

Origin of the Relative Stereoselectivity of the β -Lactam Formation in the Staudinger Reaction

Lei Jiao, Yong Liang, and Jiaxi Xu*

Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, P. R. China

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Detailed Discussion on the Isomerization of the Imine Moiety

It is unequivocal that the β -lactam products with different relative configurations are generated from zwitterionic intermediates with different configurations. To further understand how the different zwitterionic intermediates are formed, we designed and conducted the reaction of an acyl cation with an imine to simulate the formation of the zwitterionic intermediate in the Staudinger reaction. A ketene and an imine react to give a zwitterionic intermediate, while an acyl cation reacts with an imine to give an *N*-acyl iminium ion, of which imine moiety is similar to the zwitterionic intermediate and could not precede the subsequent cyclization. Thus, we can understand how the different zwitterionic intermediates are generated by analyzing experimental results.

Scheme 1. The preparation of the *N*-acetyl iminium ion **I**.

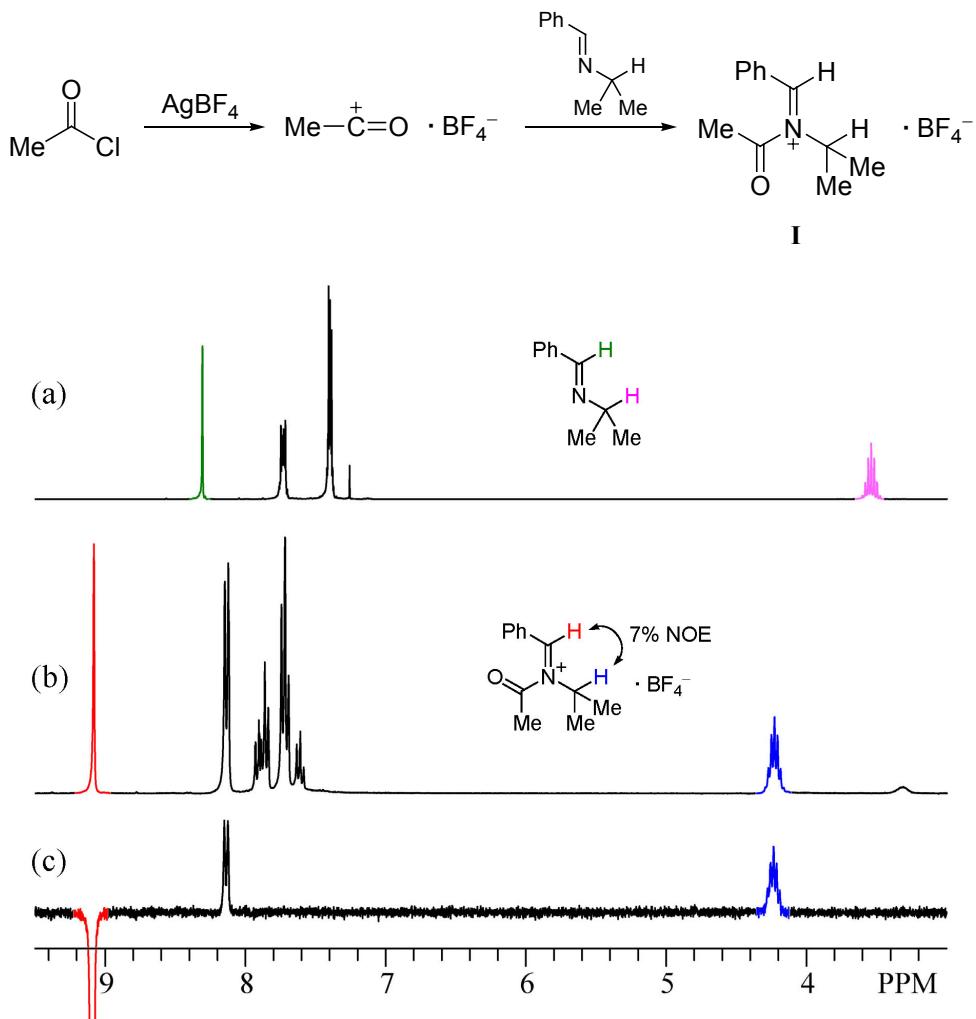


Figure 1. Partial ^1H NMR spectra: (a) the *N*-isopropyl imine; (b) the *N*-acetyl iminium ion **I**, containing small amount of benzaldehyde and *N*-isopropyl acetamide generated from the hydrolysis of **I**; and (c) 1D NOE spectrum of the iminium ion **I**.

We chose acetyl cation and *N*-isopropyl imine **2b**, which mainly produces *trans*- β -lactam in the Staudinger reaction, as the reactants to prepare *N*-acetyl iminium **I** (Scheme 1). In order to avoid the nucleophilic attack of the chloride anion,¹ acetyl cation was prepared by mixing equimolar amounts of acetyl chloride and AgBF₄ in DMSO-*d*₆. After separation of the precipitates of AgCl, it was added to a solution of imine **2b** in DMSO-*d*₆ to afford the *N*-acetyl iminium ion **I**. ¹H NMR spectra show that the chemical shift of the iminic hydrogen indeed shifts to lower field² (δ shifted from 8.31 to 9.08), which confirmed the formation of the desired *N*-acetyl iminium ion **I** (spectra **a** and **b** in Figure 1). The NOE experiment indicates that the iminium ion **I** only exists in *E* configuration (spectrum **c** in Figure 1). The prepared iminium ion **I** was heated to 80 °C to observe whether the thermal isomerization occurred. However, after maintained at such temperature for several tens of minutes, **I** gradually became messy and the iminium ion with *Z* configuration was never detected.

The above results reveal that the imine moiety in the *N*-acetyl iminium ion did not isomerize though its C=N double bond becomes weaker, and also demonstrate that the isomerization of the imine itself hardly occurs under normal reaction conditions due to its higher bond order. Considering that the imine moiety, at least in part, indeed isomerizes in the Staudinger reaction, we believe that the isomerization of the zwitterionic intermediate only occurs during the direct ring-closure step. From geometry viewpoint, the isomerization progress can be explained as follows: the theoretical investigation reveals that the stable conformation of the zwitterionic intermediate is *s-trans* **II**, but the intermediate must adopt a near planar *s-cis* configuration **IIIa** to facilitate cyclization;³ the isomerization occurring during the ring-closure process can release the steric hindrance of the *s-cis* configuration **IIIa** to form a less bulky intermediate **IIIb** (Figure 2).

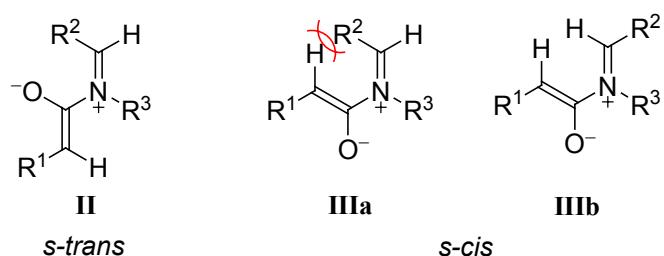


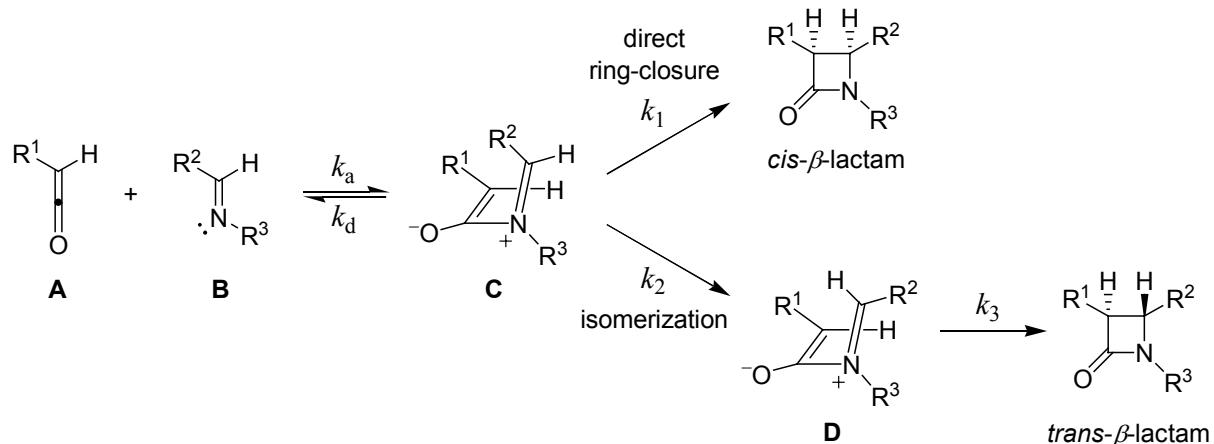
Figure 2. The configurations of the zwitterionic intermediates.

¹ Bose et al studied the NMR spectrum of a CCl₄ solution containing equimolar amounts of acetyl chloride and benzylideneaniline and found that *N*-(chlorophenyl)methyl-*N*-phenylacetamide, instead of *N*-acetyl iminium ion, was generated (the chemical shift of the iminic hydrogen shifted from 8.38 to 7.90). See: Bose, A. K.; Spiegelman, G.; Manhas, M. S. *Tetrahedron Lett.* **1971**, *12*, 3167-3170.

² Olah, G. A.; Kreienbuhl, P. *J. Am. Chem. Soc.* **1967**, *89*, 4756-4759.

³ Cossio, F. P.; Ugalde, J. M.; Lopez, X.; Lecea, B.; Palomo, C. *J. Am. Chem. Soc.*, **1993**, *115*, 995-1004.

Detailed Kinetic Treatment



According to the above kinetic system, the rate law of each reaction is:

$$\frac{d[cis]}{dt} = k_1[C] \quad (1)$$

$$\frac{d[trans]}{dt} = k_3[D] \quad (2)$$

$$\frac{d[D]}{dt} = k_2[C] - k_3[D] \quad (3)$$

$$\frac{d[C]}{dt} = k_a[A][B] - k_1[C] - k_2[C] - k_d[C] \quad (4)$$

$$\frac{d[A]}{dt} = k_d[C] - k_a[A][B] \quad (5)$$

$$\frac{d[B]}{dt} = k_d[C] - k_a[A][B] \quad (6)$$

Integrating both sides of the equations (1), (2) and (3) gives:

$$[cis] = k_1 \int [C] dt \quad (7)$$

$$[trans] = k_3 \int [D] dt \quad (8)$$

$$[D] = k_2 \int [C] dt - k_3 \int [D] dt \quad \Rightarrow \quad k_3 \int [D] dt = k_2 \int [C] dt - [D] \quad (9)$$

Thus, the ratio of *cis* and *trans* isomers could be described as follows:

$$\frac{[cis]}{[trans]} = \frac{k_1 \int [C] dt}{k_3 \int [D] dt} = \frac{k_1 \int [C] dt}{k_2 \int [C] dt - [D]} \quad (10)$$

Because the cyclization step is very fast, the concentration of the intermediate **D** is very low, i.e. $[D] \rightarrow 0$, thus:

$$\frac{[cis]}{[trans]} = \frac{k_1}{k_2} \quad (11)$$

Experimental Details

General. α -Diazocarbonyl compounds **1**,⁴ **10a–f**,⁵ and ethyl 2-diazo-3-oxo-3-phenylthio-propionate⁶ (the precursor of ketene **20**); imines **2a–c**,⁷ **5a–f**,⁷ **8a–c**,⁸ **8d**⁹ and **14a–f**⁷ were prepared according to published procedures. Toluene and xylenes were refluxed with sodium and freshly distilled prior to use. All reactions were performed under a nitrogen atmosphere. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 with TMS as an internal standard.

The Determination of the *cis* / *trans* Ratios of the Crude β -Lactam Products.

- For the reactions of diazoacetate **1** and imines **5**, the *cis* / *trans* ratios were obtained by the integral of the corresponding C(3) and C(4) protons of β -lactams in ^1H NMR spectra (protons of *cis*-isomers appear at about 4.7 and 4.9 ppm, while protons of *trans*-isomers appear at about 4.0 and 4.3 ppm) of the crude reaction mixture. See representative spectrum 1 for example.
- For the reactions of diazoketones **10** and imine **5f**, the *cis* / *trans* ratios at 140 °C were obtained by the integral of the corresponding protons C(3) and C(4) protons of β -lactams in ^1H NMR spectra (protons of *cis*-isomers appear at about 4.8 and 5.1 ppm, while protons of *trans*-isomers appear at about 4.0 and 4.5 ppm) of the crude reaction mixture. See representative spectrum 2 for example. The *cis* / *trans* ratios at 130 °C were obtained by the HPLC analysis. See representative chromatogram 3 for example.
- For the reactions of diazoacetate **1** and imines **14**, the *cis* / *trans* ratios were obtained by the integral of the corresponding C(3) and C(4) protons of β -lactams in ^1H NMR spectra (protons of *cis*-isomers appear at about 5.0 and 5.5 ppm, while protons of *trans*-isomers appear at about 4.2 and 4.9 ppm) of the crude reaction mixture. See representative spectrum 5 for example.

The Reaction of Ketene **20 with imine **2c**.** The precursor of ketene **20**, ethyl 2-diazo-3-oxo-3-phenylthio-propionate (1.3 mmol), was dissolved in 15 mL of dry toluene and was heated to reflux for 2 h. The resulting solution was cooled to 80 °C, and a solution of imine **2c** (1 mmol) in 5 mL of toluene was added during 30 minutes. After the addition, the solution was maintained at 80 °C and stirred for 12 h. The solvent was evaporated and the mixture was directly submitted to ^1H NMR analysis.

⁴ Danheiser, R. L.; Okamoto, I.; Lawlor, M. D.; Lee, T. W. *Org. Synth.* Vol. 80, 160-171.

⁵ Bridson, J. N.; Hooz, J. *Org. Synth. Coll. Vol.* 6, 386.

⁶ Padwa, A.; Sheehan, S. M.; Price, A. T. *Tetrahedron Lett.* **1994**, 35, 849-852.

⁷ Linder, M. R.; Frey, W. U.; Podlech, J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2566-2577.

⁸ Wardrop, A. W. H.; Sainsbury, G. L.; Harrison, J. M.; Inch, T. D. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1279-1285.

⁹ Nagarajan, K.; Venkateswarlu, A.; Kulkarni, C. L.; Shah, R. K. *Indian J. Chem.* **1974**, 12, 227-235.

The Calculation of the *cis / trans* Ratios at 80 °C Using the Eyring Equation

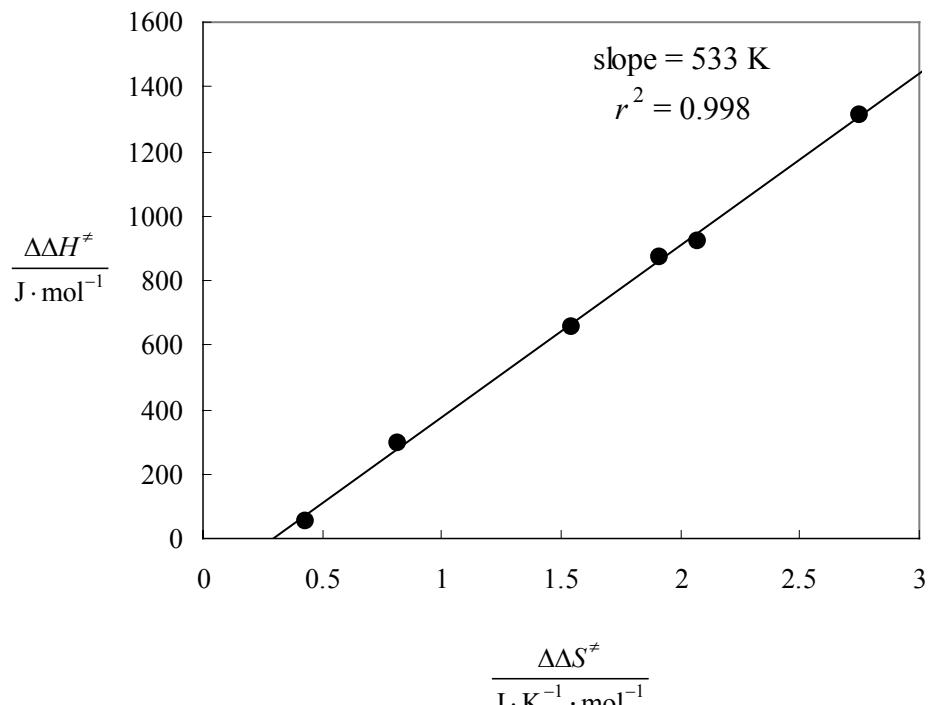
The *cis / trans* ratios at 140 and 130 °C are correlated with the Eyring Equation to give the $\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$ data, and then the *cis / trans* ratios at 80 °C were calculated (Table 1).

Table 1. The Calculation of the *cis / trans* Ratios at 80 °C

$$\log \frac{cis}{trans} = \log \frac{k_1}{k_2} = -\frac{\Delta\Delta H^\ddagger}{2.303RT} + \frac{\Delta\Delta S^\ddagger}{2.303R}$$

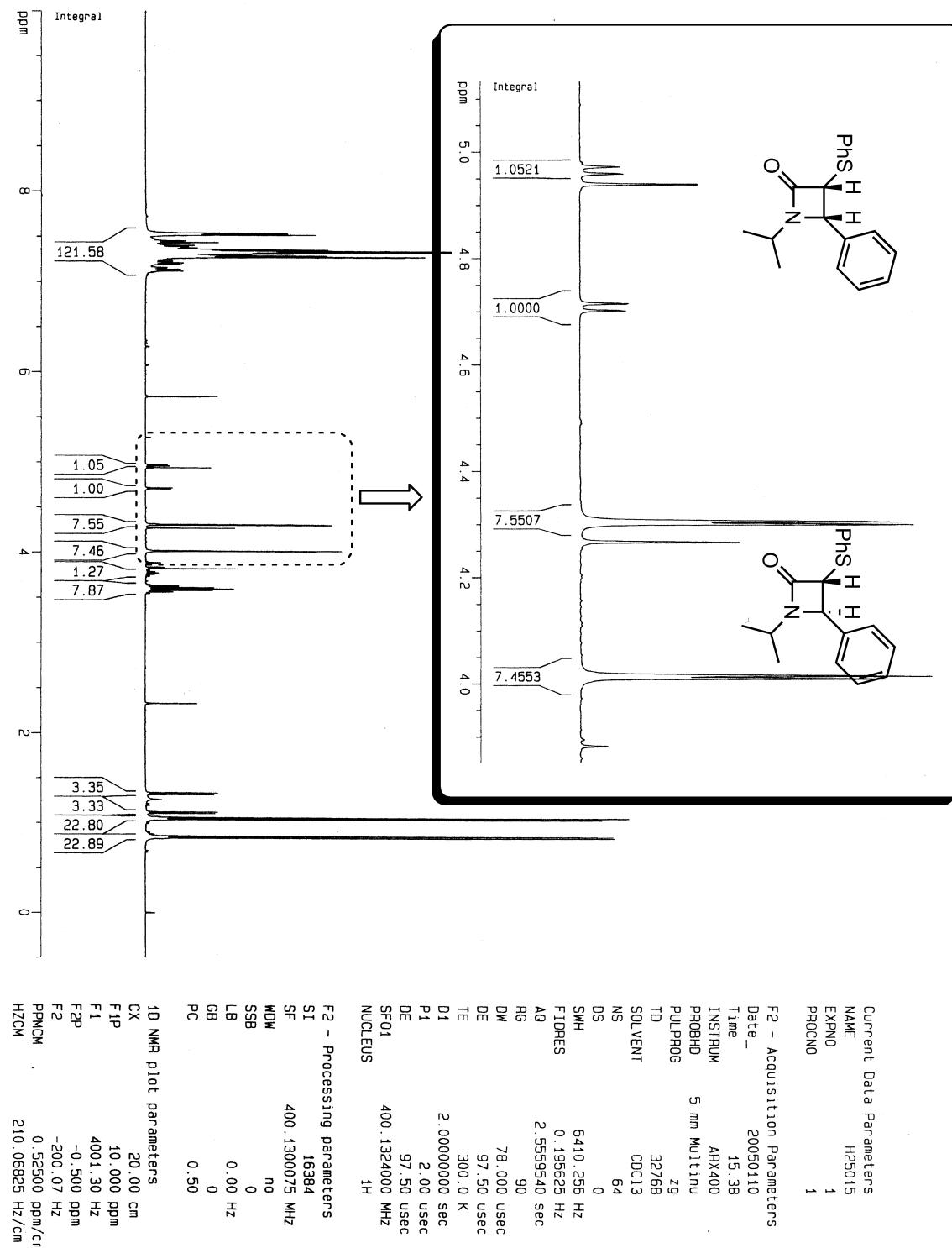
R	p-MeO	p-Me	H	p-Cl	m-Cl	p-NO ₂
<i>cis / trans</i> at 140 °C	1.95 : 1	1.23 : 1	1 : 1.15	1 : 1.47	1 : 1.63	1 : 2.71
<i>cis / trans</i> at 130 °C	1.93 : 1	1.18 : 1	1 : 1.26	1 : 1.67	1 : 1.84	1 : 3.25
$\Delta\Delta H^\ddagger / \text{kJ} \cdot \text{mol}^{-1}$	1.1	5.7	13	18	17	25
$\Delta\Delta S^\ddagger / \text{J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}$	8.2	16	29	40	37	53
<i>cis / trans</i> at 80 °C	1.85 : 1	1 : 1.08	1 : 2.15	1 : 3.52	1 : 3.74	1 : 9.4

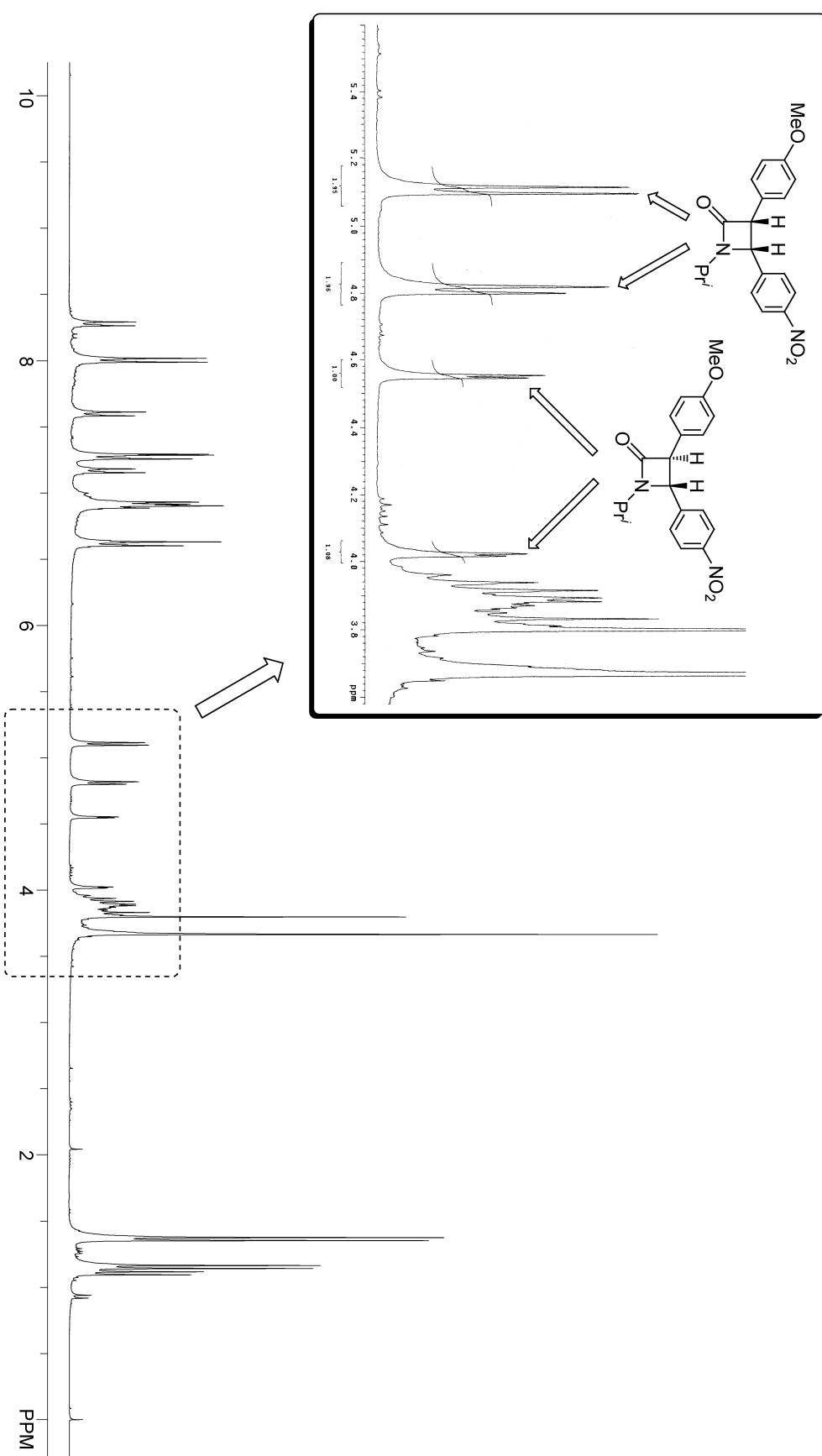
Meanwhile, $\Delta\Delta H^\ddagger$ shows a good correlation with $\Delta\Delta S^\ddagger$ (see figure below).



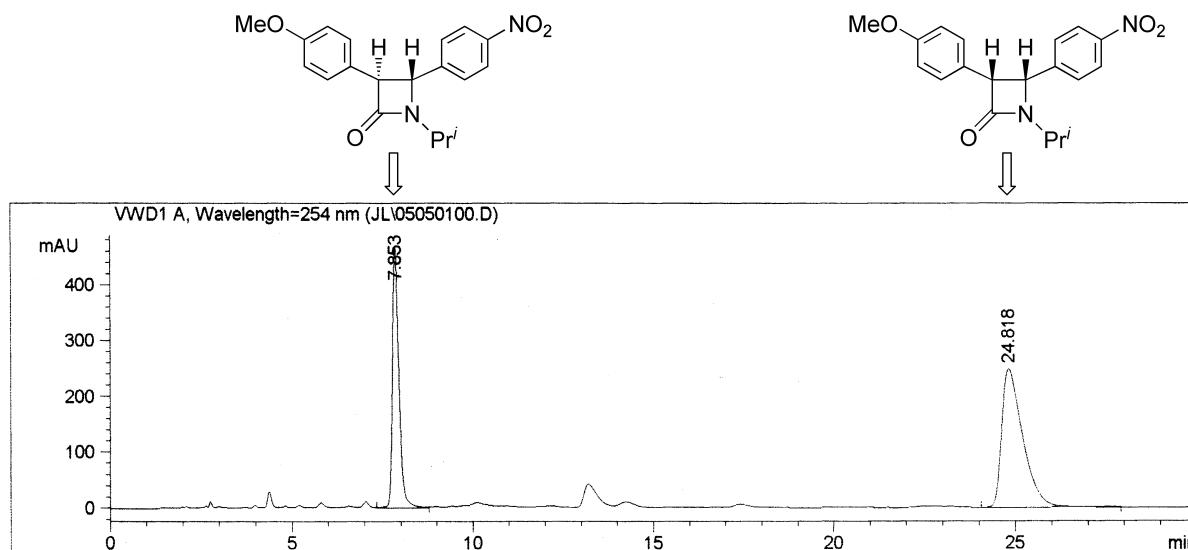
Representative Spectra and Chromatogram

1. Representative ^1H NMR Spectra of the Crude Products of the Reaction of 1 and 5c

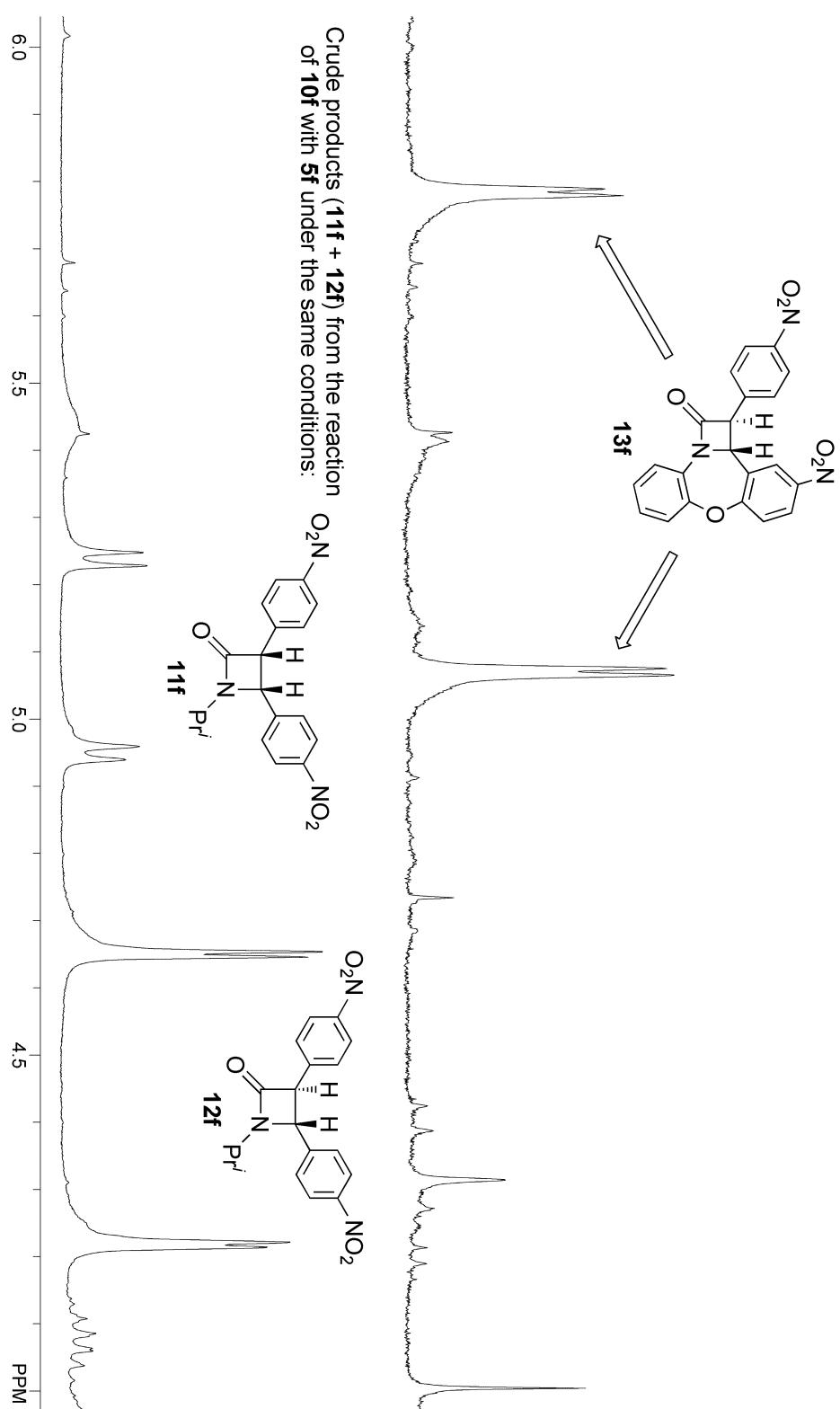


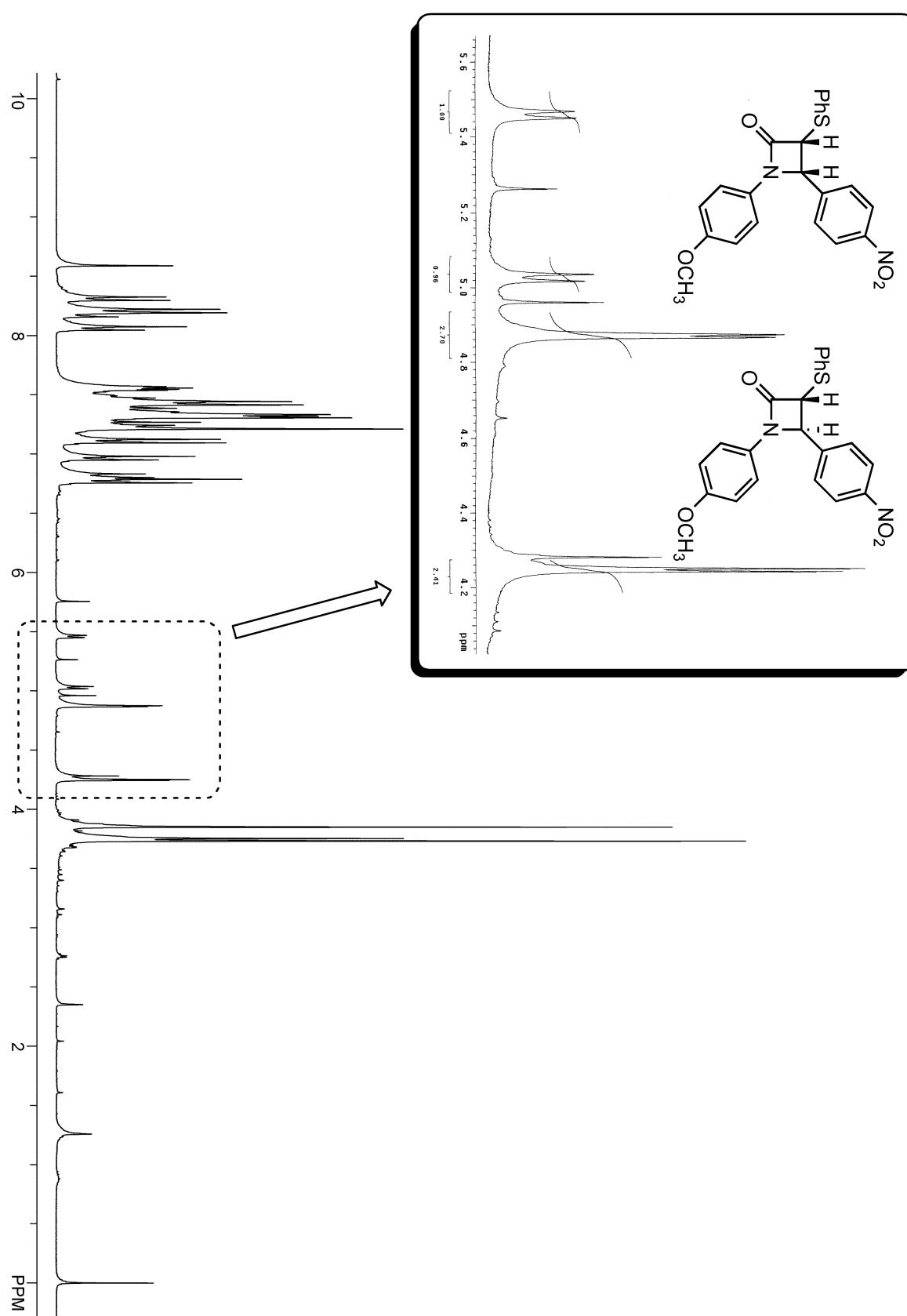
2. Representative ^1H NMR Spectra of the Crude Products of the Reaction of 10a and 5f

3. Representative HPLC Chromatogram of the Crude Products of the Reaction of 10a and 5f



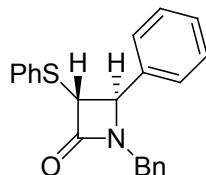
The *cis* / *trans* ratio of the 140 °C reactions were determined by ^1H NMR. Both the 140 °C and 130 °C reaction mixtures were analyzed by HPLC (Agilent ZORBAX SIL Column, elution with hexane / *i*-PrOH 95:5 at 1.00 mL·min $^{-1}$, detect at 254 nm), and the response factors of the two diastereoisomers were calculated on the basis of the determined *cis* / *trans* ratio at 140 °C by ^1H NMR. Consequently the *cis* / *trans* ratio of the 130 °C reaction was calculated using the above response factors.

4. Representative ^1H NMR Spectra of the Crude Product of the Reaction of **10f and **8d****

5. Representative ^1H NMR Spectra of the Crude Products of the Reaction of 1 and 14a

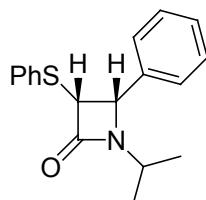
The Spectroscopic Data for the Products

(\pm)-*trans*-1-Benzyl-4-phenyl-3-phenylthioazetidin-2-one (4a)



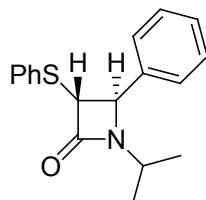
^1H NMR (300 MHz): δ 3.67 (d, $J = 15.0$ Hz, 1H), 4.15 (dd, $J = 0.5, 2.1$ Hz, 1H), 4.20 (d, $J = 2.1$ Hz, 1H), 4.80 (d, $J = 15.0$ Hz, 1H), 6.72–6.76 (m, 2H), 7.13–7.57 (m, 13H). ^{13}C NMR (75.5 MHz): δ 44.4, 61.6, 61.8, 126.5, 127.5, 127.9, 128.3, 128.5, 128.8, 129.0, 129.1, 131.0, 133.7, 134.4, 135.8, 165.7. MS (EI) m/z: 345 (M^+ , 0.5), 212 (100), 91 (61). IR ν (cm $^{-1}$): 1754. This compound has been reported in published literature;¹⁰ however, no spectroscopic data was given.

(\pm)-*cis*-1-Isopropyl-4-phenyl-3-phenylthioazetidin-2-one (3b)



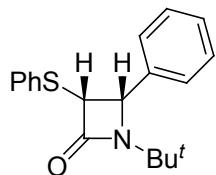
^1H NMR (300 MHz): δ 1.12 (d, $J = 6.9$ Hz, 3H), 1.33 (d, $J = 6.9$ Hz, 3H), 3.78 (m, 1H), 4.71 (d, $J = 5.4$ Hz, 1H), 4.97 (d, $J = 5.4$ Hz, 1H), 7.13–7.38 (m, 10H). ^{13}C NMR (75.5 MHz): δ 20.2, 21.1, 45.7, 58.2, 59.1, 126.7, 128.1, 128.65, 128.69, 130.5, 134.4, 135.2, 166.3. MS (ESI) m/z: 298 ($M+\text{H}^+$). IR ν (cm $^{-1}$): 1749.

(\pm)-*trans*-1-Isopropyl-4-phenyl-3-phenylthioazetidin-2-one (4b)



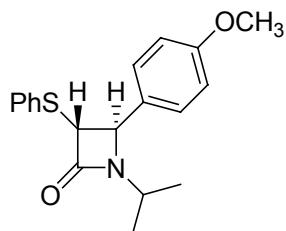
^1H NMR (300 MHz): δ 0.85 (d, $J = 6.9$ Hz, 3H), 1.06 (d, $J = 6.9$ Hz, 3H), 3.60 (m, 1H), 4.02 (d, $J = 2.1$ Hz, 1H), 4.32 (d, $J = 2.1$ Hz, 1H), 7.28–7.56 (m, 10H). ^{13}C NMR (75.5 MHz): δ 20.0, 20.7, 45.3, 60.2, 61.2, 126.4, 128.0, 128.6, 128.7, 128.9, 131.3, 133.2, 137.6, 165.6. MS (ESI) m/z: 298 ($M+\text{H}^+$). IR ν (cm $^{-1}$): 1751.

¹⁰ Sugano, Y.; Naruto, S. *Chem. Lett.*, **1989**, 1331–1334.

(\pm)-*cis*-1-*tert*-Butyl-4-phenyl-3-phenylthioazetidin-2-one (3c)

^1H NMR (300 MHz): δ 1.31 (s, 9H), 4.66 (d, $J = 5.4$ Hz, 1H), 5.00 (d, $J = 5.4$ Hz, 1H), 7.15–7.36 (m, 10H).

^{13}C NMR (75.5 MHz): δ 28.1, 54.9, 57.5, 59.3, 126.7, 128.0, 128.6, 128.7, 130.6, 134.6, 136.4, 166.5. MS (EI) m/z: 311 (M^+ , 0.8), 212 (100), 57 (13). IR ν (cm $^{-1}$): 1744.

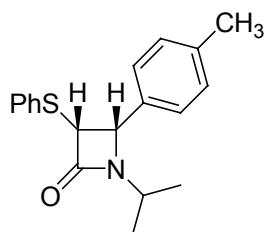
(\pm)-*trans*-1-Isopropyl-4-(4-methoxyphenyl)-3-phenylthioazetidin-2-one (7a)

^1H NMR (300 MHz): δ 0.86 (d, $J = 6.6$ Hz, 3H), 1.05 (d, $J = 6.6$ Hz, 3H), 3.60 (m, 1H), 3.80 (s, 3H), 4.02

(d, $J = 1.8$ Hz, 1H), 4.28 (d, $J = 1.8$ Hz, 1H), 6.89–7.54 (m, 9H). ^{13}C NMR (75.5 MHz): δ 19.9, 20.7, 45.0,

55.0, 60.0, 60.9, 114.1, 127.6, 127.8, 128.8, 129.3, 131.4, 132.9, 159.7, 165.5. MS (ESI) m/z: 328 ($M+\text{H}^+$).

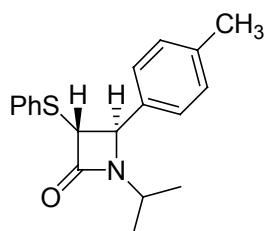
IR ν (cm $^{-1}$): 1748.

(\pm)-*cis*-1-Isopropyl-4-(4-methylphenyl)-3-phenylthioazetidin-2-one (6b)

^1H NMR (300 MHz): δ 1.12 (d, $J = 6.9$ Hz, 3H), 1.33 (d, $J = 6.9$ Hz, 3H), 2.38 (s, 3H), 3.78 (m, 1H), 4.69

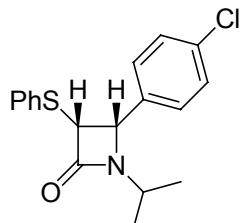
(d, $J = 5.1$ Hz, 1H), 4.95 (d, $J = 5.1$ Hz, 1H), 7.15–7.33 (m, 9H). MS (ESI) m/z: 312 ($M+\text{H}^+$).

IR ν (cm $^{-1}$): 1751.

(\pm)-*trans*-1-Isopropyl-4-(4-methylphenyl)-3-phenylthioazetidin-2-one (7b)

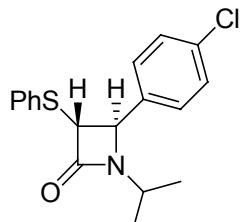
¹H NMR (300 MHz): δ 0.86 (d, $J = 6.6$ Hz, 3H), 1.05 (d, $J = 6.6$ Hz, 3H), 2.35 (s, 3H), 3.60 (m, 1H), 4.01 (d, $J = 2.1$ Hz, 1H), 4.29 (d, $J = 2.1$ Hz, 1H), 7.16–7.55 (m, 9H). ¹³C NMR (75.5 MHz): δ 20.0, 20.7, 21.0, 45.2, 60.1, 61.1, 126.4, 127.9, 128.8, 129.4, 131.4, 133.1, 134.6, 138.5, 165.6. MS (ESI) m/z: 312 (M+H)⁺. IR ν (cm⁻¹): 1751.

(±)-cis-4-(4-Chlorophenyl)-1-isopropyl-3-phenylthioazetidin-2-one (6d)



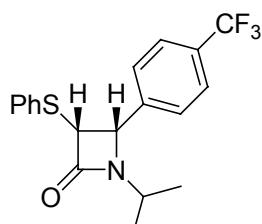
¹H NMR (300 MHz): δ 1.12 (d, $J = 6.6$ Hz, 3H), 1.32 (d, $J = 6.6$ Hz, 3H), 3.80 (m, 1H), 4.73 (d, $J = 5.4$ Hz, 1H), 4.95 (d, $J = 5.4$ Hz, 1H), 7.16–7.38 (m, 9H). ¹³C NMR (75.5 MHz): δ 20.3, 21.2, 45.7, 58.3, 58.6, 126.9, 128.4, 128.8, 129.2, 129.5, 130.5, 133.9, 134.6, 166.1. MS (ESI) m/z: 332 (M+H)⁺. IR ν (cm⁻¹): 1752.

(±)-trans-4-(4-Chlorophenyl)-1-isopropyl-3-phenylthioazetidin-2-one (7d)



¹H NMR (300 MHz): δ 0.85 (d, $J = 6.9$ Hz, 3H), 1.04 (d, $J = 6.9$ Hz, 3H), 3.61 (m, 1H), 3.99 (d, $J = 2.1$ Hz, 1H), 4.29 (d, $J = 2.1$ Hz, 1H), 7.27–7.56 (m, 9H). ¹³C NMR (75.5 MHz): δ 20.1, 20.8, 45.4, 60.5, 60.6, 127.8, 128.2, 129.0, 129.1, 131.1, 133.5, 134.5, 136.4, 165.6. MS (ESI) m/z: 332 (M+H)⁺. IR ν (cm⁻¹): 1751.

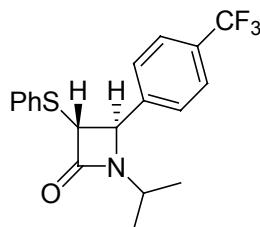
(±)-cis-4-(4-Trifluoromethylphenyl)-1-isopropyl-3-phenylthioazetidin-2-one (6e)



¹H NMR (300 MHz): δ 1.13 (d, $J = 6.6$ Hz, 3H), 1.33 (d, $J = 6.6$ Hz, 3H), 3.81 (m, 1H), 4.79 (d, $J = 5.1$ Hz, 1H), 5.02 (d, $J = 5.1$ Hz, 1H), 7.11–7.62 (m, 9H). ¹³C NMR (75.5 MHz): δ 20.3, 21.2, 45.9, 58.2, 58.7, 124.99, 125.04, 127.0, 128.5, 128.8, 130.6, 133.7, 139.5, 165.9. MS (ESI) m/z: 366 (M+H)⁺. IR ν (cm⁻¹):

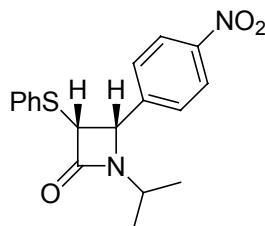
1753.

(\pm)-*trans*-4-(4-Trifluoromethylphenyl)-1-isopropyl-3-phenylthioazetidin-2-one (7e)



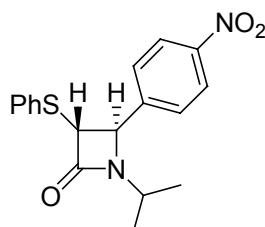
¹H NMR (300 MHz): δ 0.85 (d, J = 6.9 Hz, 3H), 1.04 (d, J = 6.9 Hz, 3H), 3.63 (m, 1H), 4.00 (d, J = 2.1 Hz, 1H), 4.36 (d, J = 2.1 Hz, 1H), 7.31–7.66 (m, 9H). ¹³C NMR (75.5 MHz): δ 20.1, 20.9, 45.7, 60.7, 60.9, 125.94, 125.99, 126.8, 128.5, 129.2, 130.8, 133.9, 142.2, 165.7. MS (ESI) m/z: 366 (M+H)⁺. IR ν (cm⁻¹): 1756.

(\pm)-*cis*-1-Isopropyl-4-(4-nitrophenyl)-3-phenylthioazetidin-2-one (6f)

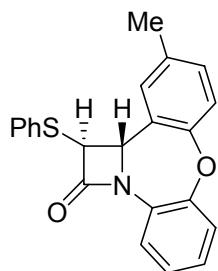


¹H NMR (300 MHz): δ 1.14 (d, J = 6.6 Hz, 3H), 1.34 (d, J = 6.6 Hz, 3H), 3.84 (m, 1H), 4.85 (d, J = 5.4 Hz, 1H), 5.11 (d, J = 5.4 Hz, 1H), 7.10–7.18 (m, 5H), 7.47–7.51 (m, 2H), 8.19–8.22 (m, 2H). ¹³C NMR (75.5 MHz): δ 20.3, 21.2, 46.0, 58.2, 58.4, 123.1, 127.1, 128.8, 128.9, 130.3, 133.3, 142.9, 147.9, 165.6. MS (ESI) m/z: 343 (M+H)⁺. IR ν (cm⁻¹): 1753.

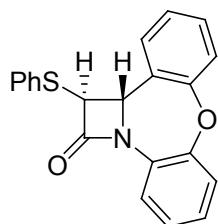
(\pm)-*trans*-1-Isopropyl-4-(4-nitrophenyl)-3-phenylthioazetidin-2-one (7f)



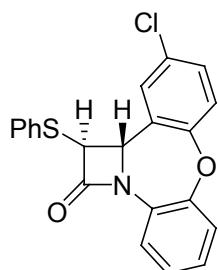
¹H NMR (300 MHz): δ 0.86 (d, J = 6.9 Hz, 3H), 1.04 (d, J = 6.9 Hz, 3H), 3.65 (m, 1H), 4.02 (d, J = 2.1 Hz, 1H), 4.42 (d, J = 2.1 Hz, 1H), 7.35–7.60 (m, 7H), 8.24–8.27 (m, 2H). ¹³C NMR (75.5 MHz): δ 20.1, 20.8, 45.7, 60.2, 61.1, 124.2, 127.2, 128.7, 129.2, 130.3, 134.1, 145.4, 148.0, 165.4. MS (ESI) m/z: 343 (M+H)⁺. IR ν (cm⁻¹): 1755.

(\pm)-*trans*-4-Methyl-2-phenylthio-azeto[1,2-*d*]dibenzo[*b,f*]oxazepin-1-one (9a)

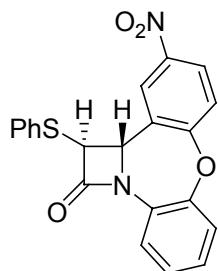
^1H NMR (300 MHz): δ 2.30 (s, 3H), 4.75 (d, $J = 3.0$ Hz, 1H), 5.46 (d, $J = 3.0$ Hz, 1H), 6.90–7.99 (m, 12H). ^{13}C NMR (75.5 MHz): δ 20.8, 56.1, 59.7, 120.0, 121.3, 121.5, 124.7, 125.1, 126.4, 128.7, 128.8, 129.4, 129.6, 130.7, 131.3, 133.8, 135.0, 144.1, 155.9, 161.9. MS (EI) m/z: 359 (M^+ , 17). IR ν (cm $^{-1}$): 1756.

(\pm)-*trans*-2-Phenylthio-azeto[1,2-*d*]dibenzo[*b,f*]oxazepin-1-one (9b)

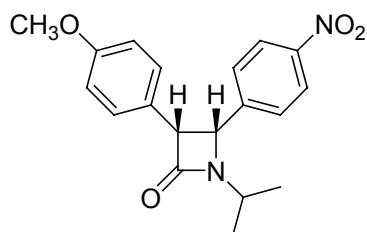
^1H NMR (300 MHz): δ 4.76 (d, $J = 2.7$ Hz, 1H), 5.48 (d, $J = 2.7$ Hz, 1H), 6.95–7.99 (m, 13H). ^{13}C NMR (75.5 MHz): δ 56.3, 59.7, 120.0, 121.5, 121.6, 124.7, 125.2, 125.3, 125.9, 128.7, 129.3, 129.4, 129.5, 130.4, 131.3, 133.7, 143.9, 158.1, 161.8. MS (EI) m/z: 345 (M^+ , 22). IR ν (cm $^{-1}$): 1736.

(\pm)-*trans*-4-Chloro-2-phenylthio-azeto[1,2-*d*]dibenzo[*b,f*]oxazepin-1-one (9c)

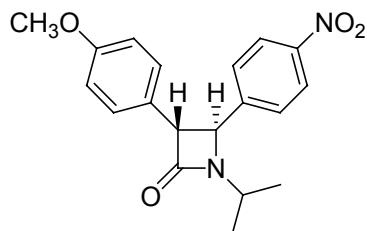
^1H NMR (300 MHz): δ 4.71 (d, $J = 2.4$ Hz, 1H), 5.42 (d, $J = 2.4$ Hz, 1H), 7.00–7.99 (m, 12H). ^{13}C NMR (75.5 MHz): δ 56.6, 59.3, 120.2, 121.5, 123.1, 124.9, 125.5, 126.2, 129.0, 129.4, 129.5, 130.2, 130.5, 131.0, 134.0, 143.7, 156.5, 161.6. MS (EI) m/z: 379 (M^+ , 28). IR ν (cm $^{-1}$): 1765.

(\pm)-*trans*-4-Nitro-2-phenylthio-azeto[1,2-*d*]dibenzo[*b,f*]oxazepin-1-one (9d)

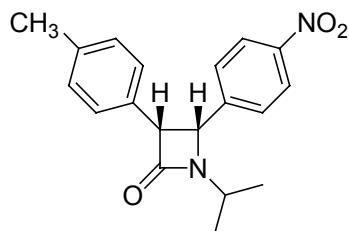
^1H NMR (300 MHz): δ 4.82 (d, $J = 3.0$ Hz, 1H), 5.42 (d, $J = 3.0$ Hz, 1H), 7.00–8.24 (m, 12H). ^{13}C NMR (75.5 MHz): δ 57.4, 59.3, 120.3, 121.5, 122.1, 122.9, 125.2, 125.9, 126.0, 128.8, 129.2, 129.6, 130.5, 130.6, 134.1, 143.0, 144.3, 161.2, 162.3. MS (EI) m/z: 390 (M^+ , 52). IR ν (cm $^{-1}$): 1753.

(\pm)-*cis*-1-Isopropyl-3-(4-methoxyphenyl)-4-(4-nitrophenyl)azetidin-2-one (11a)

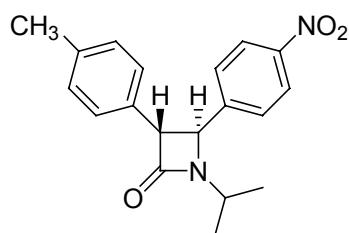
^1H NMR (300 MHz): δ 1.15 (d, $J = 6.6$ Hz, 3H), 1.36 (d, $J = 6.6$ Hz, 3H), 3.67 (s, 3H), 3.92 (m, 1H), 4.81 (d, $J = 5.7$ Hz, 1H), 5.10 (d, $J = 5.7$ Hz, 1H), 6.60–8.02 (m, 8H). ^{13}C NMR (75.5 MHz): δ 20.3, 21.3, 45.5, 55.0, 58.5, 59.6, 113.7, 123.1, 123.9, 128.2, 129.6, 144.5, 147.3, 158.5, 168.0. MS (ESI) m/z: 341 ($\text{M}+\text{H}$) $^+$. IR ν (cm $^{-1}$): 1744.

(\pm)-*trans*-1-Isopropyl-3-(4-methoxyphenyl)-4-(4-nitrophenyl)azetidin-2-one (12a)

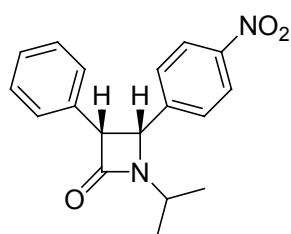
^1H NMR (300 MHz): δ 1.11 (d, $J = 6.6$ Hz, 3H), 1.37 (d, $J = 6.6$ Hz, 3H), 3.81 (s, 3H), 3.92 (m, 1H), 4.02 (d, $J = 2.1$ Hz, 1H), 4.54 (d, $J = 2.1$ Hz, 1H), 6.89–8.30 (m, 8H). ^{13}C NMR (75.5 MHz): δ 20.7, 21.3, 45.5, 55.3, 62.3, 64.1, 114.4, 124.3, 126.4, 127.2, 128.4, 146.8, 148.0, 159.3, 168.2. MS (ESI) m/z: 341 ($\text{M}+\text{H}$) $^+$. IR ν (cm $^{-1}$): 1747.

(\pm)-*cis*-1-Isopropyl-3-(4-methylphenyl)-4-(4-nitrophenyl)azetidin-2-one (11b)

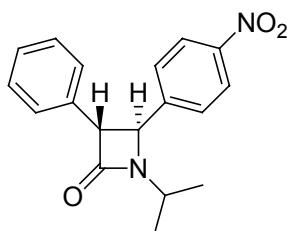
^1H NMR (300 MHz): δ 1.15 (d, $J = 6.6$ Hz, 3H), 1.36 (d, $J = 6.6$ Hz, 3H), 2.16 (s, 3H), 3.91 (m, 1H), 4.82 (d, $J = 5.7$ Hz, 1H), 5.12 (d, $J = 5.7$ Hz, 1H), 6.88–8.00 (m, 8H). ^{13}C NMR (75.5 MHz): δ 20.2, 20.8, 21.2, 45.5, 58.3, 59.9, 123.0, 128.2, 128.3, 128.8, 128.9, 136.8, 144.4, 147.2, 167.8. MS (ESI) m/z: 325 ($\text{M}+\text{H}$) $^+$. IR ν (cm $^{-1}$): 1745.

(\pm)-*trans*-1-Isopropyl-3-(4-methylphenyl)-4-(4-nitrophenyl)azetidin-2-one (12b)

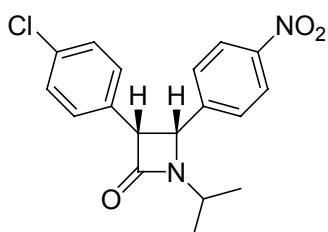
^1H NMR (300 MHz): δ 1.11 (d, $J = 6.6$ Hz, 3H), 1.36 (d, $J = 6.6$ Hz, 3H), 2.34 (s, 3H), 3.91 (m, 1H), 4.04 (d, $J = 2.4$ Hz, 1H), 4.57 (d, $J = 2.4$ Hz, 1H), 7.12–8.30 (m, 8H). ^{13}C NMR (75.5 MHz): δ 20.6, 21.0, 21.2, 45.5, 61.9, 64.3, 124.2, 127.1, 127.2, 129.6, 131.3, 137.7, 146.8, 147.9, 168.0. MS (ESI) m/z: 325 ($\text{M}+\text{H}$) $^+$. IR ν (cm $^{-1}$): 1749.

(\pm)-*cis*-1-Isopropyl-4-(4-nitrophenyl)-3-phenylazetidin-2-one (11c)

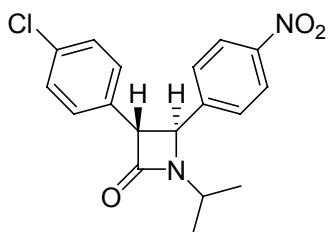
^1H NMR (300 MHz): δ 1.16 (d, $J = 6.6$ Hz, 3H), 1.37 (d, $J = 6.6$ Hz, 3H), 3.92 (m, 1H), 4.87 (d, $J = 5.7$ Hz, 1H), 5.14 (d, $J = 5.7$ Hz, 1H), 6.98–8.00 (m, 9H). ^{13}C NMR (75.5 MHz): δ 20.4, 21.3, 45.6, 58.3, 60.2, 123.1, 127.3, 128.2, 128.3, 128.5, 131.9, 144.3, 147.3, 167.6. MS (ESI) m/z: 311 ($\text{M}+\text{H}$) $^+$. IR ν (cm $^{-1}$): 1744.

(\pm)-*trans*-1-Isopropyl-4-(4-nitrophenyl)-3-phenylazetidin-2-one (12c)

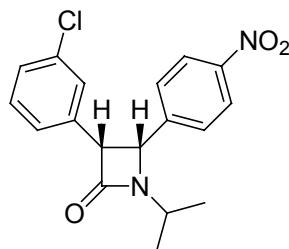
^1H NMR (300 MHz): δ 1.12 (d, $J = 6.6$ Hz, 3H), 1.37 (d, $J = 6.6$ Hz, 3H), 3.92 (m, 1H), 4.08 (d, $J = 2.4$ Hz, 1H), 4.61 (d, $J = 2.4$ Hz, 1H), 7.24–8.31 (m, 9H). ^{13}C NMR (75.5 MHz): δ 20.7, 21.3, 45.5, 61.8, 64.5, 124.3, 127.2, 127.9, 129.0, 134.3, 146.7, 148.0, 167.7. MS (ESI) m/z: 311 ($\text{M}+\text{H}$) $^+$. IR ν (cm $^{-1}$): 1749.

(\pm)-*cis*-3-(4-Chlorophenyl)-1-isopropyl-4-(4-nitrophenyl)azetidin-2-one (11d)

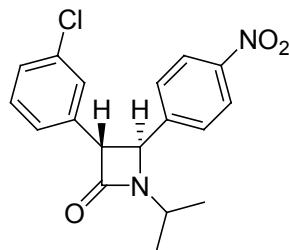
^1H NMR (300 MHz): δ 1.15 (d, $J = 6.6$ Hz, 3H), 1.37 (d, $J = 6.6$ Hz, 3H), 3.90 (m, 1H), 4.83 (d, $J = 5.7$ Hz, 1H), 5.15 (d, $J = 5.7$ Hz, 1H), 6.94–8.04 (m, 8H). ^{13}C NMR (75.5 MHz): δ 20.3, 21.2, 45.7, 58.2, 59.3, 123.3, 128.2, 128.5, 129.8, 130.5, 133.2, 143.9, 147.4, 167.1. MS (ESI) m/z: 345 ($\text{M}+\text{H}$) $^+$. IR ν (cm $^{-1}$): 1746.

(\pm)-*trans*-3-(4-Chlorophenyl)-1-isopropyl-4-(4-nitrophenyl)azetidin-2-one (12d)

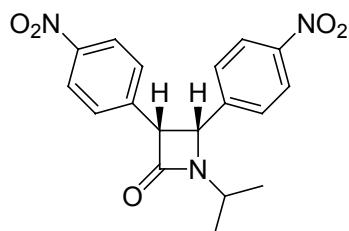
^1H NMR (300 MHz): δ 1.12 (d, $J = 6.6$ Hz, 3H), 1.37 (d, $J = 6.6$ Hz, 3H), 3.90 (m, 1H), 4.07 (d, $J = 2.1$ Hz, 1H), 4.60 (d, $J = 2.1$ Hz, 1H), 7.20–8.30 (m, 8H). ^{13}C NMR (75.5 MHz): δ 20.5, 21.1, 45.5, 61.6, 63.6, 124.2, 127.2, 128.5, 129.0, 132.8, 133.6, 146.3, 147.9, 167.1. MS (ESI) m/z: 345 ($\text{M}+\text{H}$) $^+$. IR ν (cm $^{-1}$): 1751.

(\pm)-*cis*-3-(3-Chlorophenyl)-1-isopropyl-4-(4-nitrophenyl)azetidin-2-one (11e)

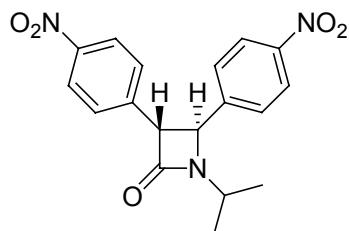
¹H NMR (300 MHz): δ 1.16 (d, J = 6.6 Hz, 3H), 1.38 (d, J = 6.6 Hz, 3H), 3.91 (m, 1H), 4.83 (d, J = 5.7 Hz, 1H), 5.16 (d, J = 5.7 Hz, 1H), 7.01–8.05 (m, 8H). ¹³C NMR (75.5 MHz): δ 20.3, 21.2, 45.7, 58.2, 59.4, 123.2, 126.6, 127.5, 128.2, 128.5, 129.5, 134.0, 134.1, 143.8, 147.4, 166.8. MS (ESI) m/z: 345 (M+H)⁺. IR ν (cm⁻¹): 1746.

(\pm)-*trans*-3-(3-Chlorophenyl)-1-isopropyl-4-(4-nitrophenyl)azetidin-2-one (12e)

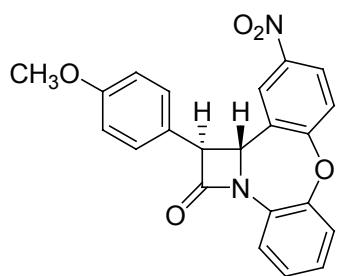
¹H NMR (300 MHz): δ 1.13 (d, J = 6.6 Hz, 3H), 1.38 (d, J = 6.6 Hz, 3H), 3.90 (m, 1H), 4.08 (d, J = 2.1 Hz, 1H), 4.62 (d, J = 2.1 Hz, 1H), 7.15–8.32 (m, 8H). ¹³C NMR (75.5 MHz): δ 20.6, 21.2, 45.6, 61.4, 63.7, 124.3, 125.4, 127.2, 127.3, 128.0, 130.2, 134.7, 136.2, 146.2, 148.0, 166.8. MS (ESI) m/z: 345 (M+H)⁺. IR ν (cm⁻¹): 1750.

(\pm)-*cis*-1-Isopropyl-3,4-bis(4-nitrophenyl)azetidin-2-one (11f)

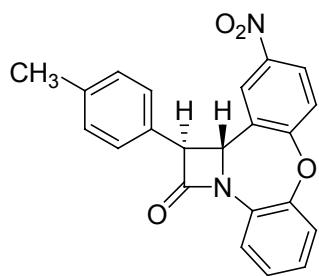
¹H NMR (300 MHz): δ 1.18 (d, J = 6.6 Hz, 3H), 1.40 (d, J = 6.6 Hz, 3H), 3.92 (m, 1H), 4.97 (d, J = 5.7 Hz, 1H), 5.27 (d, J = 5.7 Hz, 1H), 7.22–8.05 (m, 8H). ¹³C NMR (75.5 MHz): δ 20.3, 21.1, 46.0, 58.1, 59.2, 123.5, 128.1, 129.4, 130.0, 139.7, 143.3, 146.8, 147.6, 166.2. MS (ESI) m/z: 356 (M+H)⁺. IR ν (cm⁻¹): 1748.

(\pm)-*trans*-1-Isopropyl-3,4-bis(4-nitrophenyl)azetidin-2-one (12f)

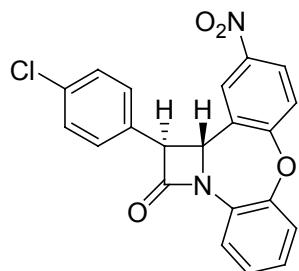
^1H NMR (300 MHz): δ 1.14 (d, $J = 6.9$ Hz, 3H), 1.38 (d, $J = 6.9$ Hz, 3H), 3.90 (m, 1H), 4.22 (d, $J = 2.1$ Hz, 1H), 4.65 (d, $J = 2.1$ Hz, 1H), 7.45–8.34 (m, 8H). ^{13}C NMR (75.5 MHz): δ 20.6, 21.3, 45.9, 61.2, 63.7, 124.3, 124.5, 127.3, 128.2, 141.6, 145.8, 147.5, 148.3, 166.0. MS (ESI) m/z: 356 ($\text{M}+\text{H}$) $^+$. IR ν (cm $^{-1}$): 1751.

(\pm)-*trans*-2-(4-Methoxyphenyl)-4-Nitro-azeto[1,2-*d*]dibenzo[*b,f*]oxazepin-1-one (13a)

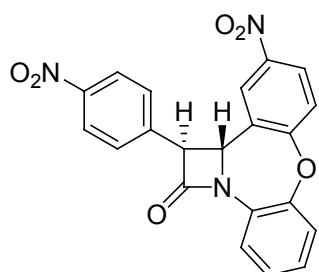
^1H NMR (300 MHz): δ 3.83 (s, 3H), 4.85 (d, $J = 3.0$ Hz, 1H), 5.60 (d, $J = 3.0$ Hz, 1H), 6.96–8.28 (m, 11H). ^{13}C NMR (75.5 MHz): δ 55.3, 58.7, 59.8, 114.6, 120.3, 121.5, 122.2, 122.9, 124.8, 125.1, 125.9, 126.0, 128.7, 129.3, 131.8, 143.0, 144.4, 159.6, 162.7, 163.6. MS (EI) m/z: 388 (M^+ , 15). IR ν (cm $^{-1}$): 1753.

(\pm)-*trans*-2-(4-Methylphenyl)-4-Nitro-azeto[1,2-*d*]dibenzo[*b,f*]oxazepin-1-one (13b)

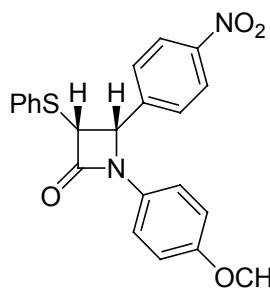
^1H NMR (300 MHz): δ 2.38 (s, 3H), 4.87 (d, $J = 3.0$ Hz, 1H), 5.63 (d, $J = 3.0$ Hz, 1H), 7.06–8.30 (m, 11H). ^{13}C NMR (75.5 MHz): δ 21.1, 59.1, 59.7, 120.3, 121.5, 122.2, 123.0, 124.8, 125.97, 126.00, 127.4, 129.4, 129.9, 130.1, 131.9, 138.2, 143.0, 144.4, 162.7, 163.5. MS (EI) m/z: 372 (M^+ , 53). IR ν (cm $^{-1}$): 1758.

(\pm)-*trans*-2-(4-Chlorophenyl)-4-Nitro-azeto[1,2-*d*]dibenzo[*b,f*]oxazepin-1-one (13d)

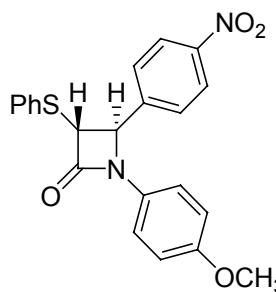
^1H NMR (300 MHz): δ 4.90 (d, $J = 3.0$ Hz, 1H), 5.65 (d, $J = 3.0$ Hz, 1H), 7.07–8.32 (m, 11H). ^{13}C NMR (75.5 MHz): δ 58.5, 59.5, 120.3, 121.6, 122.1, 123.1, 125.1, 126.1, 126.2, 128.9, 129.2, 129.5, 131.60, 131.64, 134.4, 143.0, 144.5, 162.66, 162.72. MS (EI) m/z: 392 (M^+ , 89). IR ν (cm $^{-1}$): 1747.

(\pm)-*trans*-4-Nitro-2-(4-Nitrophenyl)-azeto[1,2-*d*]dibenzo[*b,f*]oxazepin-1-one (13f)

^1H NMR (300 MHz): δ 5.04 (d, $J = 3.0$ Hz, 1H), 5.77 (d, $J = 3.0$ Hz, 1H), 7.12–8.36 (m, 11H). MS (EI) m/z: 403 (M^+ , 32). IR ν (cm $^{-1}$): 1745.

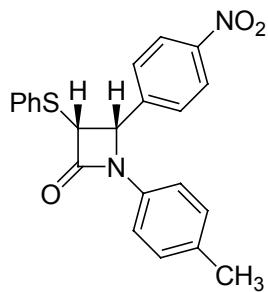
(\pm)-*cis*-1-(4-Methoxyphenyl)-4-(4-nitrophenyl)-3-phenylthioazetidin-2-one (15a)

^1H NMR (300 MHz): δ 3.75 (s, 3H), 5.02 (d, $J = 5.4$ Hz, 1H), 5.46 (d, $J = 5.4$ Hz, 1H), 6.80–8.18 (m, 13H). ^{13}C NMR (75.5 MHz): δ 55.4, 58.6, 59.3, 114.5, 118.4, 123.5, 127.4, 128.6, 129.0, 130.1, 130.8, 132.9, 141.2, 148.0, 156.6, 162.4. MS (ESI) m/z: 407 ($M+\text{H}$) $^+$. IR ν (cm $^{-1}$): 1754.

(\pm)-*trans*-1-(4-Methoxyphenyl)-4-(4-nitrophenyl)-3-phenylthioazetidin-2-one (16a)

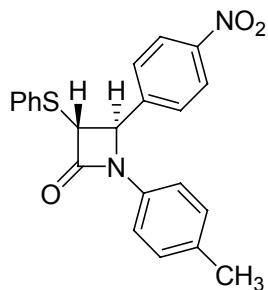
¹H NMR (300 MHz): δ 3.72 (s, 3H), 4.26 (d, J = 2.4 Hz, 1H), 4.89 (d, J = 2.4 Hz, 1H), 6.75–8.21 (m, 13H).

¹³C NMR (75.5 MHz): δ 55.3, 61.86, 61.94, 114.4, 118.4, 124.4, 126.8, 128.5, 129.3, 129.9, 131.3, 132.8, 143.6, 148.0, 156.5, 161.8. MS (ESI) m/z: 407 (M+H)⁺. IR ν (cm⁻¹): 1753.

(\pm)-*cis*-1-(4-Methylphenyl)-4-(4-nitrophenyl)-3-phenylthioazetidin-2-one (15b)

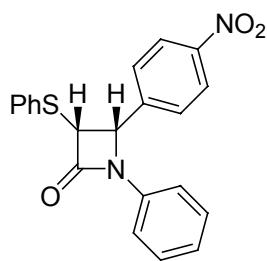
¹H NMR (300 MHz): δ 2.28 (s, 3H), 5.02 (d, J = 5.7 Hz, 1H), 5.47 (d, J = 5.7 Hz, 1H), 7.07–8.18 (m, 13H).

¹³C NMR (75.5 MHz): δ 20.9, 58.6, 59.2, 117.0, 123.5, 127.5, 128.6, 129.0, 129.8, 130.9, 132.9, 134.2, 134.6, 141.2, 148.0, 162.7. MS (ESI) m/z: 391 (M+H)⁺. IR ν (cm⁻¹): 1757.

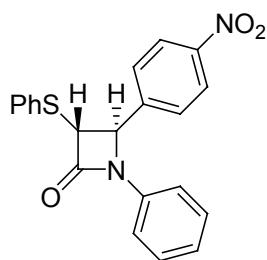
(\pm)-*trans*-1-(4-Methylphenyl)-4-(4-nitrophenyl)-3-phenylthioazetidin-2-one (16b)

¹H NMR (300 MHz): δ 2.25 (s, 3H), 4.26 (d, J = 2.4 Hz, 1H), 4.91 (d, J = 2.4 Hz, 1H), 7.05–8.21 (m, 13H).

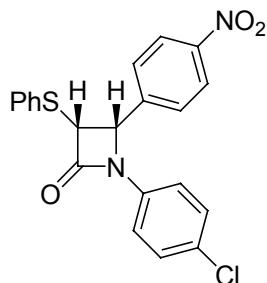
¹³C NMR (75.5 MHz): δ 20.8, 61.76, 116.9, 124.4, 126.8, 128.5, 129.3, 129.7, 131.2, 132.8, 134.0, 134.4, 143.6, 148.0, 162.1. MS (ESI) m/z: 391 (M+H)⁺. IR ν (cm⁻¹): 1757.

(\pm)-*cis*-4-(4-Nitrophenyl)-1-phenyl-3-phenylthioazetidin-2-one (15c)

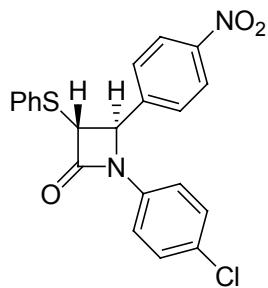
¹H NMR (300 MHz): δ 5.04 (d, J = 5.7 Hz, 1H), 5.50 (d, J = 5.7 Hz, 1H), 7.12–8.20 (m, 14H). ¹³C NMR (75.5 MHz): δ 58.6, 59.3, 117.1, 123.6, 124.8, 127.6, 128.6, 129.0, 129.4, 131.0, 132.8, 136.6, 141.0, 148.1, 163.0. MS (ESI) m/z: 377 (M+H)⁺. IR ν (cm⁻¹): 1759.

(\pm)-*trans*-4-(4-Nitrophenyl)-1-phenyl-3-phenylthioazetidin-2-one (16c)

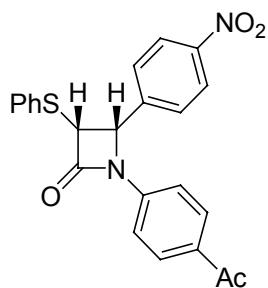
¹H NMR (300 MHz): δ 4.28 (d, J = 2.4 Hz, 1H), 4.93 (d, J = 2.4 Hz, 1H), 7.07–8.21 (m, 14H). ¹³C NMR (75.5 MHz): δ 61.80, 61.82, 116.9, 124.4, 124.7, 126.8, 128.5, 129.2, 129.3, 131.2, 132.8, 136.5, 143.5, 148.0, 162.4. MS (ESI) m/z: 377 (M+H)⁺. IR ν (cm⁻¹): 1759.

(\pm)-*cis*-1-(4-Chlorophenyl)-4-(4-nitrophenyl)-3-phenylthioazetidin-2-one (15d)

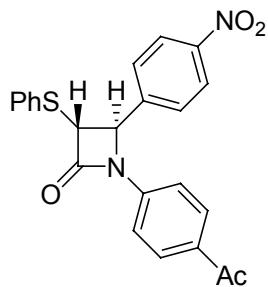
¹H NMR (300 MHz): δ 5.06 (d, J = 5.4 Hz, 1H), 5.49 (d, J = 5.4 Hz, 1H), 7.21–8.19 (m, 13H). ¹³C NMR (75.5 MHz): δ 58.8, 59.4, 118.3, 123.6, 127.6, 128.5, 129.0, 129.4, 129.9, 130.9, 132.6, 135.1, 140.5, 148.1, 163.0. MS (ESI) m/z: 411 (M+H)⁺. IR ν (cm⁻¹): 1761.

(\pm)-*trans*-1-(4-Chlorophenyl)-4-(4-nitrophenyl)-3-phenylthioazetidin-2-one (16d)

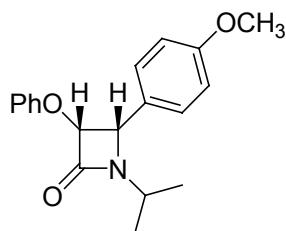
^1H NMR (300 MHz): δ 4.28 (d, $J = 2.4$ Hz, 1H), 4.89 (d, $J = 2.4$ Hz, 1H), 7.10–8.24 (m, 13H). ^{13}C NMR (75.5 MHz): δ 62.0, 62.2, 118.2, 124.6, 126.8, 128.8, 129.37, 129.42, 129.9, 130.9, 133.1, 135.0, 143.0, 148.2, 162.4. MS (ESI) m/z: 411 ($\text{M}+\text{H}$)⁺. IR ν (cm⁻¹): 1760.

(\pm)-*cis*-1-(4-Acetylphenyl)-4-(4-nitrophenyl)-3-phenylthioazetidin-2-one (15e)

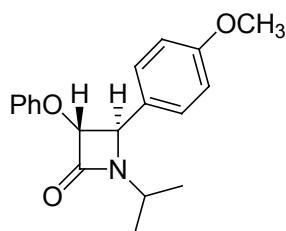
^1H NMR (300 MHz): δ 2.54 (s, 3H), 5.09 (d, $J = 5.4$ Hz, 1H), 5.57 (d, $J = 5.4$ Hz, 1H), 7.23–8.21 (m, 13H). ^{13}C NMR (75.5 MHz): δ 26.4, 59.0, 59.5, 116.8, 123.7, 127.8, 128.5, 129.1, 129.9, 131.1, 132.5, 133.3, 140.2, 140.4, 148.2, 163.4, 196.4. MS (ESI) m/z: 419 ($\text{M}+\text{H}$)⁺. IR ν (cm⁻¹): 1678, 1764.

(\pm)-*trans*-1-(4-Acetylphenyl)-4-(4-nitrophenyl)-3-phenylthioazetidin-2-one (16e)

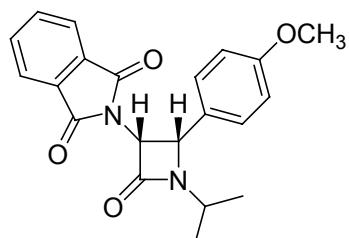
^1H NMR (300 MHz): δ 2.52 (s, 3H), 4.32 (d, $J = 2.4$ Hz, 1H), 4.98 (d, $J = 2.4$ Hz, 1H), 7.22–8.24 (m, 13H). ^{13}C NMR (75.5 MHz): δ 26.3, 62.0, 62.2, 116.6, 124.6, 126.7, 128.8, 129.4, 129.8, 130.7, 133.1, 133.2, 140.1, 142.9, 148.2, 162.8, 196.4. MS (ESI) m/z: 419 ($\text{M}+\text{H}$)⁺. IR ν (cm⁻¹): 1677, 1763.

(\pm)-*cis*-1-Isopropyl-4-(4-methoxyphenyl)-3-phenoxyazetidin-2-one (17a)

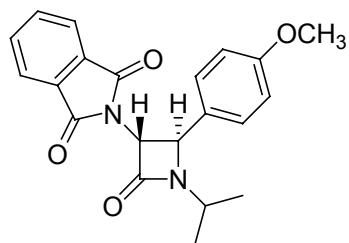
¹H NMR (300 MHz): δ 1.06 (d, J = 6.9 Hz, 3H), 1.29 (d, J = 6.9 Hz, 3H), 3.74 (s, 3H), 3.85 (m, 1H), 4.91 (d, J = 4.5 Hz, 1H), 5.32 (d, J = 4.5 Hz, 1H), 6.72–7.33 (m, 9H). ¹³C NMR (75.5 MHz): δ 20.0, 21.2, 44.8, 55.0, 60.5, 80.8, 113.4, 115.4, 121.7, 126.1, 129.0, 129.9, 156.9, 159.6, 165.3. MS (ESI) m/z: 312 (M+H)⁺. IR ν (cm⁻¹): 1751.

(\pm)-*trans*-1-Isopropyl-4-(4-methoxyphenyl)-3-phenoxyazetidin-2-one (17b)

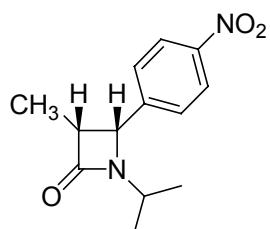
¹H NMR (300 MHz): δ 1.06 (d, J = 6.9 Hz, 3H), 1.31 (d, J = 6.9 Hz, 3H), 3.77 (m, 1H), 3.86 (s, 3H), 4.50 (d, J = 1.2 Hz, 1H), 4.92 (d, J = 1.2 Hz, 1H), 6.75–7.34 (m, 9H). ¹³C NMR (75.5 MHz): δ 20.1, 21.2, 45.1, 55.3, 62.3, 86.5, 114.4, 115.2, 121.8, 128.2, 128.9, 129.5, 157.1, 160.1, 165.1. MS (ESI) m/z: 312 (M+H)⁺. IR ν (cm⁻¹): 1759.

(\pm)-*cis*-1-Isopropyl-4-(4-methoxyphenyl)-3-(1,3-dioxoisindolin-2-yl)azetidin-2-one (18a)

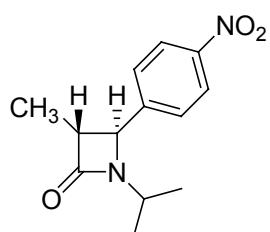
¹H NMR (300 MHz): δ 1.26 (d, J = 6.6 Hz, 3H), 1.41 (d, J = 6.6 Hz, 3H), 3.67 (s, 3H), 3.98 (m, 1H), 5.04 (d, J = 5.1 Hz, 1H), 5.38 (d, J = 5.1 Hz, 1H), 6.73–7.89 (m, 8H). ¹³C NMR (75.5 MHz): δ 20.0, 21.2, 45.6, 55.0, 59.0, 59.9, 113.6, 123.4, 125.7, 128.7, 131.2, 134.1, 159.4, 163.5, 166.9. MS (ESI) m/z: 365 (M+H)⁺. IR ν (cm⁻¹): 1719, 1755.

(\pm)-*trans*-1-Isopropyl-4-(4-methoxyphenyl)-3-(1,3-dioxoisooindolin-2-yl)azetidin-2-one (18b)

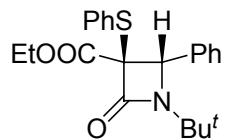
^1H NMR (300 MHz): δ 1.12 (d, $J = 6.9$ Hz, 3H), 1.41 (d, $J = 6.9$ Hz, 3H), 3.81 (s, 3H), 3.85 (m, 1H), 4.94 (d, $J = 2.4$ Hz, 1H), 5.11 (d, $J = 2.4$ Hz, 1H), 6.91–7.85 (m, 8H). ^{13}C NMR (75.5 MHz): δ 19.9, 20.6, 45.2, 55.1, 58.7, 61.7, 114.2, 123.4, 127.9, 128.9, 131.5, 134.2, 159.9, 164.6, 166.8. MS (ESI) m/z: 365 ($\text{M}+\text{H}$)⁺. IR ν (cm⁻¹): 1717, 1757.

(\pm)-*cis*-1-Isopropyl-3-methyl-4-(4-nitrophenyl)azetidin-2-one (19a)

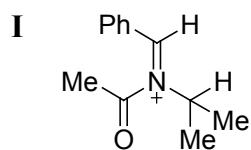
^1H NMR (300 MHz): δ 0.81 (d, $J = 7.5$ Hz, 3H), 1.16 (d, $J = 6.6$ Hz, 3H), 1.35 (d, $J = 6.6$ Hz, 3H), 3.53 (m, 1H), 3.81 (m, 1H), 4.90 (d, $J = 5.7$ Hz, 1H), 7.49–7.52 (m, 2H), 8.27–8.30 (m, 2H). ^{13}C NMR (75.5 MHz): δ 9.6, 20.3, 21.3, 45.4, 49.1, 56.8, 123.7, 128.1, 144.9, 147.7, 170.7. MS (ESI) m/z: 249 ($\text{M}+\text{H}$)⁺. IR ν (cm⁻¹): 1746.

(\pm)-*trans*-1-Isopropyl-3-methyl-4-(4-nitrophenyl)azetidin-2-one (19b)

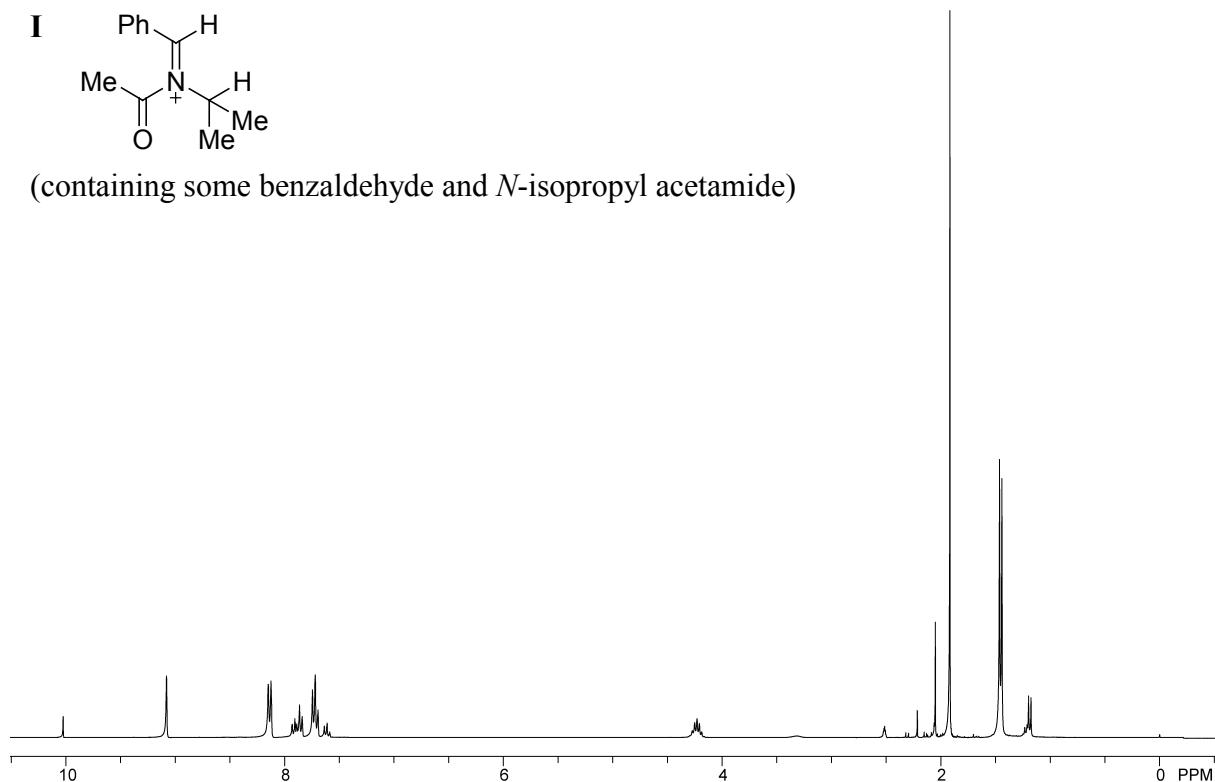
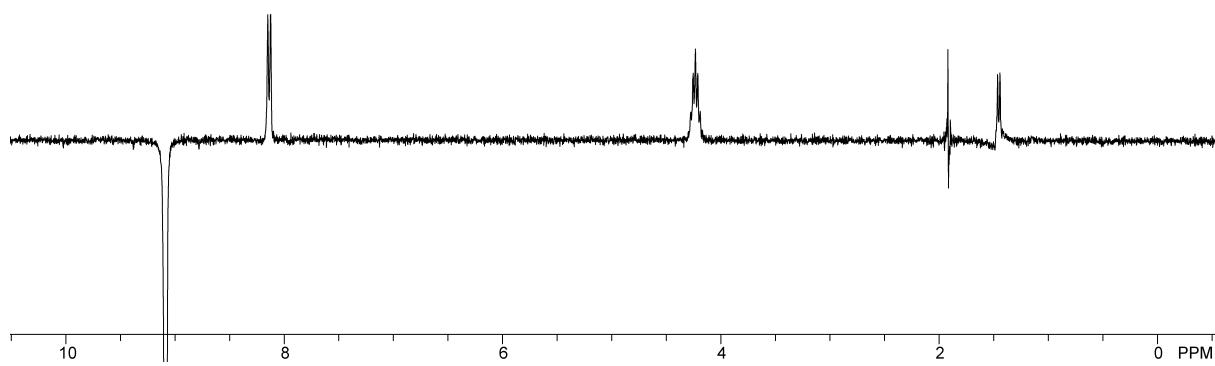
^1H NMR (300 MHz): δ 1.06 (d, $J = 6.6$ Hz, 3H), 1.29 (d, $J = 6.6$ Hz, 3H), 1.40 (d, $J = 7.5$ Hz, 3H), 2.97 (dq, $J = 1.8, 7.5$ Hz, 1H), 3.83 (m, 1H), 4.28 (d, $J = 1.8$ Hz, 1H), 7.59–7.62 (m, 2H), 8.26–8.28 (m, 2H). ^{13}C NMR (75.5 MHz): δ 12.7, 20.2, 21.0, 44.9, 54.6, 60.5, 123.9, 127.1, 147.2, 144.7, 170.3. MS (ESI) m/z: 249 ($\text{M}+\text{H}$)⁺. IR ν (cm⁻¹): 1747.

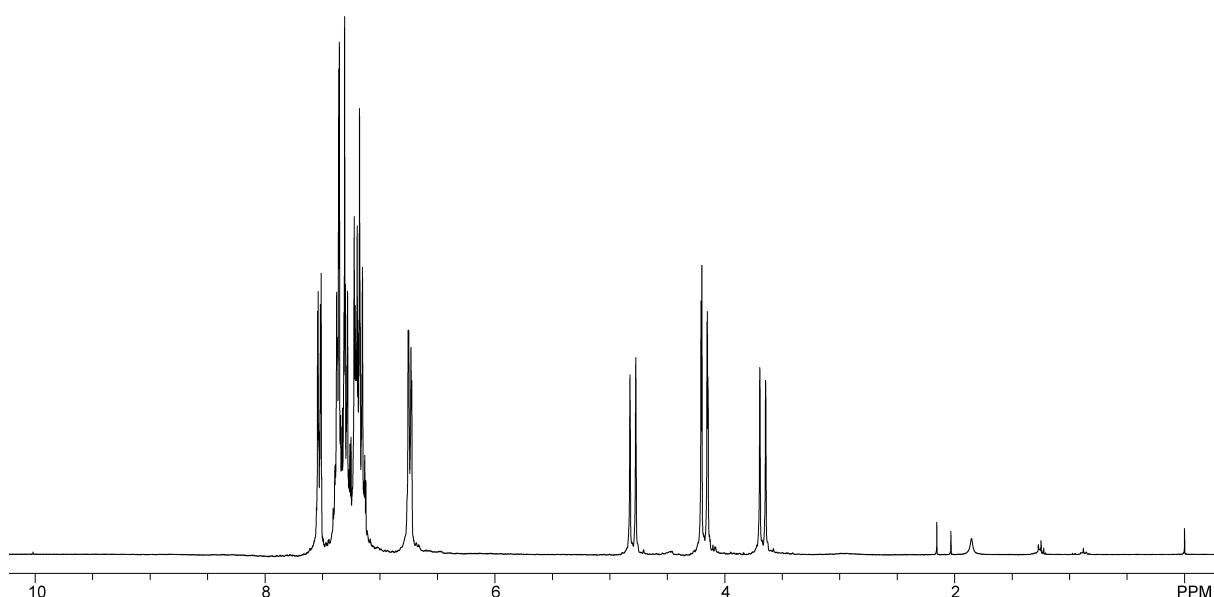
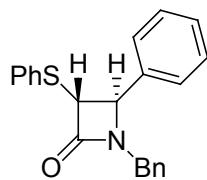
Ethyl (±)-*trans*-1-*tert*-butyl-4-phenyl-3-phenylthioazetidin-2-one-3-carboxylate (21b)

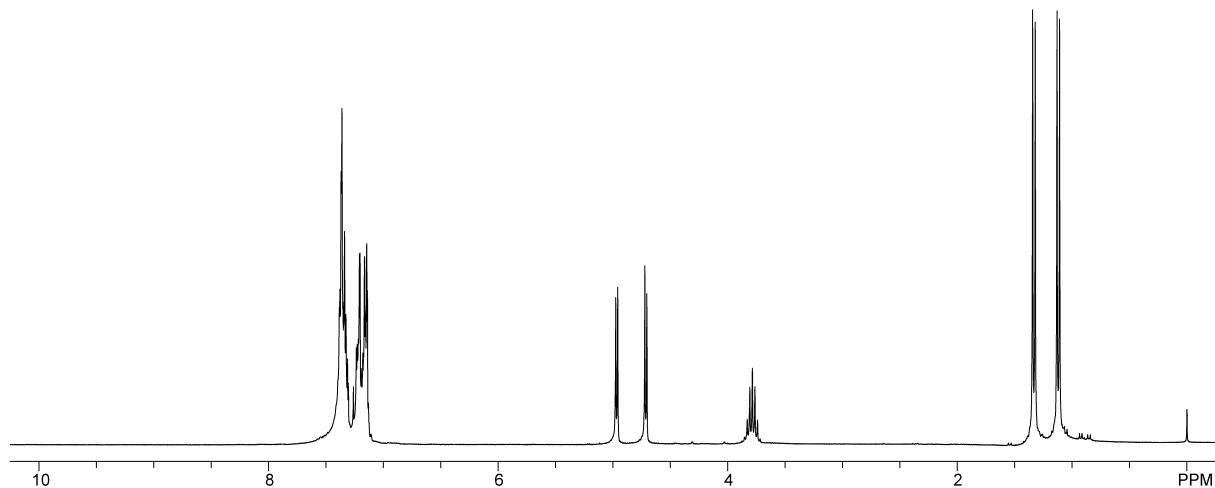
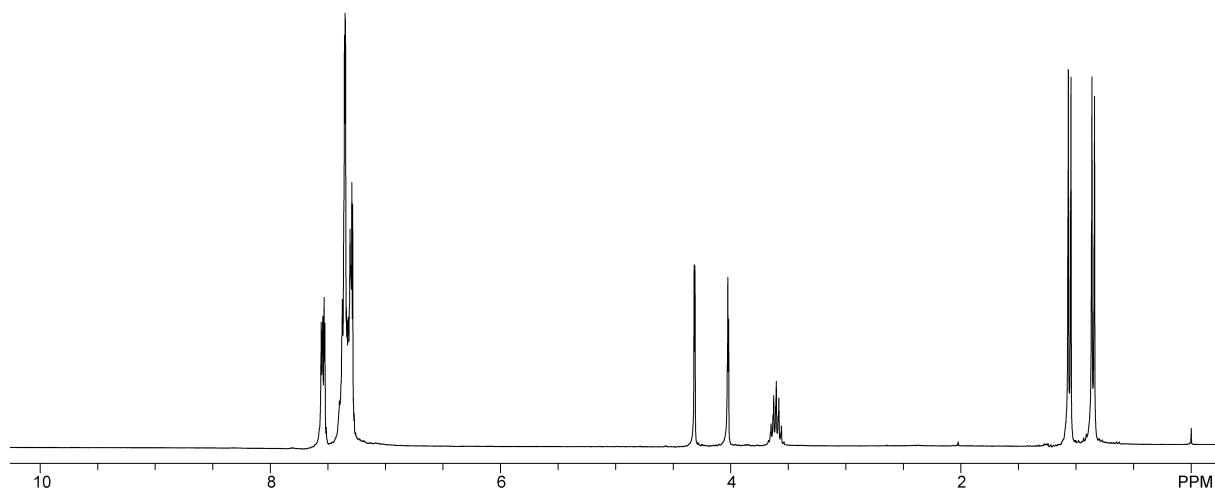
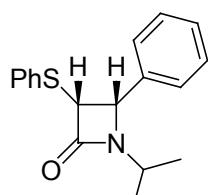
¹H NMR (300 MHz): δ 1.08 (t, $J = 7.2$ Hz, 3H), 1.33 (s, 9H), 4.12 (m, 2H), 5.23 (s, 1H), 7.10–7.38 (m, 10H). ¹³C NMR (75.5 MHz): δ 13.7, 28.0, 55.3, 62.4, 62.9, 69.4, 127.8, 128.0, 128.4, 128.7, 129.0, 130.6, 133.0, 135.2, 163.2, 167.4. MS (ESI) m/z: 384 (M+H)⁺. IR ν (cm⁻¹): 1720, 1762.

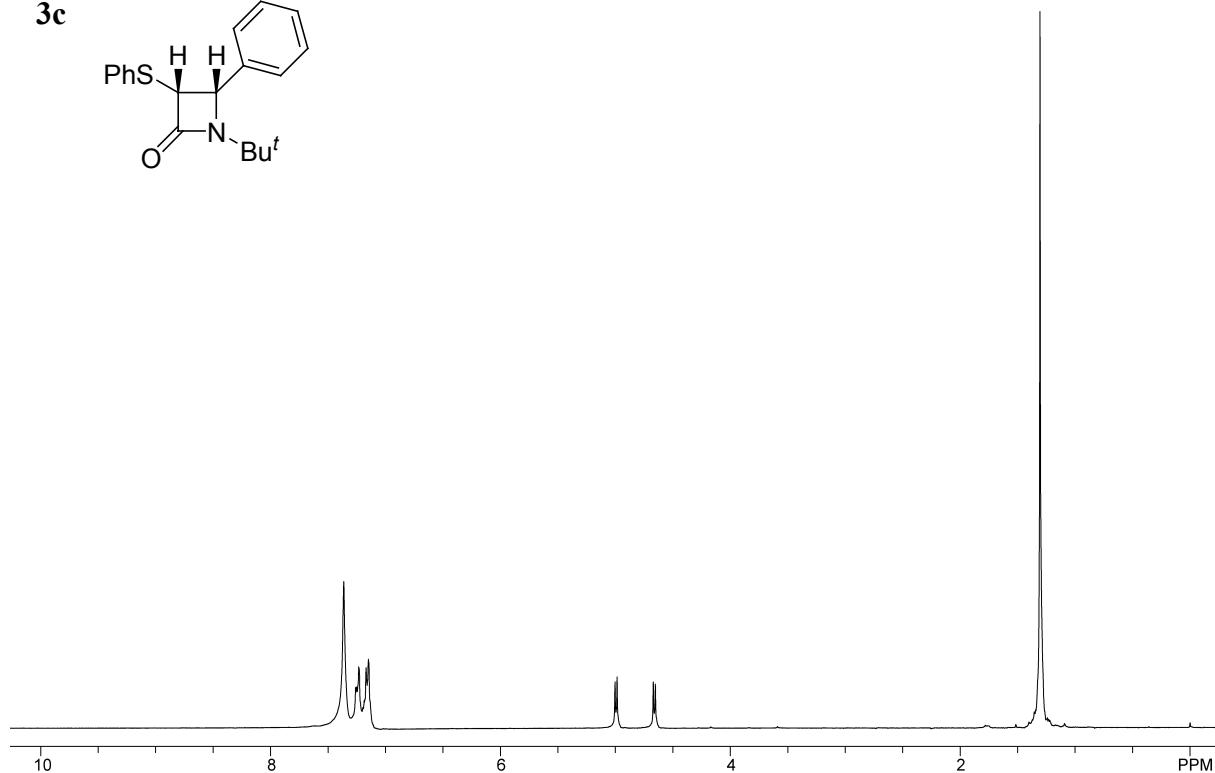
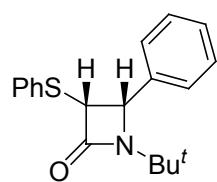
Copies of ^1H NMR Spectra of the Products

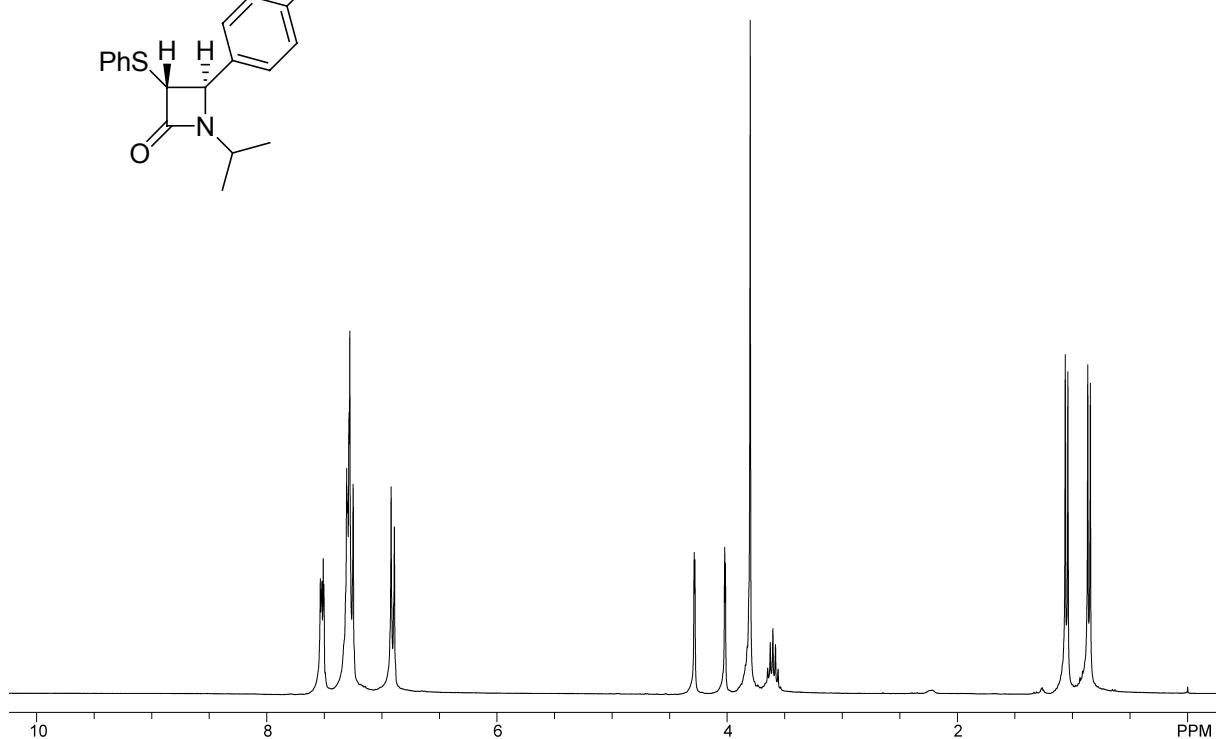
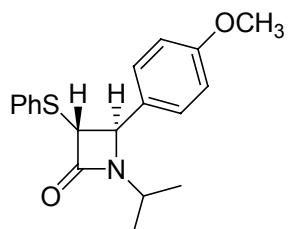
(containing some benzaldehyde and *N*-isopropyl acetamide)

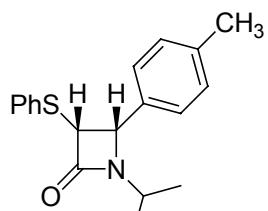
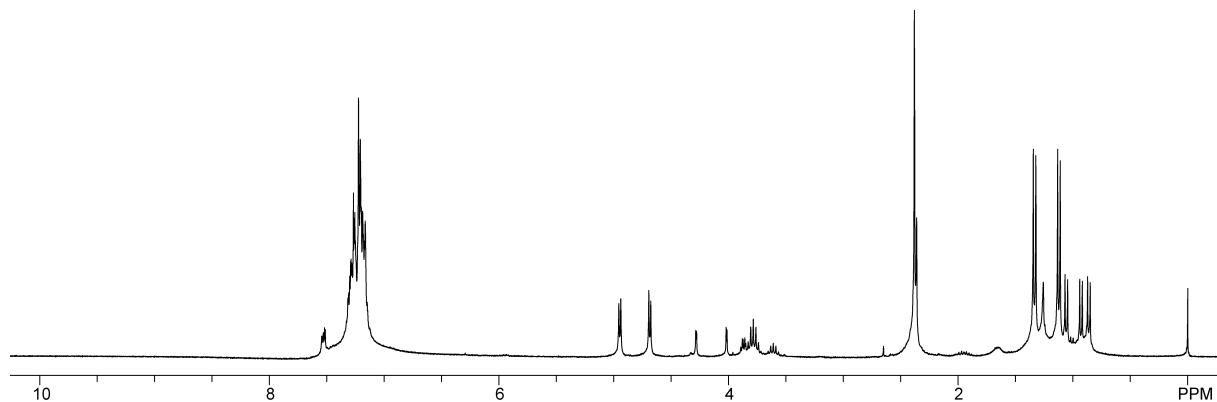
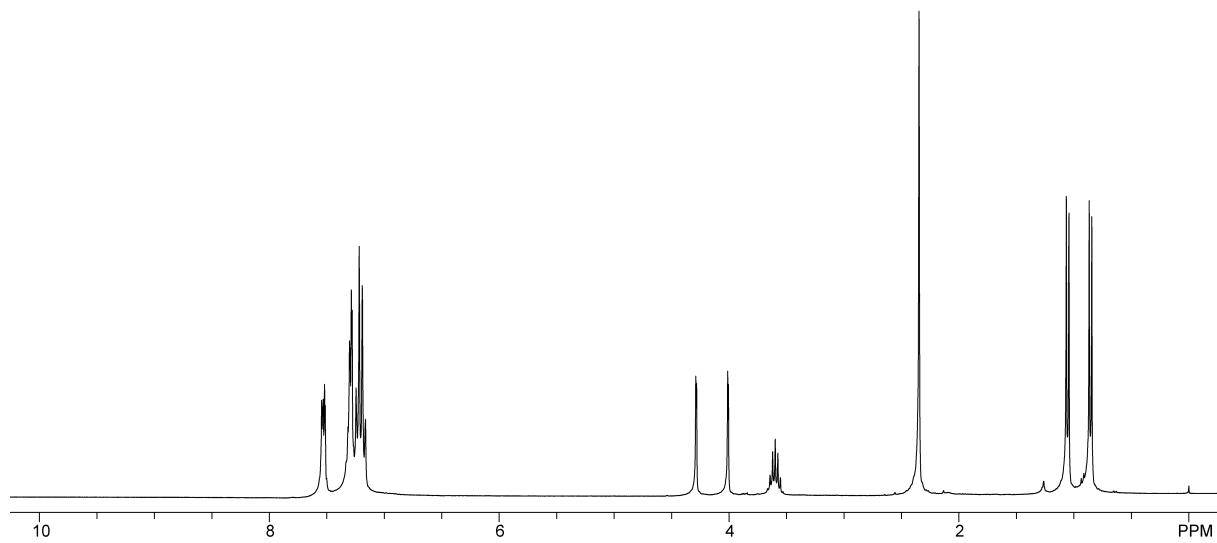
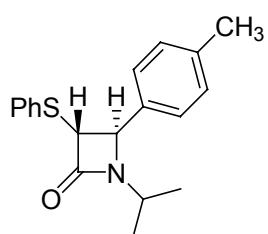
**I NOE**

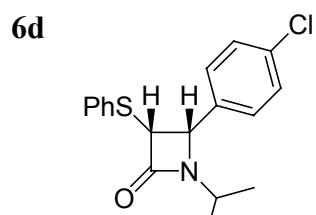
4a

3b**4b**

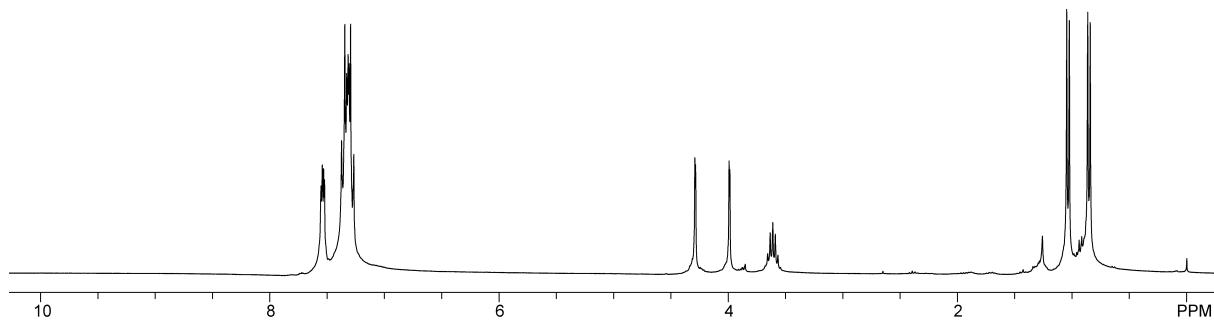
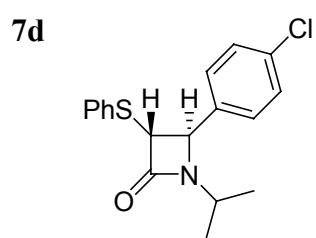
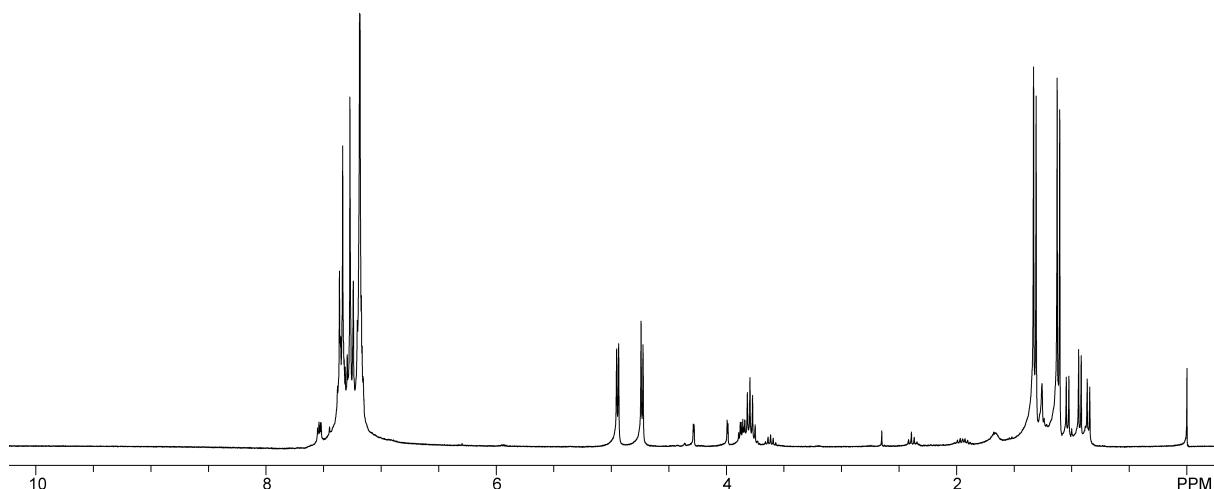
3c

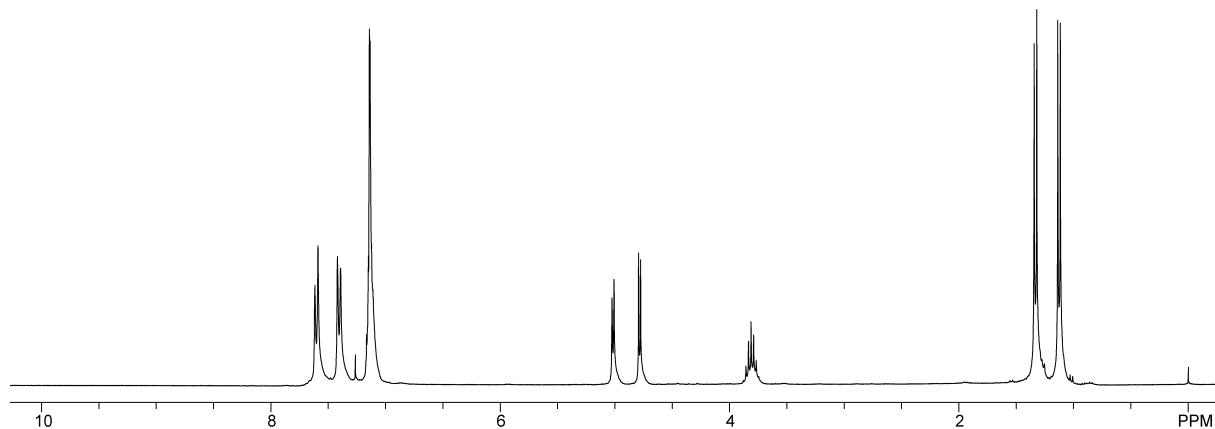
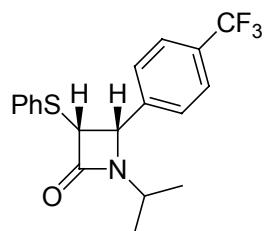
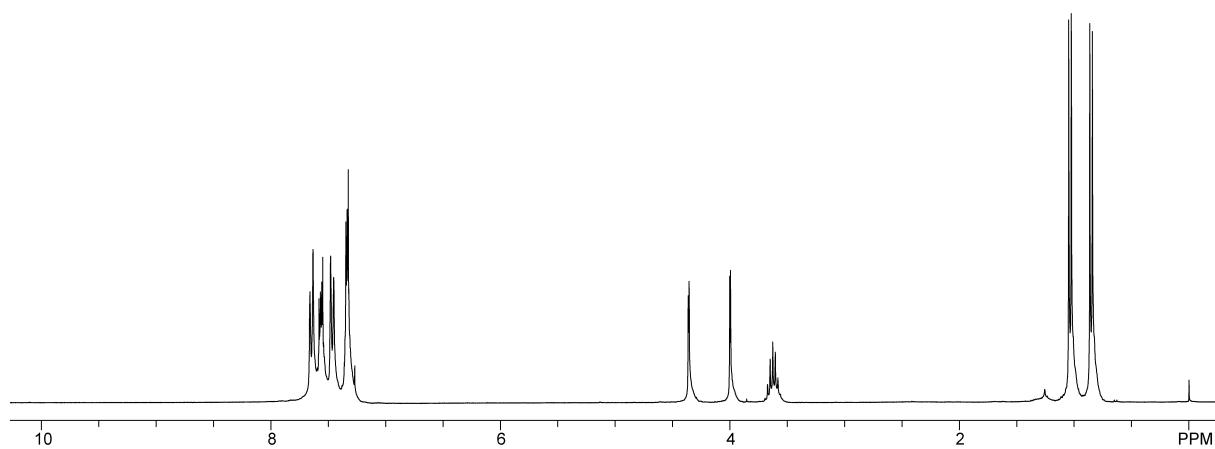
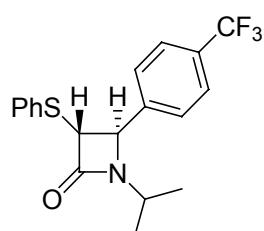
7a

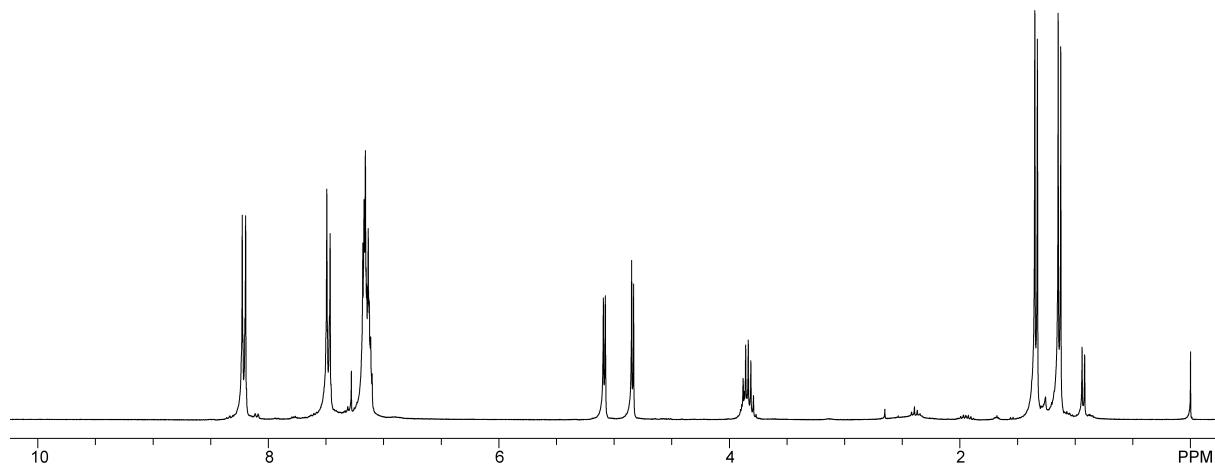
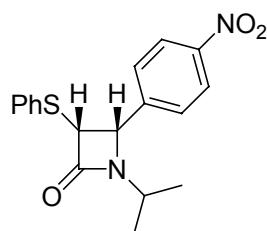
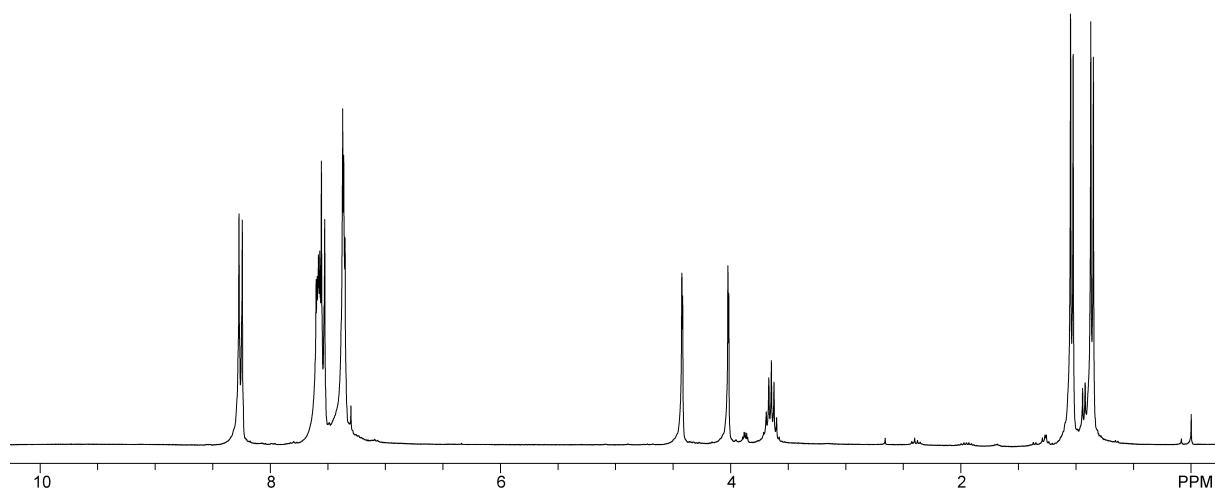
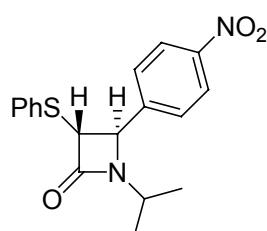
6b(containing some **7b**)**7b**

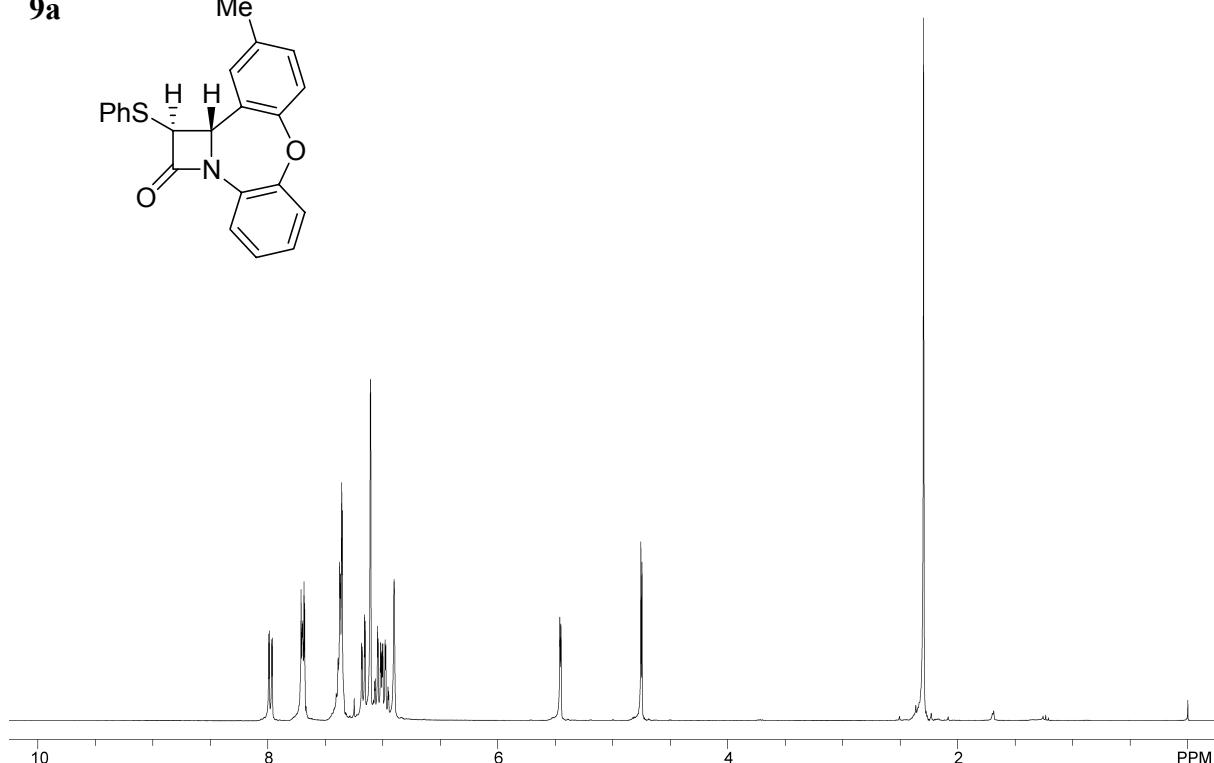
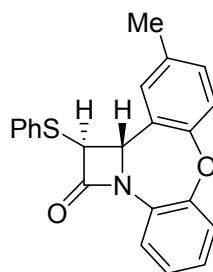
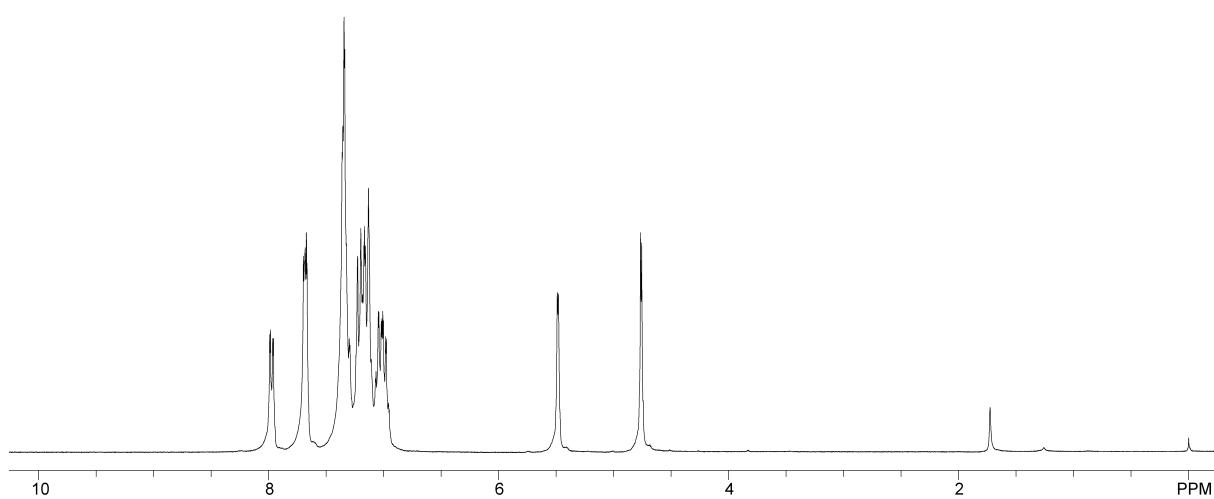
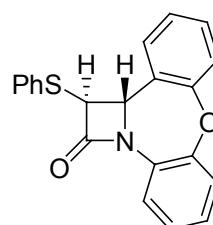


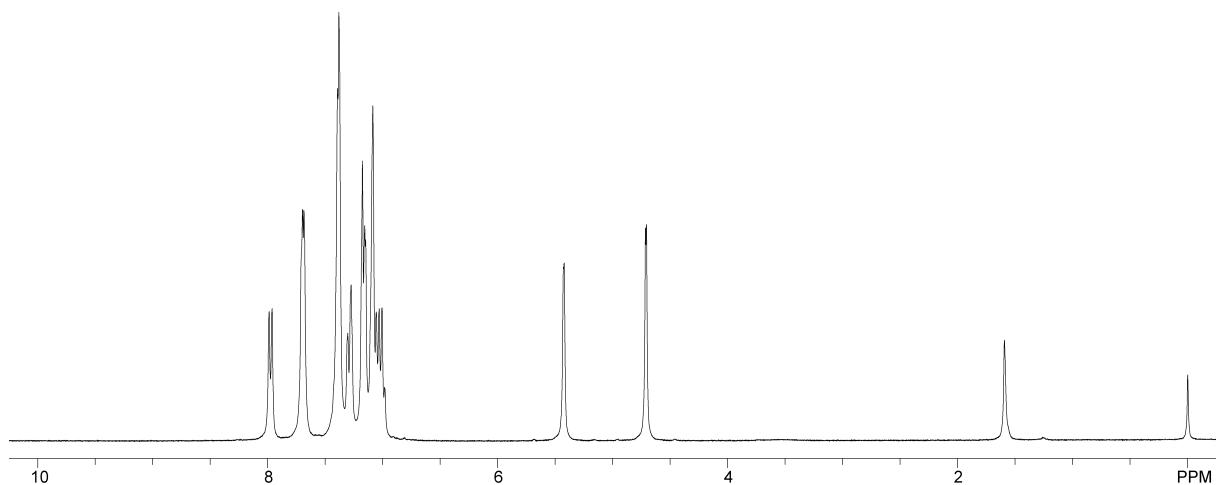
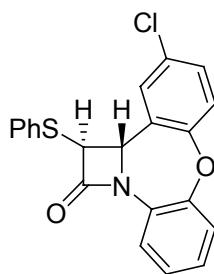
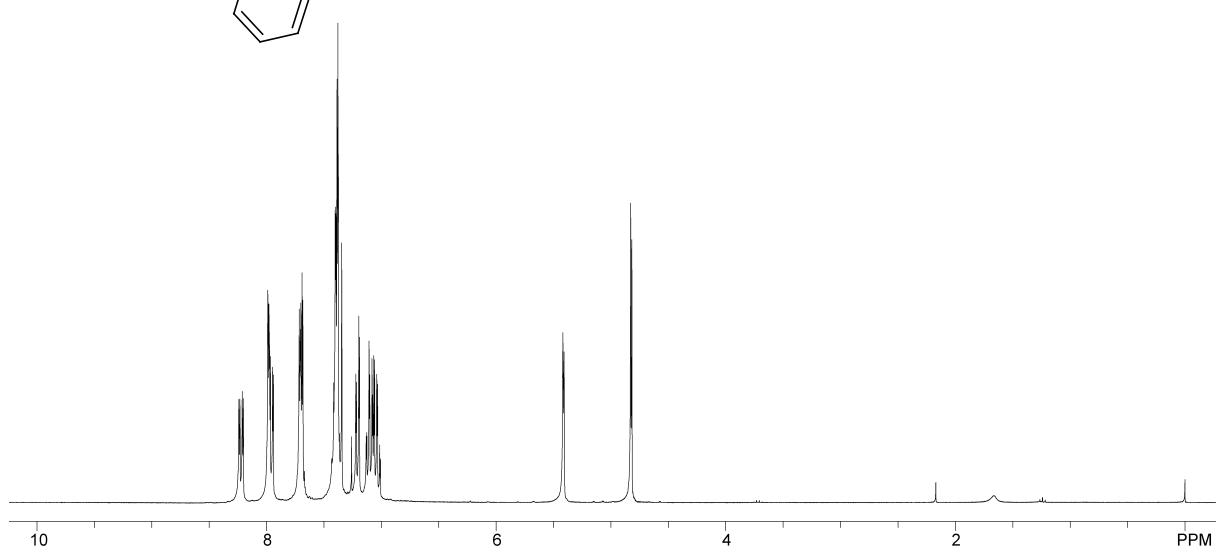
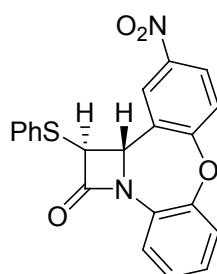
(containing some **7d**)

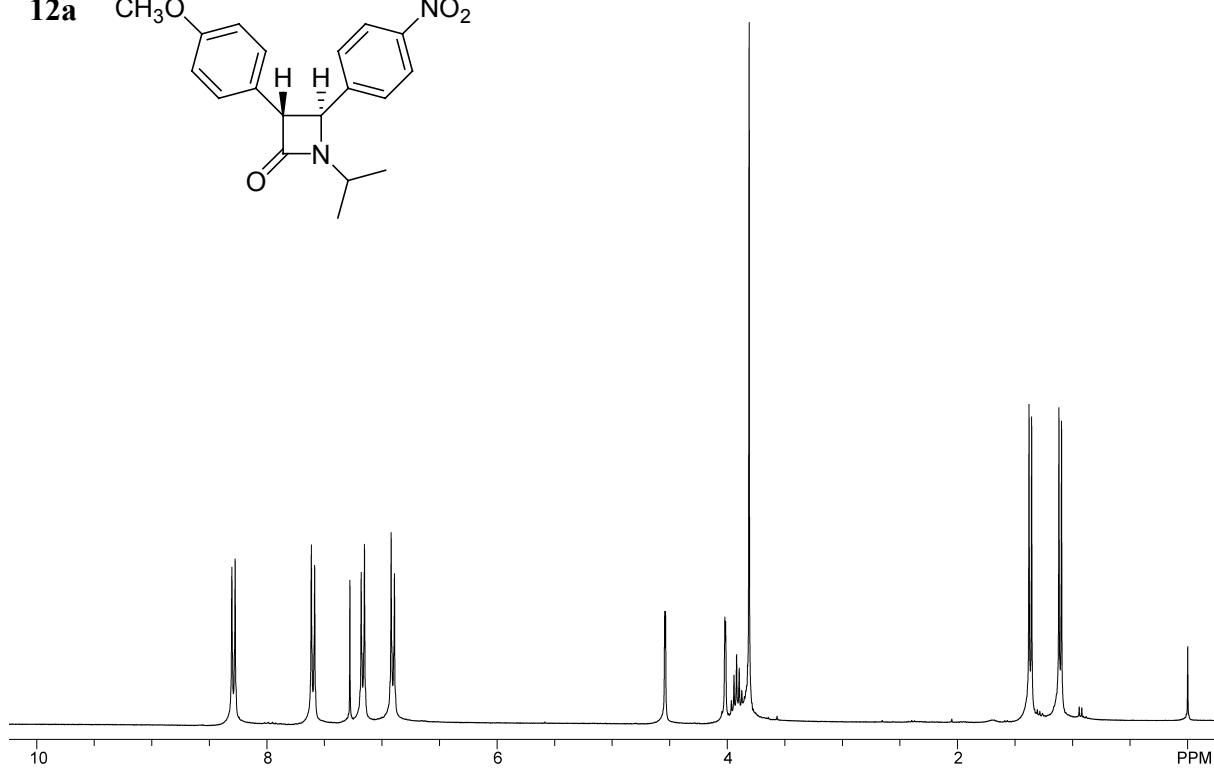
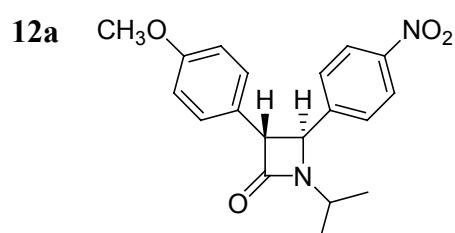
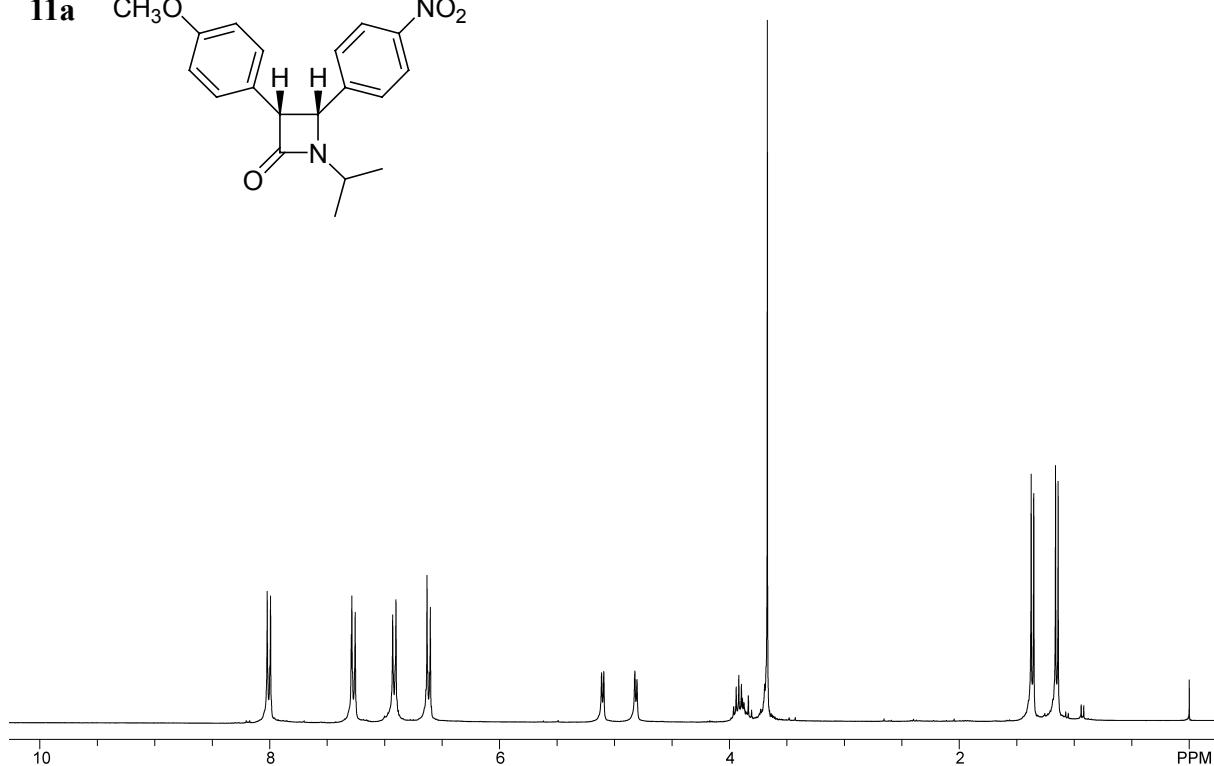
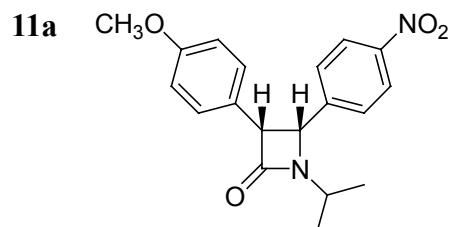


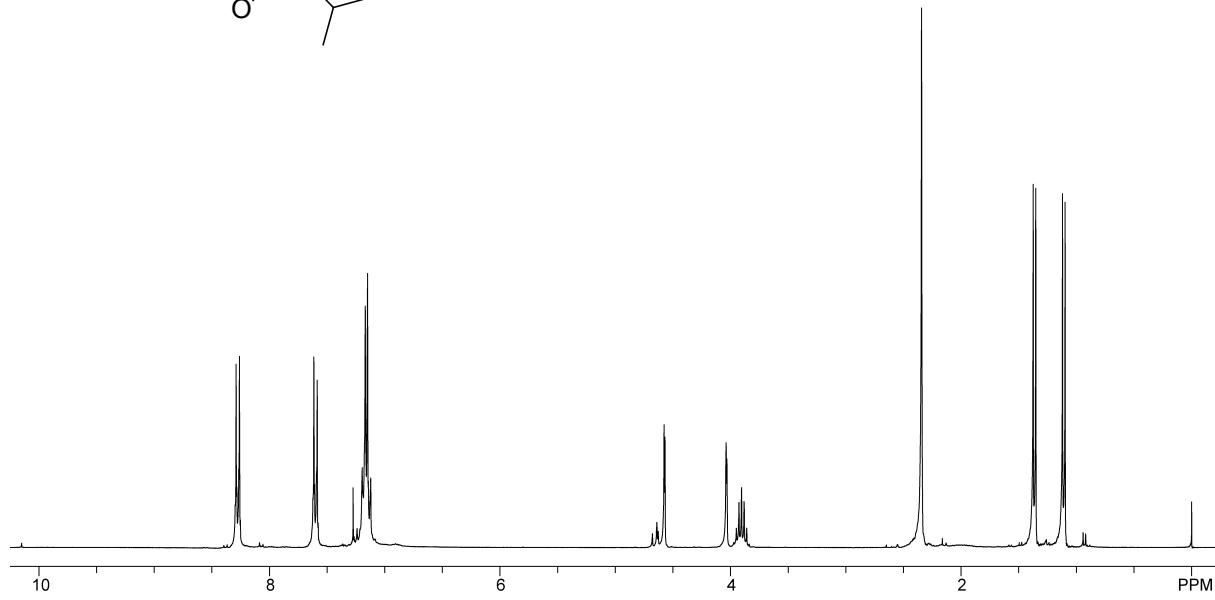
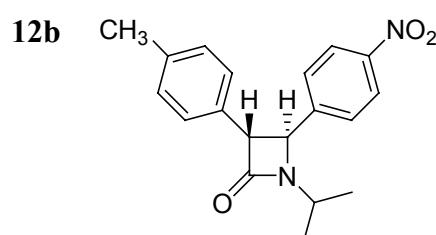
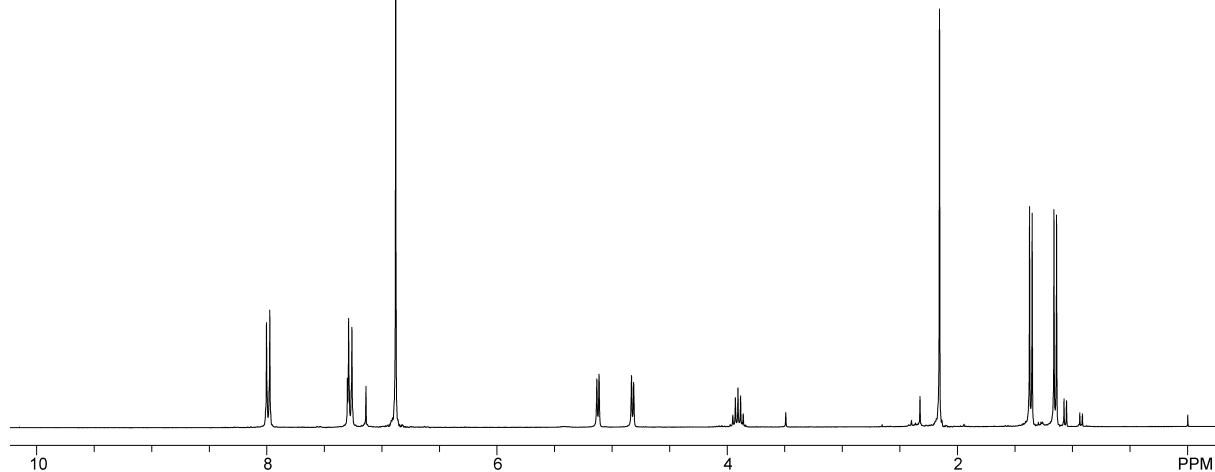
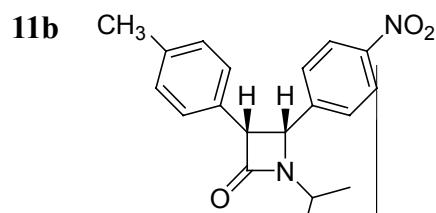
6e**7e**

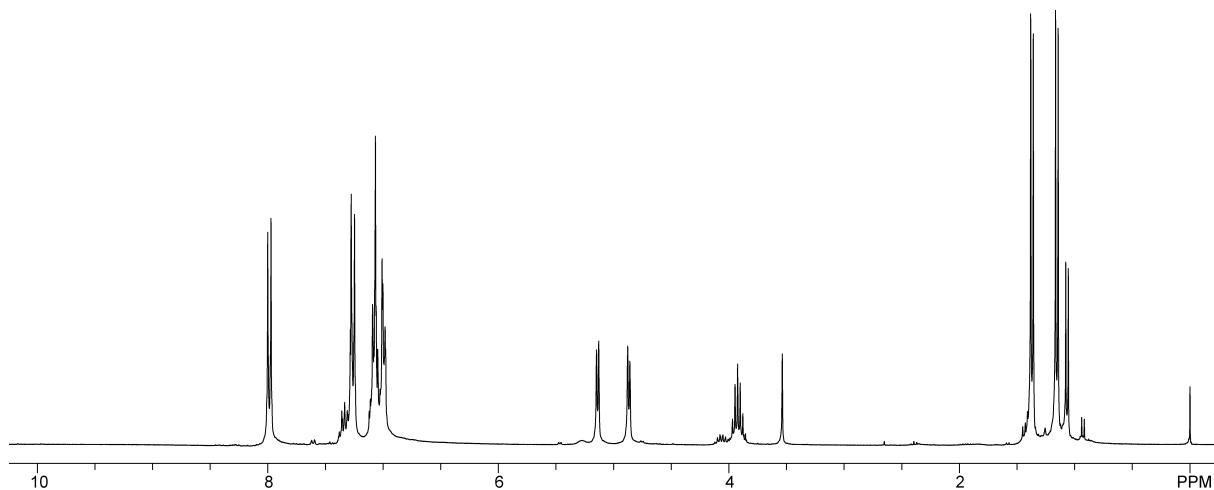
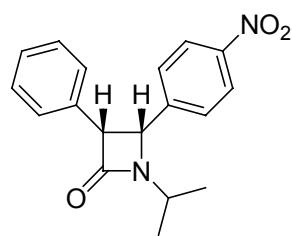
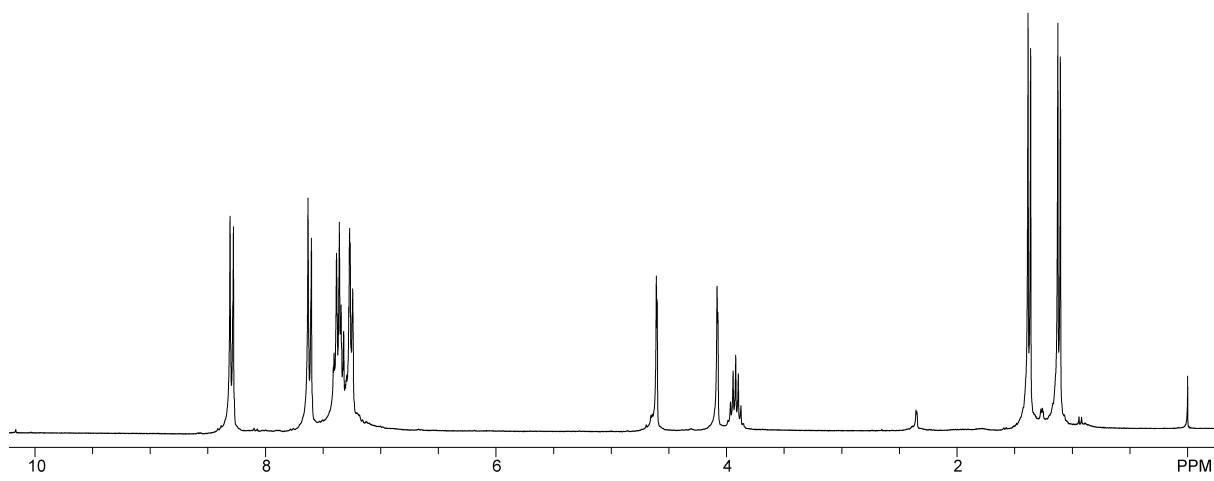
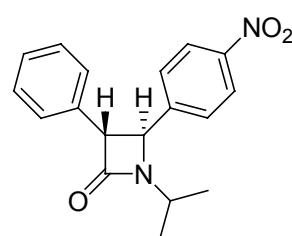
6f**7f**

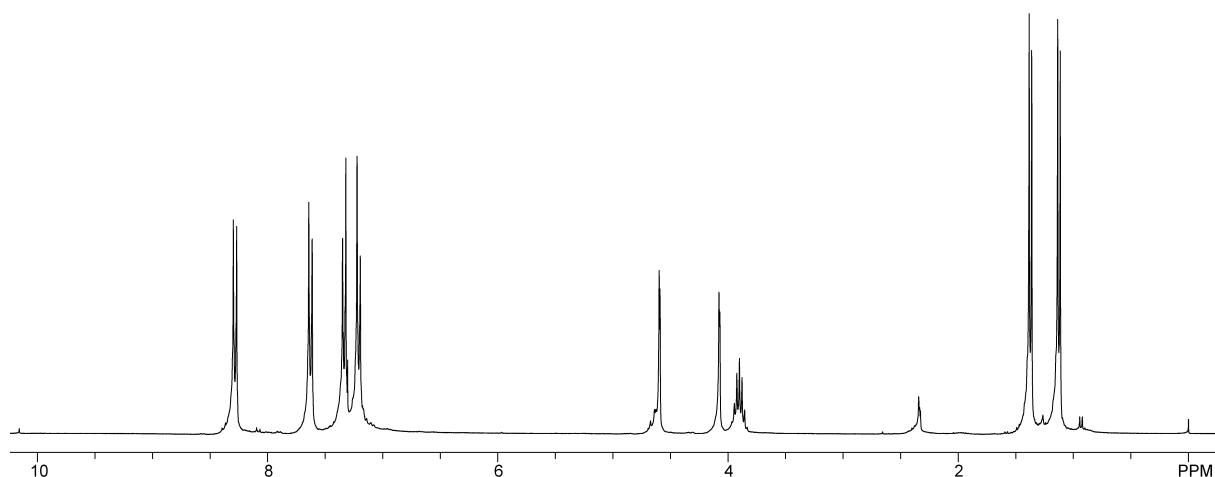
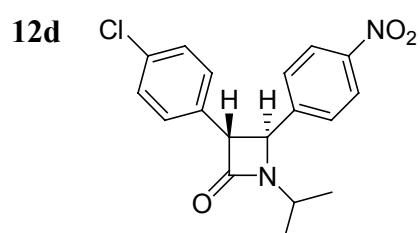
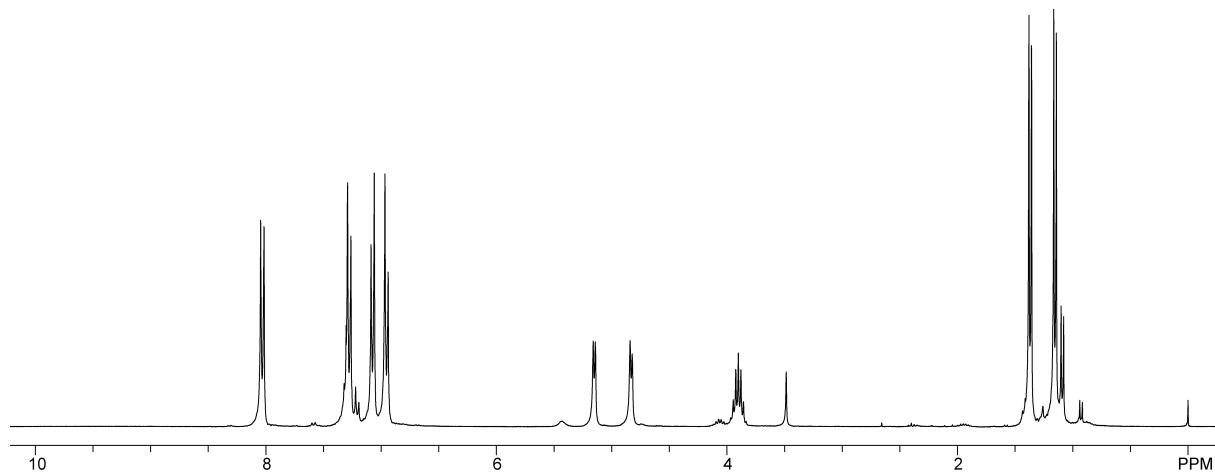
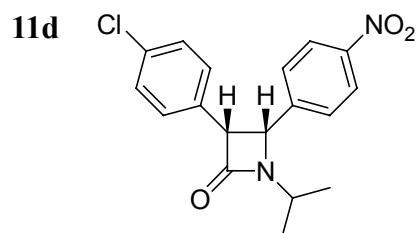
9a**9b**

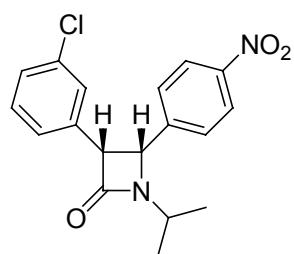
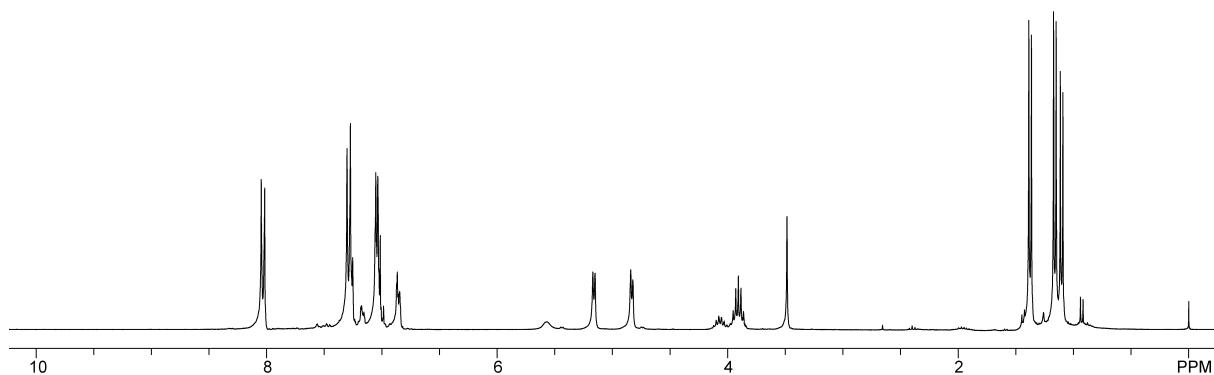
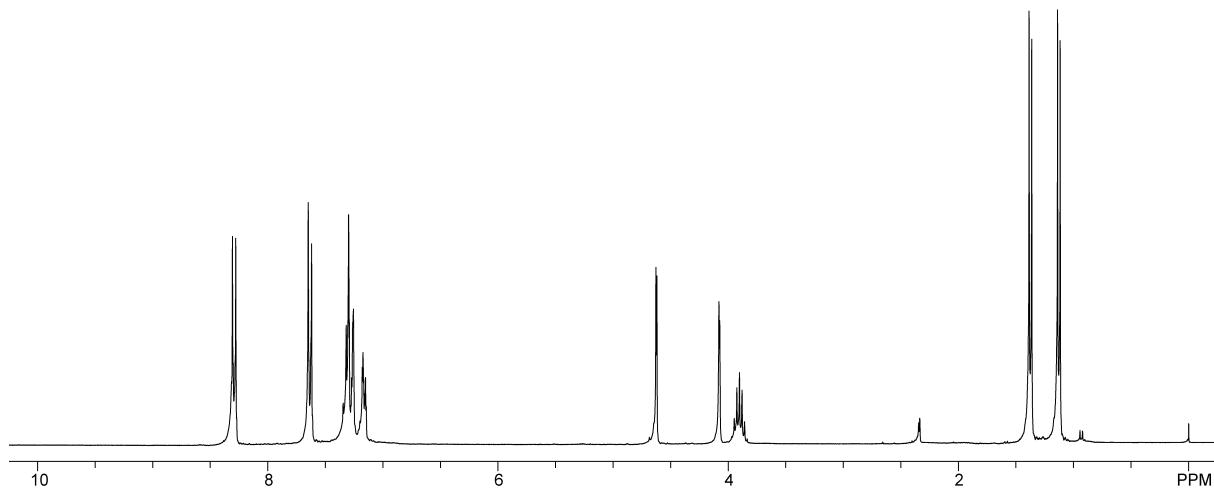
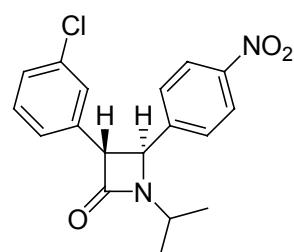
9c**9d**

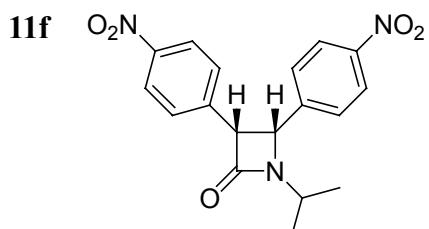




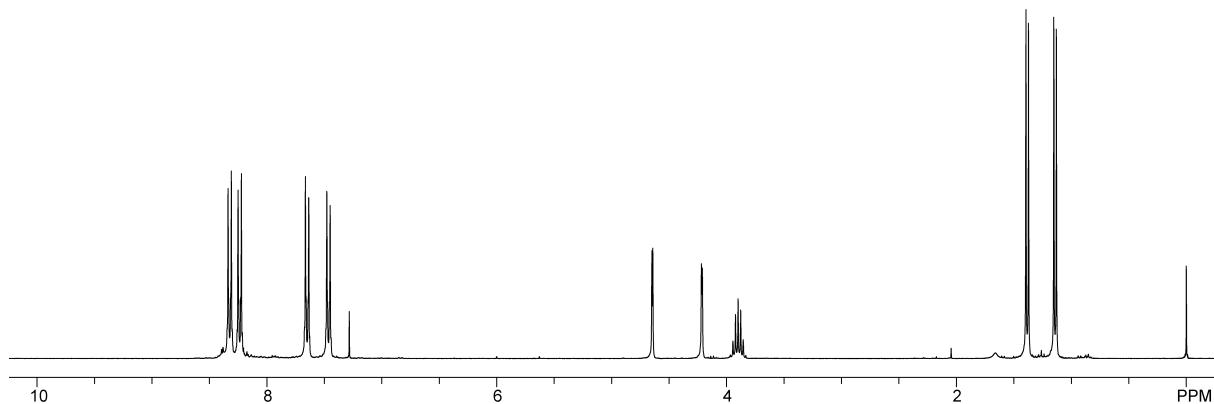
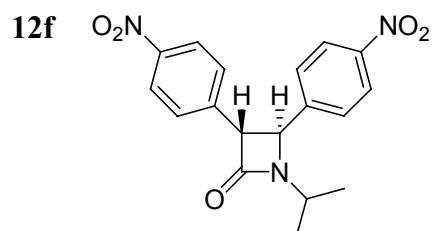
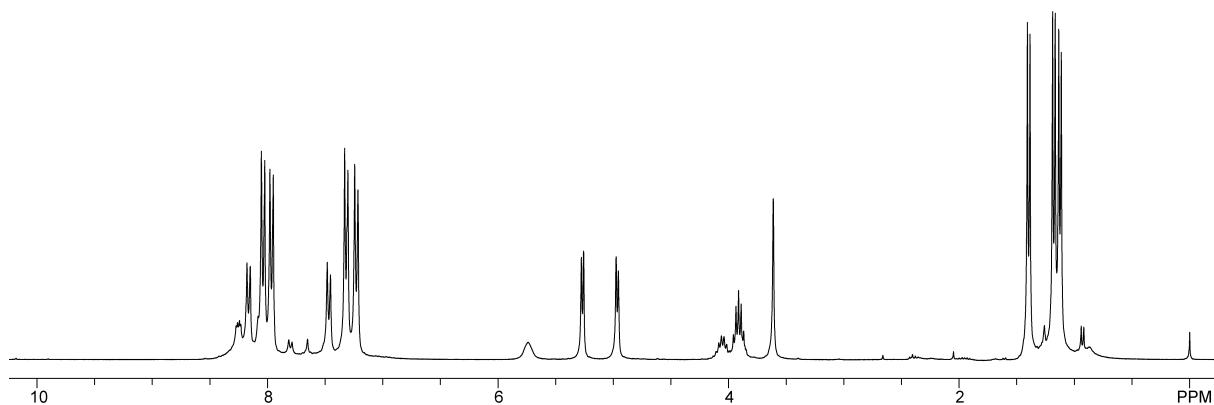
11c**12c**

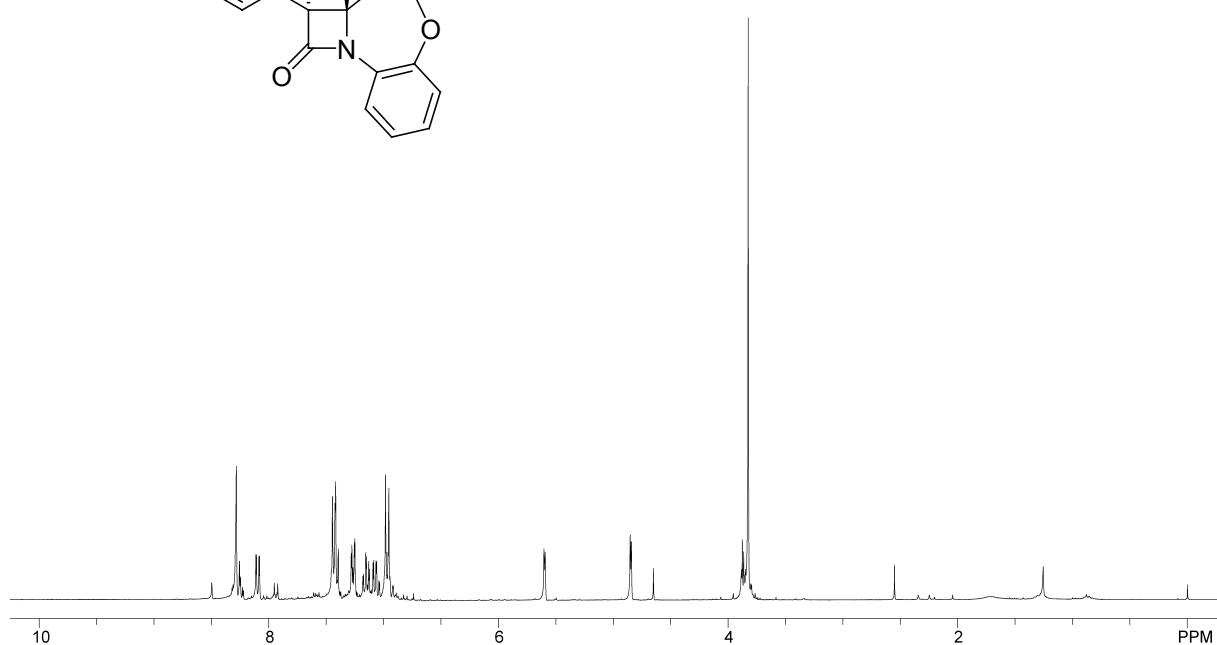
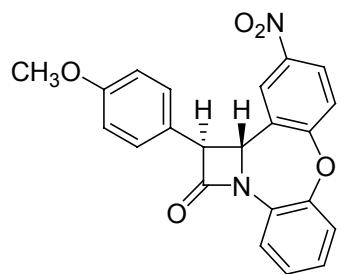
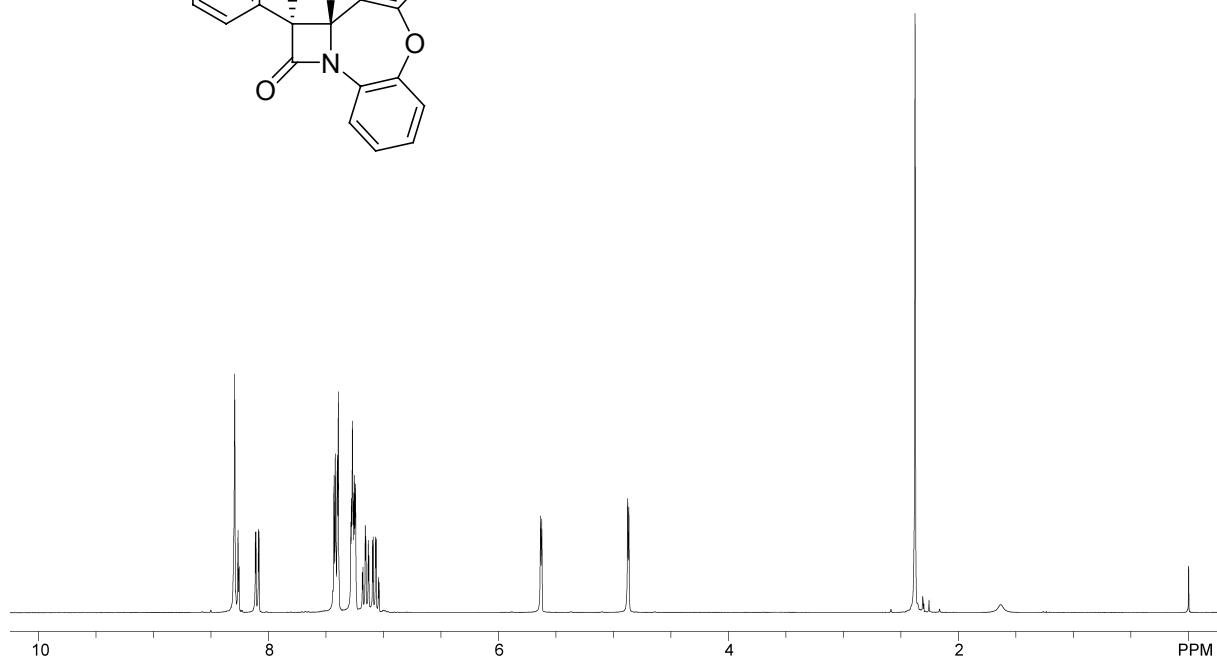
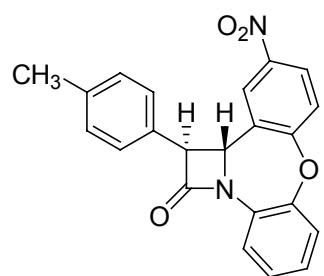


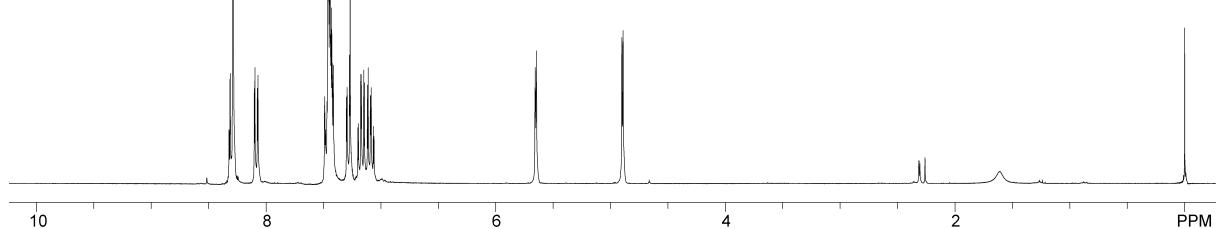
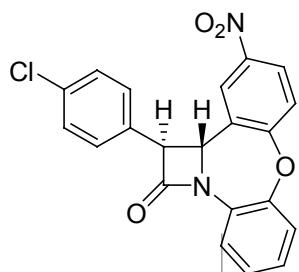
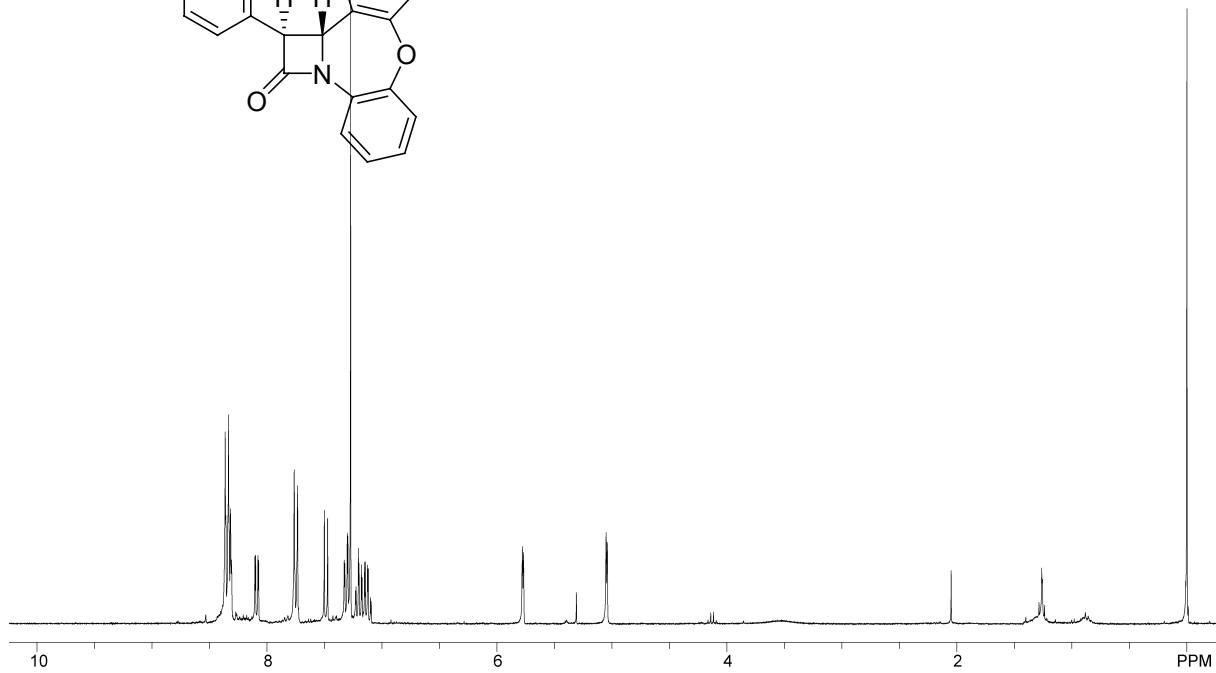
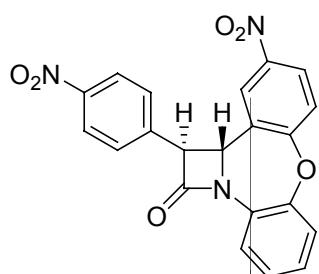
11e(containing some byproduct 2-(3-chlorophenyl)-*N*-isopropylacetamide)**12e**

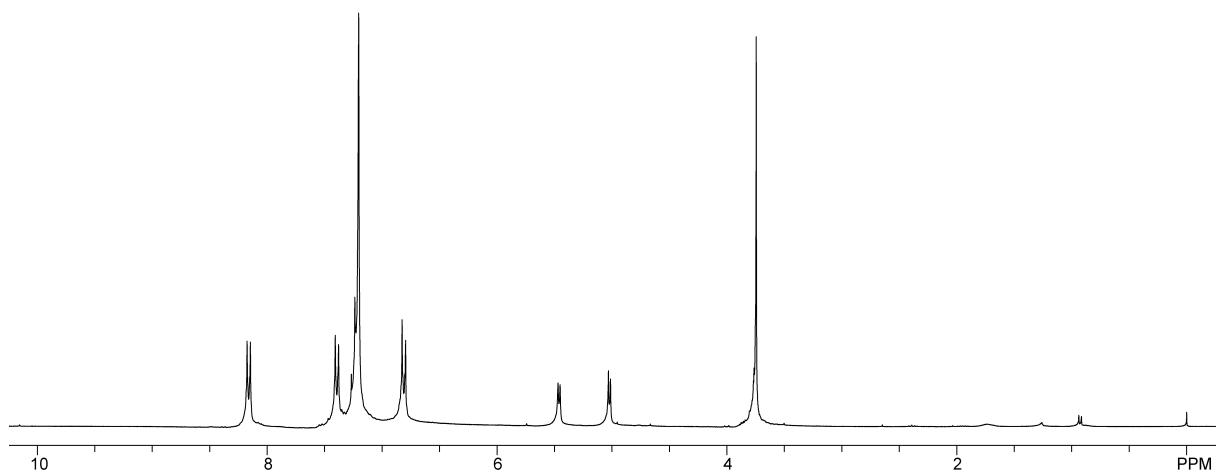
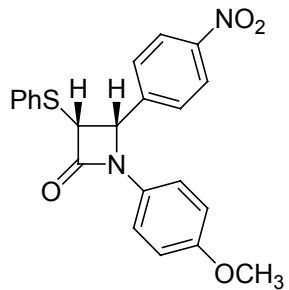
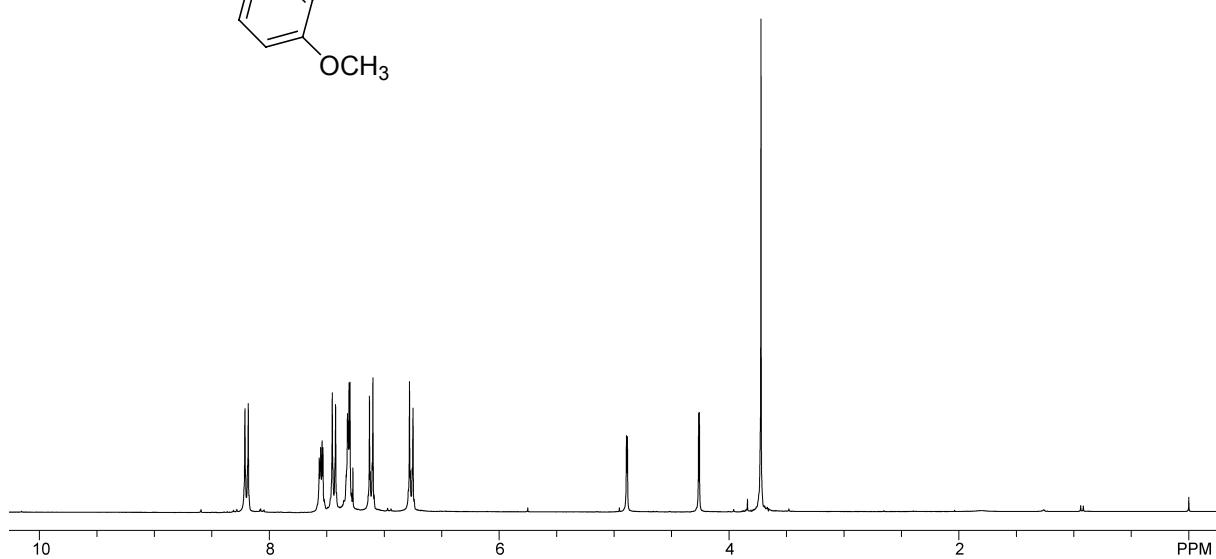
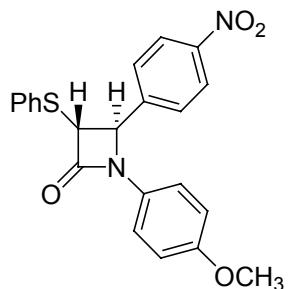


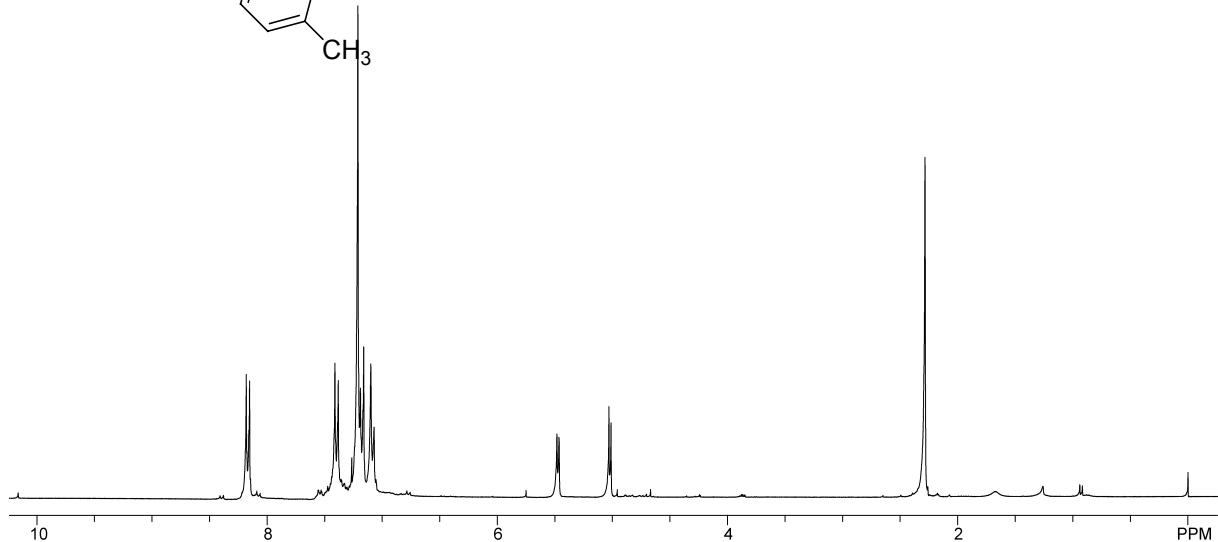
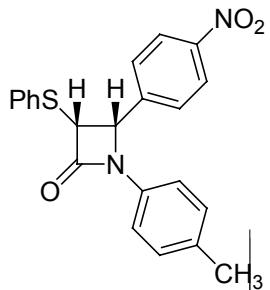
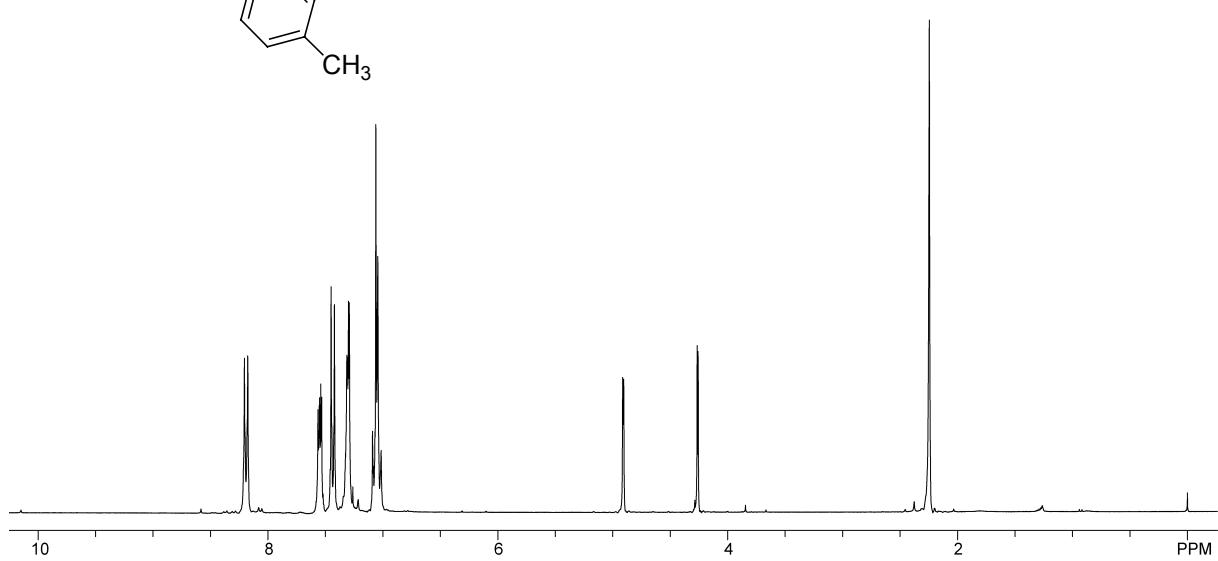
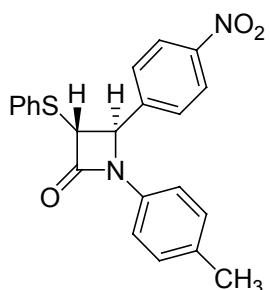
(containing some byproduct 2-(4-nitrophenyl)-N-isopropylacetamide)

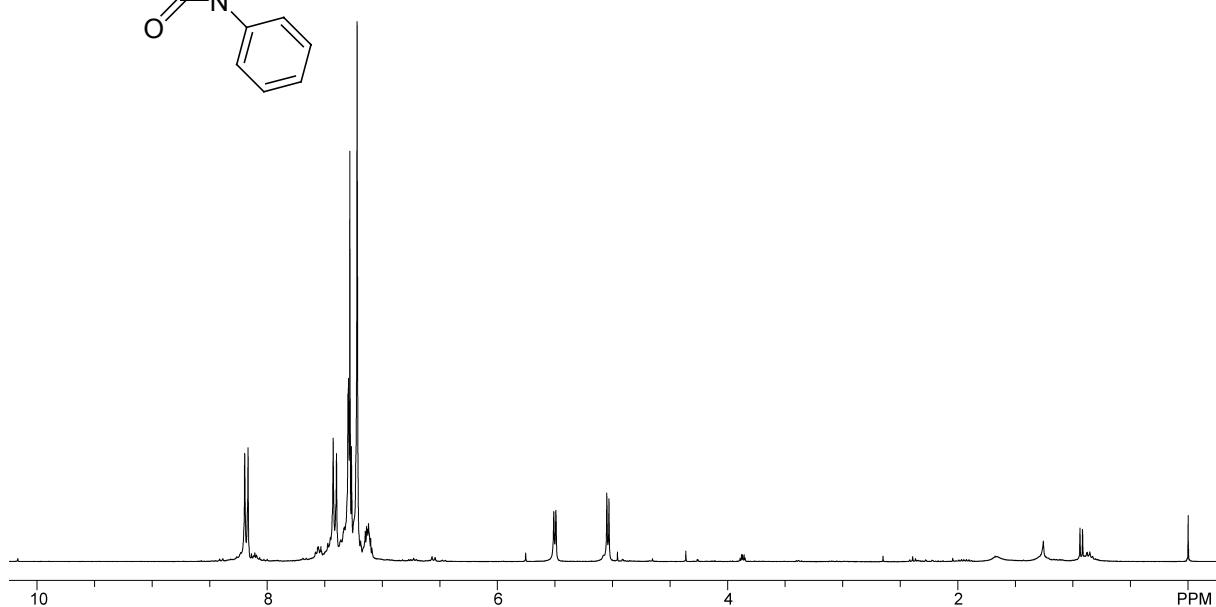
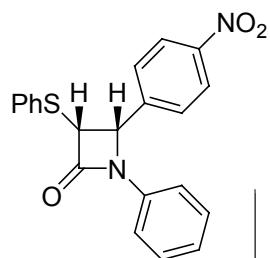
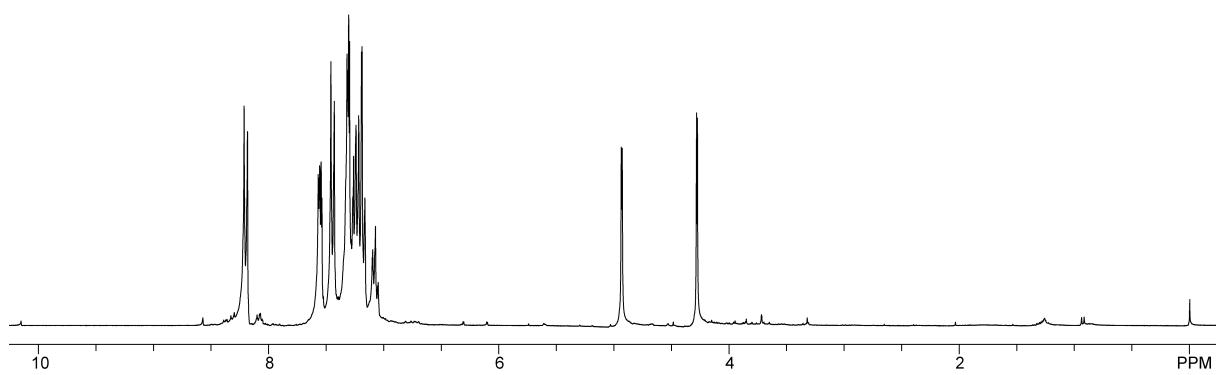
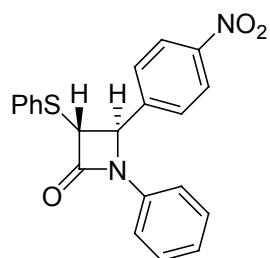


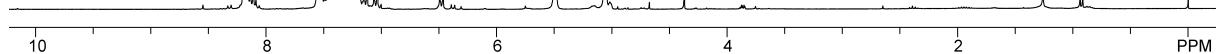
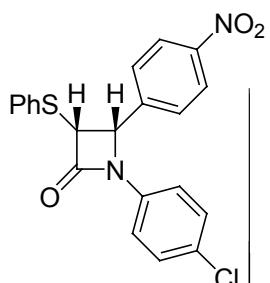
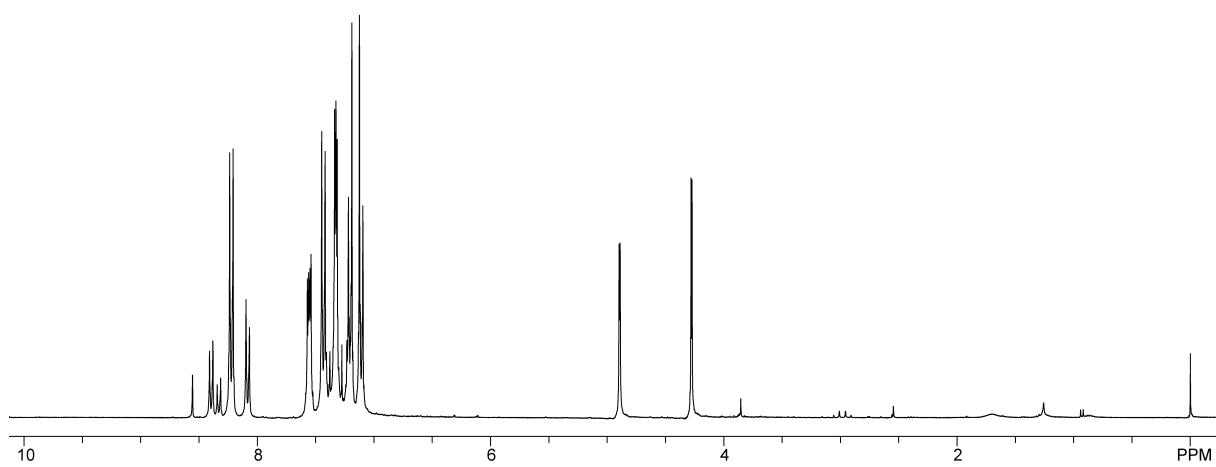
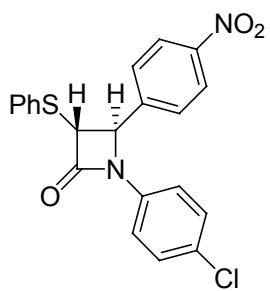
13a**13b**

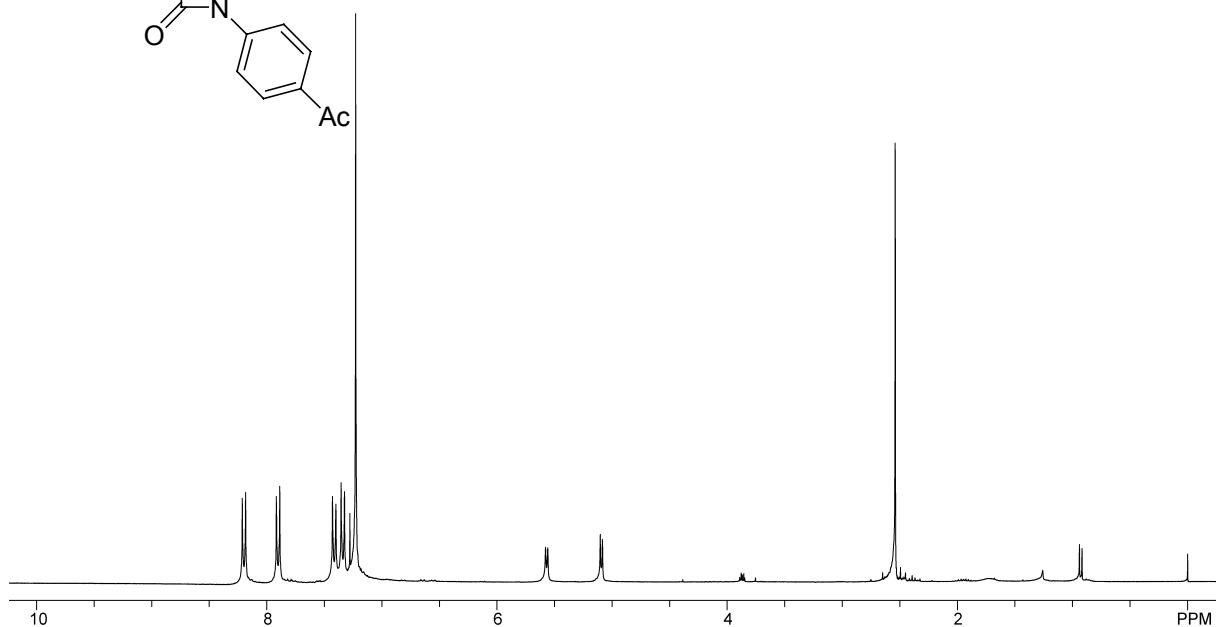
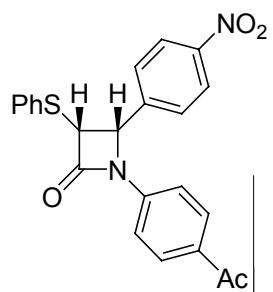
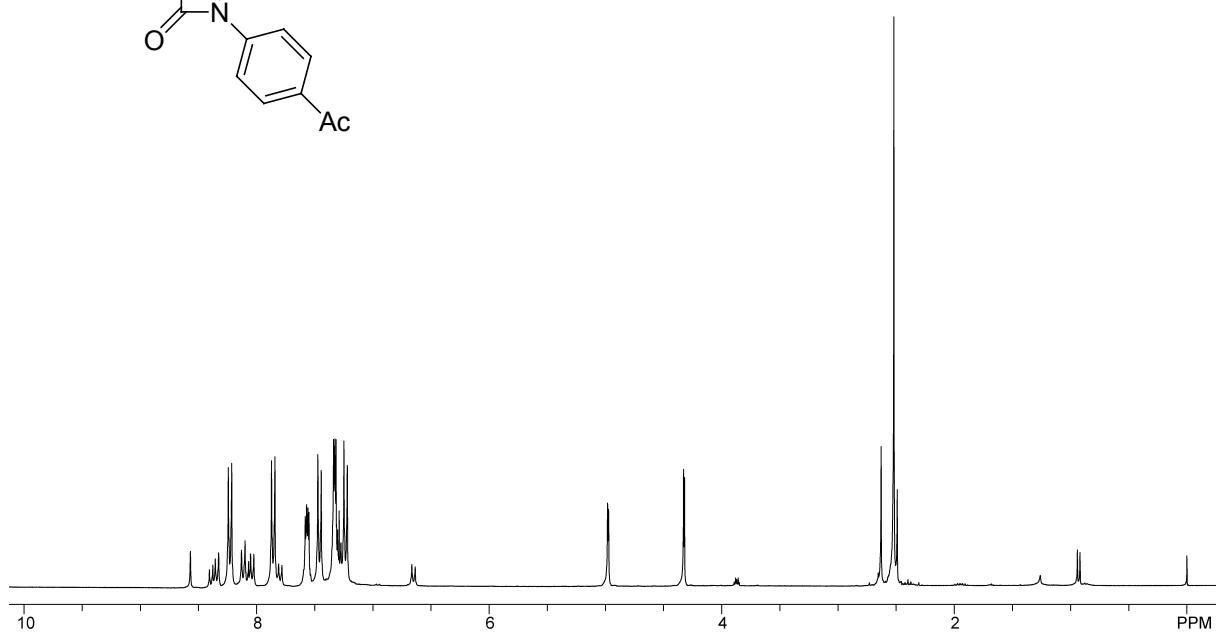
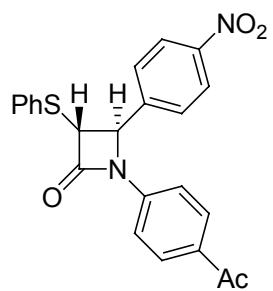
13d**13f**

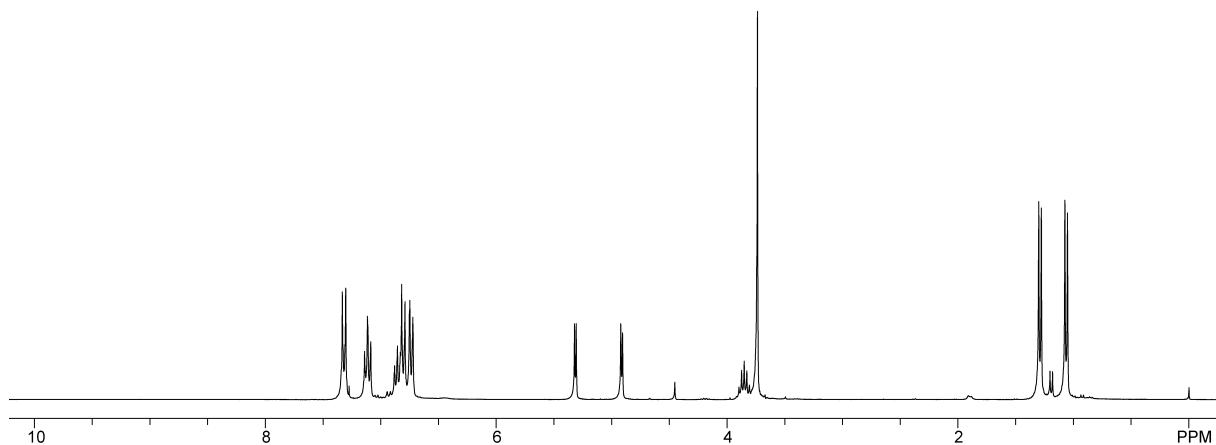
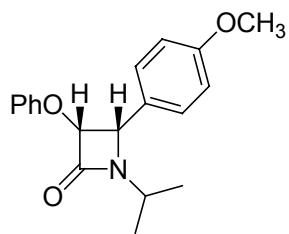
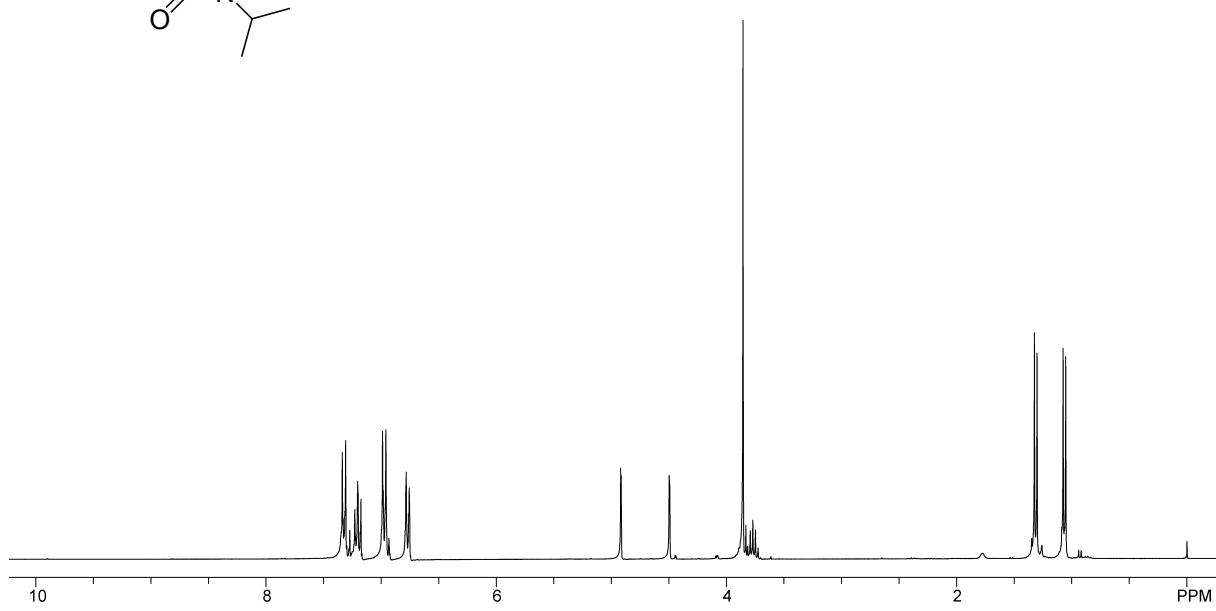
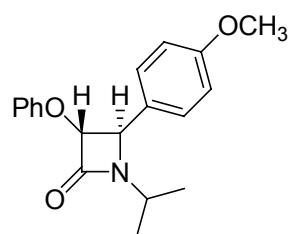
15a**16a**

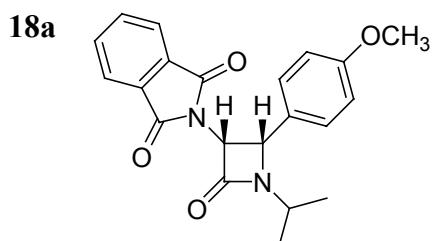
15b**16b**

15c**16c**

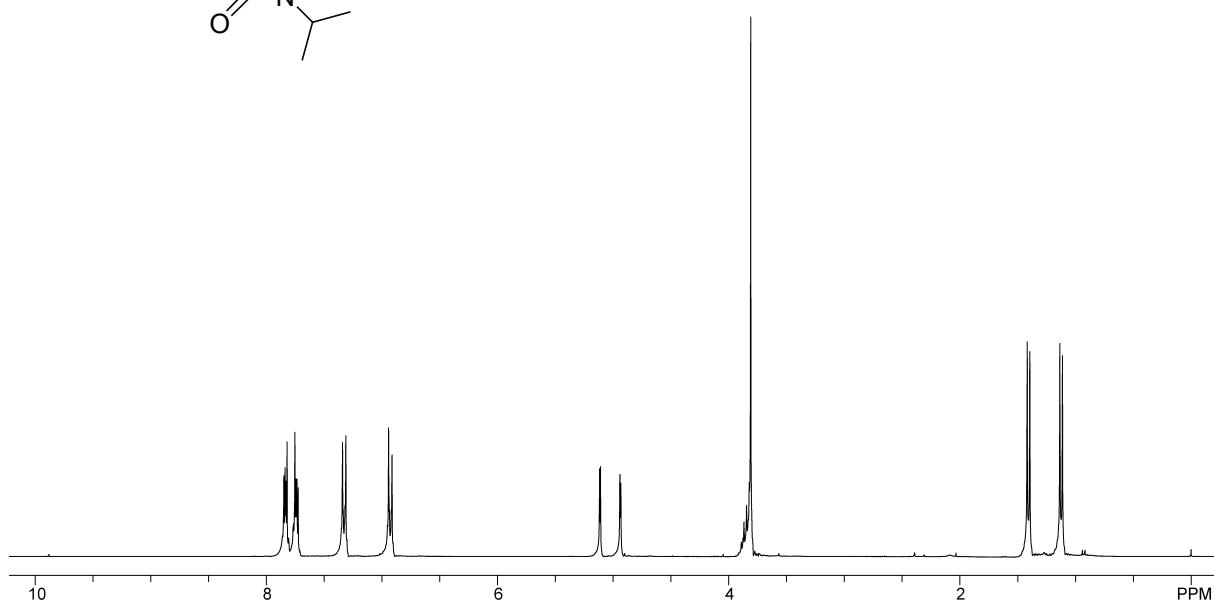
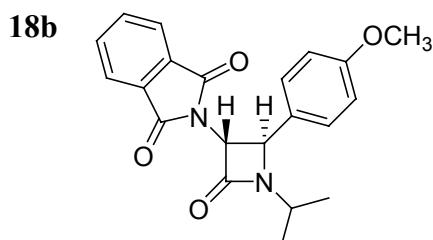
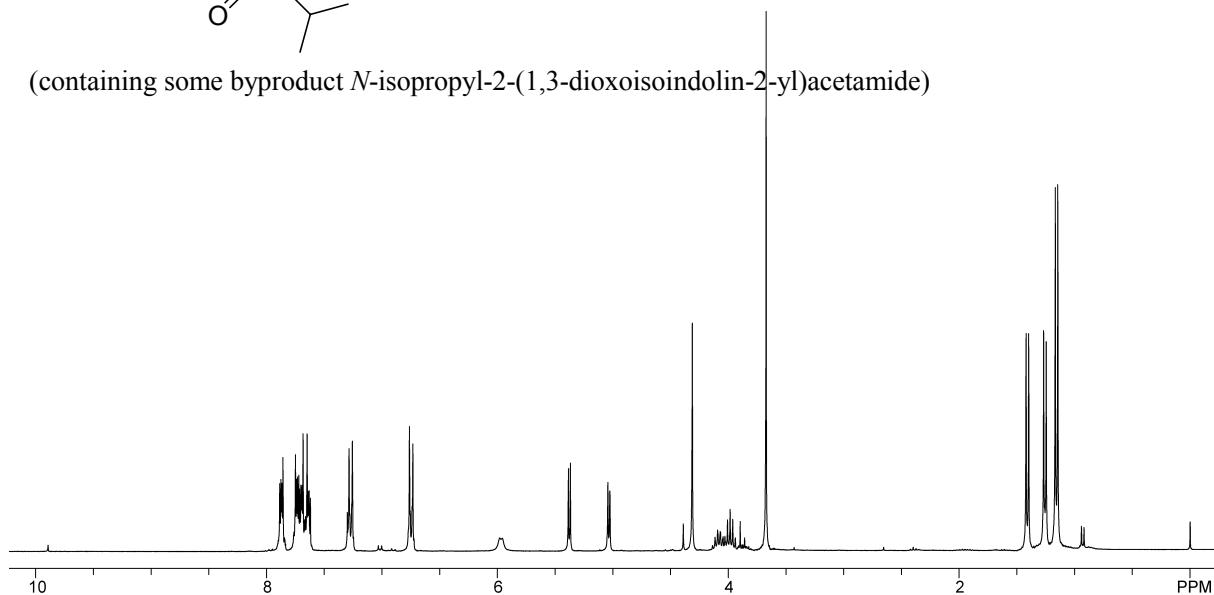
15d**16d**

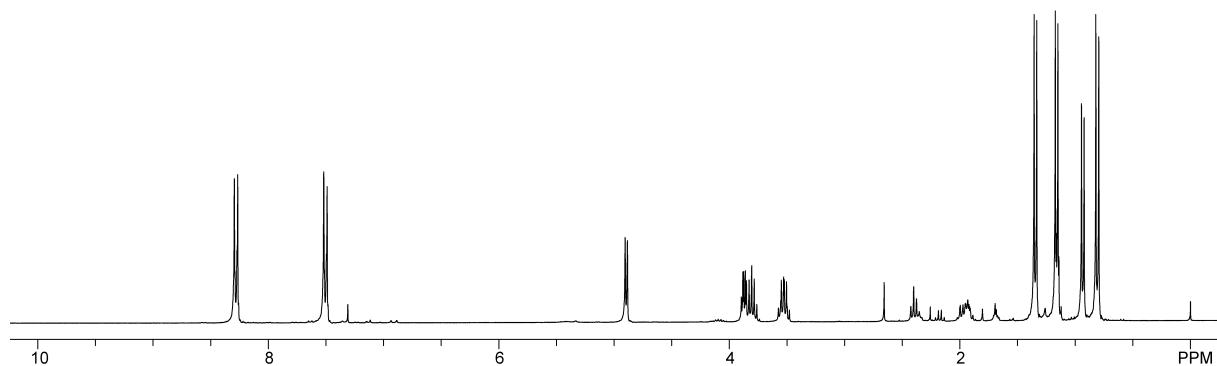
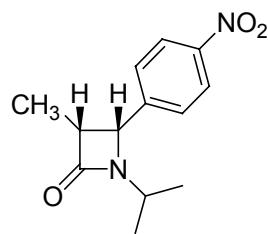
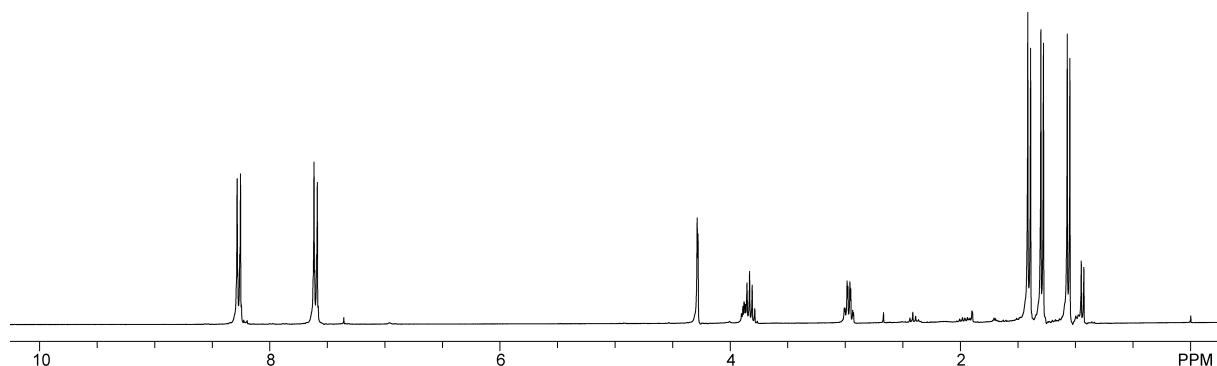
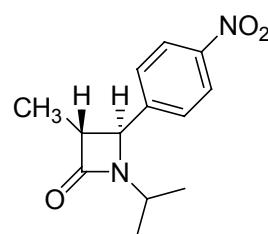
15e**16e**

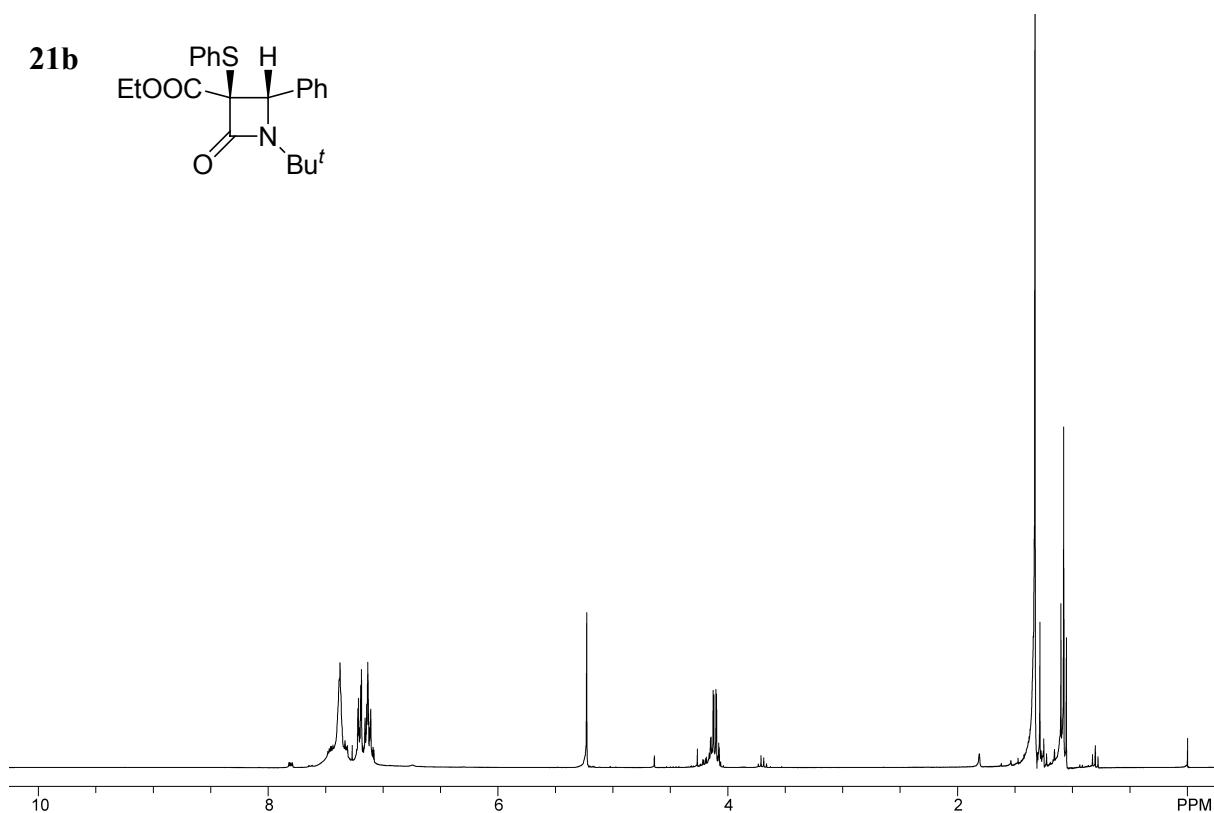
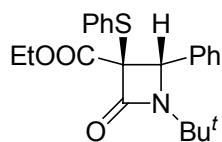
17a**17b**



(containing some byproduct *N*-isopropyl-2-(1,3-dioxoisoindolin-2-yl)acetamide)



19a**19b**

21b**21b NOE**