Supporting Information (17 pages)

Intermolecular and Intramolecular Kinetic Isotope Effects in the Nitrosoarene Ene Reaction: Experimental Verification for Reversible Intermediate Formation

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Kinetic Analysis to Estimate the Extent of Reversibility in the Ene Reaction of ArNO with the *cis/trans*-TME-d$_6$ Substrates

- assumption of no steric and secondary isotope effects:

  $\longrightarrow$ k_f, k_r, $k_a(H)$, $k_a(D)$ for *cis*-TME-d$_6$ = k_f, k_r, $k_a(H)$, $k_a(D)$ for *trans*-TME-d$_6$

  $\longrightarrow$ for *cis*-TME-d$_6$: $k_f(D) = k_f(H) = k_f$ and $k_r(D) = k_r(H) = k_r$

  $\longrightarrow$ for *trans*-TME-d$_6$: $k_a^{avg} = \dfrac{k_a(H) + k_a(D)}{2}$

- experimental data (Table 1):

$$\left\{\frac{[\mathbf{P_H}]}{[\mathbf{P_D}]}\right\}_{trans} = \left(\frac{k_H}{k_D}\right)_{trans\ (exp)} = \frac{k_a(H)}{k_a(D)} = 3.0 \ \text{ for } trans\text{-TME-d}_6:$$

$$\left\{\frac{[\mathbf{P_H}]}{[\mathbf{P_D}]}\right\}_{cis} = \left(\frac{k_H}{k_D}\right)_{cis\ (exp)} = 1.5 \ \text{ for } cis\text{-TME-d}_6:$$

- kinetic expression of the product-forming step for *cis*-TME-d$_6$:

$$\left\{\frac{[\mathbf{P_H}]}{[\mathbf{P_D}]}\right\}_{cis} = \frac{k_a(H)}{k_a(D)}\frac{[\mathbf{AI_H}]}{[\mathbf{AI_D}]} \longrightarrow \frac{[\mathbf{AI_H}]}{[\mathbf{AI_D}]} = \left\{\frac{[\mathbf{P_H}]}{[\mathbf{P_D}]}\right\}_{cis} \times \frac{k_a(D)}{k_a(H)} \qquad \text{(eq 1)}$$

- application of steady-state kinetics on *cis*-TME-d$_6$:

$$\left.\begin{array}{l} \dfrac{d\,[\mathbf{AI_H}]}{d\,t} = 0 = k_f\,[\mathbf{E}] - k_r\,[\mathbf{AI_H}] - k_a(H)\,[\mathbf{AI_H}] \\[2mm] \dfrac{d\,[\mathbf{AI_D}]}{d\,t} = 0 = k_f\,[\mathbf{E}] - k_r\,[\mathbf{AI_D}] - k_a(D)\,[\mathbf{AI_D}] \end{array}\right\} \longrightarrow \frac{[\mathbf{AI_H}]}{[\mathbf{AI_D}]} = \frac{k_r + k_a(D)}{k_r + k_a(H)} \quad \text{(eq 2)}$$

- combination of eq 1 and eq 2 to replace [$\mathbf{AI_H}$]/[$\mathbf{AI_D}$]:

$$\left\{\frac{[\mathbf{P_H}]}{[\mathbf{P_D}]}\right\}_{cis} \times \frac{k_a(D)}{k_a(H)} = \frac{k_r + k_a(D)}{k_r + k_a(H)} \qquad\qquad \text{(eq 3)}$$

- substitution into eq 3 for $k_a(H)/k_a(D) = \{[\mathbf{P_H}]/[\mathbf{P_D}]\}_{trans}$
  and $k_a(H) = \{[\mathbf{P_H}]/[\mathbf{P_D}]\}_{trans} \times k_a(H)$:

$$\left\{\frac{[\mathbf{P_H}]}{[\mathbf{P_D}]}\right\}_{cis} \times \left\{\frac{[\mathbf{P_D}]}{[\mathbf{P_H}]}\right\}_{trans} = \frac{k_r + k_a(D)}{k_r + \left\{\dfrac{[\mathbf{P_H}]}{[\mathbf{P_D}]}\right\}_{trans} \times k_a(D)} \qquad \text{(eq 4)}$$

- substitution of the experimental data into eq 4:

$$1.5 \times \frac{1}{3.0} = \frac{k_r + k_a(D)}{k_r + 3.0 \times k_a(D)}$$

- on solving for k_r and $k_a(D)$ and substitution of $k_a^{avg} = \dfrac{k_a(H) + k_a(D)}{2}$:

$$k_r = k_a(D) = 1/3\ k_a(H) = 1/2\ k_a^{avg}$$

The Problems with Pentafluoronitrosobenzene as Enophile

For the F_5C_6-NO enophile, the known[2] intermolecular and intermolecular KIE were repeated, in view of the large difference between the reported k_H/k_D value for F_5C_6-NO (1.03 ± 0.05) with TME-d_0 versus TME-d_{12} and the presently measured value for p-O_2N-C_6H_4-NO (1.98 ± 0.05, first entry in Table 1). Our remeasured for F_5C_6-NO values are now in better accord with the new nitrosoarene enophile p-O_2N-C_6H_4-NO (Table S1).

Table S1. Intermolecular and Intramolecular Kinetic Isotope Effects for the Ene Reaction of Tetramethylethylenes (TME) with Pentafluoronitrosobenzene

	k_H/k_D values			
	intermolecular	intramolecular		
enophile	TME-d_0 vs. TME-d_{12}	*cis*-TME-d_6	*trans*-TME-d_6	*gem*-TME-d_6
C_6F_5-NO[a,b]	1.20-1.77[c,d] (1.03)	1.3[e] (1.2)	3.0[e] (3.0)	(4.5)

[a] See Experimental Section for details. [c] In parenthesis is given the k_H/k_D value reported in ref 2 (Et$_2$O, 2 h, 0 °C). [c] In CH$_2$Cl$_2$ or Et$_2$O, determined by GC analysis with cyclohexane as internal standard; calculated according to k_H/k_D = ln {[A$_H$]/[A$_H$]$_0$} / ln {[A$_D$]/[A$_D$]$_0$}; error ca. 3% of the stated value. [d] Value depends on the solvent and the reaction conditions, see Table S2. [e] In CDCl$_3$, determined by ^{1}H-NMR spectroscopy; error ca. 5% of the stated value.

The intramolecular KIE for *cis*-TME-d_6 was now found to be 1.3 (±0.07), which is similar to the reported value (1.2).

We have repeated the intermolecular KIE between TME-d_0 and TME-d_{12} for this enophile many times at various conversions (10-50%), and we have found that the k_H/k_D values in dichloromethylene range between 1.20 and 1.77 (±0.05). Evidently, the exact value depends on the reaction conditions, which include the extent of conversion, the concentration of the F_5C_6-NO and the substrates, the way of nitroso-enophile addition, and the stirring rate. In ethyl ether, which was used previously as solvent,[2] the reaction proceeds slower and better behaved than in CH_2Cl_2 (ca. 2 h at 0 °C for full conversion of the enophile versus less than 30 min in CH_2Cl_2), and we observed k_H/k_D values of 1.21-1.27 at various conversions, but never 1.03 (Table S2).

Table S2. Intermolecular Kinetic Isotope Effects in the Ene Reaction of F_5C_6NO with the TME-d_0 / TME-d_{12} Substrate Pair under a Variety of Reaction Conditions

F_5C_6NO	ref 2	present[a]					
solvent	Et_2O	CH_2Cl_2[b]			Et_2O[c]		
convn [%]	not det.	12	13	48	22	35	48
equiv.	0.5	0.15	0.2	0.35		0.5	
time [min]	120		30		45	100	125
k_H/k_D value	1.03[d]	1.77	1.47[e]	1.20	1.23	1.27	1.21

[a] These k_H/k_D values were determined by GC analysis of the remaining alkenes with cyclohexane as internal standard; error < 3% of the stated value. [b] Rapid reaction, full conversion of the enophile in less than 30 min at 0 °C; k_H/k_D value depends on the reaction conditions. [c] Full conversion of the enophile in 2 h at 0 °C. [d] Determined by mass spectroscopy of the remaining alkenes. [e] Instead of 4 mL of CH_2Cl_2, 9 mL were taken.

Our procedure was similar to that used previously,[2] except we employed 2 mL of a 0.003 M solution of the alkenes in CH_2Cl_2 (Et_2O), to which the F_5C_6-NO in 2 mL of CH_2Cl_2 (Et_2O) was added, whereas previously 50 mL of a 0.015 M solution of the alkenes was used, to which the F_5C_6-NO in 20 mL Et_2O was added; thus, the concentrations in our experiments were for the olefins by a factor of 7.3 lower and for F_5C_6-NO by factors of 6 to 42. Moreover, for the determination of the k_H/k_D values we employed GC analysis on a 60-m capillary column, in which the TME-d_0 and TME-d_{12} alkenes are cleanly separated, with cyclohexane as internal standard, whereas previously MS analysis was used, in which the conversions are not specified. Low conversions were chosen for some of our experiments in view of possible local depletion effects for the highly reactive F_5C_6-NO enophile. Nevertheless, the error in the GC analysis remains below 5% also for the low conversions, since the signals are well separated and the chromatograms are very clean. We have conducted the experiments at higher conversions and lower (but still substantial) normal kinetic isotope effects were obtained; however, the results are not reproducible.

In conclusion, our present k_H/k_D values for the ene reaction of F_5C_6-NO with the TME-d_0/TME-d_{12} substrate pair clearly demonstrate the difficulties with this highly reactive enophile in mechanistic work. We recommend the use of p-O_2N-C_6H_4-NO as nitrosoarene enophile, which exhibits sufficient reactivity and provides reproducible intermolecular kinetic isotope effects.

Experimental Section

General Aspects. To obtain well-resolved NMR spectra of the hydroxylamine ene products, immediately before measurement ca. 5 μL phenylhydrazine were added to the $CDCl_3$ solution as scavenger of paramagnetic impurities. For quantitative ^{1}H-NMR analyses, a relaxation delay of 20 s with a 30° pulse was used. TLC analysis was conducted on precoated silica-gel foils 60 F_{254} (20 x 20 cm). Spots were visualized by UV irradiation (254 nm), by a 5% solution of phosphomolybdic acid in ethanol, or by a 1 N aqueous NaOH solution (for nitroso ene products). Solvents were dried by standard methods and purified by distillation before use. Commercially available substances were purified by standard procedures. The isotopic and stereochemical purity of the deuterium-labeled alkenes was determined by MS, GC, and ^{1}H-NMR analysis. The nitrosoarene ene reactions were conducted under exclusion of light and moisture.

Starting Materials. 4-Nitronitrosobenzene (ArNO) was prepared by oxidation of 4-nitroaniline with potassium monoperoxysulfate (kindly supplied by Peroxid-Chemie GmbH, Pullach bei München, Germany) according to the literature procedure[S1] and purified by recrystallization from methanol. 4-Phenyl-1,2,4-triazoline-3,5-dione (PTAD)[S2] and pentafluoronitrosobenzene[S3] were made according to literature procedures and purified by sublimation. The 2,3-dimethyl-2-butenes (*cis*-TME-d_6,[S4] *trans*-TME-d_6,[S5] *gem*-TME-d_6,[S6] and TME-d_{12}[S7]) and the 3-methyl-1-phenyl-2-butenes (**2**-d_0[S8] and **2**-d_6[S9]) were prepared as reported.

GP-1: General Procedure for the Ene Reaction with 4-Nitronitrosobenzene on the Preparative Scale. To a solution of the alkene in dry dichloromethane (200 mL) was added 4-nitronitrosobenzene at 0 °C. The reaction mixture was stirred at this temperature for 24 h until complete conversion [TLC detection, petroleum ether/ethyl ether (2:1) as

eluent]. The product was extracted from the organic layer with 4% aqueous sodium hydroxide solution (3 x 50 mL). After acidification with 98% sulfuric acid at 0 °C, the water layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were washed with water (1 x 50 mL), dried over anhydrous Na_2SO_4, and the solvent was removed (40 °C, 800 mbar). The crude ene products were purified by silica-gel flash chromatography [petroleum ether/dichloromethane (3:1) as eluent].

Ene Reaction of 4-Nitronitrosobenzene with 2,3-Dimethyl-2-butene on the Preparative Scale: *N*-Hydroxyl-*N*-(4-nitrophenyl)-*N*-(1,1,2-trimethyl-2-propenyl)amine (3a).[7] According to the general procedure (GP-1), 280 mg (3.33 mmol) of 2,3-dimethyl-2-butene (TME-d_0) were treated with 506 mg (3.33 mmol) of 4-nitronitrosobenzene. The workup yielded 606 mg (77%) of the ene product as air sensitive, yellow oil, R_f [petroleum ether/dichloromethane (4:1) as eluent] = 0.4. IR (KBr): $\tilde{v}$ 3382, 2980, 1593, 1499, 1323, 1112 cm^{-1}; ^{1}H NMR (250 MHz, CDCl$_3$): δ 1.26 (s, 6 H, 2 × CH$_3$), 1.81 (s, 3 H, CH$_3$), 4.86 (s, br, 1 H, CH), 4.90 (s, br, 1 H, CH), 7.20 (m, 2 H, CH$_2$), 8.00 (m, 2 H, CH$_2$), OH signal not detected; ^{13}C NMR (63 MHz, CDCl$_3$): δ 21.1 (2 × q), 25.2 (q), 69.8 (s), 113.5 (t), 120.1 (2 × d), 125.7 (2 × d), 143.6 (s), 152.2 (s) 157.7 (s). Anal. Calc. for C$_{12}$H$_{16}$N$_2$O$_3$ (236.3): C, 61.00; H, 6.83; N, 11.86. Found: C 60.82; H 6.64; N 11.63.

Ene Reaction of 4-Nitronitrosobenzene with 3-Methyl-1-phenyl-2-butene on the Preparative Scale: *N*-Hydroxyl-*N*-(2-methyl-1-phenylmethylpropenyl)-*N*-(4-nitro-phenyl)amine (3b).** According to the general procedure (GP-1), 1.00 g (6.85 mmol) of 3-methyl-1-phenyl-2-butene (2-d_0) were treated with 400 mg (2.63 mmol) of 4-nitronitrosobenzene. The workup yielded 462 mg (59%) of the ene product as yellow oil, R_f [petroleum ether/dichloromethane (2:1) as eluent] = 0.2. IR (KBr): $\tilde{v}$ 3551, 3087, 3029,

2972, 2926, 1594, 1550, 1515, 1335, 1253, 1005 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$): δ 1.78 (s, 3 H, CH$_3$), 3.15 (dd, J_1 = 14.1 Hz, J_2 = 6.1 Hz, 1 H, CH), 3.30 (dd, J_1 = 14.1 Hz, J_2 = 9.0 Hz, 1 H, CH), 4.59 (dd, J_1 = 9.0 Hz, J_2 = 6.0 Hz, 1 H, CH), 5.01 (s, br, 1 H, CH), 5.02 (s, br, 1 H, CH), 6.91 (m, 2 H, CH$_2$), 7.20-7.27 (m, 5 H, CH, 2 × CH$_2$), 8.00 (m, 2 H, CH$_2$), OH signal not detected; ^{13}C NMR (101 MHz, CDCl$_3$): δ 20.9 (q), 35.7 (t), 69.2 (d), 112.4 (2 × d), 115.0 (t), 125.2 (2 × d), 126.5 (d), 128.3 (2 × d), 129.1 (2 × d), 138.3 (s), 139.6 (s), 142.0 (s), 156.1 (s). Anal. Calc. for C$_{17}$H$_{18}$N$_2$O$_3$ (298.3): C, 68.44; H, 6.08; N, 9.39. Found: C 68.24; H, 6.04; N, 9.41.

GP-2: General Procedure for the Ene Reaction of 4-Nitronitrosobenzene with the Unlabeled Alkenes on the NMR Scale. Under an argon-gas atmosphere, the alkene was dissolved in 5.00 mL of argon-saturated CDCl$_3$. To this solution were added 50.0 μL of tetrachloroethane as internal standard. A 500-μL aliquot of this stock solution was taken for the ^{1}H-NMR reference spectrum. To the remaining stock solution were added 500 mg (3.29 mmol) of 4-nitronitrosobenzene at 0 °C, and the reaction mixture was stirred at this temperature for 24 h. The conversion and the product balance were determined by ^{1}H-NMR analysis, the results are given below.

Ene Reaction of 4-Nitronitrosobenzene with the Unlabeled 2,3-Dimethyl-2-butene on the NMR Scale. According to the general procedure (GP-2), 0.55 g (6.58 mmol) of 2,3-dimethyl-2-butene were treated with 500 mg (3.29 mmol) of 4-nitronitrosobenzene. The conversion was 92% (normalized to 1 equiv. of alkene), the product balance >95%.

Ene Reaction of 4-Nitronitrosobenzene with the Unlabeled 3-Methyl-1-phenyl-2-butene on the NMR Scale. According to the general procedure GP-2, 0.96 g (6.58 mmol)

3-methyl-1-phenyl-2-butene were treated with 500 mg (3.29 mmol) of 4-nitronitrosobenzene. The conversion was 78% (normalized to 1 equiv. of alkene), the product balance >95%.

GP-3: General Procedure for the Ene Reaction of 4-Nitronitrosobenzene with the Deuterium Stereo-Labeled Hexadeuterio-2,3-dimethyl-2-butenes on the ^{1}H-NMR Scale to detect the Intramolecular Kinetic Isotope Effects (KIE). In a NMR tube the alkene was dissolved in 400 μL of CDCl$_3$ at 20 °C. The tube was closed, cooled to 0 °C, and a 300-μL aliquot of a stock solution of 4-nitronitrosobenzene in CDCl$_3$ (molarity is given for the specific cases) was added in one portion. The tube was closed, vigorously shaken and, stored in an ice bath for 4 h. The conversion and the product distribution were determined by ^{1}H-NMR analysis, from which the kinetic isotope effect (KIE) was calculated.

Ene Reaction of 4-Nitronitrosobenzene with *cis*-TME-d$_6$. According to the general procedure (GP-3), 4.0 mg (4.44 μmol) of *cis*-TME-d$_6$ were treated with 4.5 mg (2.96 μmol) of 4-nitronitrosobenzene. The conversion was 88% (normalized to 1 equiv. of alkene) and the kinetic isotope effect $k_H/k_D = 1.5$.

Ene Reaction of 4-Nitronitrosobenzene with *trans*-TME-d$_6$. According to the general procedure (GP-3), 7.1 mg (7.89 μmol) of *trans*-TME-d$_6$ were treated with 8.0 mg (5.26 μmol) of 4-nitronitrosobenzene. The conversion was >95% (normalized to 1 equiv. of alkene) and the kinetic isotope effect $k_H/k_D = 3.0$.

Ene Reaction of 4-Nitronitrosobenzene with *gem*-TME-d$_6$. According to the general procedure (GP-3), 16.0 mg (17.8 μmol) of *gem*-TME-d$_6$ were treated with 18.0 mg

(11.9 μmol) of 4-nitronitrosobenzene. The conversion was 94% (normalized to 1 equiv. of alkene) and the kinetic isotope effect $k_H/k_D = 4.0$.

GP-4: General Procedure for the Ene Reaction of 4-Nitronitrosobenzene with the Perprotio/Perdeuterio-Alkene Pairs on the GC Scale for the Intermolecular Kinetic Isotope Effects (KIE) on the Basis of the Alkene Conversions. Into a 4-mL glass vial was placed the required amount of a stock sample (exact quantities are given for the specific cases) of the two alkenes and the internal standard (cyclohexane or dodecane) in 2.00 mL CH_2Cl_2 at 20 °C. A 10-μL aliquot of this solution was taken as reference GC sample. The vial was closed, cooled to 0°C and a 2-mL aliquot of a stock solution of 4-nitronitrosobenzene in CH_2Cl_2 (molarity is given for the specific cases) was added. The closed vial was vigorously shaken and stirred in the ice bath for 4 h. The conversions were determined by GC analysis, from which the kinetic isotope effect (KIE) was calculated.

Ene Reaction of 4-Nitronitrosobenzene with TME-d_0 versus TME-d_{12}. According to the general procedure (GP-4), 2.52 mg (3.00 μmol) of TME-d_0, 2.88 mg (3.00 μmol) of TME-d_{12} and 2.52 mg (3.00 μmol) cyclohexane (internal standard) were treated with 3.94 mg (2.00 μmol) of 4-nitronitrosobenzene. The conversion of TME-d_0 was 39% and of TME-d_{12} 22% [$k_H/k_D = 1.98 \pm 0.05$]. A second run was carried out under the same conditions, which gave the same k_H/k_D value.
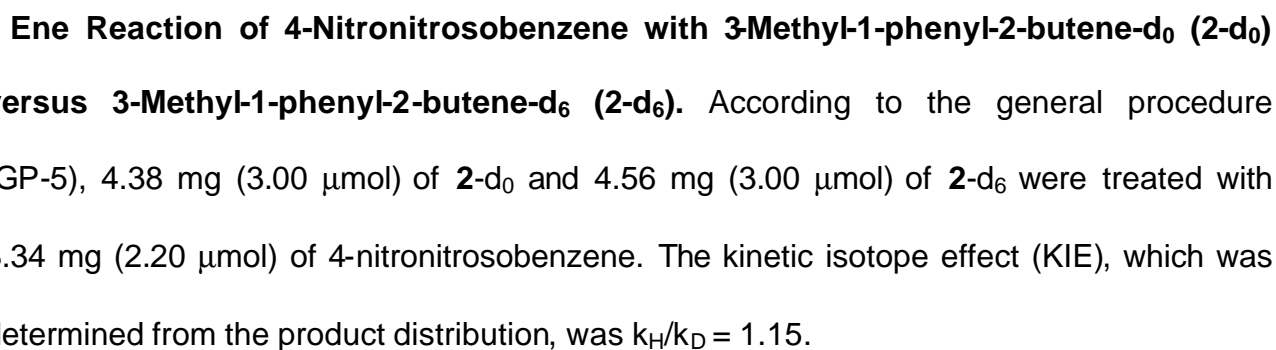
Ene Reaction of 4-Nitronitrosobenzene with 3-Methyl-1-phenyl-2-butene-d_0 (2-d_0) versus 3-Methyl-1-phenyl-2-butene-d_6 (2-d_6). According to the general procedure (GP-4), 4.38 mg (3.00 μmol) of **2**-d_0, 4.56 mg (3.00 μmol) of **2**-d_6 and 5.10 mg (3.00 μmol)

dodecane (internal standard) were treated with 4.33 mg (2.20 μmol) of 4-nitronitroso-benzene. The conversion of **2**-d_0 was 37% and of **2**-d_6 32% [$k_H/k_D = 1.18 \pm 0.04$].

GP-5: General Procedure for the Ene Reaction of 4-Nitronitrosobenzene with the Perprotio-/Perdeuterio-Alkene Pairs on the ^{1}H-NMR Scale for the Intermolecular Kinetic Isotope Effects (KIE) on the Basis of the Product Distribution. Into a NMR tube was placed the required amount of a stock solution (exact quantities are given for the specific cases) of the two alkenes in 400 μL CDCl$_3$ at 20 °C. The tube was closed, cooled to 0 °C, and a 300-μL aliquot of a stock solution of 4-nitronitrosobenzene in CDCl$_3$ (molarity is given for the specific cases) was added in one portion. The tube was closed, vigorously shaken, and placed into an ice bath for 4 h. The product distribution was determined by ^{1}H-NMR analysis, from which the kinetic isotope effect (KIE) was calculated.

Ene Reaction of 4-Nitronitrosobenzene with TME-d_0 versus TME-d_{12}. According to the general procedure (GP-5), 2.52 mg (3.00 μmol) of TME-d_0 and 2.88 mg (3.00 μmol) of TME-d_{12} were treated with 3.04 mg (2.00 μmol) of 4-nitronitrosobenzene. The kinetic isotope effect (KIE), which was determined from the product distribution, was $k_H/k_D = 2.0$. A sample ^{1}H-NMR spectrum of the crude reaction mixture is given below.

Scheme S1. ^{1}H-NMR Spectroscopic Analysis of the Product Distribution from the Intermolecular Competition between TME-d_0 and TME-d_{12} in the Ene Reaction of 4-Nitronitrosobenzene

Ene Reaction of 4-Nitronitrosobenzene with 3-Methyl-1-phenyl-2-butene-d_0 (2-d_0) versus 3-Methyl-1-phenyl-2-butene-d_6 (2-d_6). According to the general procedure (GP-5), 4.38 mg (3.00 μmol) of **2**-d_0 and 4.56 mg (3.00 μmol) of **2**-d_6 were treated with 3.34 mg (2.20 μmol) of 4-nitronitrosobenzene. The kinetic isotope effect (KIE), which was determined from the product distribution, was $k_H/k_D = 1.15$.

GP-6: General Procedure for the Ene Reaction of Pentafluoronitrosobenzene with the Deuterium Stereo-Labeled Hexadeuterio-2,3-dimethyl-2-butenes on the ^{1}H-NMR

Scale for the Intramolecular Kinetic Isotope Effects (KIE). A NMR tube was charged with the alkene in 400 μL CDCl$_3$ at 20 °C. The tube was closed, cooled to 0 °C, and a 300-μL aliquot of a stock solution of pentafluoronitrosobenzene in CDCl$_3$ (molarity is given for the specific cases) was added in one portion. The tube was closed, vigorously shaken, and placed into an ice bath for 30 min. The conversion and the product distribution were determined by ^{1}H-NMR analysis, from which the kinetic isotope effect (KIE) was calculated.

Ene Reaction of Pentafluoronitrosobenzene with *cis*-TME-d$_6$. According to the general procedure (GP-6), 4.0 mg (4.44 μmol) of *cis*-TME-d$_6$ were treated with 2.2 mg (1.12 μmol) of pentafluoronitrosobenzene. The conversion was 91% (normalized to 1 equiv. of alkene) and the kinetic isotope effect $k_H/k_D = 1.3$.

Ene Reaction of Pentafluoronitrosobenzene with *trans*-TME-d$_6$. According to the general procedure (GP-6), 2.98 mg (3.33 μmol) of *cis*-TME-d$_6$ were treated with 4.56 mg (3.00 μmol) of pentafluoronitrosobenzene. The conversion was 88% and the kinetic isotope effect $k_H/k_D = 3.0$.

GP-7: General Procedure for the Ene Reaction of Pentafluoronitrosobenzene with the TME-d$_0$ versus TME-d$_{12}$ Alkene Pair on the GC Scale for the Intermolecular Kinetic Isotope Effects (KIE). Into an 4-mL glass vial was placed the required amount of a stock sample (exact quantities are given for the specific cases) of the two alkenes in 2.00 mL CH$_2$Cl$_2$ (or Et$_2$O) at 20 °C. A 10-μL aliquot of this solution was taken for a GC reference sample. The vial was closed, cooled to 0 °C, and a 2.00 mL aliquot of a stock solution of pentafluoronitrosobenzene in CH$_2$Cl$_2$ (or Et$_2$O, molarity is given for the specific

cases) was added in one portion. The vial was closed, vigorously shaken, and stirred in an ice bath for 30 min. The conversions were determined by GC analysis, from which the kinetic isotope effect (KIE) was calculated.

Ene Reaction of Pentafluoronitrosobenzene (0.3 Equiv.) with TME-d_0 versus TME-d_{12} in CH_2Cl_2. According to the general procedure (GP-7), 2.52 mg (3.00 μmol) of TME-d_0, 2.88 mg (3.00 μmol) of TME-d_{12} and 2.52 mg (3.00 μmol) cyclohexane (internal standard) were treated with 1.97 mg (1.00 μmol) of pentafluoronitrosobenzene. The conversion of TME-d_0 was 15% and of TME-d_{12} 9.0% [$k_H/k_D = 1.77 \pm 0.05$].

Ene Reaction of Pentafluoronitrosobenzene (0.4 Equiv.) with TME-d_0 versus TME-d_{12} in CH_2Cl_2 at Lower Concentration. According to the general procedure (GP-7), 2.52 mg (3.00 μmol) of TME-d_0, 2.88 mg (3.00 μmol) of TME-d_{12} and 2.52 mg (3.00 μmol) cyclohexane (internal standard) were treated with 1.52 mg (1.20 μmol) of pentafluoronitrosobenzene. Instead of 2 x 2 mL CH_2Cl_2, 6 mL of CH_2Cl_2 were used to dissolve the alkenes and the enophile was added in 3 mL CH_2Cl_2. The overall conversion of TME-d_0 and TME-d_{12} was 13% and the calculated k_H/k_D value was 1.47 (± 0.04).

Ene Reaction of Pentafluoronitrosobenzene (0.7 Equiv.) with TME-d_0 versus TME-d_{12} in CH_2Cl_2. According to the general procedure (GP-7), 2.52 mg (3.00 μmol) of TME-d_0, 2.88 mg (3.00 μmol) of TME-d_{12} and 2.52 mg (3.00 μmol) cyclohexane (internal standard) were treated with 4.10 mg (2.08 μmol) of pentafluoronitrosobenzene. The conversion of TME-d_0 was 37% and of TME-d_{12} 32% [$k_H/k_D = 1.20 \pm 0.04$].

Ene Reaction of Pentafluoronitrosobenzene (1 Equiv.) with TME-d_0 versus TME-d_{12} in Et$_2$O. According to the general procedure (GP-7), 3.19 mg (3.80 µmol) of TME-d_0, 3.65 mg (3.80 µmol) of TME-d_{12} and 3.19 mg (3.80 µmol) cyclohexane (internal standard) in 2.5 mL of Et$_2$O were treated with 7.49 mg (3.80 µmol) of pentafluoronitrosobenzene in 2.0 mL of Et$_2$O. The conversions of TME-d_0 and of TME-d_{12} were determined by GC analysis at various reaction times, from which the kinetic isotope effects were calculated.

entry	time [min]	conversions [%][a]			k_H/k_D[b]
		TME-d_0	TME-d_{12}	overall	
1	45	24.4	20.3	22	1.23 (±0.04)
2	100	39.0	32.2	35	1.27 (±0.04)
3	125	51.7	45.2	48	1.21 (±0.04)

[a] Determined by GC analysis with cyclohexane as internal standard; error ca. 3% of the stated value. [b] Calculated according to $k_H/k_D = \ln\{[A_H]/[A_H]_0\} / \ln\{[A_D]/[A_D]_0\}$; error ca. 3% of the stated value.

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Structure Matrix

TME-d$_0$　　　TME-d$_{12}$　　　*cis*-TME-d$_6$　　　*trans*-TME-d$_6$　　　*gem*-TME-d$_6$

E-**1**　　　*Z*-**1**　　　**2**-d$_0$　　　**2**-d$_6$

AI$_H$　　　**AI**$_D$　　　**AI**$_{trans}$

DI　　　**P**$_H$　　　**P**$_D$

A　　　**B**　　　**AI**$_{tetra}$　　　**AI**$_{tri}$