Spirocyclopropanes from Intramolecular Cyclopropanation of Pyranopyrazoles and Pyranopyrimidine-diones and Lewis Acid Mediated (3+2) Cycloadditions of Spirocyclopropylpyrazolones

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## I. Optimization of the reaction conditions and stereochemical course of the intramolecular cyclopropanation reaction

Table S1. Optimization of the reaction conditions ${ }^{a}$

|  |  | $\xrightarrow[\substack{\text { DCM }(3 \mathrm{~mL}) \\ \text { Ht }}]{\substack{\text { Oxidant } \\ \text { Additive }}}$ |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
| entry | oxidant (equiv) |  | additive (equiv) | time (min) | yield $^{\text {b }}$ (\%) |
| 1 | PhIO (1.0) |  | $\mathrm{Et}_{3} \mathrm{~N}$ (1.0) | 30 | 80 |
| 2 | PhIO (1.1) |  | $\mathrm{Et}_{3} \mathrm{~N}$ (1.0) | 30 | 88 |
| 3 | PhIO (1.2) |  | $\mathbf{E t}_{3} \mathrm{~N}$ (1.0) | 30 | 92 |
| 4 | PhIO (1.3) |  | $\mathrm{Et}_{3} \mathrm{~N}$ (1.0) | 30 | 91 |
| 5 | PIDA (1.2) |  | $\mathrm{Et}_{3} \mathrm{~N}$ (1.0) | 30 | 60 |
| 6 | PIFA (1.2) |  | $\mathrm{Et}_{3} \mathrm{~N}$ (1.0) | 30 | 58 |
| 7 | $\mathrm{I}_{2}(1.2)$ |  | $\mathrm{Et}_{3} \mathrm{~N}$ (1.0) | 30 | 30 |
| 8 | $\operatorname{PIDA}(0.5)+\mathrm{I}_{2}(0.5)$ |  | $\mathrm{Et}_{3} \mathrm{~N}$ (1.0) | 30 | 70 |
| 9 | $\operatorname{PIDA}(0.5)+\mathrm{I}_{2}(0.5)$ |  | $\mathrm{Et}_{3} \mathrm{~N}$ (1.5) | 30 | 88 |
| 10 | $\operatorname{PIDA}(0.5)+\mathbf{I}_{2}(0.5)$ |  | $\mathrm{Et}_{3} \mathrm{~N}$ (2.0) | 30 | 94 |
| 11 | $\operatorname{PIDA}(0.6)+\mathrm{I}_{2}(0.6)$ |  | $\mathrm{Et}_{3} \mathrm{~N}$ (2.0) | 30 | 92 |
| 12 | $\mathrm{PhIO}(0.5)+\mathrm{I}_{2}(0.5)$ |  | $\mathrm{Et}_{3} \mathrm{~N}$ (2.0) | 40 | 60 |
| 13 | $\mathrm{PhIO}(1.0)+\mathrm{TBAI}(1.0)$ |  | $\mathrm{Et}_{3} \mathrm{~N}$ (1.0) | 45 | $50^{c}$ |
| 14 | $\mathrm{PhIO}(1.2)$ |  | $\mathrm{Et}_{3} \mathrm{~N}$ (1) | 60 | $10^{c}$ |
| 15 | $\operatorname{PIDA}(0.5)+\mathrm{I}_{2}(0.5)$ |  | $\mathrm{Et}_{3} \mathrm{~N}$ (2.0) | 30 | $70^{c}$ |
| 16 | HTIB (1.2) |  | $\mathrm{Et}_{3} \mathrm{~N}$ (2.0) | 30 | 40 |
| 17 | IBA (1.2) |  | $\mathrm{Et}_{3} \mathrm{~N}(2.0)$ | 30 | 55 |

[^0]Scheme S1. Stereochemical course of this intramolecular cyclopropanation reaction




In Scheme S1, the plausible stereochemical course of this intramolecular cyclopropanation reaction is illustrated. Both the starting materials pyranopyrimidine-dione $\mathbf{1 a}^{\mathbf{\prime}} \mathbf{\mathbf { b } ^ { \prime }}$ and pyranopyrazole 1c'd' exist as racemic mixtures. Consequently, both method A and B transform $\mathbf{1 a}^{\prime}$ and $\mathbf{1 b}$ ' to their corresponding cyclopropane $\mathbf{2 a} \mathbf{a}^{\prime}$ and $\mathbf{2 b} \mathbf{b}^{\prime}$ respectively. Thus, racemic
mixtures of spirocyclopropanes are obtained from pyranopyrimidine-diones since $\mathbf{2 a} \mathbf{a}^{\mathbf{\prime}}$ and $\mathbf{2 b}{ }^{\prime}$ bears an enantiomeric relationship to each other (Table 2, entry $\mathbf{2 a - 2 f}$ ). On the other hand, $\mathbf{1 c}{ }^{\prime}$ and $\mathbf{1 d}$ ' afford their corresponding spirocyclopropanes as the diastereomeric mixtures due to the formation of an unsymmetrical pyrazolone unit in the resulting cyclopropanes. Now, there are enantiomeric relationships between the major diastereomers $\mathbf{2} \mathbf{c}^{\prime}$ and $\mathbf{2} \mathbf{d}^{\prime}$ and between the minor isomers $\mathbf{2} \mathbf{c}^{\prime \prime}$ and $\mathbf{2 d} \mathbf{d}^{\prime \prime}$ respectively, which explains the formation of the spirocyclopropanes as the diastereomeric mixtures from the 3-methyl-pyranopyrazoles (Table 2, entry $\mathbf{2 g} \mathbf{- l}$ and $\mathbf{2 n} \mathbf{- p}$ ). The steric effect of the carbethoxy group in 3-carbethoxy-pyranopyrazoles may be the reason for the diastereospecific formation of $\mathbf{2} \mathbf{c}^{\prime \prime}$ and $\mathbf{2 d} \mathbf{d}^{\prime \prime}$ from $\mathbf{1 c}$ ' and $\mathbf{1 d}$ ' respectively (Table 2, entry $\mathbf{2 q - v}$ ).
II. X-ray Crystallography Data of Compounds $2 q$ (CCDC 1521821), 3g (CCDC 1521822) and $4 q(C C D C ~ 1521823): ~$


Figure S1. The X-ray structure of $\mathbf{2 q}$. The ellipsoid contour percent probability level is $50 \%$.


Figure S2. The X-ray structure of $\mathbf{3 g}$. The ellipsoid contour percent probability level is $50 \%$.


Figure S3. The X-ray structure of $\mathbf{4 q}$. The ellipsoid contour percent probability level is $50 \%$.
Single crystal X-ray data for compounds $2 q$ (CCDC 1521821), 3 g (CCDC 1521822) and $4 q$ (CCDC 1521823) :

Single crystals suitable for X-ray diffraction of $\mathbf{2 q}, \mathbf{3 g}$ and $\mathbf{4 q}$ were grown from ethyl acetate. The crystals were carefully chosen using a stereo zoom microscope supported by a rotatable polarizing stage. In all the cases the data were collected at 296(2) K on a CCD diffractometer with graphite monochromated $\mathrm{Mo}-\mathrm{K} \alpha$ radiation $(0.71073 \AA)$. The data were processed using the package SAINT. ${ }^{1}$ Structures were solved by direct and Fourier methods and refined by fullmatrix least squares based on F2 using SHELXTL ${ }^{2}$ and SHELXL- $97^{3}$ packages.

Table S2. Crystallographic data for the compound $\mathbf{2 q}, \mathbf{3 g}$ and $\mathbf{4 q}$

| Compounds | $\mathbf{2 q}$ | $\mathbf{3 g}$ | $\mathbf{4 q}$ |
| :--- | :--- | :--- | :--- |


| empirical formula | $\mathrm{C}_{22} \mathrm{H}_{16} \mathrm{~N}_{4} \mathrm{O}_{3}$ | $\mathrm{C}_{27} \mathrm{H}_{19} \mathrm{~N}_{5} \mathrm{OS}$ | $\mathrm{C}_{29} \mathrm{H}_{21} \mathrm{~N}_{5} \mathrm{O}_{3}$ |
| :---: | :---: | :---: | :---: |
| fw | 384.39 | 461.53 | 487.51 |
| crystal color | light-yellow | colourless | Colourless |
| crystal system | Triclinic | Monoclinic | Monoclinic |
| space group | $P-1$ | P 21/c | P 21/c |
| $a(\AA)$ | 9.9417(4) | 13.565(11) | 12.843(12) |
| $b(\AA)$ | 10.1104(4) | 11.634(9) | 11.009(10) |
| $c(\AA)$ | 10.6132(5) | 14.456(11) | 18.175(17) |
| $\alpha\left({ }^{\circ}\right)$ | 87.141(2) | 90.00 | 90.00 |
| $\beta\left({ }^{\circ}\right)$ | 69.537(2) | 93.247(12) | 103.298(12) |
| $\gamma\left({ }^{\circ}\right)$ | 75.045(2) | 90.00 | 90.00 |
| $V\left(\AA^{3}\right)$ | 964.65(7) | 2278(3) | 2501(4) |
| Z | 2 | 4 | 4 |
| $T, \mathrm{~K}$ | 296(2) | 296(2) | 296(2) |
| Wavelength (A) | 0.71073 | 0.71073 | 0.71073 |
| $2 \theta\left({ }^{\circ}\right)$ | 4.10-54.00 | 3.00-51.46 | 3.26-50.98 |
| $\mu\left(\mathrm{mm}^{-1}\right)$ | 0.091 | 0.173 | 0.087 |
| $\rho_{\text {calcd }}\left(\mathrm{g} \mathrm{cm}^{-3}\right)$ | 1.323 | 1.352 | 1.300 |
| $F(000)$ | 400 | 960 | 1024 |
| absorption correction | multi-Scan | multi-Scan | multi-Scan |
| index ranges | $-12 \leq h \leq 11$ | $-16 \leq h \leq 16$ | $-15 \leq h \leq 14$ |
|  | $-12 \leq k \leq 12$ | $-14 \leq k \leq 13$ | $-13 \leq k \leq 13$ |
|  | $-13 \leq l \leq 13$ | $-17 \leq l \leq 15$ | $-18 \leq l \leq 21$ |
| reflections collected | 10938 | 16269 | 16252 |


| independent reflections <br> $\left(R_{\text {int }}\right)$ | $4216(0.0201)$ | $4282(0.0648)$ | $4577(0.0560)$ |
| :--- | :--- | :--- | :--- |
| Goodness-of-fit on $\mathrm{F}^{2}$ | 0.787 | 1.026 | 1.005 |
| $R_{1}{ }^{a} / \mathrm{w} R_{2}{ }^{b}$ <br> $(I>2 \sigma(I))$ | $0.0419 / 0.1408$ | $0.0461 / 0.0998$ | $0.0611 / 0.1786$ |
| $R_{1}{ }^{a} / \mathrm{w} R_{2}{ }^{b}$ (for all data) | $0.0515 / 0.1613$ | $0.1012 / 0.1200$ | $0.1038 / 0.2123$ |
| Largest diff. peak/hole $/$ <br> $\mathrm{e} \AA^{-3}$ | $0.213 /-0.186$ | $0.194 /-0.226$ | $0.863 /-0.216$ |

## References:

1. APEX-II, SAINT-Plus, and TWINABS; Bruker-Nonius AXS Inc.: Madison, WI, 2004.

2 SHELXTL, version 6.10; Bruker AXS Inc.: Madison, WI, 2002.
3. Sheldrick, G. M. SHELXL-97, Crystal Structure Refinement Program; University of Göttingen: Göttingen, Germany, 1997.

## III. ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ NMR spectra for the products of Table 1,2 and 3

For compounds 2a-v, the ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ NMR spectra of samples, obtained through Method B, are provided.


















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[^0]:    ${ }^{a} 1.0 \mathrm{mmol}$ of $\mathbf{1 a}$ was taken along with 3 mL of solvent in all the cases. ${ }^{b}$ yield. ${ }^{c} \mathrm{MeOH}$ was used in place of DCM

