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THE STEREOSTRUCTURES OF [1,1'-BICYCLOHEXYL]-2,2'-DIONES: A REASSIGNMENT

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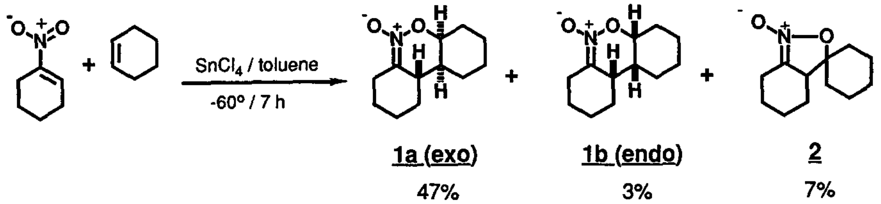
Summary: The stereostructural assignment of $\underline{C}_2$ and $\underline{C}_s$ isomers of [1,1'-bicyclohexyl]-2,2'-dione has been unambiguously established by correlation to an X-ray crystal structure and by a novel chromatographic technique.

We have recently reported[2] the [4+2]-cycloaddition of nitrocyclohexene with cyclohexene to afford the three cyclic nitronic esters **1a**, **1b**, and **2** (eq 1). While it was possible to differentiate the fused from the spiro nitronates by analysis of the ^{1}H-NMR and IR spectra

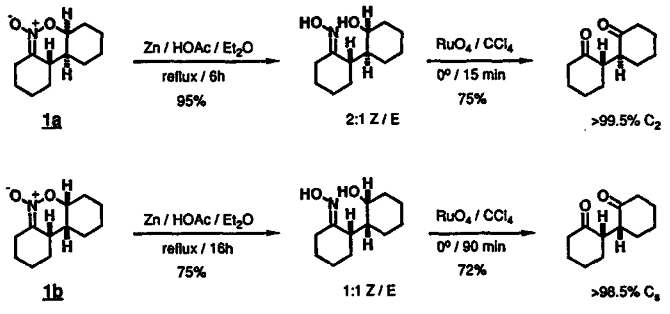


(1)

it was not possible to assign the stereostructure of the major and minor fused nitronate isomers. Our initial assignment was based solely on the expectation that the major isomer would arise from an exo-mode cycloaddition, with no obvious secondary orbital effects being at play. Thus the major and minor isomers were assigned as **1a** and **1b**, respectively. Confirmation of these assignments was deemed feasible by degradation of the nitronates to the known[3] $\underline{C}_2$ and $\underline{C}_s$ isomers of [1,1'-bicyclohexyl]-2,2'-dione.

While no direct hydrolytic method could be found which did not suffer from epimerization at the key stereocenter[2] we did develop a reduction-oxidation protocol which delivered the stereoisomeric diketones with very high selectivity from the separate cycloadducts (Scheme 1). Comparison of the ^{1}H- and ^{13}C-NMR data for the two isomers with the literature values[3] led to the surprising conclusion that the major cycloadduct **1a** was transformed to the $\underline{C}_s$ (crystalline) diastereomer and the minor cycloadduct **1b** to the $\underline{C}_2$

Scheme 1



(oily) diastereomer.[4] Since each nitronate led selectively to one of the bicyclohexyldiones no crossover could have occurred. Thus we were forced to conclude that the major cycloadduct arises from an endo transition state!

Despite this chemical correlation we were sufficiently surprised at the endo selectivity of the cycloaddition to secure this assignment by an X-ray crystal structure determination of the major nitronate.[5] As shown in Figure 1 our initial assumption

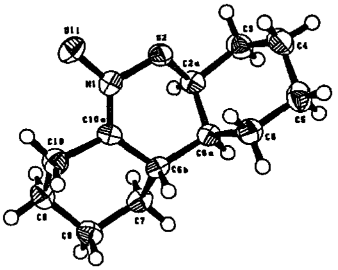


Figure 1. ORTEP drawing of **1a** at 35% probability.

was correct and the major isomer does indeed arise from an *exo pathway*! Reduction and oxidation of this compound should lead to the $\underline{C}_2$ diastereomer, casting the literature assignment in doubt.

Convincing confirmation of the validity of our assignment was obtained from the chromatographic behavior of the two isomers on a chirally functionalized silica gel adsorbent.[6,7] The top and bottom traces in Figures 2 and 3 are the simultaneous polarographic and ultraviolet absorbances of the eluate, respectively.[8] Figure 2 is the chromatogram of a 2:1 mixture (by ^{13}C-NMR) of diketones obtained from a non-selective hydrolysis[2] (H_2SO_4/THF/H_2O) of the major nitronate **1a**. Based on the polarographic deflections we assign peaks A and B as the *d*,*l*-pair and peak C as the *meso* (achiral) isomer. Figure 3 is the chromatogram of the homogeneous (by ^{13}C-NMR) diketone obtained from reductive-oxidative degradation of the major nitronate. Thus, we conclude that **1a** is

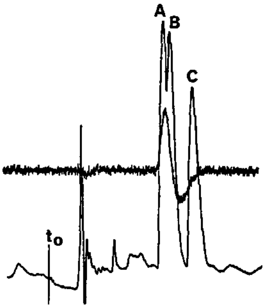


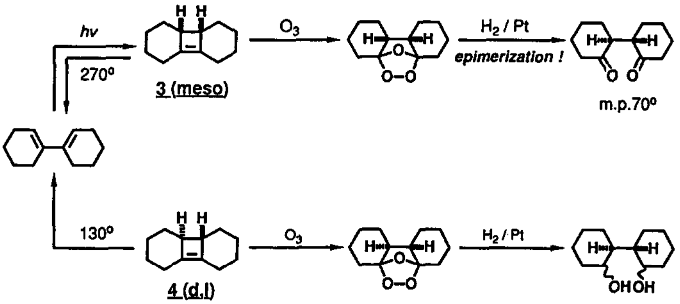
Figure 2. HPLC[7,8] trace of a 2:1 mixture of $\underline{C}_2$ and $\underline{C}_s$-diketones.

Figure 3. HPLC[7,8] trace of pure $\underline{C}_2$-diketone.

transformed to the $\underline{C}_2$-diketone which is the crystalline diastereomer and that the literature assignments are reversed.

Closer inspection of the papers in which the two diastereomers have been prepared and characterized reveals that they, in fact, were not independently assigned.[3] All correlations refer back to Criegee[9] who assigned the meso stereostructure to a crystalline diketone obtained from ozonolysis of a meso cyclobutene 3 (Scheme 2). The assignment of the cyclobutene derives from its photochemical formation from 1,1'-bicylohexenyl[10] and

Scheme 2



expected thermal stability.[11] While the structure of 3 is certain, Criegee overlooked the possibility of epimerization upon hydrogenolysis of the ozonide. Unfortunately, insufficient quantities of 4 prevented a thorough comparison of its derived diketone (the diol is the direct reduction product) thus obscuring what would have led to an inconsistency (both 3 and 4 would have afforded the same dione) and doubtless more careful experimentation. CAVEAT EMPTOR!

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References and Notes

(1) (a) Fellow of the Alfred P. Sloan Foundation (1985-1987). NSF Presidential Young Investigator (1985-1990). (b) NSF Graduate Fellow, 1984-1987.

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(4) The physical properties of the correctly assigned diketones are provided below. For the sake of clarity the correct structures for all compounds are shown throughout.

C_2 isomer: (*R**,*R**)-[1,1'-bicyclohexyl]-2,2'-dione. mp 70-71 °C ^{1}H-NMR (300 MHz, CDCl$_3$, δ): 2.85 (m, 2H); 2.34 (m, 4H); 2.15-1.00 (m, 12H). ^{13}C-NMR (75.5 MHz, CDCl$_3$, δ): 211.66, 48.91, 42.27, 30.06, 28.01, 25.38. IR (CCl$_4$): 2940s, 2865s, 1709s, 1449s, 1426m, 1345m, 1312m, 1283m, 1252m, 1229m, 1217, 1188w, 1132s, 1111w, 1059w, 1034w, 1005w, 909s. TLC: R_f = 0.31 (hex/EtOAc:4/1). HPLC[7]: $T_R(+)$ = 8.50 min, $T_R(-)$ = 9.10 min (hex/iPrOH:95/5, 0.7 mL/min).

C_2 isomer: (*R**,*S**)-[1,1'-bicyclohexyl]-2,2'-dione. ^{1}H-NMR (300 MHz, CDCl$_3$, δ): 2.8-1.2 (m, 18H). ^{13}C-NMR (75.5 MHz, CDCl$_3$, δ): 210.76, 50.26, 41.80, 29.08, 26.50, 24.99. IR (CCl$_4$): 2940s, 2865s, 1709s, 1449s, 1364m, 1339m, 1314m, 1271m, 1246m, 1231m, 1202m, 1130s, 1094m, 1059m, 1019w, 999m, 943w, 909m. TLC: R_f = 0.31 (hex/EtOAc:4/1). HPLC[7]: T_R = 10.7 min (hex/iPrOH:95/5, 0.7 mL/min).

(5) We thank Scott R. Wilson, Department of Chemistry, University of Illinois for the structure determination.

(6) We thank Professor William H. Pirkle for his assistance in the chromatography experiments. Details of the use of this chiral stationary phase will be published independently.

(7) Stationary phase: (2*S*,3*R*)-2-t-butyl-3-(3,5-dinitrobenzamido)-3-phenylpropionic acid, attached through an undecyl ester chain to the silica. Mobile phase: hex/iPrOH:95/5, 0.7 mL/min.

(8) UV detection: 0.04 Abs at 254 nm. Polarimeter detection: 580 nm.

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