Synthesis of (*E,E*)-Thiacyclodeca-4,7-diene and of Its 3-Methyl Derivative from D-Mannitol. Stereochemical and Conformational Behavior

Vande Cerè, Emrico Dalcanale, Claudio Paolucci, Salvatore Pollicino,* Edda Sandri, Lodovico Lunazzi, and Antonino Fava

Istituto di Chimica Organica, Università di Bologna, 40136 Bologna, Italy

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(*E,E*)-1,4-Cycloalkadienes are conformationally chiral species. The title compound, **1**, a ten-membered (*E,E*)-1,4-diene, has been synthesized by way of a reaction sequence where the configurations of C_3 and C_4 of D-mannitol, an enantiomerically pure starting material, were carried intact until the penultimate step. The last step was a Whitham cycloelimination of a 2-phenyldioxolane derivative, a reaction known to be stereospecific, which ought to have yielded optically active **1**. The material, however, had no appreciable optical activity, indicating a fast enantiomerization process is taking place. A dynamic ^{13}C NMR study of the 3-methyl derivative, **14**, indicates the barrier for epimerization is 11.0 kcal/mol. The enantiomerization of **1** must then have a barrier of approximately this height, too low for optical activity to be observable. The conformational motions that may bring about enantiomerization have been considered, along with another motion responsible for ^{13}C NMR signal averaging. Low-temperature experiments indicate $\Delta G^{\ddagger} \leq 6$ kcal/mol for this latter process.

To our knowledge neither (*E,E*)-1,4-cyclodecadiene nor any of its heterocyclic analogues have ever been synthesized. Yet this molecular type, while a priori not seeming to be so strained as to be highly unstable and reactive, appears to possess interesting geometrical properties that make it a good candidate for stereochemical and conformational studies. Simple geometrical considerations indicate (*E,E*)-1,4-cyclodecadienes (**1**) to be chiral species

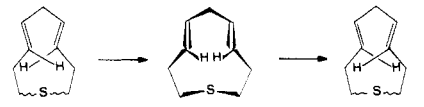
A

1 (X = S)

as shown by A, which exposes their helical shape. The compression between the 1,5-olefinic hydrogens restricting the double bonds from being coplanar forces them to rotate about their adjacent single-bond pivots and settle on somewhat diverging planes.

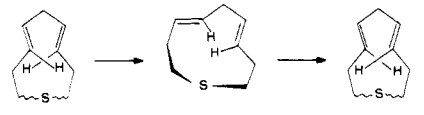
A further peculiarity suggested by molecular models is the spatial positioning of atom X (three bonds away from either double bond), which may be located either above or below the median molecular plane. This feature makes the molecule asymmetric rather than dissymmetric. However, the operation of switching the X atom from one side to the other does not bring about configurational change (A). This motion in fact is equivalent to the existence of a C_2 axis lying on the median molecular plane and passing through the bis-allylic carbon C_6 (numbering from X). So that configurational inversion can be achieved, the molecule will have to pass through a symmetrical conformation. This may be attained by rotating the double-bond planes in either of two ways. In the first, B, one of the double bonds rotates (clockwise in the P

B



$B^{\ddagger}$

C



$C^{\ddagger}$

enantiomer, counterclockwise in the M) so as to bring the hydrogens at C_4 and C_8 up against each other. The system will pass through a symmetrical conformation ($B^{\ddagger}$) characterized by a σ plane passing through X and C_6. The second, C, is the usual mechanism for chiral inversion of (*E*)-cycloalkenes[1] where one of the double bonds rotates inside out, bringing the H at C_5 (or C_7) against C_8–H (or C_4–H) across the ring, in a transition state ($C^{\ddagger}$) where the two double bonds are coplanar.

On these premises, the stereochemical and conformational behavior of (*E,E*)-1,4-cyclodecadienes appears to be worth investigating. Accordingly, we have prepared a heterocyclic analogue, *E,E*-thiacyclodeca-4,7-diene (**1**, X = S), whose synthesis and properties are described herein. The strategy we have applied consisted in the stepwise stereospecific formation of the double bonds one at a time by using enantiomerically pure precursors. In such a way, should **1** by optically stable, an enantiomerically pure compound would be obtained. As it turned out, **1** undergoes rapid enantiomerization. A study of the dynamic ^{13}C NMR behavior of **1** and of its 3-Me derivative has established the barrier for enantiomerization to be on the order of 11 kcal/mol, while that for the flipping motion of atom X is ≤6 kcal/mol.

Results and Discussion

As the chiral building block for the synthesis (Scheme I) of the title compound, **1**, natural mannitol was used that was first transformed into (*R,R*)-*cis*-2,6-dioxabicyclo-[3.3.0]octane (**2**) by an established procedure.[2,3] The diether **2** was cleaved with HBr to form (*R,R*)-1,6-dibromohexane-3,4-diol (**13**),[2] which, after acetalation, was cyclized in high dilution with Na_2S to yield the thiepane **5**.[4] The latter was α vinylated by the Tuleen–Bennet[5,6] sequence to give the α-vinylthiepane **6**. This procedure turned out to be essentially nonstereospecific insofar as all four possible diastereoisomers of **6** were obtained in comparable amounts. Methyl triflate alkylation of **6** gave a mixture of isomeric sulfonium salts, **7**, which, by treatment with *t*-BuOK in THF, ring expanded to a pair of diastereomeric ten-membered homoallylic sulfides, **8a** and **8b**, which could be separated. That only two isomers were obtained is consistent with the existence of only one chiral

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(2) Wiggins, L. F. *J. Chem. Soc.* **1945**, 4.
(3) Cope, A. C.; Shen, T. Y. *J. Am. Chem. Soc.* **1956**, *78*, 5916.
(4) Protection of the hydroxy groups was necessary for effective cyclization; high-dilution direct cyclization of **3** gave but a modest yield (32%) of 3,4-dihydroxythiepane, the major product being **2** (59%).
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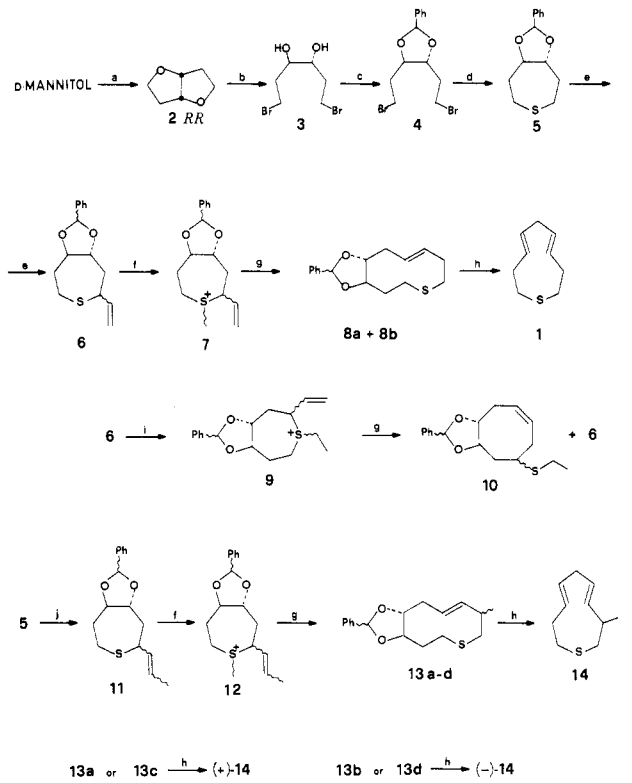
Scheme I



[a] (1) HCl 37%; (2) $SOCl_2$, pyr; (3) Raney Ni W2, Et_3N, H_2 (100 atm), 100 °C. [b] HBr (gas), CCl_4. [c] PhCHO, TsOH, $PhCH_3$. [d] Na_2S, EtOH. [e] (1) NCS, PhH; (2) C_2H_3MgBr, THF. [f] $CF_3SO_3CH_3$, CH_2Cl_2, $CaCO_3$. [g] t-BuOK, THF, −40 °C. [h] BuLi, hexane/THF, −20 °C. [i] Et_3OBF_4, CH_2Cl_2, 0 °C. [j] (1) NCS, PhH; (2) CH_3CHCH-MgBr, THF.

center (C_{12}) besides C_1 and C_{10} (whose configuration has not changed through the a–g sequence). That is, the isomers of 8 must be the (1*R*,10*R*,12*R*)–(1*R*,10*R*,12*S*) pair, and the *E* double bond is *not* an element of chirality (at ambient temperature). In other words, inversion of the chiral plane must be rapid, consistent with the known behavior of ten-membered (*E*)-cycloalkenes.[1,7]

The two isomers of 8 were separately subjected to conditions conducive to the Whitman cycloelimination,[8] yielding identical products, which proved to be the sought for (*E,E*)-thiacyclodeca-4,7-diene (1).

This material had no appreciable optical activity. Since the Whitham cycloelimination is stereospecific,[8] this finding proves that complete enantiomerization of 1 occurs within the time (~3 h) required for cycloelimination and product isolation. Moreover, the ^{13}C NMR spectrum of 1 displays only five lines, which showed no significant broadening down to −156 °C (at 25.15 MHz), indicating the signal-averaging process has an activation energy lower than ~6 kcal/mol. Since any one of the three conformational motions (A–C) discussed above would bring about signal averaging, it must be concluded that at least one of them has an energy barrier <6 kcal/mol.

A simple approach that may permit discrimination between the flipping motion (A) from the other two (B and C) consists in labeling one of the α or β carbons by means of a substituent. The resulting asymmetric system would be capable of differentiating the carbon atoms once both enantiomerizing motions B and C are frozen. (Indeed, lacking such asymmetry, the freezing of the double-bond rotations produces two enantiomers, indistinguishable by ^{13}C NMR.)

The synthesis of an asymmetrically substituted derivative was first approached in what seemed to be the simplest modification of Scheme I, that is by introducing a α-Me substituent via the S–Et derivative **9** (Scheme I). This approach, however, failed since *t*-BuOK treatment of the ethylsulfonium salt **9** did not bring about the expected 3-carbon ring expansion in any substantial amount. The major products that could be identified were **6**, the product of β elimination of ethylene (most likely arising via the α′, β mechanism)[9] and a cyclooctene derivative, **11**, which would result from 2,3-sigmatropic rearrangement of the endocyclic sulfonium ylide formed by deprotonation of **9** at C_7.

In our second approach, the synthetic scheme (Scheme I) was modified in such a way as to produce a 3-Me derivative. This was achieved by using 1-propenylmagnesium bromide in lieu of vinylmagnesium bromide in the vinylation step (step j). The isomeric mixture of α-(1-propenyl) derivatives thus obtained (**12**) was subjected to the usual methylation and rearrangement steps to produce **13** as a mixture of four diastereoisomers (**a–d**). (The doubling of isomers with respect to the corresponding unsubstituted systems (**8**) is consistent with the presence of the additional chiral center at C_3.) All four isomers **13a–d** were separated by column chromatography and characterized. Separately subjected to the Whitham cycloelimination (step h), the first and third eluted isomers, **13a** and **13c**, gave the same dextrorotatory product (+)-**14**, while the second eluted isomer, **13b**, gave (−)-**14**. In every case, the optical rotatory power was identical within experimental error ($[\alpha]^{23}_D$ 8.45 ± 0.5° (*c* 1.4, hexane)). While the product **14** is optically active, its room-temperature ^{13}C NMR spectrum has only ten signals. Thus the optical activity is due only to the chiral center at C_3, and the samples of (+)- and (−)-**14** thus obtained must be enantiomerically pure. From the sign of the optical rotation, it appears that **13a** and **13c** have the same configuration at C_3, opposite to that of the **13b** and **13d** pair.

As the temperature was lowered to −30 °C, the ten-line spectrum of **14** separated into two sets of lines (intensity ratio ~4:1), indicative of two unequally populated diastereomeric conformers whose interconversion is frozen (in the NMR time scale) at this temperature. Accurate lineshape analysis in the −32 to −60 °C range yielded an interconversion energy barrier of 11.3 kcal/mol. This barrier must be related to a conformational process that results in the inversion of the sign of the ring helix; hence process B or C but not A. Indeed if the S atom flipping process (A) was frozen but either process B or C was fast, the ^{13}C NMR spectrum would still show *one* ten-signal set.

The information gained on the 3-Me substituted derivative can be extended to the parent system, **1**, since the 3-Me group is not expected to substantially affect the energetics of any of the three processes, A–C. That is, the energy barrier for enantiomerization of **1** must be in the neighborhood of 11 kcal/mol, and therefore there is no hope to ever observe its chirooptical properties unless a method is found capable of generating it at very low temperature (<−100 °C). Such a conclusion may be safely

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(8) (a) Bridges, A. J.; Whitman, H. G.; *J. Chem. Soc., Chem. Commun.* **1974**, 142. (b) Hines, J. N.; Peagram, M. J.; Thomas, E. J.; Whitham, G. H. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2332. (c) Jones, M.; Temple, P.; Thomas, E. J.; Whitham, G. H. *Ibid.* **1974**, 433.

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extended to the homocyclic as well as to other heterocyclic analogues.

As to which process, B or C, is responsible for enantiomerization, our data provide no positive evidence. However, the height of the energy barrier, close to that for chiral inversion of (*E*)-cyclodecenes,[1,7] suggests process B as the more likely.

About the energy barrier for the flipping motion A, the only conclusion that may be drawn at this time is that it must be lower than ~6 kcal/mol.

Further investigations on this system (force field molecular structure and reaction path, sulfur extrusion toward the synthesis of cyclononadienes and -trienes) are in progress in this laboratory.

Experimental Section

Proton NMR spectra were recorded at 60 or 100 MHz on Varian EM-360L and XL-100 instruments, respectively. The latter was used for obtaining proton-noise-decoupled ^{13}C NMR spectra at 25.15 MHz by the FT technique. Single-frequency off-resonance spectra were obtained by irradiation at δ −4 in the proton spectrum. Unless otherwise stated, ^1H and ^{13}C shifts are given in parts per million from Me_4Si in $CDCl_3$. For the low-temperature experiments in $CHFCl_2$ or in 1:1 CF_2Cl_2–CHF_2Cl solvent mixture, the samples were prepared by connecting the 10-mm NMR tube, containing the sample and some acetone-d_6 for deuterium locking, to a vacuum line. The solvent was then admitted in gaseous form and condensed with liquid nitrogen, the tube being sealed in vacuo. The temperature was measured with a thermocouple inserted in a dummy tube before and after each spectral determination. Spectra simulation was carried out using the DNMR programs developed by Binsch.[10]

GLC analyses were carried out with a Hewlett-Packard 5700 instrument equipped with a flame ionization detector ($^1/_8$ in. × 3 m column, 10% Xe-60 or 10% C 20M on Chromosorb W).

Solvents and reagents were obtained dry as follows: Benzene, dichloromethane, and *tert*-butyl alcohol were distilled from calcium hydride. Tetrahydrofuran, dried over sodium and distilled, was redistilled from $LiAlH_4$ immediately before use. Pyridine was distilled from KOH. Toluene was dried and distilled from sodium metal. All reactions involving organolithium reagents were carried out under nitrogen, the reagent being introduced by syringe through a rubber stopper.

(*R*,*R*)-(+)-2,6-Dioxabicyclo[3.3.0]octane (2) was obtained according to the procedure of Cope and co-workers[3] by Raney Ni reduction of (1*R*,4*S*,5*R*,8*S*)-4,8-dichloro-2,6-dioxabicyclo-[3.3.0]octane [bp 153–155 °C, $[\alpha]^{25}_D$ 15.3 (*c* 1.38, $CHCl_3$); $[\alpha]^{22}_D$ 9.4 (*c* 4.00, H_2O) (lit.[3] bp 153–155 °C, $[\alpha]^{25}_D$ 9.0 (*c* 4.00, H_2O))]. The dichloride had been prepared from mannitol by following the procedure of Wiggins.[2]

(4*R*,5*R*)-(+)-4,5-Bis(2-bromoethyl)-2-phenyl-1,3-dioxolane (4) was obtained from (*R*,*R*)-(+)-1,6-dibromohexane-3,4-diol[3] (25.5 g, 93 mmol, in 77 mL of toluene) and freshly distilled benzaldehyde (11.2 mL, 111 mmol). The mixture was heated at reflux for 5 h in the presence of *p*-toluenesulfonic acid catalyst (0.14 g), with water being continuously removed (Dean–Stark separator). After cooling, the solution was extracted with 5% aqueous $NaHCO_3$ (10 mL) and dried over $CaSO_4$. Solvent evaporation under reduced pressure, followed by distillation, gave 25.0 g (74.5%) of the title compound: bp 170–173 °C (0.6 mm); $[\alpha]^{20}_D$ 66.2° (1.14, EtOH); ^1H NMR δ 7.4 (m, 5 H, Ar H), 5.80 (s, 1 H, OCHO), 3.97 (m, 2 H, OCH), 3.48 (t, 4 H, CH_2Br), 2.1 (m, 4 H, $BrCH_2CH_2$); ^{13}C NMR δ 137.4, 129.5, 128.5, 126.6, (C_1, C_4, C_2, C_3 of Ph ring), 103.1 (C_2), 79.9 and 78.8 (C_4 and C_5, interchangeable), 36.1 and 36.0 (CH_2Br), 29.3 (CCH_2C).

(1*R*,7*R*)-(−)-9-Phenyl-8,10-dioxa-4-thiabicyclo[5.3.0]decane (5) was prepared in EtOH from **4** (125 g, 343 mmol, in 1500 mL) and sodium sulfide monohydrate (99.5 g, 414 mmol, in 1500 mL). The two solutions were simultaneously added in a high dilution apparatus to 2000 mL of refluxing EtOH at a 300 mL/day rate. (The Na_2S solution was freshly prepared every day.) At the end of the addition the reaction mixture was further refluxed for 8 h. The residue after solvent evaporation was crystallized from pentane; yield 11.4 g (84.5%); mp 53 °C; $[\alpha]^{19}_D$ −67.4° (*c* 1.09, EtOH); *m/e* 235 (loss of benzylidenic H from the molecular ion); ^1H NMR δ 7.45 (m, 5 H, Ar H), 5.94 (s, 1 H, OCHO); 4.14 (m, 2 H, OCH), 2.68 (m, 4 H, SCH_2), 2.5 and 2.0 (m, 4 H overall, SCH_2CH_2); ^{13}C NMR δ 138.6, 129.1, 128.3, 126.5 (C_1, C_4, C_2, C_3 of Ph ring), 103.2 (C_9), 82.5 and 80.4 (C_1, C_7, interchangeable), 30.6 and 30.9 (C_3, C_5 interchangeable), 32.0 and 33.1 (C_2 and C_6, interchangeable). Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.83. Found: C, 66.21; H, 6.85.

(1*R*,7*R*)-9-Phenyl-3-vinyl-8,10-dioxa-4-thiabicyclo[5.3.0]-decane (6) was obtained as a comparable mixture of four diastereoisomers by coupling vinylmagnesium bromide with the corresponding 3-chloro derivative, prepared[4,5] from **5** (4.0 g, 16.9 mmol, in 64 mL of benzene) and *N*-chlorosuccinimide (2.5 g, 18.2 mmol). The benzene solution was added dropwise over 45 min to an ice-cooled solution of the Grignard reagent [prepared from vinyl bromide (3.67 mL, 53.3 mmol) and magnesium (1.32 g, 54.4 mmol) in 55 mL of THF]. After warming to room temperature, the reaction mixture was decomposed with 20% aqueous NH_4Cl and extracted with ether. The oily residue after solvent evaporation was chromatographed (silica gel, 10% ether/light petroleum ether), affording four fractions.

The first eluted material (0.32 g) has, in the olefinic region, protons in excess of the expected single vinyl appendage and must be an elimination product. Both ^{13}C and ^1H NMR spectra are consistent with a mixture of two about equally abundant 2-phenyl-4-vinyl-5-(3-thiapent-4-en-1-yl)-1,3-dioxolane isomers: ^{13}C NMR δ 134.9 and 134.5 (C_4—CH=), 131.8 and 131.9 (S-CH=), 118.6 and 119.3 (C_4CH=CH_2), 110.5 and 110.3 (SCH=CH_2), 103.5 and 103.3 (C_2), 84.0, 82.4, 80.9, and 79.6 (C_4 and C_5, interchangeable), 31.8 and 31.4 (C_5CH_2), 27.7 and 27.7 (CH_2S); ^1H NMR: δ 7.35 (m, 5 H, Ar H), 5.80 (s) superimposed on 6.3–4.9 (m, 7 H overall, acetalic plus olefinic H), 4.0 (m, 2 H, OCHCHO), 2.7 (m, 2 H, SCH_2), 1.9 (m, 2 H, CH_2CH_2S).[11]

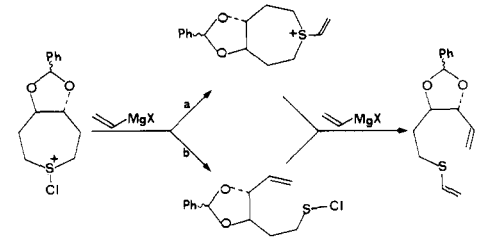
The second fraction (0.82 g, 21%) appears to consist of three diastereoisomers of **6** (~3:1:1 ratio) as evinced from the ^{13}C NMR spectrum. The more abundant isomer exhibits the following signals: δ 137.7 (CH=), 115.5 (=CH_2), 103.2 (C_9), 82.7 and 78.9 (C_1 and C_7, interchangeable), 47.4 (C_3), 39.8 (C_2), 30.1 and 28.3 (C_5 and C_6, interchangeable). The aromatic ring carbons occur at 138.2, 129.0, 128.2, 126.4 (C_1, C_4, C_3, C_2 of Ph ring). The two minor isomers show the following ^{13}C signals: 138.5, 138.2, 115.1, 115.0, 103.0, 102.7, 81.8, 81.6, 79.8, 79.1, 46.1, 45.3, 36.1, 35.4, 34.7, 29.7, 29.5. The third fraction (0.86 g, 22%) consisted of the three isomers of **6** described above in roughly equal amounts. The fourth fraction (1.00 g) consisted of the starting material, **5** (~60%), and the fourth isomer of **6**. This could be separated by chromatography (20% ether/light petroleum ether) and had the following ^{13}C NMR: 138.5, 129.0, 128.2, 126.4, (C_1, C_4, C_3, C_2 of Ph ring), 137.6 (=CH), 115.5 (=CH_2), 102.7 (C_9), 80.8 and 80.4 (C_1 and C_7, interchangeable), 47.4 (C_3), 38.8 (C_2), 30.7 and 27.6 (C_5 and C_6, interchangeable).

This material was combined with those from the second and third fractions and used in the methylation step. The overall yield of **6** was 56%.

(1*R*,7*R*)-4-Methyl-9-phenyl-3-vinyl-8,10-dioxa-4-thioniabicyclo[5.3.0]decane Trifluoromethanesulfonates (7). To the

(10) Binsch, G.; Klein, D. A.; *QCPE* DNMR Program No. 140, University of Indiana, Bloomington, IN.

(11) A likely route for the formation of these ring-opened products is through coupling of the Grignard reagent with a chlorosulfonium intermediate from **5** to give a sulfonium salt which then undergoes base-catalyzed elimination. Alternatively, the chlorosulfonium ion might first undergo elimination to a sulfenyl chloride, which would couple with the Grignard:



mixtures of diastereomeric **6** (2.06 g, 7.84 mmol) dissolved in CH_2Cl_2 (60 mL) a CH_2Cl_2 solution of methyl triflate was added dropwise at 0 °C. (The reaction was best performed in the presence of suspended $CaCO_3$ to eliminate any free acid and avoid polymerization.) The mixture was warmed to room temperature and stirred for 3 h. After filtration, the solvent was removed under reduced pressure to give 3.35 g of crude sulfonium salts as a viscous material. The substance tends to polymerize on standing and was therefore used immediately in the subsequent rearrangement step.

(*E*)-(1*R*,10*R*)-12-Phenyl-11,13-dioxa-4-thiabicyclo[8.3.0]tridec-7-enes 8a and 8b. A solution of the crude sulfonium salts **7** (3.35 g, 7.84 mmol) in 70 mL of THF/*t*-BuOH (10:1 v/v) was treated at −40 °C with *t*-BuOK (0.879 g, 7.84 mmol). After 1.5 h at −40 °C, the mixture was quenched with H_2O (10 mL), neutralized with dilute HCl, and extracted with ether. Evaporation of solvent left a residue (1.73 g), which by GLC analysis consisted of at least three products; chromatographic separation (SiO_2, 15% ether/light petroleum ether) gave four fractions. The first eluted material (0.150 g) appeared to be a mixture of several minor products and was discarded. The second (0.274 g) and fourth (0.130 g) eluted materials were the two diastereoisomers of the title compound, **8a** and **8b**, respectively, while the third fraction (0.880 g) was a 5:4 mixture of **8a** and **8b**. They were separated by chromatography (SiO_2, 15% ether/light petroleum ether). The faster eluting isomer **8a**, recrystallized from pentane, was characterized as follows: mp 87–87.5 °C; $[\alpha]^{20}_D$ −19.8° (*c* 0.53, EtOH); ^{1}H NMR: δ 7.4 (m, 5 H, Ar H), 5.80 (s, 1 H, acetalic H), 5.5 (m, 2 H, olefinic H), 4.44 and 3.97 (m, 2 H overall, OHCCHO), 3.0–1.7 (m, 10 H, CH_2); ^{13}C NMR, δ 132.2 and 127.2 (C_7 and C_8, interchangeable), 102.5 (C_{12}), 80.2 and 79.8 (C_1 and C_{10}, interchangeable), 35.3, 32.5, 32.2 (two signals), 30.9 (C_2, C_3, C_5, C_6, C_9, unassigned). The aromatic carbons occur at 137.4, 129.3, 128.3, 126.7 (C_1, C_4, C_2, C_3 of Ph ring).

The slower eluting isomer, **8b** was characterized as follows: mp 56 °C; $[\alpha]^{20}_D$ −47.6° (*c* 0.42, EtOH); ^{1}H NMR δ 7.45 (m, 5 H, Ar H), 5.87 (s, 1 H, acetalic H), 5.6 (m, 2 H, olefinic H), 4.50 and 3.90 (m, 2 H overall, OCHCHO), 3.1–1.6 (m, 10 H, CH_2); ^{13}C NMR 132.0 and 128.1 (C_7 and C_8, interchangeable), 103.0 (C_{12}), 81.8 and 78.7 (C_1 and C_{10}, interchangeable), 35.9, 32.6 (two signals), 32.0, 30.2 (C_2, C_3, C_5, C_6, C_9, unassigned).

(*E*,*E*)-Thiacyclodeca-4,7-diene. To a solution of **8a** in THF (0.44 g, 1.6 mmol, in 6.3 mL) cooled at −20 °C, 2.3 mL of 1.5 M BuLi (3.4 mmol) in hexane was added dropwise by syringe under nitrogen. After stirring at −20 °C for 30 min, water was added and the mixture extracted with pentane. After drying and solvent evaporation, the residue [0.46 g, three major peaks in GLC (10% Xe 60)] was separated by column chromatography (SiO_2, 3% ether/light petroleum ether). The first eluted material (0 14 g, 57.5%) was the title compound (*m*/*e* 154), which proved to be completely devoid of optical activity. The olefinic protons in the ^{1}H NMR spectrum give rise to a symmetrical ten-line spectrum centered at δ 5.50. Irradiation at δ 2.7 gave rise to an AB quartet, J = 16.0 Hz (*E* double bond), $\Delta\nu$ = 46 Hz at 60 MHz. Irradiation at δ 2.9 and 2.5 decouples the low and high field parts of the quartet, respectively. Since the bis-allylic protons (at C_6) are likely to resonate downfield with respect to the allylic protons at C_3 and C_9, the low-field olefinic resonance can be assigned to the protons at C_5 and C_7. The rest of the spectrum consists of two multiplets centered at δ 2.7 and 2.1 (6 H and 4 H, respectively), pertaining to the bis-allylic plus allylic protons, and to the α-methylenes, respectively. The ^{13}C NMR consists of five signals: 139.5 (C_5, C_7), 128.6 (C_4, C_8) [assignment based on the shieldings effects due to Me group at C_3 (see below)], 38.2 (C_2, C_{10}), 36.1 (C_6), 34.1 (C_3, C_9). For the low-temperature (down to −156 °C) ^{13}C NMR experiments, the sample was dissolved in a 1:1 $CCl_2F_2/CHClF_2$ mixture. Anal. Calcd for $C_9H_{14}S$: C, 70.07; H, 9.15. Found: C, 71.43; H, 9.28.

(1*R*,7*R*)-9-Phenyl-3-((*E*)-1-propenyl)-8,10-dioxa-4-thiabicyclo[5.3.0]decane (11) was obtained as a mixture of diastereoisomers by in situ coupling the 3-chloro derivative of **5** with (*E*)-1-propenylmagnesium bromide in THF, as described for **6**. The crude mixture [6.27 g (from 6.00 g, 25.4 mmol of **5**)] was chromatographed (10% ether/light petroleum ether). The first eluted material (1.51 g) consisted of two isomers of a product homologous to that obtained in the preparation of **6** (see above), 2-phenyl-4-vinyl-5-(*E*-3-thiahex-4-en-1-yl)-1,3-dioxolane: ^{13}C NMR δ 135.0 and 134.6 (C_4-CH=), 124.4, 124.5 (SCH=CHCH$_3$), 125.6 and 125.5 (SCH=), 119.2 and 118.5 (=CH_2), 103.5 and 103.3 (OCHO), 84.0, 82.4, 80.7, 79.4 (OC_4HC_5HO), 33.1 and 32.7 (C_5CH_2), 30.1 (two signals, CH_2S), 14.6 (two signals, CH_3); ^{1}H NMR δ 7.35 (m, 5 H, Ph H), 5.98 and 5.82 (two singlets superimposed to a multiplet), 6.1–5.0 (6 H overall, acetalic plus olefinic H), 4.00 (m, 2 H, OCHCHO), 2.70 (m, 2 H, SCH_2), 1.85 (m, 2 H, C_5CH_2), 1.72 (d, 3 H, =C-CH_3).

The subsequent chromatographic fractions consisted of various isomeric mixtures of **11**, the last fraction being contaminated by starting material (**5**), which was separated (0.080 g) by chromatography using 20% ether/light petroleum ether as eluant. The various fractions containing **11** were combined to give 3.83 g (58%) of the title compound. The ^{1}H NMR of the combined isomers shows the following: δ 7.5 (m, 5 H, Ar H), 5.96 (s, 1 H, acetalic H), 5.50 (m, 2 H, ethylenic H), 4.6–3.5 (extended m, 3 H, methyne H), 3.1–2.0 (m, 6 H, CH_2), 1.70 (d, J = 8 Hz, 3 H, CH_3). Anal. Calcd for $C_{16}H_{20}O_2S$: C, 69.53; H, 7.29. Found: C, 69.41; H, 7.24.

(*E*)-(1*R*,10*R*)-6-Methyl-12-phenyl-11,13-dioxa-4-thiabicyclo[8.3.0]tridec-7-enes 13a–d. The mixture of isomeric **11** (3.36 g, 12.1 mmol) was S-methylated as described above for **8a–b** to give 4.69 g of crude sulfonium salt **12**. This was used immediately in the subsequent ring-expansion reaction, as described above for **7**, to yield 3.09 g of a crude sulfide that by TLC (SiO_2, 15% ether/light petroleum ether) appears to consist of at least four major products [GLC analysis (10% Carbowax 20M, 200 °C) revealed only three major peaks]. The four products (**13a–d**, in order of decreasing elution rate, 62.1% overall) were separated by column chromatography and crystallized from EtOH (**13c** did not crystallize, however). **13a** (0.55 g): mp 104 °C; $[\alpha]^{21}_D$ 5.4 (*c* 1.01, $CHCl_3$); ^{1}H NMR δ 7.5 (m, 5 H, Ar H), 5.90 (s, 1 H, acetalic H), 5.6 (m, 2 H, olefinic H), 4.7 and 4.0 (m, 1 H each, OCH), 3.2–1.6 (m, 9 H, methylenes and C**H**CH_3), 1.07 (d, 3 H, CH_3); ^{13}C NMR δ 137.6, 129.3, 128.3, 126.7 (C_1, C_4, C_2, C_3 of Ph ring), 137.5 (C_7), 125.0 (C_8), 102.4 (C_{12}), 80.3 and 78.7 (C_1 and C_{10}, interchangeable), 40.6 (C_5), 39.9 (C_6), 33.7, 32.6, 32.0 (C_2, C_3, C_9, interchangeable), 19.5 (CH_3). **13b** (0.56 g): mp 83 °C; $[\alpha]^{21}_D$ −52.6° (*c* 1.15, $CHCl_3$); ^{1}H NMR δ 7.5 (m, 5 H, Ar H), 5.89 (s, 1 H, acetalic H), 5.5 (m, 2 H, olefinic H), 4.4 and 3.8 (m, 1 H each, OCH), 3.0–1.5 (m, 9 H, methylenes and C**H**CH_3), 1.03 (d, 3 H, CH_3); ^{13}C NMR δ 137.6, 129.3, 128.3, 126.6 (C_1, C_4, C_2, C_3 of Ph ring), 139.5 (C_7), 123.7 (C_8), 102.7 (C_{12}), 80.8 and 79.9 (C_1 and C_{10}, interchangeable, 39.8 (C_5), 36.0 (C_6), 36.6, 31.5, 30.3 (C_2, C_3, C_9, interchangeable), 19.9 (CH_3). **13c** (0.52 g) oil: $[\alpha]^{21}_D$ −20.6° (*c* 1.14, $CHCl_3$); ^{1}H NMR δ 7.5 (m, 5 H, Ar H), 5.83 (s, 1 H, acetalic H), 5.6 (m, 2 H, olefinic H), 4.7 and 4.0 (m, 1 H each, OCH), 3.2–1.6 (m, 9 H, methylenes and C**H**CH_3), 1.05 (d, 3 H, CH_3); ^{13}C NMR δ 137.4, 129.4, 128.4, 126.8 (C_1, C_4, C_2, C_3 of Ph ring), 137.2 (C_7), 125.9 (C_8), 102.9 (C_{12}), 81.4 and 77.8 (C_1 and C_{10}, interchangeable), 40.5 (C_5), 39.7 (C_6), 34.8, 31.7, 30.8 (C_2, C_3, C_9, interchangeable), 19.5 (CH_3). **13d** (0.56 g): mp 78 °C; $[\alpha]^{21}_D$ −105.0° (*c* 1.00, $CHCl_3$); ^{1}H NMR 7.5 (m, 5 H, Ar H), 5.87 (s, 1 H, acetalic H), 5.5 (m, 2 H, olefinic H), 4.4 and 3.8 (m, 1 H each, OCH), 3.0–1.5 (m, 9 H, methylenes and C**H**CH_3), 1.03 (d, 3 H, CH_3); ^{13}C NMR δ 137.7, 129.3, 128.3, 126.6 (C_1, C_4, C_2, C_3 of Ph ring), 139.4 (C_7), 124.5 (C_8), 103.1 (C_{12}), 81.8 and 79.4 (C_1 and C_{10}, interchangeable), 39.9 (C_5), 36.1 (C_6), 36.6, 31.9, 29.9 (C_2, C_3, C_9, interchangeable), 19.8 (CH_3). Anal. Calcd for $C_{17}H_{22}O_2S$: C, 70.31; H, 7.64. Found: C, 69.81; H, 7.72.

It is noteworthy that the ^{1}H NMR spectra of the **13a**/**13c** pair are essentially identical and so are the spectra of the **13b**/**13d** pair. The ^{13}C NMR spectra also display remarkable regularities within each pair. In spite of this, there appears to be no sufficient ground to assign the configuration of each isomer.

(+)- and (−)-(*E*,*E*)-3-Methylthiacyclodeca-4,7-diene ((+)-**14** and (−)-**14**) were obtained from **13a** (or **13c**) and **13b**, respectively, as described above for **1**. Whitham cycloelimination of **13a** (0.347, 1.2 mmol) gave, after workup, (+)-**14** (0.094 g, 77.5%) as a volatile oil: $[\alpha]^{23}_D$ 8.44° (*c* 1.48, *n*-C_6H_{14}). Anal. Calcd for $C_{10}H_{16}S$: C, 71.35; H, 9.58. Found: C, 72.05; H, 9.66. Similarly, **13c** gave (+)-**14** ($[\alpha]^{23}_D$ 8.87° (*c* 1.26, *n*-C_6H_4)), and **13b** gave (−)-14 ($[\alpha]^{23}_D$ −8.46° (*c* 1.30, *n*-C_6H_{14}).

The signs of the optical rotation of the various samples of **14** indicate **13a** and **13c** to have the same configuration at C_3 (hence they differ for the configuration at C_{12}). Obviously the **13b**/**13d** pair has the same configuration at C_3, opposite to that of the

13a/13c pair; ^{1}H NMR δ 5.83 (q, 2 H, C_5H and C_7H), 5.07 (m, 2 H, C_4H and C_8H), 2.7 and 2.1 (m, 9 H overall, bis-allylic, allylic, and methyne H), 0.99 (d, 3 H, CH_3) (irradiation at δ 2.8 and 2.4 decouples the low- and high-field part, respectively, of an AB quartet with J = 16 Hz (E double bonds)); ^{13}C NMR (at ambient temperature) δ 139.7 (C_7), 135.9 and 135.4 (C_4 and C_5, interchangeable), 128.4 (C_8), 45.6 (C_2), 39.1 (C_3), 38.8 (C_{10}), 35.9 and 34.2 (C_6 and C_9, interchangeable), 18.8 (CH_3). At -90 °C in $CHFCl_2$ two sets of signals obtain having the same line width (intensity ratio ~4:1). By variable-temperature ^{13}C NMR (-90 to -30 °C) the resonances of corresponding carbons have been identified as follows (minor conformer in parentheses): 140.7 (142.0), C_7; 138.1 (135.0), C_5; 135.6 (137.4), C_4; 129.3 (128.1), C_8; 45.7 (45.7), C_2; 42.0 (36.1), C_3; 39.3 (39.1), C_{10}; 37.4 (37.0), 35.4 (35.1), C_6 and C_9, interchangeable; 21.2 (15.7), CH_3.

The kinetic parameters of the exchange process (ΔG^*) = 11.0 ± 0.2 kcal/mol) were evaluated by computer simulation of the line shapes in the -32 to -60 °C range. The pair of lines having the largest chemical shift difference was selected (the CH_3 lines), which also are unencumbered by overlapping signals.

Unsuccessful Ring Expansion of 4-Ethyl-9-phenyl-3-vinyl-8,10-dioxa-4-thioniabicyclo[5.3.0]decane Tetrafluoroborate. Sulfide **6** (1.31 g, 5 mmol) in 40 mL of CH_2Cl_2 was reacted with triethyloxonium tetrafluoroborate (1.04 g, 5.5 mmol), as described for the preparation of the methyl derivative (**7**), to give 1.78 g of crude sulfonium salt. This was immediately treated with t-BuOK as described for the preparation of **8**, to give 1.12 g of a mixture of several products (TLC and GLC). Partial chromatographic separation (15% ether/light petroleum ether) showed the material to be largely made up (^{13}C NMR) of the four isomers of **6**, i.e., the products of β elimination of ethylene from **9**. Two minor products were also partially separated, each characterized in the ^{1}H NMR spectra by a quartet, δ 2.54 and 2.52, and a triplet, δ 1.22 and 1.24, respectively, indicative of the presence of a SCH_2CH_3 grouping. Both were tentatively assigned structure **10**, arising from a 2,3-sigmatropic shift of the endocyclic ylide from **9**. Since none of the chromatographic fraction showed any evidence in the ^{1}H NMR of the methyl doublet expected in the product of three-carbon ring expansion (5-methyl-12-phenyl-11,13-dioxa-4-thiabicyclo[8.3.0]tridec-7-ene), the separation of the reaction products was not pursued further.

Registry No. **1**, 82134-56-3; **2**, 82188-38-3; **3**, 82188-39-4; **4**, 82134-50-7; **5**, 82134-51-8; **6**, 82134-52-9; **7**, 82134-54-1; **8** (isomer 1), 82134-55-2; **8** (isomer 2), 82188-40-7; **11**, 82134-57-4; **12**, 82134-59-6; **13** (isomer 1), 82134-60-9; **13** (isomer 2), 82188-41-8; **13** (isomer 3), 82188-42-9; **13** (isomer 4), 82188-43-0; (+)-**14**, 82149-52-8; (-)-**14**, 82149-53-9; (1*R*,4*S*,5*R*,8*S*)-4,8-dichloro-2,6-dioxobicyclo[3.3.0]octane, 82188-37-2; D-mannitol, 69-65-8.

Notes

Tropone Revisited

I. David Reingold* and Laurence J. DiNardo

Department of Chemistry, Middlebury College, Middlebury, Vermont 05753

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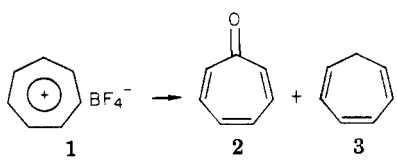
We recently reported a new synthesis of tropone (**2**) which involved heating tropylium fluoborate (**1**) in dimethyl sulfoxide (Me_2SO).[1] Soon after publication we received word that the reaction did not work well for some people;[2] and, indeed, on moving from Pennsylvania to Vermont, we ourselves occasionally had some difficulty reproducing our yields.[3] On the other hand, others reported no problems.[4] Faced with these conflicting results, we have embarked on a reinvestigation of the reaction and report our results herein.

When tropylium fluoborate is heated in Me_2SO, a 1:1 mixture of tropone (**2**) and cycloheptatriene (**3**) is produced over the course of several hours (eq 1). There is no intermediate detectable by NMR spectroscopy, and the reaction appears to be quantitative. Addition of solid anhydrous sodium carbonate to the reaction mixture markedly accelerates the reaction and causes the vigorous evolution of carbon dioxide. Thus, a mixture of tropylium fluoborate and Me_2SO is converted quickly to tropone and cycloheptatriene on addition of solid sodium carbonate at room temperature. After workup the yield of tropone (corrected for Me_2SO contamination) is consistently 45-49% based on tropylium salt, which is 90-98% of expected tropone.



1 2 3 (1)

The mechanism of the reaction and the source of the oxygen that ends up on the tropone remain unknown, but it is clear that the mechanism proposed by us[1] and others,[5] which involves a dimethyl sulfoxonium salt in a process related to the Corey-Kim oxidation,[6] is not correct, for this does not account for the generation of cycloheptatriene along with the tropone. Furthermore, on the analytical scale, the sodium carbonate catalyzed reaction works equally well in dimethylformamide and, with heating, in acetone, tetraglyme, and acetonitrile. On a preparative scale, tropone can be generated in acetonitrile without distillation, as all the byproducts can be removed by filtration or evaporation.[7] Ditropyl ether is a tempting intermediate to propose for this transformation, because it is known to disproportionate slowly into tropone and

(1) Garfunkel, E.; Reingold, I. D. *J. Org. Chem.* **1979**, *44*, 3725.
(2) Ledlie, D., personal communication; Gribble, G. W., personal communication.
(3) Reingold, I. D.; Halsey, D., unpublished results.
(4) Thummel, R. P., personal communication.
(5) Kitahara, Y.; Funamizu, M. Japanese Patent 11 122; *Chem. Abstr.* **1963**, *59*, 10012b.
(6) Corey, E. J.; Kim, C. U. *J. Am. Chem. Soc.* **1972**, *94*, 7586; *J. Org. Chem.* **1973**, *38*, 1233.
(7) Despite efforts to exclude moisture, some ditropyl ether was produced when this was done in the summer; winter reactions gave clean tropone. Ditropyl ether was not a problem in the summer when Me_2SO was the solvent, but then a distillation is necessary to remove the Me_2SO. If time is not of the essence, ditropyl ether presents no problem, as it disproportionates to tropone and cycloheptatriene within a few days (see note 8).

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