were washed (acid, 5% NaOH, brine), dried ($MgSO_4$), concentrated, and evaporatively distilled (100 °C (0.25 mm)) to give 180 mg (91% yield) of spirocyclic ketone: IR (film) 1715 (C=O), 3100 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 0.9 (d, J = 6 Hz, 3 H, $CHCH_3$), 5.1–5.4 (d, 1H, CH_2CH=C**H**), 5.5–5.8 (m, 1 H, CH_2C**H**=CH); ^{13}C NMR δ 9.2 (C-12), 18.9 (C-10), 22.4 (C-4), 24.7 (C-11), 25.3 (C-9), 35.8 (C-5), 41.1 (C-3), 43.8 (C-6), 53.9 (C-1), 127.2 (C-8), 136.1 (C-7), 213.0 (C-2).

Cyclization of Alcohol 1c. Allylic alcohol **1c** (370 mg, 1.6 mmol) was combined with 75 mL of dry formic acid and heated to 55 °C under N_2 for 11 h. The cooled solution was diluted with water (200 mL) and extracted with methylene chloride (3 × 100 mL). The combined extracts were washed (water, bicarbonate, brine), dried ($MgSO_4$), and concentrated to give 390 mg of crude formate: IR (film) 1730 (C=O), 1150 (CO), 3040 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 4.6–5.8 (m, 3 H, HC=CH and C**H**OH), 7.9 (s, 1 H, HC=O). Analysis by VPC (Carbowax, 185 °C) showed one major peak with a shoulder and shorter retention time peaks believed to be hydrocarbon.

The above mixture of formates (370 mg) was treated with an excess of lithium aluminum hydride in ether to cleave the formate esters. The resulting mixture was chromatographed on silical gel to give 90 mg of hydrocarbons eluted with hexane and 260 mg of alcohols eluted with methanol. The alcohol mixture was evaporatively distilled (125 °C (0.2 mm)) to give 200 mg of an oil which partially solidified upon standing. Analysis by VPC (Carbowax, 185 °C) showed three peaks with long retention times (>7 min). The first peak, 7.5 min, contained 5.7% of the total area, the second, 9 min, contained 13% of the area, and the third peak, 11.5 min, contained 80% of the area. The mixture of alcohols was partially separated on an alumina column (TLC grade) by using 30% CH_2Cl_2/hexane. The major isomer **12** had the following spectroscopic properties: IR (film) 3400 (OH), 1035 (CO), 3020 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 3.25–3.8 (m, 1 H, C**H**OH), 5.0–5.3 (bd, 1 H, CH_2CH=C**H**), 5.5–5.79 (m, 1 H, CH_2C**H**=CH); ^{13}C NMR ($CDCl_3$) δ 14.0 (CH_3), 18.8, 20.3, 23.4, 24.9, 25.3, 29.6, 34.4, 35.7, 36.5, 40.8 (C-6), 54.5 (C-1), 73.1 (C-2), 126.6 (C-8), 137.6 (C-7).

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Registry No. 1a, 70681-88-8; **1b**, 70681-89-9; **1c**, 70681-90-2; **2a**, 70079-75-3; **2b**, 70681-91-3; **2c**, 70681-92-4; **3**, 5323-87-5; **4**, 70681-93-5; **4** formate, 70681-94-6; **5**, 70681-95-7; **5** formate, 70681-96-8; **6**, 16133-76-9; **6** *p*-nitrobenzoate, 70681-97-9; **7**, 70681-98-0; **8**, 70681-99-1; **11**, 70682-00-7; **11** formate, 70682-01-8; **11** ketone, 70682-02-9; **12**, 70682-03-0; **12** formate, 70703-18-3; iii, 70682-05-2; iv, 70682-23-4; 1-bromo-4-pentene, 1119-51-3; *trans*-4-hexen-1-ol, 928-92-7; *trans*-4-hexenyl chloride, 62614-72-6; *trans*-4-nonen-1-ol, 16695-34-4; *trans*-4-nonenyl chloride, 16427-36-4; spiro[5.5]undecane-2,8-dione, 70682-04-1.

Convenient Syntheses of 5,5,9-Trimethyl-*trans*-1-decalone and 6β-Hydroxy-5,5,9β-trimethyl-*trans*-1-decalone

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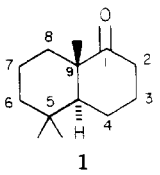
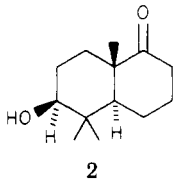
Convenient syntheses of 5,5,9-trimethyl-*trans*-1-decalone (1) and 6β-hydroxy-5,5,9β-trimethyl-*trans*-1-decalone (2) involve (1) the Robinson annelation of 2-methyl-1,3-cyclohexanedione with ethyl vinyl ketone, (2) selective ketalization of 5,9-dimethyl-$\Delta^{5,10}$-octal-1,6-dione at the nonconjugated carbonyl group with ethylene glycol, (3) reductive methylation of 1-ethylenedioxy-5,9-dimethyl-$\Delta^{5,10}$-2-octalone, (4) Wolff–Kishner reduction or dissolving-metal reduction of 1-ethylenedioxy-5,5,9-trimethyl-*trans*-1-decalone, and (5) acid-catalyzed hydrolysis of 1-ethylenedioxy-5,5,9-trimethyl-*trans*-decalin or of 1-ethylenedioxy-6β-hydroxy-5,5,9β-trimethyl-*trans*-decalin to form 1 and 2, respectively.

The value of 5,5,9-trimethyl-*trans*-1-decalone[2] (1) and 6β-hydroxy-5,5,9β-trimethyl-*trans*-1-decalone (2) as



1



2

synthetic intermediates has been demonstrated in the synthesis of several terpenes.[3] In connection with several projected syntheses in our respective laboratories,[4] we required convenient, stereocontrolled preparations of these bicyclic intermediates. Particularly important, both for our work and for others who might anticipate utilizing these terpene precursors, is the requirement that preparations of racemic 1 and 2 be efficient and exercise highly effective stereocontrol to avoid tiresome and sometimes difficult isomer separations. We now report a short synthetic sequence for the preparation of 1 and 2 in approximately 50% overall yield from 2-methyl-1,3-cyclohexanedione which exercises the requisite stereocontrol while maintaining the C-1 carbonyl oxidation state throughout the sequence. Both the overall yield and

(1) Direct correspondence to D.S.W. at Central Research, Pfizer, Groton, Conn., or to P.L.S. at The University of Texas at San Antonio.

(2) We are using the common name of the parent compound 1 to avoid the cumbersome 3,4,4aα,5,6,7,8,8a-octahydro-5,5,8aβ-trimethyl-1(2*H*)-naphthalenone. And to avoid confusion, comparable common names and the skeletal numbering system shown for 1 have been used for all related compounds in this study.

(3) For several examples, see ref 5–7 as well as the following: (a) N. Danieli, Y. Mazur, and F. Sondheimer, *Tetrahedron*, **23**, 509 (1967); (b) E. Ghera and F. Sondheimer, *Tetrahedron Lett.*, 3887 (1964).

(4) Several additional manuscripts are now in preparation. See also ref 12a.

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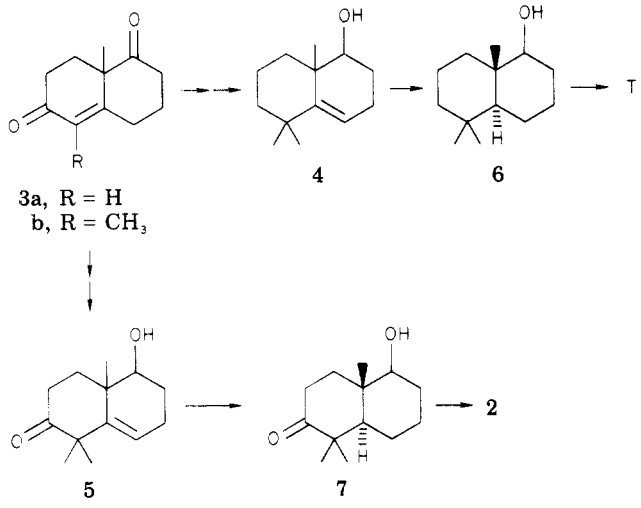
Scheme I

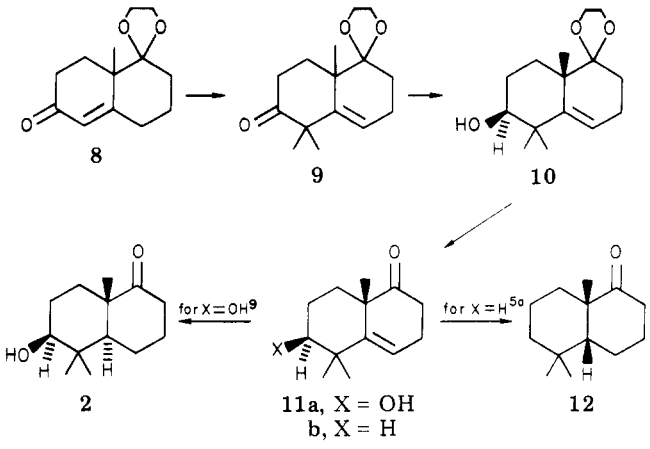


operational simplicity eclipse the previously reported preparations of **1** and **2**.

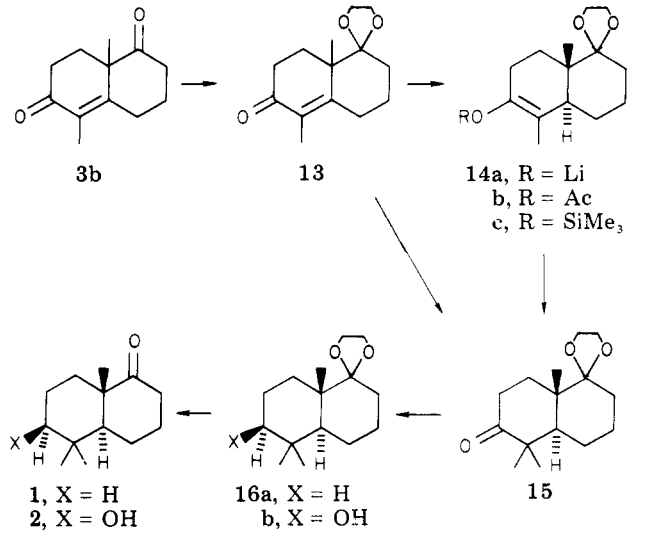
As in the present study, most previously reported syntheses of **1** and **2** have utilized the Wieland–Miescher ketone **3a**[5,6] or its methyl analogue **3b**[7] which are readily available from Robinson annelations of 2-methyl-1,3-cyclohexanedione. A common feature of these published procedures, as shown in Scheme I, is the stereoselective hydrogenation of the octalols **4** and **5** to secure the trans-fused decalols **6** and **7**, respectively.[8] It would appear[5a] that reduction of the C-1 ketone to the C-1β alcohol prior to catalytic hydrogenation is necessary to guarantee selective generation of the trans rather than the cis ring fusion. Subsequent reoxidation of the C-1β alcohol to a C-1 ketone proved satisfactory for the conversion of **6** to **1** but additional protection/deprotection steps were required to effect the redox reversal of the carbonyl and hydroxyl groups in the conversion of **7** to **2**.[6] Moreover, we felt that a more efficient scheme for the synthesis of **1** and **2** might be devised which would avoid the necessity for proceeding through the C-1β alcohol.

This notion was incorporated into one attractive approach to **2**, in which the catalytic hydrogenation of the ketol **11a** was reported to furnish, predominantly, the *trans*-decalone **2**.[9] This result, shown in Scheme II, stands in direct contrast to the catalytic hydrogenation of **11b** which led predominantly to the *cis*-decalone **12**.[5a] In order to reconcile this apparent anomaly, we have reinvestigated the preparation of **2** illustrated in Scheme II but have encountered several difficulties. Both the methylation of **8** and the lithium tri-*tert*-butoxyaluminum hydride reduction of **9** required chromatography to separate **9** from small amounts of overmethylation byproduct and to separate **10** from its 6α epimer. Alternative reductions of **9** using various aluminum hydrides, sodium borohydride, or lithium in ammonia also led to unsatisfactory mixtures. The most troubling aspect of this entire procedure was our inability to effect stereoselective catalytic hydrogenation

Scheme II



Scheme III



of **11a** to afford the trans-fused product **2**. Despite variations in experimental conditions, we invariably obtained complex mixtures which appear to contain products both of nonspecific hydrogenation and of partial overreduction of the C-1 carbonyl. Accordingly, we sought a new preparation of compounds **1** and **2**.

Since dissolving-metal reduction[10] offered an alternative to catalytic hydrogenation as a method for establishing the requisite trans ring fusion, we turned our attention to Scheme III. Robinson annelation of 2-methyl-1,3-cyclohexanedione with ethyl vinyl ketone afforded **3b** which underwent regioselective ketalization,[11,12] generating **13** in 65–70% overall yield. Application of Stork's reductive methylation procedure[10] *with rigorous exclusion of oxygen* furnished **15** bearing both the requisite trans ring fusion and *gem*-dimethyl moiety in 80% yield after chromatography. In an attempt to suppress the amount of unalkylated and overalkylated decalone byproducts, we examined the use of cosolvents (THF, glyme, HMPA) at

(5) For a seven-step route to **1** from **3a**, see: (a) J. D. Cocker and T. G. Halsall, *J. Chem. Soc.*, 3441 (1957); (b) F. Sondheimer and D. Elad, *J. Am. Chem. Soc.*, **79**, 5542 (1957).

(6) For an eleven-step route to **2** from **3a**, see F. Sondheimer and D. Elad, *J. Am. Chem. Soc.*, **80**, 1967 (1958).

(7) For a seven-step route to **1** from **3b**, see N. Ototani, T. Kato, and Y. Kitahara, *Bull. Chem. Soc. Jpn.*, **40**, 1730 (1967).

(8) An exception is the synthesis of (−)-(9*S*,10*S*)-**1** from (+)-manool: G. Ohloff, W. Giersch, K. H. Schultz-Elte, and C. Vial, *Helv. Chim. Acta*, **59**, 1140 (1976).

(9) R. E. Ireland, "Organic Synthesis", Prentice-Hall, Englewood Cliffs, N.J., 1969, pp 40–44, 50–52.

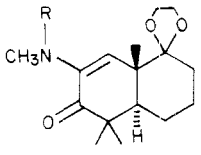
(10) (a) G. Stork, P. Rosen, and N. L. Goldman, *J. Am. Chem. Soc.*, **83**, 2965, (1961); (b) G. Stork and S. D. Darling, *ibid.*, **86**, 1761 (1964).

(11) (a) Y. Kitahara, A. Yoshikoshi, and S. Oida, *Tetrahedron Lett.*, 1763 (1964); (b) R. E. Ireland et al. and W. S. Johnson et al., *J. Am. Chem. Soc.*, **92**, 5743 (1970).

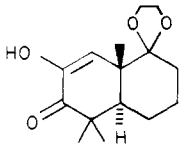
(12) (a) C. L. Edwards, Ph.D. Thesis, The University of Texas at Austin, Austin, Texas, 1974; (b) D. L. Snitman, M.-Y. Tsai, and D. S. Watt, *Synth. Commun.*, **8**, 195 (1978). (c) We found it most convenient to carry the ketalization slightly beyond completion (that is, ensure consumption of starting endione) by forming a small amount of bis(ketal). Both chromatography and direct crystallization (if seeded) then proceed smoothly, since the bis(ketal), unlike the endione, is highly mobile during chromatography and highly soluble during crystallization.

several reaction temperatures as well as variations in the amount and rate of addition of methyl iodide. These efforts failed to increase the yield of **15** or to reduce the amounts of those byproducts which necessitated chromatography.

The facile base-induced oxidation of ketone **15** merits some comment. As noted above, direct reductive methylation of **13** required the rigorous exclusion of oxygen. If this precaution was not heeded, particularly during evaporation of the ammonia, a mixture was obtained in which the α-aminoenone **17a** and not ketone **15** was the



17a, R = H
b, R = Ac



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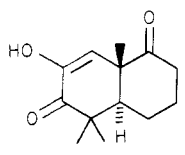

19

major product. Further support for this structural assignment was obtained by conversion of **17a** to its acetamide **17b** which also exhibited spectral data in accord with the proposed structure. Partial hydrolysis of **17a** in aqueous acid produced the ketal diosphenol **18** and the keto diosphenol **19**. Autoxidation[13] of **15** also provided a sample of **18** and further substantiated the assignment of structure **17a** to the product of the "reductive methylation" experiment. We surmise that **17a** was derived from air oxidation of **15**, followed by Schiff base formation, tautomerization, and N-methylation. Indeed, when air was rigorously excluded during the evaporation of ammonia, **15** was the predominant product.

As illustrated in Scheme III, we also investigated the methylation of the enolate **14a** in ethereal, ammonia-free solvents. Following evaporation of solvent in the lithium/ammonia reduction of **13**, the residual enolate **14a** was intercepted as its enol acetate **14b** or enol silyl ether **14c**.[14] Regeneration of enolate **14a** from the enol acetate **14b** (by treatment with 2 equiv of methyllithium) and subsequent methylation in either glyme or THF proved no more satisfactory than direct alkylation in ammonia. As evidenced by extraneous high-field doublets in its NMR spectrum, the product mixture contained unalkylated, α'-alkylated, and/or overalkylated byproducts. Since formation of these byproducts may be attributed to the presence of lithium *tert*-butoxide during the methylation step, methylation was attempted under quenching conditions in the absence of excess base. Thus, regeneration of enolate **14a** from the enol silyl ether **14c** (by treatment with 1 equiv of methyllithium) and subsequent methylation in glyme with a large excess of methyl iodide at ambient temperature furnished a crude product which displayed few extraneous high-field doublets in the NMR spectrum. Facile isolation of **15** in 80% yield was achieved by direct crystallization of the crude reaction product, and the yield was increased to 92% by chromatography of the mother liquors. In summary, ammonia-free methylation of enolate **14a** in the absence of other bases required an additional synthetic operation but allowed more facile isolation of purified **15** and furnished this product in higher yield than did direct reductive methylation.

As anticipated in Scheme III, the decalone **15** proved to be a valuable precursor to both **1** and **2**. Wolff–Kishner reduction of **15** produced the ketal **16a** which was directly hydrolyzed to decalone **1** in 86% yield from **15** and 50–55% overall yield from **3b**. Reductions of the C-6 ketone in **15** to the 6β-alcohol **16b** were somewhat complicated by the formation of varying amounts of the 6α epimer.[15] Best results (10% or less of the 6α contaminant) were obtained by using lithium in ammonia–ethanol, which allowed isolation of isomer-pure **16b** in 70–75% yield by simple crystallization. Hydride reductions of **15** proved less satisfactory and, whenever concentrations of the 6α epimer exceeded 15% of the product mixture,[15] cocrystallization of both epimeric alcohols interfered with purification. Hydrolysis of **16b** furnished the desired product **2** in near-quantitative yield. Intermediate purification of **16b** (from the lithium in ammonia–ethanol reduction) proved unnecessary, since direct hydrolysis of crude **16b** furnished readily crystallized ketol **2** in 82% yield from **15** and 49–53% overall yield from **3b**. Current investigations utilizing intermediates **1** and **2** in terpene syntheses will be reported in due course.

Experimental Section

Infrared spectra were determined on a Perkin-Elmer Infracord or Beckman IR-5A spectrophotometer. The abbreviation TF denotes thin film. Ultraviolet spectra were determined on a Cary 14 spectrophotometer. NMR spectra were determined on a Varian EM-390, A60, or A60A spectrometer or on a Perkin-Elmer R-12 spectrometer. Mass spectra were determined on a Varian MAT CH5 or Du Pont-Consolidated Electrodynamics Corp. Model 21-491 mass spectrometer. Parent ion molecular weights of purified samples were determined by peak matching with appropriate perfluorokerosene peak fragments by using a Du Pont-Consolidated Electrodynamics Corp. Model 21-110 high-resolution mass spectrometer and are denoted by the abbreviation HRMS. Melting points were determined with either a Thomas-Hoover or Fisher-Johns apparatus and are uncorrected. Elemental analyses were performed by Atlantic Microlabs or Chemalytics, Inc.

1-Ethylenedioxy-5,5,9-trimethyl-*trans*-6-decalone (15). Procedure A. Direct Reductive Methylation of 13. To a solution of 2.36 g (10 mmol) of **13**,[11,12] 740 mg (10 mmol, 1 equiv) of anhydrous *tert*-butyl alcohol, 30 mL of anhydrous THF, and 300 mL of anhydrous ammonia in a 1-L three-necked flask, equipped with an overhead mechanical stirrer[16] and dry ice–acetone condenser and swept by a slow stream of nitrogen vented through the condenser, was added 168 mg (24 mmol, 1.2 equiv) of lithium wire. The blue color persisted for 10 min.[16] To the colorless enolate solution was added 14.2 g (100 mmol, 10 equiv) of methyl iodide. After the reaction mixture was stirred for 1 h, the dry ice–acetone condenser was replaced by a water-jacketed condenser. Aided by the slow stream of nitrogen, the ammonia was evaporated over a 1-h period by using a steam bath. The product was diluted with 150 mL of water and extracted into 300 mL of ether. The ether solution was washed with 150 mL of brine and dried over anhydrous magnesium sulfate. The crude product (2.71 g) was purified by liquid–liquid chromatography on Woelm silica gel, using 1:3 ethyl acetate–hexane, to afford 2.02 g (80%) of **15**: IR ($CHCl_3$) 5.88 μm; NMR ($CDCl_3$) δ 1.03, 1.05 and 1.23 (three s, 9, C-5 and C-9 CH_3), 3.91 (m, 4, OCH_2CH_2O); mass spectrum (70 eV) *m/e* (relative intensity) 252 (7, M^+), 209 (76), 112 (33), 99 (100), 84 (41). Anal. ($C_{15}H_{24}O_3$): C, H.

Procedure B. Enol Silyl Ether Approach. To a solution of 9.3 mg (1.34 mmol) of lithium wire in 15 mL of anhydrous ammonia was added, dropwise under a nitrogen atmosphere, a

(13) H. Mori, V. S. Gandhi, and E. Schwenk, *Chem. Pharm. Bull.*, **10**, 842 (1962).

(14) (a) H. O. House and B. M. Trost, *J. Org. Chem.*, **30**, 2502 (1965) (and references cited therein); (b) G. Stork and P. F. Hudrlik, *J. Am. Chem. Soc.*, **90**, 4462, 4464 (1968); (c) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969).

(15) A convenient spectral probe was demonstrated for determining the amounts of 6α epimer present in crude reaction mixtures of 6β-alcohol **16b**: the alcohol mixture was converted to a mixture of methoxymethyl ethers in near quantitative yield by the action of sodium hydride and chloromethyl methyl ether in THF. Although the AB patterns of the acetal methylene chromophores overlapped at $\delta \sim 4.75$ in the NMR spectrum, there was sufficient resolution to allow quantitation of the 6α epimer.

(16) In the absence of efficient mechanical stirring, the blue color persisted for several hours. Magnetically stirred reactions gave erratic results; the deposition of a gummy precipitate invariably fouled the stirring.

solution of 150 mg (0.64 mmol) of **13** and 47 mg (0.64 mmol) of *tert*-butyl alcohol in 1 mL of anhydrous THF. The mixture was allowed to stir for 15–20 min during which time additional lithium wire was added, if necessary, to maintain the blue color of the solution. One drop of isoprene was added to decompose residual lithium, and the ammonia was replaced by THF. A quenching solution of chlorotrimethylsilane (0.4 mL) and triethylamine (0.1 mL) in 2 mL of THF (centrifuged to remove ammonium salts) was added at 25 °C. The mixture was stirred for 4 h and then added to a rapidly stirred, cold aqueous sodium bicarbonate–pentane mixture. The pentane layer and additional pentane extracts were combined, washed with brine, and dried over anhydrous magnesium sulfate. Evaporation of solvent afforded 195 mg (99%) of **14c** as a clear oil. NMR analysis showed a single compound which was used directly without purification: IR (TF) 5.98 μm; NMR ($CDCl_3$) δ 0.14 (s, 9, $Si(CH_3)_3$), 0.93 (s, 3, C-9 CH_3), 1.52 (broadened d, J = 2 Hz, 3, C-5 CH_3), 3.90 (m, 4, OCH_2CH_2O); mass spectrum (70 eV) m/e 310 (M^+), 99 (base), 73.

To 3.90 mL of 1.65 M ethereal methyllithium (~6.4 mmol) in 25 mL of anhydrous glyme was added, dropwise at 25 °C, a solution of 2.0 g (6.45 mmol) of enol silyl ether **14c** in 12 mL of glyme (distilled from sodium–benzophenone). After the reaction mixture was stirred at room temperature for 1 h, the enolate solution was quenched by rapid addition of 12 mL (approximate 30-fold excess) of methyl iodide. The solution was stirred for an additional 0.5 h, and the product **15** was isolated (1.64 g crude) as described in procedure A. Analysis of the crude product by NMR revealed only trace amounts of unalkylated, α′-alkylated, and/or polyalkylated ketones. Crystallization from 1:1 pentane–ether gave 1.32 g of ketone **15** (80% yield from **13**), mp 48–50 °C. Repeated recrystallization from pentane–ether gave an analytical sample, mp 49.5–50 °C. Chromatography, as described in procedure A, of the residues obtained by evaporation of the mother liquors allowed isolation of an additional 0.18 g of **15**, thus raising the isolated yield to 92%.

1-Ethylenedioxy-7-(*N*-methylamino)-5,5,9-trimethyl-*trans*-Δ^7-6-octalone (17a). Procedure A described for the preparation of **15** was repeated, except that the use of a nitrogen stream was omitted. The ammonia was allowed to evaporate in the hood over an 18-h period. The crude product (2.90 g) displayed a number of components including a small amount of **15** according to thin-layer and vapor-phase chromatographic analysis. The major component was isolated by liquid–liquid chromatography on Woelm silica gel, using 1:3 ethyl acetate–hexane, to afford 991 mg (36%) of **17a**: IR (KBr) 3.17, 6.02, 6.15 μm; NMR ($CDCl_3$) δ 1.13, 1.23 and 1.32 (three s, 9, C-5 and C-9 CH_3), 2.64 (s, 3, $NHCH_3$), 3.98 (m, 4, OCH_2CH_2O), 4.03–4.20 (m, 1, $NHCH_3$, exchanges with D_2O), 5.50 (s, 1, C-8 vinyl H); mass spectrum (70 eV) m/e (relative intensity) 279 (78, M^+), 207 (93), 192 (91), 164 (100), 152 (31); UV (CH_3OH) λ_{max} 309 nm (ε 3900).

An analytical sample was prepared by two recrystallizations from hexane; mp 90–90.5 °C. Anal. ($C_{16}H_{25}NO_3$): C, H, N.

1-Ethylenedioxy-7-(*N*-methyl-*N*-acetylamino)-5,5,9-trimethyl-*trans*-Δ^7-6-octalone (17b). To 82 mg of **17a** in 10 mL of anhydrous pyridine was added 1.5 mL of acetic anhydride. The solution was stirred for 17 h at 25 °C. The product was diluted with ether, washed successively with saturated copper sulfate solution, water, and brine, and dried over anhydrous magnesium sulfate. The crude product (131 mg) was chromatographed on a 20 × 20 cm Merck silica gel F254 preparative-layer (2 mm thick) plate in ethyl acetate. A band (R_f 0.30) was eluted to afford 89 mg (97%) of **17b**: IR (KBr) 5.95, 5.99 sh, 6.10 μm; NMR ($CDCl_3$) δ 1.10, 1.21 and 1.32 (three s, 9, C-5 and C-9 CH_3), 1.90 (s, 3, $N(CH_3)COCH_3$), 2.99 (s, 3, $N(CH_3)COCH_3$), 4.00 (m, 4, OCH_2CH_2O), 6.94 (s, 1, C-8 vinyl H); mass spectrum (70 eV) m/e (relative intensity) 321 (100, M^+), 278 (52), 209 (38), 192 (50), 164 (68).

An analytical sample was prepared by recrystallization from ether; mp 124–125 °C. Anal. ($C_{18}H_{27}NO_4$): C, H, N.

1-Ethylenedioxy-7-hydroxy-5,5,9-trimethyl-*trans*-Δ^7-6-octalone (18) from the Hydrolysis of 17a. A solution of 150 mg of **17a** in 6 mL of 1:2:3 1 M hydrochloric acid–glacial acetic acid–THF was stirred for 10 h at 25 °C. The product was diluted with ether, washed successively with water, saturated sodium bicarbonate, and brine, and dried over anhydrous magnesium sulfate. The crude product (125 mg) was chromatographed on a 20 × 20 cm Merck silica gel F254 preparative-layer (2 mm thick) plate in 1:2 ether–hexane. After two developments in this solvent system, two poorly resolved bands were apparent. The bands were eluted and the impure products were subjected to further purification as follows.

A band (R_f 0.63) afforded 90 mg (62%) of an off-white solid. This product was recrystallized twice from hexane and a third time from hexane–ethyl acetate to afford 9.7 mg of **18**: mp 132–133 °C; IR (KBr) 3.08, 6.10, 6.95 μm; NMR ($CDCl_3$) δ 1.15, 1.26 and 1.36 (three s, 9, C-5 and C-9 CH_3), 3.98 (m, 4, OCH_2CH_2O), 6.05 (s, 1, C-7 OH, exchanges with D_2O), 6.50 (s, 1, vinyl H); mass spectrum (70 eV) m/e (relative intensity) 226 (57, M^+), 251 (46), 151 (10), 112 (44), 85 (100); UV (CH_3OH) λ_{max} 267 nm (ε 8900). Anal. ($C_{15}H_{22}O_4$): C, H.

A band (R_f 0.54) afforded 50 mg of a yellow oil. This product was rechromatographed on a 20 × 20 cm Merck silica gel F254 analytical (0.25 mm thick) plate in 1:2 ethyl acetate–hexane. After two developments a band (R_f 0.43) was eluted to afford 1.2 mg of **19**: IR ($CHCl_3$) 2.92, 5.84, 5.97, 6.05 μm; NMR ($CDCl_3$) δ 1.21, 1.23 and 1.48 (three s, 9, C-5 and C-9 CH_3), 6.01 (s, 1, C-7 OH), 6.68 (s, 1, vinyl H); mass spectrum (70 eV) m/e (relative intensity) 222 (100, M^+), 211 (50), 165 (21), 148 (35), 124 (84).

1-Ethylenedioxy-7-hydroxy-5,5,9-trimethyl-*trans*-Δ^7-6-octalone (18) from the Oxidation of 15. The procedure of Mori, Gandhi, and Schwenk[13] was repeated by using 294 mg of **15** in 45 mL of 1 M potassium *tert*-butoxide in *tert*-butyl alcohol under 15 psi of oxygen in a Parr shaker for 2 h to afford 71 mg (23%) of **18** which had spectra identical with those of **18** prepared from the hydrolysis of **17a**.

5,5,9-Trimethyl-*trans*-1-decalone (1). A solution of 1.35 g (5.35 mmol) of **15**, 600 mg of hydrazine dihydrochloride, and 7 mL of hydrazine hydrate in 25 mL of anhydrous triethylene glycol was refluxed at 125 °C under a nitrogen atmosphere for 2.5 h. To this hot solution was added 2.0 g of potassium hydroxide. The hydrazine and water were removed by distillation, and the reaction was heated at 190 °C for 4 h. The solution was cooled, diluted with water, and extracted with hexane. The organic layers were combined and washed with water and brine and dried over anhydrous magnesium sulfate. The solvents were evaporated to afford 1.18 g of crude **16a**.

If desired, this product may be isolated and purified by preparative chromatography on Merck silica gel F254, using 1:24 ethyl acetate–hexane: IR ($CHCl_3$) 3.34, 6.85, 8.43 μm; NMR ($CDCl_3$) δ 0.83, 0.86 and 1.05 (three s, 9, C-5 and C-9 CH_3), 3.93 (m, 4, OCH_2CH_2O); mass spectrum (70 eV) m/e (relative intensity) 238 (15, M^+), 262 (6), 213 (8), 199 (100), 186 (18). Anal. ($C_{15}H_{26}O_2$): C, H.

A solution of 1.18 g of crude **16a** in 25 mL of 1:2:3 1 M hydrochloric acid–glacial acetic acid–THF was stirred for 4 h at 25 °C. The product was diluted with ether, washed successively with water, saturated sodium bicarbonate, and brine, and dried over anhydrous magnesium sulfate. The crude product (947 mg) was chromatographed on four 20 × 20 cm Merck silica gel F254 preparative-layer (2 mm thick) plates in 1:4 ethyl acetate–hexane.

A band (R_f 0.54) afforded 894 mg (86%) of **1**: IR (TF) 5.90 μm; NMR ($CDCl_3$) δ 0.91, 0.95 and 1.16 (three s, 9, C-5 and C-9 CH_3); mass spectrum (70 eV) m/e (relative intensity) 194 (84, M^+), 184 (61), 161 (55), 96 (91), 55 (100). Anal. ($C_{13}H_{22}O$): C, H.

6β-Hydroxy-5,5,9β-trimethyl-*trans*-1-decalone (2). To 6 mg (0.8 mmol) of lithium wire in 4 mL of anhydrous ammonia under a nitrogen atmosphere was added a solution of 100 mg (0.4 mmol) of **15** and 92 mg (2 mmol) of ethanol in 2 mL of anhydrous THF. The solution was stirred for 1.5 h during which time lithium wire was periodically added in order to maintain the blue color. Isoprene was then added to decompose the residual lithium, and the mixture was poured into saturated aqueous ammonium chloride. Extraction with ether, washing with brine, drying over anhydrous magnesium sulfate, and evaporation of the ethereal solvent produced 95 mg (95% crude) of 6β-alcohol **16b** (containing approximately 10% of the 6α epimer).[15] That the reduction was complete was confirmed by the absence of a carbonyl absorption in the IR spectrum. This crude mixture of alcohols was suitable for use in the next step.

However, if desired, **16b** could be isolated by careful recrystallization from pentane to furnish **16b** in 74% isolated yield. Further recrystallization produced an analytical sample: mp

106–106.5 °C; IR (TF) 2.90 μm (broad); NMR ($CDCl_3$) δ 0.78, 0.97, 1.03 (three s, 9, C-5 and C-9 CH_3), 3.25 (m, 1, C-6α H), 3.92 (m, 4, OCH_2CH_2O); mass spectrum (70 eV) *m/e* 254 (M^+), 99 (base), 86. Anal. ($C_{15}H_{26}O_3$): C, H; also by HRMS.

Crude **16b** (prepared above and containing *10% or less* of the 6α epimer) was used directly to prepare **2**. To a solution of 2 mL of 1:5:6 concentrated hydrochloric acid–water–tetrahydrofuran under a nitrogen atmosphere was added 28 mg (0.11 mmol) of **16b**. The solution was stirred for 30 min. Extraction with ether, washing successively with water and brine, drying over anhydrous magnesium sulfate, and evaporation of solvents gave 22 mg of crude **2** contaminated with small amounts of its 6α epimer. Recrystallization from hexane produced 19 mg (82%) of crystalline **2** as a single isomer, mp 72–73 °C, whose spectral data were identical with those of the known compound: lit.[6] mp 72–73 °C. In a similar run, purified **16b** was hydrolyzed to **2** which was isolated as a crystalline sample in 96% yield: IR ($CHCl_3$, 10% solution) 2.77, 2.85, 5.90 μm; NMR ($CDCl_3$) δ 0.91, 1.04, 1.16 (three s, 9, C-5 and C-9 CH_3), 3.22 (m, 1, C-6α H).

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Registry No. 1, 16776-05-9; **2**, 56985-41-2; **13**, 33760-61-1; **14a**, 70197-35-2; **14b**, 70197-36-3; **14c**, 69905-28-8; **15**, 70197-37-4; **16a**, 70197-38-5; **16b**, 70224-20-3; **17a**, 70197-39-6; **17b**, 70197-40-9; **18**, 70197-41-0; **19**, 70197-42-1; **16b** 6α-epimer, 70197-32-9.

Preparation of Benzocyclic [2.2.1] Azoxy Compounds

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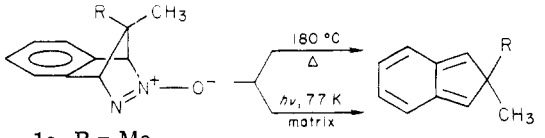
Benzobicyclic azoxy compounds, used as thermal and photochemical precursors of isoindenes, are synthesized from 2,2-dialkyl-1,3-indandiones via a four-step sequence in which the key step is a sequential hydrolysis–oxidation procedure in which the use of a vibromixer is absolutely essential.

Benzobicyclic azoxy compounds of the type 1, where R



1a, R = Me
b, R = Et
c, R = CH_2◁
d, R = *i*-Pr
e, R = CH_2Ph

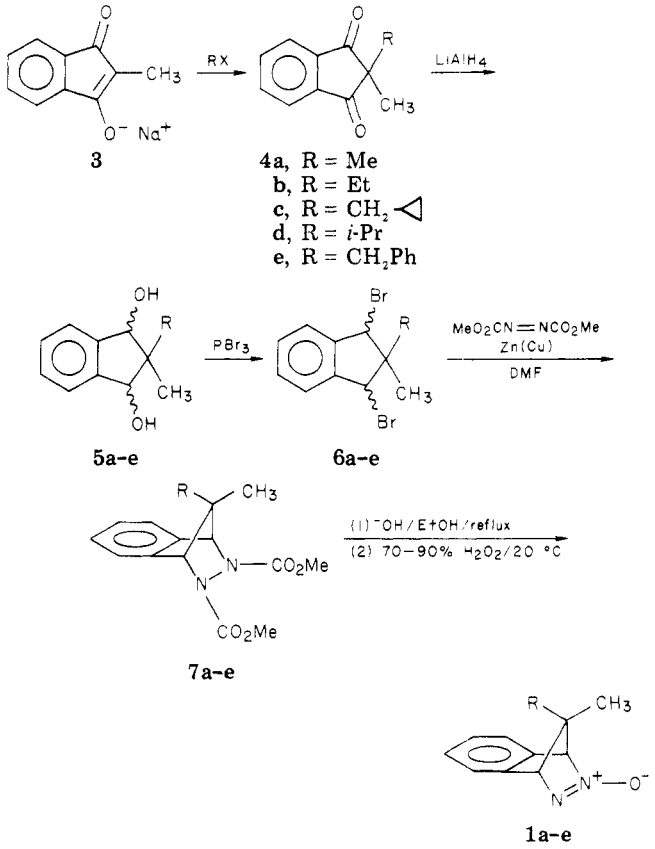
2a–e

= methyl, ethyl, cyclopropylcarbinyl, isopropyl, and benzyl, were required as thermal and/or photochemical precursors of the interesting series of isoindenes **2**.[1-3] The thermal stability of these azoxy compounds made them much more desirable precursors than the analogous azo compounds which should lose N_2 below room temperature.[4]

Snyder had previously prepared numerous cyclic, cis azoxy compounds by a combination hydrolysis–oxidation procedure.[5] Unfortunately, his method was not effective for the synthesis of the benzannelated series which we required. Our procedure is outlined in Scheme I.

Two features of our procedure proved to be *absolutely* essential for successful synthesis of the benzannelated azoxy compounds. First the vibromixer was found to be indispensable, particularly in the oxidation step where solubility of the organic species in the medium becomes a real problem.[6] Second, the oxidation procedure must,

Scheme I



in all cases, be carried out as a *separate* step and at a temperature not to exceed room temperature. The oxidation of the presumed hydrazine intermediate, **8**, is quite exothermic; hence the addition of H_2O_2 must be very slow.

The major side products of these oxidative procedures were the keto alcohols **9** which are probably formed via

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(2) W. R. Dolbier, Jr., K. Matsui, J. Michl, and D. V. Horak, *J. Am. Chem. Soc.*, **99**, 3876 (1977).
(3) W. R. Dolbier, Jr., K. E. Anapolle, K. Matsui, J. M. Riemann, L. McCullagh, and D. Rolison, *J. Org. Chem.*, accompanying paper.
(4) C. R. Flynn and J. Michl, *J. Am. Chem. Soc.*, **96**, 3280 (1974).
(5) J. P. Snyder, V. T. Bandurco, F. Darack, and H. Olsen, *J. Am. Chem. Soc.*, **96**, 5158 (1974), and references therein.
(6) The Vibromixer (Chemapec Inc., Hoboken, N.J., or Chemap Gmbh, Dusseldorf, West Germany) is an agitator, utilizing a vertical vibrating motion, which is particularly effective in dispersing heterogenous mixtures.

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