IR (neat) 1690, 1440, 1100–1250 (br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.1 (3 H, s), 6.15 (1 H, s), 7.3–8.1 (10 H, m); ^{13}C NMR ($CDCl_3$) δ 134.79, 133.30, 129.98, 129.77, 128.99, 128.74, 128.13, 70.1 (d), 59.5 (q); MS (70 eV), *m/e* 254, 178, 165, 121, 105, 77. Anal. Calcd for $C_{16}H_{14}SO$: C, 75.58; H, 5.55. Found: C, 74.22; H, 5.32. The spectral data for **4** (mp 86–89 °C) are reported below (^1H NMR and ^{13}C NMR data were collected at room temperature): UV (cyclohexane) λ_{max} 418 nm ($\epsilon \sim 600$), 314 (8300), 233 (14 000); IR ($CHCl_3$) 1600, 1460, 1320, 1220, 1100 cm^{-1}; ^1H NMR δ 3.2 (s), 3.3 (s), 3.6 (s), 4.0 (s), 7.0–7.4 (m) [singlets at δ 3.2 and 3.6 and δ 3.3 and 3.4 are of the same intensity]; ^{13}C NMR ($CDCl_3$) δ 216.37 (s), 216.05 (s), 159.55 (s), 156.43 (s), 138.17 (s), 137.25 (s), 135.07 (s), 133.29 (s), 130.3–126.98 (8 peaks), 58.62 (q), 58.38 (q), 58.18 (q), 58.06 (q); MS (70 eV), *m/e* 284, 151, 105, 77. Anal. Calcd for $C_{17}H_{16}SO_2$: C, 71.82; H, 5.67. Found: C, 71.55; H, 5.74.

Both ^{13}C and ^1H NMR spectra indicate the presence of two isomers at room temperature. However, attempts to separate these isomers using column (silica gel) and thin-layer (silica gel and alumina) chromatography were not successful. Therefore, it was thought that these are conformational and not geometrical isomers.

^1H NMR spectra were run at variable temperatures (−60–150 °C) in Me_2SO-d_6. Spectra remained unaltered in the temperature range −60–100 °C. However, broadening and coalesceing of four OCH_3 peaks (δ 3.2, 3.3, 3.6, 4.0) were observed in the range 100–120 °C and above 120 °C only two peaks (δ 3.2 and 3.8) corresponding to OCH_3 groups, expected for a single isomer of **4** was observed. No attempts were made to record ^{13}C NMR spectra at different temperatures. We suggest that **4** exists in solution at room temperature as noninterconvertible conformational isomers. Such hindrance for rotation around C–C single bonds carrying thiocarbonyl as opposed to carbonyl is known and can be attributed to the larger size of the sulfur atom.[9]

X-ray Analysis of 4. Slow evaporation of the benzene–chloroform solution of **4** gave platelike crystals: a = 8.729 (1) Å, b = 20.227 (3) Å, c = 9.523 (1) Å, β = 114.69 (1)°, V = 1527.7 Å^3, molecular formula $C_{17}H_{16}O_2S$, Z = 4, d_{measd} (flotation in aqueous KI) = 1.24 g/cm^3, d_{calcd} = 1.239 g/cm^3, space group $P2_1/n$. Intensity data were collected on a Enraf-Nonius CAD-4 diffractometer using monochromated Cu K_α radiation in $\omega/2\theta$ scan mode for a crystal of dimensions 1.0 × 0.8 × 0.3 mm^3. A total of 2510 reflections were collected out of which 2002 were significant [$|F_0| \geq 3\sigma(|F_0|)$]. The structure was solved by direct methods (MULTAN 80).[14] The full-matrix least-squares refinement of the positional and anisotropic thermal parameters of 20 non-hydrogen atoms and positional and isotropic thermal parameters of 16 hydrogen atoms (kept fixed in the final cycles) using the weigting scheme $w = 1/[\sigma^2(F) + 0.18|F|^2]$ has led to a final R value of 7.0% for significant reflections.

3. Oxidation of Diphenylcyclopropenethione. a. Direct Excitation. Diphenylcyclopropenethione (0.01 M) in chloroform, acetonitrile, or ethanol was irradiated (450-W mercury lamp or 500-W tungsten lamp) while nitrogen, without passing through alkaline pyrogallol, was bubbled through. After 48 h of irradiation, diphenylacetylene was isolated in 80% yield. The reaction was followed by TLC and the primary product was identified to be diphenylcyclopropenone. By an independent control experiment we showed that diphenylcyclopropeneone could be converted to diphenylacetylene in the above solvents with either of the above irradiations.[8] Surprisingly, formation of **2** was not detected under these conditions.

b. Dye Sensitization. Dye-sensitized irradiation of **1** was conducted by irradiating aerated solutions of **1** (0.01 M) in the presence of appropriate dyes (10^{-4} M, methylene blue, or 100 mg of polymer-bound rose bengal). Selective excitation of the dye was achieved with Corning glass filter CS-2.58. Diphenylcyclopropenone was the only isolated product (65%).

c. Singlet Oxygen Generated by the Decomposition of Triphenyl Phosphite Ozonide. Triphenyl phosphite ozonide was prepared at −78 °C in dichloromethane by following the reported procedure.[15] The above solution was warmed to −10 °C at which time oxygen evolution was visible and at this stage **1** was added. Upon keeping the reaction mixture at room temperature for about an hour, diphenylcyclopropenone was isolated as the only product (75%).

4. Control Experiments. Refluxing **1** in benzene and methanol for more than 24 h did not yield products **2–4**. **1** is stable under these conditions.

Diphenylcyclopropenone failed to react with singlet oxygen generated by dye sensitization or by thermal decomposition of triphenyl phosphite ozonide.

Acknowledgment. Department of Science and Technology, Government of India is thanked for financial support. S.S. and M.M.B. thank CSIR for research fellowships. We are especially indebted to Mr. V. Jayathertha Rao and Mrs. B. Sundari for experimental assistance at the initial stages of the project and to Professor J. A. Moore and referees for useful comments.

Registry No. 1, 2570-01-6; 2, 35093-32-4; 3, 82246-85-3; (*E*)-4, 82246-86-4; oxygen, 7782-44-7.

Supplementary Material Available: Atomic coordinate and thermal parameter tables for **4** (6 pages). Ordering information is given on any current masthead page.

(14) Main, P. (1980) MULTAN 80 system of computer programs for the automatic solutions of crystal structures from X-ray diffraction data. Department of Physics, University of York, York, England.

(15) Murray, R. W.; Kaplan, M. L. *J. Am. Chem. Soc.* **1969**, *91*, 5358.

Reactions of Alkoxypyrylium Salts with Dimethylsulfonium Methylide and Nitromethane Anion

Michael E. Garst* and Janice D. Frazier

Department of Chemistry, D-006, University of California, San Diego, La Jolla, California 92093

Received February 16, 1982

The nucleophilic reactions of certain pyrylium salts have been studied in detail and are the subject of extensive reviews.[1] Apparently, 2- or 4-alkoxypyrylium salts have not been examined in this context. These salts, prepared by the O-alkylation of common pyrones,[2,3] would yield specific polysubstituted benzenes when treated with a heteroatom-stabilized nucleophile. Few alternative methods permit construction of benzene rings, containing several substituents, from nonbenzenoid precursors.[4] In this note, we report that the reaction of four pyrylium salts with dimethylsulfonium methylide[5] and with the anion of nitromethane does yield benzenoids.

The reactions of pyrylium salts with ylides have been the subject of four brief reports. 2,4,6-Triphenylpyrylium perchlorate (**15**) with triphenylphosphonium methylide[6] and **5** with a carboalkoxyphosphonate[7] provided the expected benzene derivatives. The two reports of sulfur ylide reactions describe unprecedented ylide products. Tamura[8]

(1) (a) Dimroth, K.; Wolf, K. H. In "New Methods of Preparative Organic Chemistry"; Foerst, W., Ed.; Springer-Verlag: New York, 1964; Vol. III, pp 357–423. (b) Balaban, A. T.; Schroth, W.; Fischer, G. *Adv. Heterocycl. Chem.* **1969**, *10*, 241–326. (c) Balaban, A. T. In "New Trends in Heterocyclic Chemistry"; Mitra, R. B.; Ayyangar, N. R.; Gogte, V. N.; Acheson, R. M.; Cromwell, N., Eds.; Elsevier: New York, 1979, pp 79–111.

(2) Beak, P.; Lee, J.-K. *J. Org. Chem.* **1975**, *40*, 147–148.

(3) (a) Meerwein, H.; Hinz, G.; Hoffman, P.; Kroning, E.; Pfeil, E. *J. Prakt. Chem.* **1936**, *147*, 257. (b) Fisher, B. E.; Hodge, J. E. *J. Org. Chem.* **1964**, *29*, 776–781.

(4) (a) For Diels–Alder reactions, see Danishefsky, S. *Acc. Chem. Res.* **1981**, *14*, 400–406, and Bryson, T. A.; Donelson, D. M. *J. Org. Chem.* **1977**, *42*, 2930–2931. (b) For annulations, see Boger, D. L.; Mullican, M. D. *J. Org. Chem.* **1980**, *45*, 5002–5004.

(5) For a preliminary communication of the formation of **3**, **4**, **6**, and **7**, see Garst, M. E.; Frazier, J. D. *Heterocycles* **1981**, *16*, 17–19.

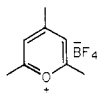
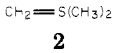
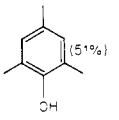
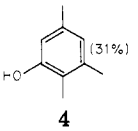
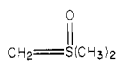
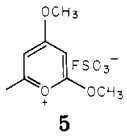
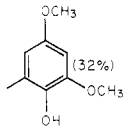
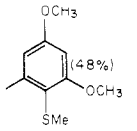
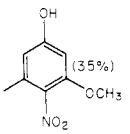
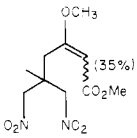
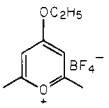
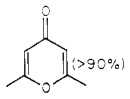
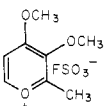
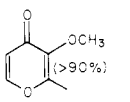
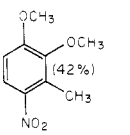
(6) Markel, G. *Angew. Chem.* **1962**, *74*, 696.

(7) Griffin, D. A.; Staunton, J. *J. Chem. Soc., Chem. Commun.* **1975**, 675–676.

(8) Tamura, Y.; Sumoto, K.; Ikeda, M. *Chem. Ind. (London)* **1972**, 498–499.

0022-3263/82/1947-3553$01.25/0

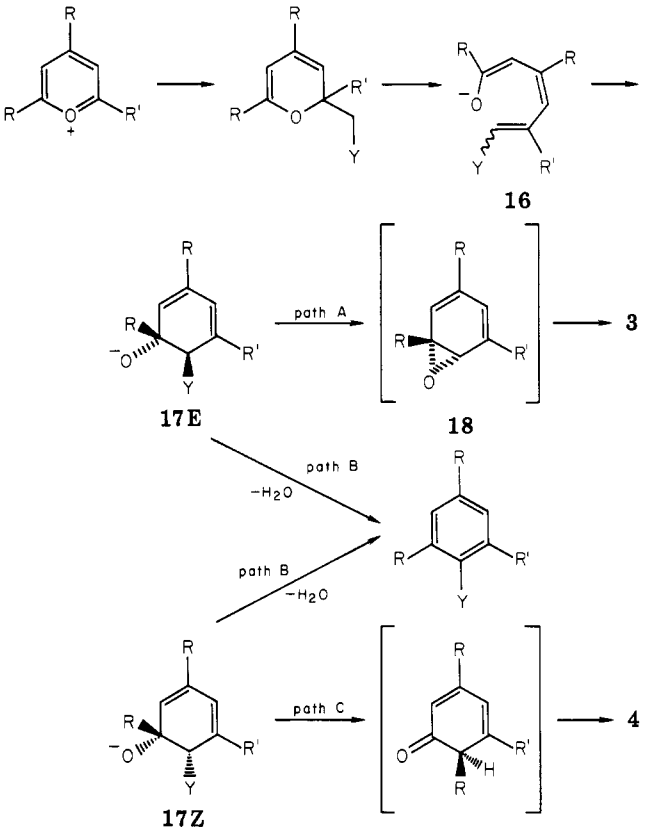
Table I

pyrylium salt	anion	product (yield)
 1	 2	 3 (51%);  4 (31%)
1	 2	4 (80%)
 5	2	 6 (32%);  7 (48%)
5	$^-CH_2NO_2$	 8 (35%);  9 (35%)
 10	2	 11 (>90%)
 12	2	 13 (>90%)
12	$^-CH_2NO_2$	 14 (42%)

reported that 2,4,6-triphenylpyrylium perchlorate and dimethylsulfoxonium methylide yielded 1,3,5-triphenylbenzene, a reaction requiring the oxidative elimination of methyl sulfone.[9] Katritzky[10] observed that triarylpyrylium salts and phenylmethylsulfonium phenacylides provided furyl chalcones, the structure of which was established by X-ray crystallography. Mechanistic rationale for the formation of these chalcones remains to be clarified. Although the Dimroth group[11] has examined the reaction of triarylpyrylium salts with nitromethane, 4-alkoxy-2,6-dimethylpyrylium salts are the only alkoxy salts previously reported to undergo addition of nitromethane.[12]

Our results with four crystalline pyrylium salts are summarized in Table I.[13,14] In all instances, the product structures were apparent from the usual spectral data and in many cases were confirmed by comparison with an authentic aromatic sample. The relationship of the substituents on phenols **6** and **8** was established by examination of the NMR spectra of the corresponding acetates. The constitution of the only nonaromatic product (**9**) was apparent from the ^1H and ^{13}C NMR data. In order for us to establish the relationships **6** and **7**, this mixture was treated with ceric ammonium nitrate[15] to provide only 2-methoxy-6-methylbenzoquinone in 80% yield.

Scheme I



From the data in Table I, conclusions about the mechanism and generality of the reactions of alkoxypyrylium salts with nucleophiles can be drawn. A single mechanistic scheme accounts for this range of products (Scheme I). Initial nucleophilic addition at the 2-position of the pyrylium salt is followed by a base-catalyzed elimination reaction, yielding a conjugated keto ylide or nitroanion (**16**). Cyclization of the resulting triene anion **16** via a nucleophilic addition or a [3,3]sigmatropic reaction affords an alkoxide anion **17**. Three reaction pathways are possible for anion **17**. When Y = NO_2, dehydration occurs, regardless of the stereochemistry, to provide the observed nitrobenzene (path A). When Y = SMe_2^+, the (*E*)-betaine can close to arene oxide **18**, which after the expected NIH shift would provide phenols (path A). The process is illustrated by the isolation of phenols **3** and **6**. We failed to isolate or trap (added mercaptide or *N*-phenyl-1,3,4-triazene-2,5-dione) the known, albeit unstable, arene oxide **18** (R = R′ = CH_3).[16] Betaine **17Z** cannot close to an epoxide. When the appendages are methyl groups and Y = SMe_2^+, a carbonium ion migration affords the phenol **4** (path C). When a better leaving group is present (Y = $SO(CH_3)_2^+$), this rearrangement pathway C predominates

(9) We have repeated the reaction of **15** with dimethylsulfoxonium methylide. Analysis of the crude reaction product by MS using direct inlet with temperature programming for sample introduction indicated $C_{24}H_{18}O$ and $C_{24}H_{18}$ in a 1:5 ratio. Treatment of **15** with **2** provided only $C_{24}H_{18}O$. In both instances, these $C_{24}H_{18}O$ products were phenolic (IR 3600 cm^{-1}) but a mixture of isomers.

(10) Katritzky, A. R.; Rizvi, S. Q. A.; Suwinski, J. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2489–2492.

(11) Dimroth, K.; Laubert, G. *Angew. Chem.* **1969**, *81*, 392–393.

(12) (a) Ohta, M.; Kato, H. *Bull. Chem. Soc. Jpn.* **1959**, *32*, 707–710. (b) Dimroth, K. *Angew. Chem.* **1960**, *72*, 331–358.

(13) 2,3-Dimethoxypyrylium fluoborate and 2,4-dimethoxy-6-pentylpyrylium fluorosulfate were prepared and determined to be homogeneous by NMR spectroscopy but were not crystalline. Treatment of these viscous oils with **2** or nitromethane anion under a variety of conditions afforded mixtures containing only traces of aromatic material or pyrones.

(14) Alkoxy salts **5**, **10**, and **12** also yielded complex mixtures when treated with dimethylsulfoxonium methylide in Me_2SO solvent.

(15) Jacob, P.; Callery, P. S.; Shulgin, A. T.; Castagnoli, N. *J. Org. Chem.* **1976**, *41*, 3627–3629.

(16) Kaubisch, N.; Daly, J. W.; Jerina, D. M. *Biochemistry* **1972**, *11*, 3080–3088.

over path B to afford only 4. Newman[17] observed path A–B competition in an analogous betaine. The alkoxy moieties (R, R') in 17 inductively destabilize the carbonium intermediate, favoring path B over path C. Unfortunately, the failure of 12 to undergo addition with 2 precludes accurate determination of the resonance vs. inductive effects of the alkoxy groups on this reaction. The anion from nitromethane apparently adds to both the 2- and the 6-positions but not to the 4-position, regardless of the electrophilicity of that position. When an ester is generated after elimination (16, R = OCH_3; Y = NO_2), dehydration and a second addition competes with cyclization.[18]

The reactions of alkoxypyrylium salts with nucleophiles have severe requirements. The 2-position of the pyrylium salt must be at least as electrophilic as the 4-position for addition of sulfur ylides. Even when the α-position is unhindered yet less electrophilic, as in 12, ylide 2 provides dealkylation. Furthermore, for reactions with 2 pyrylium salt must be exceptionally pure; even trace impurities inhibit this process. Nitromethane anion yields aromatics from 4-alkoxypyrylium salts by net replacement of the pyrylium oxygen by a carbon containing a nitro group. 2-Alkoxypyrylium salts give additional products with this anion. The reactions of alkoxypyrylium salts with these nucleophiles may find use in benzene and quinone syntheses.

Experimental Section

The general experimental and instrumental techniques have been reported previously.[19] The GC column used was 6 ft × 0.25 in., containing 3% DEXIL 300 on Supelcoport and programmed at an initial temperature of 110 °C for 2 min following injection and then increased by 20 °C per minute until 280 °C. Retention times are the time after the appearance of ether solvent.

2,4,6-Trimethylphenol (3) and 2,3,5-Trimethylphenol (4). To a suspension of 1.08 g (6.35 mmol) of trimethylsulfonium fluoborate in 10 mL of THF at −20 °C was added 3.60 mL (6.35 mmol) of *n*-butyllithium.[20] This suspension became homogeneous over 15 min, was cooled to −78 °C, and stirred for 30 min. We added 2,4,6-trimethylpyrylium fluoborate[21] (0.81 g, 3.18 mmol) in one batch using a solid addition funnel. This suspension gradually became homogeneous. After 5 h at −78 °C, the solution was quenched with an equal volume of 10% aqueous HCl. This solution was washed with CH_2Cl_2 (3 × 20 mL), and the pooled CH_2Cl_2 layers were dried over $MgSO_4$ and filtered. We removed the solvent at ambient temperature and 2.7 kPa using a Buchi rotary evaporator to provide 0.35 g (82%) of 3 and 4 in a 62:38 ratio. Compounds 3 and 4 exhibited NMR, MS, and GC data, which was identical with authentic samples.[22]

2,3,5-Trimethylphenol (4). A solution of 2.3 mmol of dimethylsulfoxonium methylide in Me_2SO/THF was prepared according to Corey and Chaykovsky[23] and cooled to −5 °C. Pyrylium salt 1 (0.24 g, 1.2 mmol) was added in one batch. The solution was stirred at −5 °C for 1 h and then at room temperature for 7 h. Processing as above afforded 0.15 g (80%) of 4.

2,4-Dimethoxy-6-methylphenol (6) and 2,4-Dimethoxy-6-methylthioanisole (7). From 6.4 mmol of 2 and 0.81 g (3.2 mmol) of 5[7] there was obtained 1.0 g of solid. Preparative layer chromatography on silica gel (hexane/EtOAc, 4:1) afforded analytical samples: 4-methoxy-6-methyl-2-pyrone, 20% yield by GC (t_R = 7.5 min); 15% isolated yield. 6:[23] 32% yield GC (t_R = 7.1 min); 25% isolated; IR 3600 (br d) cm^{-1}; NMR δ 2.27 (s, 3 H), 3.72 (s, 3 H), 3.82 (s, 3 H), 6.25 (d, J = 2 Hz, 1 H), 6.32 (d, J = 2 Hz, 1 H); mass spectrum (70 eV) m/z 168 (M^+). 7: 48% yield by GC (t_R 9.7 min); 20% isolated yield; IR 2900, 1580, 1450, 1315, 1190, 1150, 1080, 800 cm^{-1}; NMR δ 2.25 (s, 3 H), 2.50 (s, 3 H), 3.80 (s, 3 H), 3.90 (s, 3 H), 6.30 (d, J = 2 Hz, 1 H), 6.40 (d, J = 2 Hz, 1 H); mass spectrum (70 eV), m/z 198 (M^+), 181, 109, 97, 83, 82, 81; HRMS, m/z observed 198.0726, $C_{10}H_{14}O_2S$ requires 198.0714.

Methylation (dimethyl sulfate, K_2CO_3, H_2O) or acetylation (acetic anhydride, potassium acetate) of 6 yielded the expected derivatives. Methyl ether of 6: NMR (partial spectrum) δ 6.2 (d, J = 2 Hz, 1 H) and 6.3 (d, J = 2 Hz, 1 H); mass spectrum (70 eV), m/z 182 (M^+). Acetate of 6: NMR δ 2.1 (s, 3 H), 2.3 (s, 3 H), 3.7 (s, 3 H), 3.8 (s, 3 H), 6.2 (d, J = 2 Hz, 1 H), 6.3 (d, J = 2 Hz, 1 H); mass spectrum (70 eV), m/z 210 (M^+).

Treatment of a crude sample of 6 and 7 with ceric ammonium nitrate according to the procedure of Castagnoli[15] gave 2-methoxy-5-methylbenzoquinone[25] in 80% yield: IR 3360, 2940, 1700, 1670, 1650, 1600 cm^{-1}; NMR δ 2.0 (s, 3 H), 3.8 (s, 3 H), 5.9 (d, J = 2 Hz, 1 H), 6.5 (d, J = 2 Hz, 1 H); MS (70 eV), m/z 152 (M^+), 124, 122, 109, 69 (100), 68, 66, 53, 40.

3-Methoxy-5-methyl-4-nitrophenol (8) and Methyl 3-Methoxy-5-methyl-5-(nitromethyl)-6-nitro-2-hexenoate (9). According to the Ohta[12] procedure, a solution of potassium *tert*-butoxide, prepared from 0.030 g (0.767 mmol) of potassium in 2.0 mL of *tert*-butyl alcohol, was treated with 0.80 mL of nitromethane, followed by 0.100 g (0.394 mmol) of 5. This solution was refluxed for 4 h, cooled, and processed as before to afford 0.065 g (71%) of 8 and 9 in a 1:1 ratio. Analytical samples were obtained by chromatography on silica gel (hexane/EtOAc, 7:3). 8:[26] R_f 0.49; mp 96–98 °C; IR 3340, 2920, 1610, 1590, 1460, 1290, 1190, 1170, 875 cm^{-1}; NMR (360 MHz) δ 2.62 (s, 3 H), 3.85 (s, 3 H), 6.37 (d, J = 2.8 Hz, 1 H), 6.43 (d, J = 2.8 Hz, 1 H); mass spectrum (70 eV), m/z 183 (M^+), 166, 153, 136, 125, 111, 106, 94, 77, 65, 59 and 51. 9: R_f 0.35; IR 2920, 1690, 1610, 1540, 1410, 1360 cm^{-1}; NMR (at 360 MHz) δ 1.20 (s, 3 H), 3.12 (s, 2 H), 3.66 (s, 3 H), 3.69 (s, 3 H), 4.66 (d, J = 13 Hz, 2 H), 4.77 (d, J = 13 Hz, 2 H), 5.21 (s, 1 H); ^{13}C NMR δ 169.3 (s), 167.5 (s), 94.7 (d), 79.8 (t), 79.8 (t), 55.5 (q), 51.1 (q), 38.2 (s), 36.3 (t), 20.7 (q); mass spectrum (70 eV), m/z 245, 217, 198, 183, 169, 155, 145, 123, 113 (100), 109, 98, 91, 69, 59, 55; HRMS observed, m/z 245.076998; $C_9H_{13}N_2O_6$ ($M^+ - OCH_3$) requires 245.0754.

From 0.020 g (0.1 mmol) of 8, 0.10 mL of acetic anhydride, and 0.90 g of potassium acetate there was obtained 0.014 g of the acetate: NMR δ 2.3 (s, 3 H), 2.4 (s, 3 H), 3.85 (s, 3 H), 6.55 (d, J = 2 Hz, 1 H), 6.65 (d, J = 2 Hz, 1 H).

Reaction of 10 and 12 with 2. According to the above procedure, reaction of 10[3a] and 12[3b] with 2 provided only the starting pyrones 11[22] and 13, respectively. 13: alumina TLC (hexane/EtOAc, 4:1) R_f 0.5; NMR δ 2.30 (s, 3 H), 3.80 (s, 3 H), 6.30 (d, J = 6 Hz, 1 H), 7.55 (d, J = 6 Hz, 1 H); mass spectrum (70 eV), m/z 140 (M^+).

1,2-Dimethoxy-3-methyl-4-nitrobenzene (14). Accordingly, a solution of 0.15 g (6.3 mmol) of sodium, 4 mL of nitromethane, and 12 mL of *tert*-butyl alcohol was refluxed for 3 h, treated with 1.2 mmol of 12, and refluxed again for 4 h to give 0.10 g (42%) of 14, accompanied by 13. Thick-layer chromatography on alumina (hexane/EtOAc, 4:1) afforded an analytical sample of 14: R_f 0.66; IR 2910, 1700, 1590, 1560, 1490, 1460, 1330, 1260, 1210, 1070, 800, 790 cm^{-1}; NMR δ 2.50 (s, 3 H), 3.80 (s, 3 H), 3.90 (s, 3 H), 6.75 (d, J = 8 Hz, 1 H), 7.70 (d, J = 8 Hz, 1 H); mass spectrum (70 eV), m/z 197 (M^+), 180 (100), 152, 136, 121, 106, 93, 77, 65, 59, 51; HRMS observed, m/z 197.068792; $C_9H_{11}NO_4$ requires 197.0686.

Acknowledgment. We are grateful to the Cancer Research Coordinating Committee for partial support and to the NIH (Shared Instrument Grant GM 27583) for purchase of the mass spectrometer.

Registry No. 1, 773-01-3; 2, 40651-06-7; 3, 527-60-6; 4, 697-82-5; 5, 52911-90-7; 6, 53887-78-8; 6 methyl ether, 38790-14-6; 6 acetate,

(17) Newman, M. S.; Lee, L.-F. *J. Org. Chem.* **1974**, *39*, 1446.
(18) 4-Methoxy-6-methyl-2-pyrone is stable under these conditions.
(19) Garst, M. E.; Bonfiglio, J. N.; Grudoski, D. A.; Marks, J. *J. Org. Chem.* **1979**, *45*, 2307–2315.
(20) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353–1364.
(21) Balaban, A. T.; Boulton, A. J. In "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. V, pp 1112–1113.
(22) Purchased from the Aldrich Chemical Co.
(23) Corey, E. J.; Chaykovsky, M. In ref 21; pp 755–757.
(24) Späth, E.; Pailer, M.; Gergely, G. *Chem. Ber.* **1940**, *73*, 795–804.
(25) Singh, J. M.; Turner, A. B. *J. Chem. Soc., Perkin Trans. 1* **1974**, 2556–2559.
(26) Henrich, F.; Nachtigall, G. *Chem. Ber.* **1903**, *36*, 889–895.

53547-97-0; 7, 77635-33-7; 8, 82209-16-3; 8 acetate, 82209-18-5; 9, 82228-57-7; 10, 457-23-8; 11, 1004-36-0; 12, 82209-15-2; 13, 4780-14-7; 14, 82209-17-4; nitromethane, 75-52-5; 2-methoxy-5-methylbenzoquinone, 614-13-1.

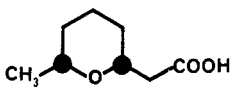
Stereospecific Synthesis of Racemic (*cis*-6-Methyltetrahydropyran-2-yl)acetic Acid, a Constituent of the Glandular Secretion from the Civet Cat

Youseung Kim and Bradford P. Mundy*

Department of Chemistry, Montana State University, Bozeman, Montana 59717

Received April 20, 1982

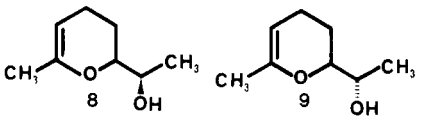
The glandular secretion of the civet cat (*Viverra civetta*) is known as civet and is one of the few animal-derived perfume materials. A recent examination of the constituents of civet[1] resulted in the isolation of a minor component (2 mg from 1 kg) whose constitution was determined by spectral[1] and synthetic means[2] to be **1**. We now report a new, simple, stereospecific synthesis of this natural product.



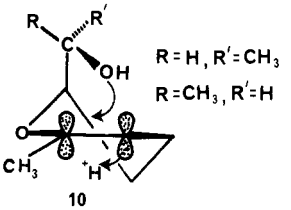
1

Our approach was based on the observations that (a) the 6,8-dioxabicyclo[3.2.1]octane system is reductively cleaved to form a pyran[3] and that (b) *cis*-2,6-disubstituted pyrans are thermodynamically more stable than the trans isomers.[2b] Also, as a consequence of our interest in insect pheromones having the 6,8-dioxabicyclo[3.2.1]octane skeleton,[4] we had experience with these systems as well as a supply of starting material. The overall synthetic route is outlined in Scheme I.

Dimerization of methyl vinyl ketone gave the well-characterized product **3**.[5] Sodium borohydride reduction of **3** resulted in a 50:50 mixture of the threo and erythro isomers **8** and **9**, respectively. Although the direction of

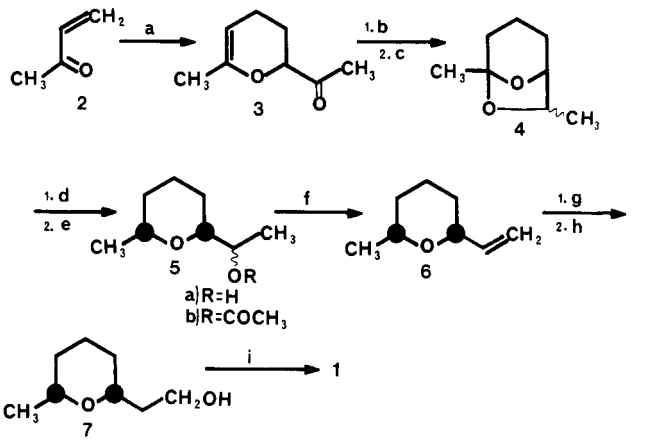


hydride delivery *does* determine the threo–erythro relationships of the alcohols and is in turn reflected in the exo–endo ratios of **4** (via **10**), these effects are not essential



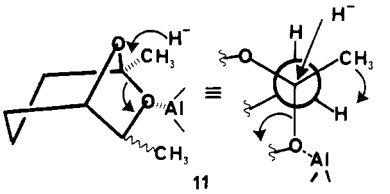
10

Scheme I. Synthesis of a Component of Civet[a]



[a] (a) 185 °C, 2 h; (b) $NaBH_4$/*i*-PrOH; (c) $TsOH/C_6H_6$; (d) AlH_3; (e) AcCl/Pyd; (f) 450 °C, N_2; (g) B_2H_6; (h) H_2O_2/OH^-; (i) CrO_3/H_2SO_4 or PDC.

to the success of our approach. Reduction of **4** with H_2–Pd/C gave a mixture of reduction products **5**; however, the differential reactivity of the two isomers of **4** toward reduction[3] resulted in difficulty in achieving high yields. This was easily circumvented by use of AlH_3. The formation of cis stereochemistry by this procedure is readily rationalized by considering an intermediate aluminum complex and S_N2 hydride displacement **11**.[6]



11

With the required cis stereochemistry established, the only requirement in order to complete the synthesis was to effect hydroxyl group transposition from **5a** to **7**. This was achieved by pyrolysis of the acetate ester, followed by hydroboration of the resulting alkene, to give **7**. Other elimination reactions (the tosylate in Me_2SO, the hydrazone in sodium glycolate, and xanthate pyrolysis) were attempted; however, none were as effective. Oxidation of **7** with Jones reagent or PDC gave **1**.

The product, a crystalline material (mp 48–51 °C), exhibited spectral characteristics consistent with the assigned structure and in agreement with the literature data. No trace of the trans isomer, reported[1] to be a liquid, could be found.

Experimental Section

The preparations of **3** and **4** have been previously reported.

Preparation of 1-(*cis*-6-Methyltetrahydropyran-2-yl)-ethanol (5a). To a gray solution of $AlCl_3$ (107.8 g, 0.808 mol) in 250 mL of anhydrous Et_2O was added dropwise LAH (7.7 g, 0.202 mol) in 100 mL of anhydrous Et_2O in an ice bath under N_2. Swirling with ether was repeated several times until all the hydride was added and the gray slurry was stirred for 1 h.

A solution of ketal **4** (57.4 g, 0.404 mol) in 100 mL of anhydrous Et_2O was added at a rate sufficient for gentle refluxing. The mixture was refluxed for 3 h. Excess hydride was destroyed by the dropwise addition of ca. 10 mL of water, followed by 2 N

(1) Maurer, B.; Grieder, A.; Thommen, W. *Helv. Chim. Acta* **1979**, *62*, 44, 1096.
(2) (a) See ref 1. (b) Seebach, D.; Pohmakotr, M. *Helv. Chim. Acta* **1979**, *62*, 843.
(3) Lipkowitz, K. B.; Mundy, B. P.; Matsko, T. H. *J. Org. Chem.* **1976**, *41*, 371.
(4) Mundy, B. P.; Lipkowitz, K. B.; Dirks, G. W. *Heterocycles* **1977**, *6*, 51.
(5) Mundy, B. P.; Lipkowitz, K. B.; Dirks, G. W. *Synth. Commun.* **1975**, *5*, 7.
(6) (a) Colonge, J.; Buendia, J.; Guignard, H. *Bull. Soc. Chem. Fr.* **1969**, 956. (b) In their discussions on the relationships of erythro alcohol → ketal and threo alcohol → ketal, no direct comments could be made on the resulting stereochemistry after carbon–oxygen bond cleavage, since the compounds utilized in the study were not substituted at C-5.

0022-3263/82/1947-3556$01.25/0