compound **11a** as a foul-smelling light yellow oil in almost quantitative yield: ^{13}C NMR ($CDCl_3$, Me_4Si) δ 8.57, 13.16, 18.45, 127.51, 142.39; ^1H NMR ($CDCl_3$, Me_4Si) δ 1.82 (s, 3 H), 3.91 (s, 4 H), 5.55 (s, 1 H).

3,4-Dimethyl-2,5-dihydrotellurophene 1,1-Dichloride (8b). 2,3-Dimethyl-1,3-butadiene (2.4 g, 29.3 mmol) was added at room temperature to a suspension of $TeCl_4$ (2.0 g, 7.4 mmol) in acetonitrile (60 mL) and stirred for 30 min when the temperature was slowly raised to reflux. The solution gradually darkened, and after 3 h of reflux it was filtered from a small amount of elemental tellurium and evaporated to give a semisolid which could be crystallized from acetonitrile. The yield of compound **8b** was 1.1 g, 53%: mp 215-216 °C dec; mass spectrum *m/e* (relative intensity, only peaks stronger than 30% of the base peak above *m/e* 100) 260 (34), 258 (63), 256 (63), 254 (45), 212 (38), 210 (39), 147 (39), 145 (37), 138 (74), 136 (100), 134 (84), 130 (34), 122 (37), 121 (66), 119 (53), 109 (34), 107 (66), 105 (50); IR (KBr) 2980 (w), 2960 (w), 2920 (w), 2910 (w), 1655 (m), 1430 (m), 1385 (s), 1375 (m), 1365 (m), 1120 (w), 1110 (w), 985 (w), 900 (w), 780 (s); ^1H NMR ($CDCl_3$, Me_4Si) δ 1.9 (s, 6 H), 4.3 (s, 4 H). Anal. ($C_6H_{10}Cl_2Te$) C, H.

3,4-Dimethyl-2,5-dihydrotellurophene (11b). 3,4-Dimethyl-2,5-dihydrotellurophene 1,1-dichloride was shaken thoroughly with a mixture of ethyl ether and excess $Na_2S{\cdot}9H_2O$ (5% aqueous) until all material had dissolved. Drying ($CaCl_2$) and evaporation of the organic phase yielded compound **11b** as a foul-smelling light yellow oil in almost quantitative yield: ^1H NMR ($CDCl_3$, Me_4Si) δ 1.6 (s, 6 H), 4.0 (s, 4 H).

Preparation of Diaryltellurides from 2,5-Dihydrotellurophene 1,1-Dichloride (4). General Procedure. 2,5-Dihydrotellurophene 1,1-dichoride (0.50 g, 1.98 mmol) was added at room temperature to a stirred ether solution (50 mL) of *a* millimole of the appropriate Grignard reagent. A slow gas evolution could immediately be observed, and the stirring was continued for another hour at room temperature when the reaction mixture was poured into a saturated solution of NH_4Cl (50 mL). The organic phase was separated and the aqueous phase extracted once with ethyl ether (50 mL). The combined ether extracts were washed with water, dried ($CaCl_2$), and evaporated to yield an oil or a semisolid of the corresponding diaryltelluride. The following diaryltellurides were prepared according to the general procedure.

Diphenyl Telluride (*a* = 6.4 mmol): yield 0.04 g (70%). The compound is an oil and was isolated as diphenyltellurium dichloride by treatment with Cl_2 gas in CCl_4 (10 mL) at room temperature; mp 159-160 °C (lit.[21] 159 °C).

Bis(4-methylphenyl) Telluride (*a* = 4.09 mmol): yield 0.54 g (88%); mp 66 ° (lit.[22] 69-70 °C).

Di-2-thienyl telluride was prepared according to the general procedure except that 2-thiethyllithium was employed instead of the Grignard reagent and that the reaction mixture was refluxed 30 min after addition of the tellurium dichloride **4** (*a* = 5.3 mmol): yield 0.46 g (79%); mp 49-50 °C (lit.[23] 50.5 °C).

Reaction of 2,5-Dihydrotellurophene with H_2O_2. H_2O_2 (35% aqueous, 0.20 g, 2.05 mmol) was added dropwise to a stirred solution of 2,5-dihydrotellurophene (0.36 g, 1.98 mmol) in THF (15 mL) at 0 °C. The white precipitate that immediately separated was filtered off and dried, but the material exploded violently upon attempted weighing.

In another identical experiment it was found that the precipitate could be dissolved by addition of $NaHCO_3$ (5% aqueous, 50 mL) to the THF suspension. Neutralization of this solution with HCl (2 M aqueous) followed by several extractions with CH_2Cl_2 afforded 2,5-dihydrotellurophene 1,1-dichloride (**4**) 0.20 g (40%), identical with the compound described above. When H_2SO_4 (2 M, aqueous) was used instead of HCl in the neutralization, no organic material could be extracted from the aqueous phase.

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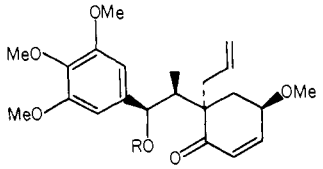
The Synthesis of Megaphone

George Büchi* and Ping-Sun Chu

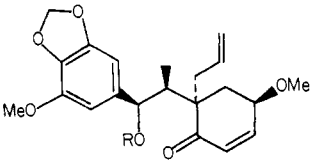
Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts, 02139. *Received October 20, 1980*

Abstract: Condensation of 4,4,5-trimethoxy-2-[3-[(methylsulfonyl)oxy]propyl]-2,5-cyclohexadien-1-one (**7**) with 1,2,3-trimethoxy-5-(1-(*Z*)-propenyl)benzene in dichloromethane, in the presence of 1 equiv of stannic chloride, gave (2β,3β,3aα)-3,3a-dihydro-5-methoxy-3-methyl-3a-[3-[(methylsulfonyl)oxy]propyl]-2-(3,4,5-trimethoxyphenyl)-6-(2*H*)-benzofuranone (**6**). Subsequent regio- and stereoselective hydrogenation of the 4,5 double bond with 5% Rh on carbon gave a single dihydro derivative **5**. Elimination of methanesulfonic acid with the use of Sharpless' method followed by reduction of the carbonyl group and rearrangement gave racemic megaphone (**1**) characterized by its naturally occurring acetate (**2**).

In the course of an extensive search for antitumor agents among plant metabolites the late S. M. Kupchan and his co-workers isolated megaphone (**1**), megaphone acetate (**2**), and megaphyllone



1, R = H
2, R = $COCH_3$



3

(**3**) from an alcoholic extract of *Aniba megaphylla Mez*, (*Lauraceae*).[1] These neolignans[2] exhibit "inhibitory activity, in vitro, against cells derived from human carcinoma of the nasopharynx (KB)".[3] Both gross structure and stereochemistry of megaphone (**1**) were deduced tentatively from chemical and spectroscopic data. An X-ray crystallographic analysis confirmed the conclusions reached and established the molecular conformation, as well as the absolute stereochemistry. The first total synthesis of megaphone (**1**) and its acetate (**2**) is described in this paper.

Retrosynthetic analysis suggested that megaphone (**1**) could be synthesized by reduction of the vinylogous ester **4**, which in turn could be prepared from mesylate **5**. The latter should be available from the selective hydrogenation of the cyclohexadienone **6** which might result from an acid-catalyzed condensation of the *p*-benzoquinone ketal **7** with 1,2,3-trimethoxy-5-(1-(*Z*)-propenyl)benzene.[4,5] This approach (Scheme I) appeared at-

(1) Kupchan, S. M.; Stevens, K. L.; Rohlfing, E. A.; Sickles, B. R.; Sneden, A. T.; Miller, R. W.; Bryan, F. R. *J. Org. Chem.* **1978**, *43*, 586-590.

(2) Review: Gottlieb, O. R. In "Progress in the Chemistry of Organic Natural Products"; Herz, W.; Grisebach, H.; Kirby, G. W., Eds.; Springer-Verlag/Wien: Austria, 1978, Vol. 35, pp 1-72.

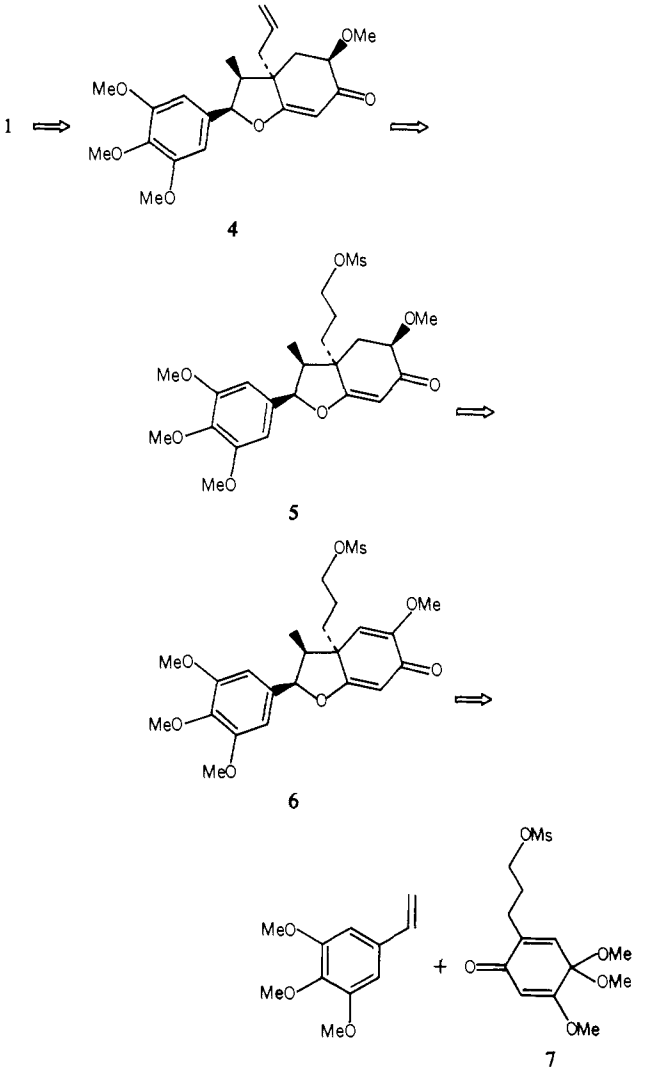
(3) The KB activity was assayed under the auspices of the National Cancer Institute. **1**, **2**, and **3** showed cytotoxicity against KB cell culture at 1.70, 1.75, and 2.55 μg/mL, respectively.

(4) Büchi, G.; Mak, C.-P. *J. Am. Chem. Soc.* **1977**, *99*, 8073-8075.

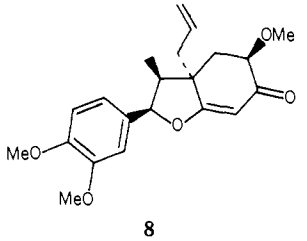
(5) Mak, C.-P. Ph.D. Dissertation, Massachusetts Institute of Technology, 1978.

0002-7863/81/1503-2718$01.25/0

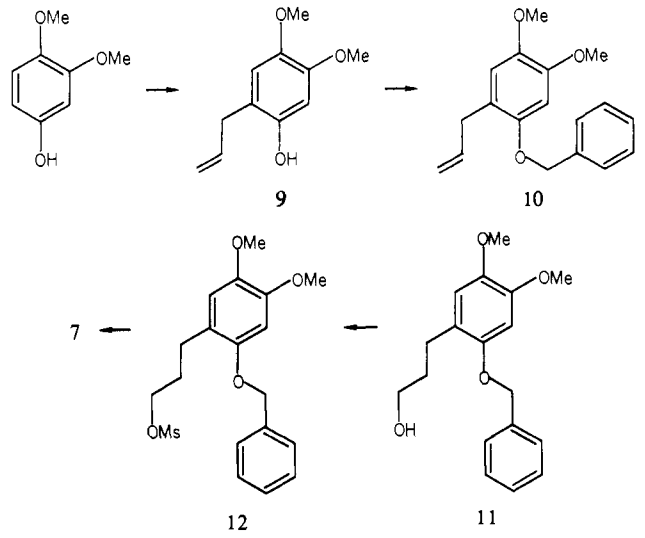
Scheme I



tractive because it would not only allow the synthesis of megaphone (**1**) but also of megaphyllone (**3**) and the related neolignan porosin (**8**),[6] provided other olefins were utilized in the cycloaddition reaction.



The required *p*-benzoquinone ketal **7** was prepared as follows. Claisen rearrangement of the allyl ether derived from 3,4-dimethoxyphenol[7] gave **9** in 83% yield accompanied by the isomeric 3,4-dimethoxy-2-(2-propenyl)phenol (7% yield). Benzylation of **9** followed by hydroboration of **10** with disiamylborane and oxidation produced a single, crystalline alcohol **11**. Mesylate **12**[8] was then hydrogenolyzed and the resulting phenol oxidized with



DDQ in methanol.[9] Samples of ketal **7** deteriorated rapidly on storage, and the compound was, therefore, used in the next step without further purification.

Condensation of the ketal **7** with 1,2,3-trimethoxy-5-(1-(*Z*)-propenyl)benzene[10] in dichloromethane at −30 °C using 1 equiv of stannic chloride was complete after 20 min and yielded the benzofuranone **6** in 48% yield. The spectral properties of **6** agreed well with those of related compounds prepared previously in this laboratory[4,5] and with porosin (**8**).[6a] A high-field three-proton doublet (δ 0.53, d, J = 7 Hz), in particular, means that the methyl group and the trimethoxybenzene ring are cis oriented. The trans arrangement of methyl and allyl substituents results from endo orientation of the addends in the transition state.[4,5]

Conversion of benzofuranone **6** to its dihydro derivative **5** demands a selective hydrogenation of the 4,5-double bond. Although similar reductions using platinum in ethanol[11] or in acetic acid[12] have been accomplished, both procedures failed to give tolerable yields in the case at hand. Catalysts other than platinum were examined, and the currently preferred method calls for hydrogenation over a 5% rhodium on carbon catalyst in methanol solution.[13] This hydrogenation, although highly stereoselective yielding only a single dihydroderivative **5** (33% based on recovered starting material) unfortunately, produces also more highly saturated compounds with presently unknown structures. An examination of a 250 MHz NMR spectrum of **5** revealed the stereochemistry already indicated. The methine proton adjacent to the methoxy group exhibits both axial-axial and axial-equatorial vicinal coupling. Consequently the methoxy group is pseudoequatorial and situated in the plane of the carbonyl group, a fact which may explain the appearance of an NMR singlet at a field lower than anticipated for a methoxy group bonded to an sp^3 carbon atom. These measurements, incidentally, correspond closely with those made with porosin (**8**).[6] The allyl group present in megaphone (**1**) could now be regenerated, and this was easily accomplished by converting the mesylate to the phenylselenide

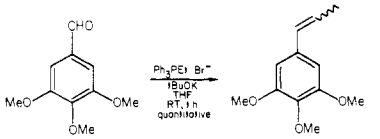
(6) (a) Aiba, C. J.; Filho, R. B.; Gottlieb, O. R. *Phytochemistry* **1973**, *12*, 413–416. (b) Aiba, C. J.; Gottlieb, O. R.; Yoshida, M.; Mourão, J. C.; Gottlieb, H. E. *Ibid.* **1976**, *15*, 1031–1032.

(7) Godfrey, I. M.; Sargent, M. V.; Elix, J. A. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1353–1354.

(8) Method of Crossland, R. K.; Servis, K. L. *J. Org. Chem.* **1970**, *35*, 3195–3196.

(9) Procedure of Büchi, G.; Chu, P. S.; Hoppmann, A.; Mak, C. P.; Pearce, A. *J. Org. Chem.* **1978**, *43*, 3983–3985.

(10) 1,2,3-Trimethoxy-5-(1-(*Z*)-propenyl)benzene was prepared as follows:



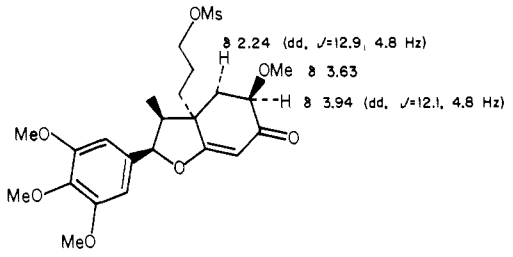
Z:*E* ≃ 7:3

The mixture of olefins was separated by spinning band distillation.

(11) Lima, O. A.; Gottlieb, O. R.; Magalhães, M. T. *Phytochemistry* **1972**, *11*, 2031–2037.

(12) Brophy, G. C.; Mohandas, J.; Slaytor, M.; Sternhell, S.; Watson, T. R.; Wilson, L. A. *Tetrahedron Lett.* **1969**, 5159–5162.

(13) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S.; Siret, P.; Keck, G. E.; Gras, J.-L. *J. Am. Chem. Soc.* **1978**, *100*, 8031–8034.



5

followed by oxidation with sodium periodate.[14]

Initial attempts to synthesize megaphone (**1**) from **4** by sequential treatments with lithium aluminum hydride and 1 N aqueous sulfuric acid[15] failed. Efforts to effect the second step with iodine in tetrahydrofuran[18] were equally unpromising. Instability of megaphone (**1**) to acidic agents seemed to cause these failures, and indeed consecutive treatments of ketone **5** with diisobutylaluminum hydride, methanesulfonyl chloride–triethylamine, and water produced megaphone (**1**) in 42% yield. Comparison of ^{1}H NMR and IR spectra of synthetic and natural megaphone (**1**) seemed to indicate identity but was not convincing because megaphone (**1**) in solution is an equilibrium mixture of hydroxy ketone and hemiketal.[1] The spectra of the secondary acetate (**2**) prepared by acetylation of synthetic megaphone, on the other hand, were identical with those of natural material.

Experimental Section

Melting points were determined on a hot-stage microscope. The following spectrometers and solvents were used: IR, Perkin-Elmer 397 ($CHCl_3$; bands are given in cm^{-1}); ^{1}H NMR, Varian T-60, Bruker mm 250 ($CDCl_3$ unless otherwise stated; chemical shifts are reported in ppm relative to Me_4Si as internal standard and coupling constants are in Hz); UV, Perkin-Elmer Hitachi 200 (EtOH, absorptions are given in nm); MS, Varian Mat 44 (results are quoted as *m/e*). Microanalyses were performed by the Robertson Laboratory, Florham Park, N.J. Flash chromatography (diameter of column, weight of silica gel used, solvent system) were done according to Still,[18] except that the silica gel used was obtained from ICN Life Sciences Group, Cleveland, Ohio, Cat. No. 402826 (particle size 32–63 μm).

Reagents and solvents were purified and dried as follows. Stannic chloride and methanesulfonyl chloride were distilled from P_2O_5 under reduced pressure. THF was distilled from sodium benzophenone ketyl immediately before use. Dichloromethane was distilled from P_2O_5 and triethylamine was distilled from CaH_2. Both were stored over activated molecular sieves 4A.

4,5-Dimethoxy-2-(2-propenyl)phenol (9). A solution of 3,4-dimethoxyphenol (2.098 g, 13.6 mmol), potassium carbonate (3.7 g, 26.8 mmol), and allyl bromide (2.4 mL, 3.4 g, 27.7 mmol) in acetone (30 mL) was stirred and refluxed under argon for 7 h. Additional allyl bromide (1.2 mL, 1.7 g, 13.7 mmol) was added, and the solution was refluxed for another 11 h. The solution was then cooled and filtered through a pad of Celite with the aid of dichloromethane. The filtrate was concentrated in vacuo and the residue filtered through silica gel (30 g) in petroleum ether–EtOAc (4:1 (v/v), 250 mL). Removal of the solvents in vacuo gave pure allyl ether which was stirred and heated neat at 235 to 240 °C (oil bath) under argon for 45 min. The solution was cooled and flash chromatography (50 mm; 120 g; hexane–EtOAc, 3:1 v/v, 500 mL; 2:1 (v/v), 200 mL; then 1:1 (v/v) gave 0.192 g of 3,4-dimethoxy-2-(2-propenyl)-phenol[19] (7% yield) and 2.204 g (83% yield) of phenol **9**: mp 42–42.5 °C (hexane–diethyl ether); IR (CCl_4) 3450, 2830, 1640, 1620, 1510, 1460, 1450, 1410, 1200, 1035, 1000, and 915 cm^{-1}; NMR (CCl_4) δ 3.25 (br d, 2, *J* = 6 Hz), 3.55 (s, 3), 3.75 (s, 3), 4.80–5.23 (m, 2), 5.57–6.20 (m, 1), 6.28 (s, 2), 6.60 (s, 1); MS *m/e* (relative intensity, %) 194 (M$^+$, 100), 179 (84). Anal. ($C_{11}H_{14}O_3$) C, H.

1,2-Dimethoxy-4-(phenylmethoxy)-5-(2-propenyl)benzene (10). A solution of phenol **9** (1.764 g, 9.1 mmol), potassium carbonate (2.537 g, 18.4 mmol), potassium iodide (1.6 g, 9.6 mmol), and benzyl bromide (1.6 mL, 2.3 g, 13.5 mmol) in DME (25 mL) was stirred and refluxed under argon for 13 h. The solution was cooled and filtered. Insoluble salts were washed thoroughly with ether, and the filtrate was concentrated in vacuo. The residue was then taken up in ether (100 mL), washed with water (once with 50 mL) and brine (once with 50 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (50 mm; 100 g; hexane, 500 mL, then hexane–EtOAc, 2:1 (v/v)) gave 2.390 g (93% yield) of benzyl ether **10**: IR (CCl_4) 1640, 1610, 1510, 1465, 1400, 1225, 1040, 1000, and 920 cm^{-1}; NMR (CCl_4) δ 3.32 (br d, 2, *J* = 6 Hz), 3.72 (s, 6), 4.93 (br s, 2), 4.77–5.23 (m, 2), 5.60–6.30 (m, 1), 6.45 (s, 1), 6.62 (s, 1), 7.30 br s, 5); MS *m/e* (relative intensity, %) 284 (M$^+$, 24), 193 (54), 91 (100). Anal. Calcd for $C_{18}H_{20}O_3$: 284.1412. Found: 284.1435.

4,5-Dimethoxy-2-(phenylmethoxy)benzenepropanol (11). Borane-tetrahydrofuran (0.78 M, 6.4 mL, 5.0 mmol) was stirred and cooled (ice bath) under argon while 2-methyl-2-butene (1.1 mL, 10.4 mmol) was added via syringe. The solution was stirred for 2 h, and benzyl ether **10** (0.929 g, 3.3 mmol) in THF (3 mL) was added via syringe. After being stirred for 1 h, the mixture was removed from the ice bath and stirring was continued for 1 h. Water (1 mL) was added, followed by a 10% NaOH solution (1.3 mL, 3.3 mmol). Aqueous hydrogen peroxide (30%) (1.3 mL, 11.5 mmol) was then added while the temperature of the solution was kept between 20 and 25 °C with the aid of an ice bath. The solution was stirred at room temperature for 1 h and was then extracted with ether (twice). The combined ether extracts were washed with saturated $NaHCO_3$ solution (once), saturated Na_2SO_3 solution (once), and brine (once), dried ($MgSO_4$), filtered, and concentrated in vacuo. Crystallization from hexane–EtOAc afforded 0.450 g of alcohol **11**. The mother liquor was concentrated and purified by flash chromatography (30 mm, 30 g, petroleum ether–EtOAc 1:1 (v/v)). Fractions judged to be identical by TLC were pooled to give 0.387 g of alcohol **11**. The combined yield was 86% and alcohol **11** had mp 63.5–64.5 °C (hexane–EtOAc): IR ($CHCl_3$) 3520, 1610, 1510, 1465, 1190, and 1040 cm^{-1}; NMR ($CDCl_3$) δ 1.50–2.03 (m, 3), 2.68 (t, *J* = 7 Hz, 2), 3.55 (t, *J* = 6 Hz, 2), 3.82 (s, 6), 5.03 (br s, 2), 6.57 (s, 1), 6.70 (s, 1), 7.38 (br s, 5); MS *m/e* (relative intensity, %) 302 (M$^+$, 18), 211 (28), 91 (100). Anal. ($C_{18}H_{22}O_4$) C, H.

4,5-Dimethoxy-2-(phenylmethoxy)benzenepropanol Methanesulfonate (12). To a stirred and cooled (ice bath) solution of alcohol **11** (0.905 g, 3.0 mmol) and triethylamine (0.6 mL, 0.536 g, 4.3 mmol) in dichloromethane (15 mL) under argon was added methanesulfonyl chloride (0.3 mL, 0.444 g, 3.9 mmol) via syringe. The solution was subsequently stirred for 80 min. Dichloromethane (50 mL) was added and the solution was washed with ice cold water (once with 50 mL), ice cold 10% hydrochloric acid (once with 50 mL), saturated $NaHCO_3$ solution (once with 50 mL), and brine (once with 50 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. Flash chromatography (30 mm, 36 g, hexane–EtOAc 1:1 (v/v)) gave 0.979 g (86%) of pure mesylate **12**. Crystallization gave prisms: mp 55–56 °C (diethyl ether); IR ($CHCl_3$) 1610, 1510, 1465, 1355, 1190, 1170, and 1025 cm^{-1}; NMR ($CDCl_3$) δ 1.68–2.37 (m, 2), 2.72 (t, *J* = 7 Hz, 2), 2.87 (s, 3), 3.83 (s, 6), 4.17 (t, *J* = 6 Hz, 2), 5.03 (br s, 2), 6.58 (s, 1), 6.72 (s, 1), 7.38 (br s, 5); MS *m/e* (relative intensity, %) 380 (M$^+$, 4), 193 (55), 91 (100). Anal. ($C_{19}H_{24}O_6S$) C, H.

(2β,3β,3aα)-3,3a-Dihydro-5-methoxy-3-methyl-3a-[3-[(methylsulfonyl)oxy]propyl]-2-(3,4,5-trimethoxyphenyl)-6(2*H*)-benzofuranone (6). A solution of benzyl ether **12** (1.007 g; 2.7 mmol) and 10% Pd/C (90 mg) in methanol (40 mL) was hydrogenated at room temperature. After 3 h, the solution was filtered through a pad of Celite and the Celite and catalyst were washed thoroughly with methanol and with dichloromethane. The filtrate was concentrated in vacuo and the crude phenol was used without purification. To a stirring solution of the phenol obtained as described above in methanol (15 mL) was added DDQ (0.670 g, 3.0 mmol) at room temperature. After 15 min, the solution was diluted with dichloromethane (50 mL), washed with saturated $NaHCO_3$ solution (twice with 50 mL) and brine (once with 50 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude quinone ketal **7** was used without further purification. To a stirring and cooled (−30 °C, bromobenzene–dry ice) solution of the quinone ketal and 1,2,3-trimethoxy-5-(1-(*Z*)-propenyl)benzene (1.111 g, 5.3 mmol) in dichloromethane (28 mL) under argon was added stannic chloride (0.3 mL, 0.668 g, 2.6 mmol) via syringe. The solution was stirred for 20 min, diluted with 5% hydrochloric acid (20 mL) and warmed to room temperature. After extraction with dichloromethane (twice) the combined extracts were washed with saturated $NaHCO_3$ solution (once) and brine (once), dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by flash chromatography (50 mm; 90 g; EtOAc, 500 mL, then EtOAc–acetone, 9:1 (v/v)). Fractions containing the desired product were pooled and concentrated in vacuo. Crystallization from methanol–dichloromethane gave 0.613 g (two crops, 48% overall yield) of **6**. Recrystallization gave analytically pure **6**: mp 164–166 °C (EtOAc–CH_2Cl_2);

(14) Sharpless, K. B.; Young, M. W. *J. Org. Chem.* **1975**, *40*, 947–949.
(15) Gannon, W. F.; House, H. O. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. V, pp 294–296.
(16) Kieczykowski, G. R.; Quesada, M. L.; Schlessinger, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 782–790.
(17) Danheiser, R. L. Ph.D. Dissertation, Harvard University, 1978. We are indebted to Professor Danheiser for bringing this method to our attention.
(18) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.
(19) Büchi, G.; Chu, P. S. *J. Org. Chem.* **1978**, *43*, 3717–3719.

IR($CHCl_3$) 2840, 1650, 1610, 1590, 1500, 1460, 1355, 1235, 1170, and 1060 cm^{-1}; NMR ($CDCl_3$) δ 0.53 (d, J = 7.0 Hz, 3), 1.49–2.32 (m, 4), 2.56–2.79 (m, 1), 3.03 (s, 3), 3.70 (s, 3), 3.85 (s, 3), 3.87 (s, 6) 4.11–4.35 (m, 2), 5.44 (s, 1), 5.92 (s, 1), 5.98 (d, J = 4.8 Hz, 1), 6.43 (s, 2); UV (95% EtOH) 243 nm (sh, log ϵ 4.16), 258 (4.28), 291 (sh, 3.68); MS m/e (relative intensity, %) 482 (M^+, 1), 208 (81), 79 (100). Anal. ($C_{23}H_{30}O_9S$) C, H.

(2β,3β,3aα,5β)-3,3a,4,5-Tetrahydro-5-methoxy-3-methyl-3a-[3-[(methylsulfonyl)oxy]propyl]-2-(3,4,5-trimethoxyphenyl)-6(2*H*)-benzofuranone (5). A solution of benzofuranone **6** (0.354 g, 0.73 mmol) in methanol (50 mL) containing 5% Rh/C (49 mg) was hydrogenated under an atmospheric pressure of hydrogen. After 105 min, the solution was filtered through a pad of Celite with the aid of dichloromethane and the filtrate was concentrated in vacuo. Flash chromatography (40 mm, 66 g, EtOAc–acetone 9:1 (v/v)) of the mixture gave 0.076 g of the desired product **5** (22% yield, 33% based on recovered starting material) and 0.121 g of unreacted benzofuranone **6**. Crystallization gave analytically pure **5**: mp 149–151 °C ($CHCl_3$–hexane); IR ($CHCl_3$) 1660, 1630, 1600, 1505, 1460, 1355, 1180, and 1130 cm^{-1}; NMR ($CDCl_3$) δ 0.55 (d, J = 7.4 Hz, 3), 1.80–2.15 (m, 5), 2.24 (dd, J = 12.9, 4.8 Hz, 1), 2.62–2.45 (m, 1), 3.08 (s, 3), 3.63 (s, 3), 3.85 (s, 3), 3.88 (s, 6), 3.94 (dd, J = 12.1, 4.8 Hz, 1), 4.48–4.26 (m, 2), 5.58 (s, 1), 5.86 (d, J = 4.8 Hz, 1), 6.46 (s, 2); MS m/e (relative intensity, %) 484 (M^+, 17) 406 (17), 221 (53), 79 (100); UV (95% EtOH) 257 nm (log ϵ 4.38). Anal. ($C_{23}H_{32}O_9S$) C, H.

(2β,3β,3aα,5β)-3,3a,4,5-Tetrahydro-5-methoxy-3-methyl-3a-(2-propenyl)-2-(3,4,5-trimethoxyphenyl)-6(2*H*)-benzofuranone (4). To a stirring suspension of 4,4′-dichlorodiphenyl diselenide (39 mg, 0.10 mmol) in absolute ethanol (1 mL) was added slowly, under a heavy argon atmosphere, small quantities of solid $NaBH_4$ until a colorless solution was obtained. The solution was then cooled in an ice bath for 20 min. Benzofurane **5** (53 mg, 0.11 mmol) in THF (1 mL) was then added and the solution was stirred for 55 min. Sodium periodate (0.199 g, 0.93 mmol) in 50% aqueous THF (3 mL) was added and stirring was continued for 25 min. The ice bath was removed and the solution was then heated at 70 °C (oil bath) for 150 min. The solution was diluted with water (10 mL) and extracted with EtOAc (3× 20 mL). The combined organic extracts were washed with 5% $NaHCO_3$ solution (1× 20 mL) and brine (1× 20 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. Flash chromatography (20 mm, 16 g, EtOAc) gave 23 mg (54% yield) of benzofuranone **4**: mp 137–139 °C ($CHCl_3$–hexane); IR ($CHCl_3$) 2825, 1655, 1630, 1590 cm^{-1}; UV (95% EtOH) 260 nm (log ϵ 4.40); NMR ($CDCl_3$) δ 0.54 (d, J = 7.4 Hz, 3), 1.91 (t, J = 12.3 Hz, 1), 2.32 (dd, J = 12.5, 5.2 Hz, 1). 2.45–2.75 (m, 3), 3.60 (s, 3), 3.85 (s, 3), 3.87 (s, 6), 4.01 (dd, J = 12.1, 5.2 Hz, 1), 5.28–5.39 (m, 2), 5.60 (s, 1), 5.85 (d, J = 5.2 Hz, 1), 5.87–6.04 (m, 1), 6.42 (s, 2). Anal. Calcd for $C_{22}H_{28}O_6$: 388.1886. Found: 388.1887.

Megaphone (1): To a cooled (ice bath) and stirring solution of benzofuranone **4** (23 mg, 0.06 mmol) in THF (0.3 mL) was added DIBAH (1 M in hexane, 0.15 mL, 0.15 mmol) via syringe. After 45 min, 3 drops of saturated NH_4Cl solution were added, followed by ether (5 mL), solid NH_4Cl (25 mg), and Celite (0.15 g). The solution was stirred at room temperature for 30 min and filtered through $MgSO_4$ and the cake washed with ether. Concentration of the filtrate in vacuo gave a colorless oil which was dissolved in THF (0.1 mL) containing Et_3N (16 μL, 12 mg, 0.12 mmol). The solution was then cooled to −55 to −60 °C with stirring and methanesulfonyl chloride (9 μL, 13 mg, 0.12 mmol) was added. The mixture was then stirred for 15 min, and 0.2 mL of H_2O/THF/Et_3N (3:2:1) was added. After the solution was warmed to room temperature, it was diluted with Et_2O, washed with water (once) and brine (once), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (20 mm, 16 g, hexane–EtOAc 1:1 (v/v)) gave 10 mg (42% yield) of megaphone (**1**): IR (CCl_4) 3600, 3375, 2830, 1665, 1590, 1500, 1460, 1230, and 1005 cm^{-1}; NMR ($CDCl_3$) δ 0.77 (d, J= 7.4 Hz, 3), 1.95 (br q, J = 7.0 Hz, 1), 2.13–2.49 (m, 3), 2.59 (dd, J = 14.7, 6.6 Hz, 1), 3.47 (s, 3), 3.83 (s, 3), 3.88 (s, 6), 4.17–4.28 (m, 1), 4.56–4.79 (br s, 1), 5.03 (br s, 1), 5.24 (br s, 1), 5.29 (br s, 1), 5.73–5.98 (m, 1), 6.03 (dd, J = 10.3, 2.2 Hz, 1), 6.66 (s, 2), 7.00 (d, J = 10.3 Hz), 0.60 (d, J = 7.7 Hz, hemiketal Me), 3.37 (s, hemiketal OMe), 6.47 (s, aromatic hemiketal).

Megaphone Acetate (2). Racemic megaphone acetate (**2**) prepared according to the literature[1] was a colorless oil: IR (CCl_4) 2840, 1745, 1680, 1590, 1510, 1460, 1420, 1230, 1130, 1010, 960, 920 cm^{-1}; NMR ($CDCl_3$) δ 0.93 (d, J = 7 Hz, 3), 1.87 (dd, J = 13.2, 9.9 Hz, 1), 2.13 (s, 3), 2.25–2.40 (m, 3), 2.55 (q, J = 7 Hz, 1), 3.46 (s, 3), 3.82 (s, 3), 3.88 (s, 6), 4.17–4.27 (m, 1), 4.95–5.03 (m, 1) 5.04 (br s, 1), 5.49–5.64 (m, 1), 5.67 (s, 1), 6.01 (dd, J = 10.3, 2.2 Hz, 1), 6.55 (s, 2), 6.91 (dt, J = 10.3, 1.8 Hz, 1).

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Kinetics and Mechanism of the Oxidation of (α-Hydroxyalkyl)chromium Complexes by Copper(II) and Iron(III) Ions

Andreja Bakač and James H. Espenson*

Contribution from the Ames Laboratory and Department of Chemistry, Iowa State University, Ames, Iowa 50011. *Received July 10, 1980*

Abstract: Copper(II) and iron(III) ions react with (α-hydroxyalkyl)chromium(2+) complexes (alkyl = methyl, ethyl, 2-propyl) in water or in aqueous alcohol solutions leading to the cleavage of the chromium–carbon bond. The immediate products are Cr^{2+}, the reduced metal ion (Cu^+ or Fe^{2+}), and the corresponding aldehyde or ketone. The reactions obey the rate law $-d[CrROH^{2+}]/dt = (k + k'[H^+]^{-1})[CrROH^{2+}][M]$, where M = Cu^{2+} or Fe^{3+}. The dominant k' term has the following values in 1 M aqueous parent alcohol (methanol, ethanol, and 2-propanol, respectively): $CrCH_2OH^{2+}$, k'_{Cu} = 0.251 s^{-1}, k'_{Fe} = 0.496 s^{-1}; $CrCH(CH_3)OH^{2+}$, 1.46, 0.481; $CrC(CH_3)_2OH^{2+}$, 0.574, 1.90. The reactivity toward Cu^{2+} and Fe^{3+} is significantly diminished upon substitution of the OH hydrogen by an alkyl group. Copper(II) does not react with (α-alkoxyalkyl)chromium(2+) complexes at all, while iron(III) shows some reactivity with k'_{Fe} = 0.0127 s^{-1} ($CrCH_2OCH_3^{2+}$) and 0.0400 s^{-1} ($CrCH(CH_3)OC_2H_5^{2+}$), both in 1 M methanol. A mechanism proposed for the oxidation of (α-hydroxyalkyl)chromium(2+) complexes by copper(II) and iron(III) consists of the oxidant attack at the alcoholic OH group followed by a slow electron-transfer step.

The Fischer–Tropsch process is one in which hydrocarbon fuels and alcohols can be synthesized from mixtures of carbon monoxide and hydrogen obtained from coal and water. The mechanism of the heterogeneous process is not completely understood, however, and this poses one impediment to its commercial development where the distribution of products is crucial.[1] One possible

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