5.71, 7.41, 7.55, 8.33, 8.77, 9.26, 9.71 μm; MS, m/e 308 ($M^+$).

Anal. Calcd for $C_8H_{11}S_2O_5F_3$: C, 31.17; H, 3.60; S, 20.80; F, 18.49. Found: C, 31.34; H, 3.44; S, 20.83; F, 18.16.

**1,2-Dimethylcyclopentenone (5b).** Cyclic keto sulfone **4b** (0.155 g, 0.503 mmol) and 0.14 g (1.01 mmol) of finely ground anhydrous potassium carbonate were combined in 6 mL of dry THF and heated to reflux under nitrogen for 5 h. The solution was cooled to room temperature, evaporated in vacuo, and extracted with ether. This was filtered through Celite, and the filtrate was evaporated in vacuo to give a pale yellow liquid, 0.058 g (100%), homogeneous on TLC: $^1H$ NMR ($CDCl_3$) δ 1.7 (br s, 3 H), 2.05 (s, 3 H), 2.1–2.6 (m, 4 H); IR ($CH_2Cl_2$) 5.92, 6.06 μm; MS, m/e 110 ($M^+$) (lit. ref 8).

**α-Methylmesyltriflone (2c).** See synthesis of **2a**. After the addition of methyl iodide and subsequent warming to 0 °C, the reaction was quenched with excess 1 N HCl. Ether extraction affords colorless crystals in 95% yield: mp 74–75 °C (methylene chloride/petroleum ether); $^1H$ NMR ($CDCl_3$) δ 1.95 (d, J = 7 Hz, 3 H), 3.30 (s, 3 H), 4.60 (q, J = 7 Hz, 1 H).

Anal. Calcd for $C_4H_7S_2O_4F_3$: C, 20.00; H, 2.94; S, 26.69; F, 23.73. Found: C, 20.19; H, 2.75; S, 26.93; F, 23.37.

**6-Methyl-6-[(trifluoromethyl)sulfonyl]tetrahydrothiopyran-3-one 1,1-Dioxide (4c).** This compound was synthesized according to method A above: 30% yield; mp 116–117 °C; $^1H$ NMR ($CDCl_3$) δ 2.0 (br s, 3 H), 2.25–3.28 (m, 4 H), 4.51 (AB q, J = 12 Hz, 2 H); IR ($CH_2Cl_2$) 5.70, 7.38, 7.47, 8.33, 8.82, 9.16, 9.35 μm.

Anal. Calcd for $C_7H_9S_2O_5F_3$: C, 28.57; H, 3.08; S, 21.79; F, 19.37. Found: C, 28.58; H, 3.06; S, 21.98; F, 19.03.

**3-Methyl-2-cyclopentenone (5c).** See procedure for **5b** (reaction time 7 h): yield 50%;[9] $^1H$ NMR ($CDCl_3$) δ 2.15 (br s, 3 H), 2.3–2.7 (m, 4 H), 5.9 (q, J = 1 Hz, 1 H); IR (neat) 3.32, 5.86, 6.15, 7.02, 7.14, 7.30, 7.60, 7.84, 8.16, 8.55, 8.85, 10.05, 11.98 μm (lit. ref 8).

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**Registry No.** 1, 93916-15-5; **2a**, 93916-04-2; **2a**·$2Li^+$, 96247-06-2; **2b**, 93915-93-6; **2b**·$2Li^+$, 96247-07-3; **2c**, 93915-89-0; **2c**·$Li^+$, 96247-08-4; **3a**, 96247-09-5; **3b**, 96247-10-8; **3c**, 96247-11-9; **4a**, 96247-12-0; **4a′**, 96247-13-1; **4b**, 96247-14-2; **4b′**, 96247-15-3; **4c**, 96247-16-4; **4c′**, 96247-17-5; **5a**, 1128-08-1; **5b**, 1121-05-7; **5c**, 2758-18-1; **6**, 96247-18-6; **7**, 96247-19-7; **8**, 96247-20-0; $CF_3SO_2F$, 335-05-7; $CH_3(CH_2)_4I$, 628-17-1; $MeSO_2Me$, 67-71-0; acrolein, 107-02-8.

(9) This low yield was partly due to the instability of **5c**.

# Methylation of Polysubstituted Electron-Rich Aromatics and Their Birch Reduction

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3,4,5-Trimethoxybenzoic, 3,5-dimethoxybenzoic, and (3,5-dimethoxyphenyl)acetic acids, and their esters, react with either 1 or 2 mol of (methylthio)methyl chloride (MTM-Cl) and zinc chloride to form the 2-mono- or 2,6-bis[(methylthio)methyl] (MTM) derivatives, which yield the corresponding methyl derivatives with Raney nickel. Normal Birch reduction also removes the methylthio group and, in the benzoic acids, the aromatic ring is converted to dihydroresorcinols. In the phenylacetic acid case, only with more vigorous reduction conditions is the dihydroresorcinol formed.

In the course of other studies directed toward the synthesis of quassinoids, we had occasion to require practical syntheses of the 2,6-dimethyl-3,5-dimethoxy and -3,4,5-trimethoxy aromatic acids **1c–3c** (Chart I). The most amenable approach to these compounds seemed to be electrophilic aromatic substitution of two one-carbon synthons on an appropriate aromatic acid or ester. However, traditional methods for effecting this transformation proved futile. Strong Lewis acid conditions were known to promote demethylation of methoxy groups when conjugated to electron-withdrawing substituents (e.g., 1; R = OMe → R = OH), and formylation reactions (such as Gattermann or Gattermann–Koch) would be expected to stop at the monoacylation stage. Hydroxymethylation/chloromethylation reactions using chloromethyl methyl ether, generated in situ from formaldehyde/hydrochloric acid/methanol, were ineffective in alkylating 3,4,5-trimethoxybenzoic acid **1a** or ester **1b**.[2] Reaction of methyl gallate (3,4,5-trihydroxybenzoate) with formaldehyde/hydrochloric acid/methanol did result in substitution at the two residual aromatic positions, but the product proved to be the diarylmethane bis(lactone) **4a**, characterized as **4b** after permethylation. Compound **4** presumably arises from interception of a transiently generated quinomethane species by unreacted methyl gallate.

To surmount these problems we sought a reagent to activate the alkylation but create a poor leaving group at the benzylic position. We now report that chloromethyl methyl sulfide (MTM-Cl), catalyzed by zinc chloride in either methylene chloride or 1,2-dichloroethane, is an excellent reagent for effecting this alkylation and for generating compounds **5–8**. Chloromethyl methyl sulfide had been used in the past under strong Lewis acid conditions ($TiCl_4$)[3] for alkylating simple aromatics, and recently, Tamura and co-workers have described the use of ethyl chloromethyl thioglycolate for this same purpose.[4] We find that either predominant monoalkylation (to **5**) or bisalkylation (**6–8**) can be achieved by choice of stoichiometry or reaction times and that regioselectivity of alkylation using compounds **2a,b** or **3a,b** strongly favors reactions at the 2- and 6-positions, with virtually no substitution at the 4-position. Prolonged reaction times after

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(2) For an example of strong Lewis-acid-catalyzed alkylation of a 1-alkyl-3,4,5-trimethoxybenzene, see: Rapoport, H.; Champion, H. H. *J. Am. Chem. Soc.* **1951**, *73*, 2239.

(3) Gross, H.; Matthey, C. *Chem. Ber.* **1964**, *97*, 2606.

(4) Tamura, Y.; Tsugoshi, T.; Annoura, H.; Ishibachi, H. *Synthesis* **1984**, 326.

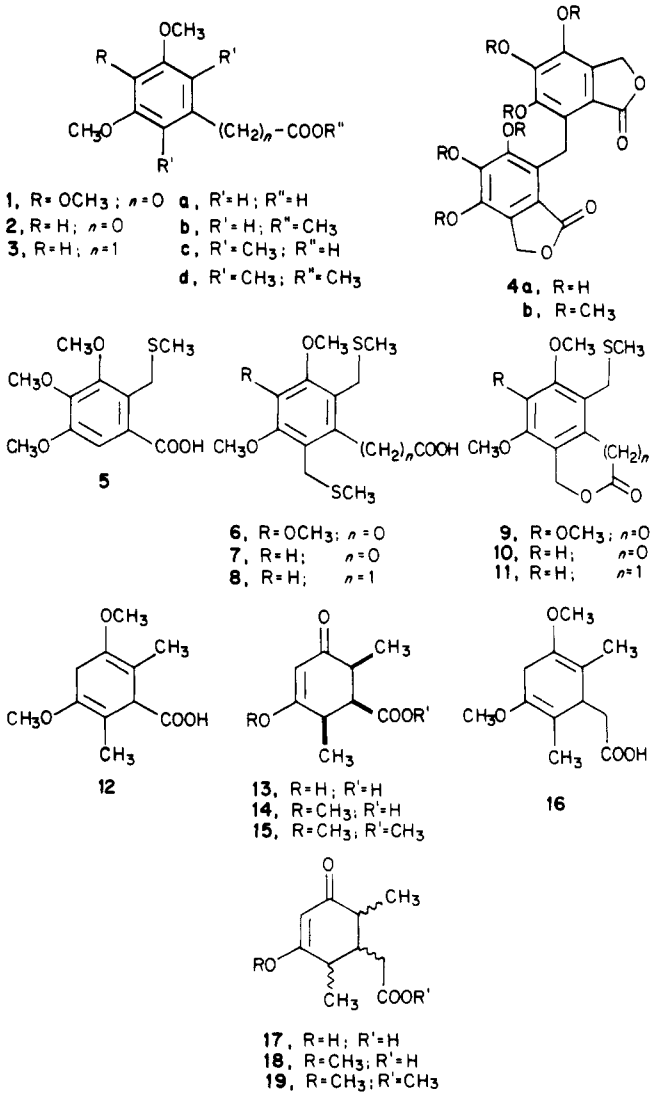
0022-3263/85/1950-2112$01.50/0 

**Table I. Properties of Compounds Synthesized**

| compd | mp, °C | % yield | MS[a] | NMR[b] |
|---|---|---|---|---|
| **4b** | 199–200 | 47 | 460 | 3.52 (6), 3.87 (6), 3.93 (6), 5.04 (2), 5.23 (4) |
| **5** | 99–102 | 40 | 272 (225) | 2.10 (3), 3.95 (3), 3.98 (3), 4.00 (3), 4.25 (2), 7.45 (1) |
| **6** | oil | 77 | | 2.08 (6), 3.92 (13), 10.2 (1) |
| **6-Me**[c] | oil | 81 | 346 | 2.01 (6), 3.80 (3), 3.90 (13) |
| **7-Me**[c] | 60–61 | 75 | 316 (269) | 1.99 (6), 3.75 (4), 3.85 (6), 3.90 (3), 6.50 (1) |
| **8** | oil | 82 | | 2.10 (6), 3.75 (2), 3.82 (4), 3.94 (6), 6.53 (1) |
| **8-Me**[c] | oil | 84 | 330 (235) | 2.04 (4), 3.68 (6), 3.85 (9), 4.02 (2), 6.42 (1) |
| **9a**[d] | 88–89 | 72 | 238 | 2.54 (3), 3.87 (3), 3.98 (3), 4.01 (3), 5.20 (2) |
| **10** | 148–149 | 75 | 254 | 2.10 (3), 3.97 (6), 4.20 (2), 5.16 (2), 6.75 (1) |
| **11**[e] | 151–153 | 70 | 268 (221) | 2.00 (3), 3.70 (4), 3.84 (6), 5.28 (2), 6.40 (1) |
| **1c** | 183–186 | 86 | | 2.25 (6), 3.85 (6), 3.95 (3), 11.2 (1) |
| **1c-Me**[c] | 43–48 | 79 | | 2.10 (6), 3.74 (6), 3.84 (6) |
| **2c** | 183–184 | 84 | 210 | 2.19 (6), 3.85 (6), 6.50 (1), 10.8 (1) |
| **3c** | 195–197 | 95 | 224 | 2.15 (6), 3.76 (2), 3.83 (6), 6.48 (1) |
| **3c-Me**[c] | 60–62 | 87 | 238 | 2.05 (6), 3.59 (3), 3.60 (2), 3.76 (6), 6.35 (1) |
| **13** | 189–192 dec | 68 | 184 (111) | 1.03 (6 d, $J$ = 6), 3.00 (3 br), 3.70 (3 br) |
| **14** | 151–153 dec | 72 | 198 (112) | 1.11 (3 d, $J$ = 7), 1.24 (3 d, $J$ = 7), 2.6 (1 m), 3.15 (2 m), 3.70 (3), 5.40 (1) |
| **15** | 87–90 | 82 | | 1.16 (3 d, $J$ = 7), 1.22 (3 d, $J$ = 7), 2.6 (1 m), 3.1 (2 m), 3.65 (3), 3.69 (3), 5.43 (1) |
| **18**[f,g] | oil | 73 | | 0.98 (3 d, $J$ = 7), 1.24 (3 d, $J$ = 6), 2.0–2.8 (5 m), 3.64 (3), 5.18 (1) |
| **19**[f] | oil | 50 | 226 (153, 112) | 1.14 (3 d, $J$ = 7.0), 1.17 (3d, $J$ = 7.5), 2.21 (1 dd, $J$ = 6, 16), 2.34 (1 dd, $J$ = 6.5, 16), 2.55 (1 dq, $J$ = 5, 7), 2.75 (1 dddd, $J$ = 5, 5, 6, 6.5), 2.92 (1 dq, $J$ = 5, 7.5), 3.68 (6), 5.31 (1) |

[a] Mass spectrum, $m/z$ parent (major). [b] NMR ($CDCl_3$), chemical shift, ppm (number of hydrogens); all peaks are singlets unless otherwise noted ($J$ values in Hz). [c] Methyl ester. [d] Dethiomethylated **9** (Raney nickel). [e] Anal. Calcd for $C_{13}H_{16}SO_4$ (found): C, 58.15 (58.17); H, 6.01 (5.97); S, 11.95 (11.91); O, 23.85 (23.95). [f] NMR for separated all-cis isomer. [g] $Me_2SO$-$d_6$ at 125 °C.

**Chart I**



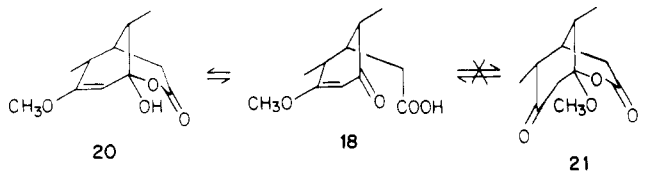

initial alkylation result in intramolecular displacement of one of the methylthio groups by the carboxyl group to generate the lactones **9–11**, and this process is particularly facile when one starts with the carboxylic esters **1b–3b**. Furthermore it appears that alkylation of esters **1b–3b** is both kinetically faster and truly catalytic in zinc chloride, compared to acids **1a–3a**, which require longer reaction times and stoichiometric quantities of Lewis acid.

Reductive conversion of the (methylthio)methyl group to a methyl group can be routinely performed on a multigram scale using Raney nickel, without affecting any lactone present. Alternatively, both types of benzylic heterosubstituent can be removed, with concomitant reduction of the aromatic ring, by submitting the benzoic acid derivatives **6**, **7**, **9**, or **10** to standard Birch reduction conditions using sodium in liquid ammonia/ethanol at −78 °C. The resultant exceedingly sensitive diene **12** can be converted to the crystalline dihydroresorcinol derivative **13** by rapid quenching with aqueous HCl. Reaction of **12** with cold methanolic oxalic acid hydrate gives **14**, in which one enol ether has been hydrolyzed and the second isomerized into conjugation.[5] Reaction of either **13** or **14** with diazomethane gives the crystalline all-cis enol ether ester **15**, with no other isomers being detected.

Birch reduction (excess sodium, liquid ammonia/ethanol, −33 °C) does not dearomatize the polysubstituted phenylacetic acid derivatives (**8** and **11**) but strips them of heteroatom substituents to give the crystalline dimethyl aromatic acid **3c**. We found, however, that more forcing conditions served to reduce the benzene ring as well. Thus the use of lithium in methylamine with *tert*-butyl alcohol at −5 °C converted **3c** or **11** to **16**, and analogous acidic workup conditions gave the homologue **17**, with HCl, or **18**, with oxalic acid; diazomethane afforded **19**. In these compounds the all-cis isomer predominated but was not the exclusive product. Properties of these products are listed in Table I.

In contrast to **14**, the higher homologue stereoisomer mixture **18** was in rapid equilibrium with pseudoacids **20**. Variable-temperature NMR studies indicate that **18** does not cyclize to **21** since the vinyl proton signal was among the first to sharpen at higher temperatures. However,

(5) For an example of oxalic acid workup for Birch reduction without isomerization, see: Wilds, A. L.; Nelson, N. A. *J. Am. Chem. Soc.* **1953**, *75*, 5366.



20 18 21

reaction of 18 (20) with diazomethane gave 19 exclusively.

This economical, experimentally simple procedure appears to be a valuable one for aromatic methylation of even sterically hindered electron-rich arenes, which also may further be dearomatized under the more vigorous Birch reduction conditions.

## Experimental Section

Unless otherwise indicated, reactions were carried out under nitrogen. Commercial materials were used as received with the following exceptions. Chloromethyl methyl sulfide (MTM-Cl) and *tert*-butyl alcohol were distilled and stored over 4-Å molecular sieves, the former in the freezer. Other dry solvents were distilled from appropriate desiccant immediately prior to use. Diazomethane was generated from *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide ("Diazald") and was stored as an ether solution over KOH pellets in a freezer. Pyrophoric metals and metal hydrides, which were provided packed in oil, were washed several times with petroleum ether immediately prior to use.

Where aqueous workup of reactions is mentioned, this consisted of extraction with the designated solvent(s), washing the combined organic layers with brine, final drying of the organic phase with $MgSO_4$, filtration of the dried solution through either a sintered-glass funnel or a plug of glass wool, and evaporation of the organic solvent at reduced pressure. Purification of reaction products by either distillation or sublimation was in all cases effected by bulb-to-bulb vacuum techniques using a Buchi Kugelrohr oven.

Spectral verification of the products obtained was facilitated by the following instruments: infrared, Perkin-Elmer Model 137, using polystyrene as a calibration standard; NMR, Perkin-Elmer R-32 (CW, 90 MHz), Bruker WH-90 (FT, 90 MHz). High-field NMR decoupling experiments were performed on a modified Bruker 270-MHz instrument. Unless otherwise noted, NMR spectra were run in $CDCl_3$ or $CCl_4$ with chemical shifts reported in parts per million (ppm) downfield of $Me_4Si$ as internal standard. Mass spectra were recorded on either an AEI MS9 or an AEI MS12 electron-impact mass spectrometer, usually at 70 eV. NMR and mass spectra and melting points are recorded in Table I. Elemental analysis was conducted by Galbraith Laboratories. Melting points were obtained by using sealed capillary tubes in a Mel-Temp apparatus and, although internally consistent, are not corrected.

**Bis[7-(4,5,6-trimethoxyphthalidyl)]methane (4b).** Methyl 3,4,5-trihydroxybenzoate ($M_r$ = 180, 100 mg, 0.55 mmol) and 2.40 g (excess) of *sym*-trioxane were dissolved in 70 mL HCl(g)/MeOH at 0 °C, allowed to warm to room temperature, and stirred for 20 h, after which the excess reagents and some of the solvent were removed on a steam bath for 1 h. The residual solvent was evaporated off at room temperature to produce a copious pink-tinted solid insoluble in methanol or acetone but soluble in aqueous base. This was suspended in 40 mL of water/methanol (1:1), the flask was flushed with $N_2$, and 3 mL of dimethyl sulfate was added. Solid KOH pellets were added piecemeal over 2 h, alternating with more methyl sulfate if a red (phenolate?) color persisted more than 5 min. After this red color no longer appeared from KOH addition, an additional 1 g of KOH was added to destroy any residual methyl sulfate, and the reaction was stirred overnight at room temperature. After it was ascertained that the solution was still alkaline, the methanol was evaporated at room temperature and the aqueous layer was extracted with ether. The aqueous layer was acidified (HCl) to pH 1, creating an insoluble interphase, but extraction with ether gave 72 mg of light yellow solid (47%), which was crystallized from dichloromethane/petroleum ether.

**2-[(Methylthio)methyl]-3,4,5-trimethoxybenzoic Acid (5).** 3,4,5-Trimethoxybenzoic acid ($M_r$ = 212, 20.3 g, 95.7 mmol) was added to a refluxing suspension of 41.63 g of $ZnCl_2$ (356 mmol), 16 mL of MTM-Cl ($M_r$ = 96.9, $d$ = 1.153 g/cm$^3$, 190 mmol), and 175 mL of dry dichloromethane. The reaction was refluxed with a drying tube for 48 h. After this time, 20 mL of water was added to the still heterogeneous suspension, and the reaction was refluxed an additional 5 h and cooled; the layers were separated, and the aqueous layer (pH 1) was extracted with fresh dichloromethane. The combined organic layers were evaporated, dissolved in saturated sodium bicarbonate solution, and extracted with ether to remove 112 mg of ether-soluble yellow oil. The aqueous layer was reacidified with HCl to pH 1, extracted with dichloromethane, dried, and filtered and the solvent was evaporated to give 19.23 g of pale salmon-colored oil (80.5%), which spontaneously crystallized. This was recrystallized from dichloromethane/petroleum ether.

**Methyl [2,6-Bis((methylthio)methyl)-3,5-dimethoxyphenyl]acetate (8).** Methyl 3,5-dimethoxyphenylacetate ($M_r$ = 212, 111 mg, 0.53 mmol), 5.6 mol % $ZnCl_2$, 2 equiv of MTM-Cl, and 16 mL of dry 1,2-dichloroethane were refluxed under $N_2$ for 8 h. The reaction was cooled, and extracted with dichloromethane vs. 1 N HCl, and the solvents were evaporated. The product was prep-plated on silica with 1:1 $CH_2Cl_2/CCl_4$, and the major band was extracted to give 145 mg of pale oil (84%).

**4,6-Dimethoxy-7-[(methylthio)methyl]phthalide (10).** Methyl 3,5-dimethoxybenzoate ($M_r$ = 196, 13.02 g, 66.3 mmol), 8.91 g of zinc chloride ($M_r$ = 136, 65.5 mmol), and 11.8 mL of chloromethyl methyl sulfide ($M_r$ = 96.6, $d$ = 1.153 g/cm$^3$, 140 mmole were mixed in 200 mL of 1,2-dichloroethane and refluxed with a drying tube for 28 h. After this time, the thick gummy mixture was cooled, quenched with 1 M HCl, and extracted with $CHCl_3$. Workup produced 12.68 g of yellow solid (76%), which was crystallized from hot acetone.

**2,6-Dimethyl-3,4,5-trimethoxybenzoic Acid (1c).** 2,6-Bis-[(methylthio)methyl]-3,4,5-trimethoxybenzoic acid ($M_r$ = 332, 1.5 g, 4.5 mmol) was dissolved in 50 mL of MeOH, and 25 mL of water was added. NaOH (10.5 g) was added over 10 min to the ice-cooled solution, which darkened somewhat, and 8 g of $NiAl_2$ was added batchwise over 20 min. The suspension was allowed to warm to room temperature over 2 h, brought to reflux overnight, cooled, and filtered through Celite, and the solvents were removed. The residuum was extracted with ether vs. 1 N HCl to give 1.21 g of amber oil. Back-extraction of the ether layer vs. saturated $NaHCO_3$ followed by reacidification of the aqueous layer and extraction with ether gave 0.93 g (86%) of off-white solid. This was recrystallized from hot ether.

**4,6-Dimethyl-5-carboxycyclohexane-1,3-dione (13).** The crude Birch product obtained from 2.90 g of 2,6-dimethyl-3,5-dimethoxybenzoic acid ($M_r$ = 210, 13.8 mmol), 20 mL of dry ethanol, 5 mL of dry THF, 100 mL of ammonia, and 2.3 g of $Na^0$, after quenching with 6 g of $NH_4Cl$ and evaporating the solvents in an $N_2$ stream overnight, was, without exposure to air, immediately treated with 50 mL of 1 N HCl. This was extracted with ether and dichloromethane. The organic layers were combined and the solvents evaporated to give 1.742 g of pale oil (68.5%), which spontaneously crystallized.

**4,6-Dimethyl-5-carbomethoxy-3-methoxycyclohex-2-en-1-one (15).** The crude product from the previous reaction ($M_r$ = 184, 38.6 mg, 0.27 mmol) was dissolved in 3 mL of THF and 1 mL MeOH, to which was added 4 mL of ethereal diazomethane solution (0.35 M, 1.4 mmol) at room temperature. After the mixture was allowed to stand for 30 min, the solvents and excess diazomethane were evaporated and the product was crystallized from hot petroleum ether to give 36.2 mg (82.5%) of white needles, mp 86.5–89.5 °C.

**(2,6-Dimethyl-3,5-dimethoxyphenyl)acetic Acid (3c).** Crude [2,6-bis((methylthio)methyl)-3,5-dimethoxyphenyl]acetic acid 11.3 g, 35.76 mmol) was dissolved in 100 mL of absolute ethanol and cooled under $N_2$ to −78 °C, at which point 400 mL of ammonia was distilled in. $Na^0$ (14 g) was added piecemeal over 2 h as the reaction was allowed to warm to −33 °C. When the blue color had finally dissipated, the reaction was recooled to −78 °C, quenched with 35 g of solid $NH_4Cl$, and allowed to warm to room temperature in an $N_2$ stream overnight. The residual volatiles were aspirated away, and the reaction was quenched with 6 N HCl to pH 1 and extracted with ether. The organic layer was dried and filtered and the solvent removed to give 9.8 g of off-white

solid (95%). This was crystallized from hot carbon tetrachloride/petroleum ether to give white light fluffy needles, mp 195.0–196.5 °C dec.

**Methyl (3-Methoxy-4,6-dimethyl-1-oxocyclohex-2-en-5-yl)acetate (19).** (2,6-Dimethyl-3,5-dimethoxyphenyl)acetic acid ($M_r$ = 224.2, 215 mg, 0.95 mmol) was dissolved in 20 mL of dry THF and 30 mL of dry *tert*-butyl alcohol and cooled under $N_2$ to −78 °C, at which time 100 mL of dry methylamine was distilled in. $Li^0$ (1.5 g, 216 mmol) was added all at once, and the reaction was warmed to −5 °C, no blue color being present until the reaction reached −15 °C. The temperature was maintained at −5 °C (ice/brine) for 20 min, when an additional 15 mL of *tert*-butyl alcohol was added. After about 5 min the blue color dissipated, and the flask was recooled to −78 °C, quenched with 30 g of $NH_4Cl$(s), and allowed to warm to room temperature overnight in a stream of nitrogen. The residual volatiles were aspirated off, the vacuum was broken with 40 mL of 1 M HCl, and the remaining mixture was extracted with ether. Workup produced 139 mg of pale oil (73%). This was immediately dissolved in 2 mL of MeOH and 2 mL of THF, and 15 mL (excess) of ethereal diazomethane was added. After 10 minutes, the volatiles were evaporated and the sweet-smelling resultant oil was distilled [Kugelrohr, 100 °C (0.01 mm Hg)] to give 107 mg (50%) of clear oil. The mixture of isomers (NMR 5.25 (1 h, br s), 3.62 (3 H, s), 3.60 (3 H, s), 2.9–2.1 (5 H, m), 1.25–1.00 (6 H, m)) was separated on silica TLC (ether/petroleum ether, 1:4, developed 7 times) to give the major kinetic product pure, which was assigned the all-cis configuration on the basis of 270-MHz decoupling experiments.

**(3-Methoxy-4,6-dimethyl-1-oxocyclohex-2-en-5-yl)acetic Acid (18).** (3,5-Dimethoxy-2,6-dimethylphenyl)acetic acid ($M_r$ = 224, 790 mg, 3.52 mmol) was dissolved in 10 mL of dry THF and 10 mL of dry *tert*-butyl alcohol and cooled to −78 °C, and 100 mL of methylamine was distilled in. The reaction was warmed to −5 to −10 °C, and 0.5 g of $Li^0$ ($M_r$ = 7, 70 mmol) was added piecemeal over 30 min. The blue solution was quenched with 5 mL of MeOH and recooled to −78 °C, 200 mmol of $NH_4Cl$ was added, and the reaction was warmed to room temperature in an $N_2$ stream. The residual volatiles were aspirated off, the flask was cooled to 0 °C, and the vacuum was broken with 40 mL of saturated oxalic acid dihydrate in MeOH to pH 2. The solvent was evaporated, and the residuum was extracted with ether vs. pH 2 water. Workup produced 953 mg of pale oily semisolid, contaminated by a little oxalic acid. The product was distilled [120 °C (0.01 mmHg)] to give 544 mg of pale oil (73%). The isomer mixture could with difficulty be separated by TLC (50% $C_6H_6$, 50% ether, 1% HOAc, developed 4 times on 0.25-mm silica, or 80% $C_6H_6$, 20% ether, 1% HOAc, developed 10 times on 1-mm silica) to give two bands predominantly. The lower, and major, band was assigned the all-cis configuration (NMR, Table I). The higher, and lesser, band appeared to contain two isomers: NMR ($CDCl_3$) 5.34 (1 H, v br), 3.69 (3 H, br s), 3.0–2.0 (5 H, v br), 1.26 (3 H, br), 1.17 (3 H, br); NMR ($Me_2SO$-$d_6$, 125 °C) 5.26 (0.25 H, s), 5.21 (0.75 H, s), 3.66 (3 H, s), 2.6–1.9 (5 H, br), 1.25 (0.8 H, d, $J$ = 6.8 Hz), 1.21 (0.8 H, d, $J$ = 8.0 Hz), 1.09 (2.2 H, d, $J$ = 6.7 Hz), 0.98 (2.2 H, d, $J$ = 7.0 Hz).

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**Registry No.** **1a**, 118-41-2; **1b**, 1916-07-0; **1c**, 96213-26-2; **1d**, 96213-27-3; **2a**, 1132-21-4; **2b**, 2150-37-0; **2c**, 96213-28-4; **3a**, 4670-10-4; **3b**, 6512-32-9; **3c**, 96213-29-5; **3d**, 96213-30-8; **4a**, 96213-31-9; **4b**, 96213-32-0; **5**, 96213-33-1; **6**, 96227-67-7; **6** methyl ester, 96213-34-2; **7**, 96213-35-3; **7** methyl ester, 96213-36-4; **8**, 96213-37-5; **8** methyl ester, 96213-38-6; **9**, 96213-39-7; **9a**, 75339-75-2; **10**, 96213-40-0; **11**, 96213-41-1; **12**, 96227-68-8; **13**, 96213-42-2; **14**, 96213-43-3; **15**, 96213-44-4; **16**, 96227-69-9; **17**, 96213-45-5; **18** (*all-cis*), 96213-46-6; **18**, 96290-75-4; **19** (*all-cis*), 96213-47-7; **19**, 96290-45-8; **20**, 96213-48-8; MTMCl, 2373-51-5; $ZnCl_2$, 7646-85-7; 3,4,5-trihydroxybenzoic acid methyl ester, 99-24-1; 1,3,5-trioxane, 110-88-3.

# Synthesis of 2,2-Disubstituted 7-Methylenenorbornanes with 2-Exo Functionality by Diels–Alder Reaction of 5,5-Dimethoxytetrachlorocyclopentadiene[1]

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Diels–Alder reaction of 5,5-dimethoxytetrachlorocyclopentadiene (**2**) with methyl methacrylate gave only the *endo*-carbomethoxybicycloheptene adduct **4N**, confirmed by single-crystal X-ray analysis. Methylation of the endo adduct **3** of methyl acrylate and **2** gave only **4N**. Saponification and dehalogenation of **3** gave carboxy ketal **7**, whose methyl ester **9** also gave only *endo*-carbomethoxy product **10** upon alkylation. Reaction of **2** with methacrylonitrile gave a 3.5:1 exo/endo product mixture, whose major isomer **11X** was hydrolyzed to its carboxamide (**12X**). Conversion of **12X** to its carboxylic acid (**6X**) by acidic *n*-butyl nitrite was accompanied by a pentachloro byproduct (**19**) derived from internal methoxylation of the carboxy group by the C7 ketal. Dehalogenation of **6X** and hydrogenation gave saturated carboxy ketal **20**. Hydrolysis of **20** gave the lactol **22** of the keto acid. Treatment of **22** with diazomethane gave keto ester **25**; treatment of **20** with diazomethane gave ester **24**, whose ketal function could not be selectively hydrolyzed to give **25**, only **22** being isolated. Wittig reaction of **25** provided the 7-methylene ester **26**, also available by direct Wittig treatment of **22** followed by esterification.

For a study concerning haptophilic control of hydrogenation stereochemistry,[2] we undertook the synthesis of system **1**, in which the group R was to be modifiable to produce functions of differing size and polarity. Our ap-

(1) Taken in part from the Ph.D. Thesis of J. K. W., Rutgers University, 1984.

(2) Thompson, H. W.; Naipawer, R. E. *J. Am. Chem. Soc.* **1973**, *95*, 6379.

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