The Catalytic Hydrogenation of Substituted 4-Chromanones and 4-Chromanols

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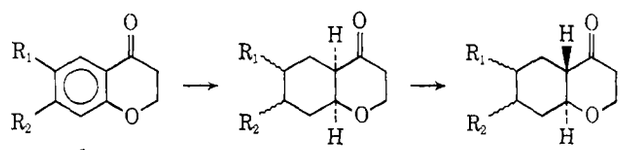
Received April 3, 1973

The catalytic hydrogenation over ruthenium of 6- and 7-carbomethoxy-4-chromanone, 6-methyl-4-chromanone, 6-carbomethoxy-4-chromanol, and the ethylene ketal of 6-carbomethoxy-4-chromanone has been attempted. Conditions were found for the ketones leading to perhydro alcohols as the major products. Electron-donating ring substituents appear to minimize significantly any competing hydrogenolyses.

The catalytic hydrogenation of the aromatic rings of 4-chromanones, while not reported in the literature,[1] provides an attractive route for the preparation of analogs of *cis*- and *trans*-decalin containing an oxygen atom as one of the ring constituents[2] (Scheme I).

SCHEME I



1 2 3

a, $R_1 = CO_2CH_3$; $R_2 = H$

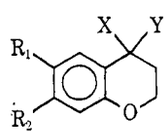
b, $R_1 = CH_3$; $R_2 = H$

c, $R_1 = H$; $R_2 = CO_2CH_3$

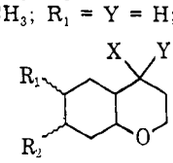
The major difficulty lay in the choice of catalyst and reaction conditions, so as to minimize hydrogenolysis of either the benzylic carbonyl groups[1,3] (as such or in a reduced form) or the phenolic carbon–oxygen bond,[4] and suggested primary emphasis on ruthenium catalysts.

The desired starting materials, **1a–c**, were prepared by literature methods[5,6] and exhibited the expected spectral properties.[7] To evaluate the optimum benzylic functionality, 6-carbomethoxy-4-chromanone (**1a**) was reduced with sodium borohydride to the 6-carbomethoxy-4-chromanols (**4**) and also converted to the ethylene ketal **5**.

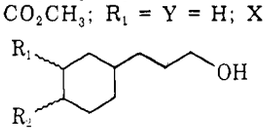
Preliminary experiments using ruthenium catalysts in 80% aqueous ethanol for the hydrogenation of 6-carbomethoxy-4-chromanone (**1a**) led to complete hydrogenolysis of the benzylic carbon–oxygen bond and extensive reduction of the aromatic ring. The hydrogenolysis products 6-carbomethoxychroman (**6**) and saturated material with gross structure **7** (R = CH_2CH_3) were obtained in a 1:2 ratio, and evidence was obtained that **6** was converted to **7** under the reaction conditions. Hydrogenation of **1a** in 90% aqueous methanol over 5% ruthenium on charcoal at 100° and 1950 psig for 20 hr proved satisfactory for extensive aromatic ring hydrogenation with less hydrogenolysis. Chromatography of 800 mg of crude reaction mixture permitted isolation of 290 mg of a mixture of perhydro alcohols[8] **8**, 260 mg of hydrogenated and benzylically hydrogenolyzed **7** (R = CH_3), and 160 mg of hydrogenated and benzylically and phenolically hydrogenolyzed **9**. Under these reaction conditions, ring



4, $R_1 = CO_2CH_3$; $R_2 = Y = H$; $X = OH$
5, $R_1 = CO_2CH_3$; $R_2 = H$; $XY = -O(CH_2)_2O-$
6, $R_1 = CO_2CH_3$; $R_2 = X = Y = H$
10, $R_1 = CO_2CH_3$; $R_2 = Y = H$; $X = OCH_3$
13, $R_1 = CH_3$; $R_2 = X = Y = H$
14, $R_2 = CO_2CH_3$; $R_1 = X = Y = H$
18, $R_2 = CO_2CH_3$; $R_1 = Y = H$; $X = OH$



7, $R_1 = CO_2R$; $R_2 = X = Y = H$
8, $R_1 = CO_2CH_3$; $R_2 = Y = H$; $X = OH$
11, $R_1 = CO_2CH_3$; $R_2 = Y = H$; $X = OCH_3$
12, $R_1 = CH_3$; $R_2 = Y = H$; $X = OH$
15, $R_2 = CO_2CH_3$; $R_1 = X = Y = H$
16, $R_2 = CO_2CH_3$; $R_1 = Y = H$; $X = OH$



9, $R_1 = CO_2CH_3$; $R_2 = H$
17, $R_1 = H$; $R_2 = CO_2CH_3$

(1) (a) For results of Raney nickel hydrogenations of 7-methoxy- and 7-hydroxy-4-chromanone, see R. T. Blickenstaff and I. Y. C. Tao, *Tetrahedron*, **24**, 2495 (1968), and P. Naylor, G. R. Ramage, and P. Schofield, *J. Chem. Soc.*, 1190 (1958). (b) For the results of hydrogenations of 4-chromenones, see R. Mozingo and H. Adkins, *J. Amer. Chem. Soc.*, **60**, 669 (1938). (c) For typical results on hydrogenation of flavones, see M. Suzuki and T. Oda, *Nippon Kagaku Zasshi*, **89**, 878 (1968) [*Chem. Abstr.*, **70**, 57575*r* (1969)]; S. Fujise, *et al.*, *Nippon Kagaku Zasshi*, **84**, 81 (1963) [*Chem. Abstr.*, **60**, 5445*a* (1964)]; S. Mitsui, *et al.*, *J. Chem. Soc. Jap., Pure Chem. Sect.*, **72**, 339 (1951) [*Chem. Abstr.*, **46**, 8102*i* (1952)].

(2) The stereochemical designations at the bridgeheads in the perhydro products obtained in this work are arbitrarily chosen to reflect the cis or trans relationships and are not meant to imply absolute configurations.

(3) (a) W. John, P. Günther, and M. Schmeil, *Ber.*, **71**, 2637 (1938); (b) R. L. Augustine, "Catalytic Hydrogenation," Marcel Dekker, New York, N. Y., 1965, pp 81–84, 110–111, and 135.

(4) Reference 3b, pp 72–73.

(5) J. Lichtenberger and R. Geyer, *Bull. Soc. Chim. Fr.*, 282 (1963).

(6) J. Colonge and A. Guyot, *Bull. Soc. Chim. Fr*, 325 (1958).

(7) The melting point of 6-carbomethoxy-4-chromanone (**1a**), 72.5–74.5°, was significantly different from the value of 130° reported previously.[5] However, elemental analyses, spectral data, and the method of preparation confirm the assigned structure.

(8) After Jones oxidation[9] gas chromatographic analysis suggested the presence of three ketones. Based on the known preference[10] for cis addition in catalytic hydrogenations and on small-scale equilibration studies[11] involving the ketones, it appears reasonable to assign cis ring fusions (**2a**) to the major isomers.

(9) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. 1, Wiley, New York, N. Y., 1967, pp 142–144.

(10) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962, pp 350–353; J. March, "Advanced Organic Chemistry," McGraw-Hill, New York, N. Y., 1968, pp 591–596.

(11) G. Schwartzkopf, unpublished observations.

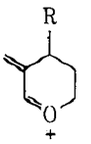
hydrogenation was essentially complete and benzylic hydrogenolysis amounted to ~60%.

Reduction of alcohol **4** in 90% aqueous methanol over ruthenium resulted in slower ring reduction and almost quantitative benzylic hydrogenolysis. Products obtained were aromatic ester **6** (50–60% yield), saturated ester **7** (R = CH_3; 30–40% yield), and <10% each of the methyl ethers of the starting alcohol (**10**) and the reduced alcohol (**11**). Ketal **5** was found to be unstable on refluxing in 90% aqueous methanol for 19 hr, producing 30–40% ketone **1a**. Addition of sodium bicarbonate prevented this hydrolysis. However, reduction of the ketal in aqueous methanol containing sodium bicarbonate over ruthenium did not lead to reaction of any kind. Based on these results, keto systems (**1**) were used exclusively in subsequent experiments.

Two questions remained to be investigated. The first was whether the carbomethoxy group exerted a significant influence through electron withdrawal. Hydrogenation of 1.0 g of 6-methyl-4-chromanone (**1b**) in 90% aqueous methanol over ruthenium produced a mixture of at least six components. The two major components, constituting ~65% of vacuum-distilled material (540 mg), were isolated by preparative vapor phase chromatography[12] and identified as isomeric saturated alcohols (**12**). A minor component appeared to be 6-methylchroman (**13**) from mass spectral evidence.

The second question was whether the carbomethoxy group exerted a significant influence by virtue of being para to the chroman oxygen function. Hydrogenation of 7-carbomethoxy-4-chromanone (**1c**) in aqueous methanol over ruthenium produced 830 mg of an oil which was subjected to column chromatography. The three products isolated were 140 mg of 7-carbomethoxychroman (**14**), 190 mg of hydrogenolyzed saturated ester **15**, and 360 mg of an isomeric mixture of the desired saturated alcohols[13] **16**. Approximately 80 mg of impure hydrogenated and benzylically and phenolically hydrogenolyzed **17** was also obtained, but resisted separation from 7-carbomethoxy-4-chromanol (**18**). These products correspond to ~80% aromatic ring hydrogenation with ~50% benzylic hydrogenolysis and are similar enough to those obtained from 6-carbomethoxy-4-chromanone (**1a**) to suggest that the only substituent-effect difference in the 6- and 7-carbomethoxy-4-chromanone hydrogenations is a slight increase in the hydrogenolysis of the phenolic carbon-oxygen bond when the carbomethoxy group is in the 6 position.

In obtaining mass spectra of the various reaction products, we have uncovered a useful feature in the spectra of all of the saturated bicyclic compounds (**7**, **11**, **12**, and **15**) except the carbomethoxy alcohols (**8** and **16**). In these compounds, the base peak at 70 eV corresponds to a fragment of gross structure **19** irrespective of the nature of the substituent R in position 4 and of the nature or position of substituents in the other ring. The generality of this behavior in related heterocyclic systems[14] and the actual structure of such fragments remain to be explored.



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In summary, catalytic hydrogenation conditions have been established for the reduction of 6- and 7-substituted chromanones so that the major components obtained will be the perhydro alcohols. Electron-donating ring substituents appear to minimize significantly any competing hydrogenolyses. However, the limited range of substituents studied suggests caution in the application of these results.

Experimental Section

Melting points and boiling points are uncorrected. Nmr spectra were recorded on a Varian A-60A instrument using solutions in deuteriochloroform. Ir spectra were determined with a Beckman IR-10 spectrophotometer, with only major absorptions being cited. Mass spectral analyses were obtained at 70 eV. Elemental analyses were performed by Alfred Bernhardt Mikroanalytisches Laboratorium, Elbach, West Germany.

6-Carbomethoxy-4-chromanone (**1a**).—This compound was prepared from *p*-cresol in 27% overall yield by the method of Lichtenberger and Geyer[5] and was obtained from hexane as a pale orange solid: mp 72.5–74.5° (lit.[5] mp 130°); ir (Nujol) 1710 cm^{-1} (C=O); nmr δ 8.21 (d, 1, J = 2 Hz, H-5), 7.98 (dd, 1, J = 2, 8 Hz, H-7), 6.73 (d, 1, J = 8 Hz, H-8), 4.55 (t, 2, J = 6 Hz, OCH_2CH_2), 3.88 (s, 3, OCH_3), 2.80 (t, 2, J = 6 Hz, CH_2-CH_2C=O).

Anal. Calcd for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 63.72; H, 4.80.

6-Methyl-4-chromanone (**1b**).—This compound was prepared from 2-carboxyethyl *p*-tolyl ether in 30% yield by the method of Colonge and Guyot:[6] mp 28–32° (lit.[6] mp 34°); ir (Nujol) 1690 cm^{-1} (C=O); nmr δ 7.69 (d, 1, J = 2 Hz, H-5), 7.31 (dd, 1, J = 2, 9 Hz, H-7), 6.88 (d, 1, J = 9 Hz, H-8), 4.51 (t, 2, J = 6.5 Hz, OCH_2CH_2), 2.77 (t, 2, J = 6.5 Hz, CH_2CH_2C=O), 2.30 (s, 3, CH_3).

7-Carbomethoxy-4-chromanone (**1c**).—This compound was prepared from *m*-cresol in 4.5% overall yield by the method of Lichtenberger and Geyer[5] and was obtained from methanol as white crystals: mp 108–109° (lit.[4] mp 103°); ir (Nujol) 1685 (ketone C=O), 1720 cm^{-1} (ester C=O); nmr δ 7.93 (d, 1, J = 8 Hz, H-5), 7.61 (d, 1, J = 2 Hz, H-8), 7.60 (dd, 1, J = 2, 8 Hz, H-6), 4.69 (t, 2, J = 6 Hz, OCH_2CH_2), 3.93 (s, 3, OCH_3), 2.83 (t, 2, J = 6 Hz, CH_2CH_2C=O).

6-Carbomethoxy-4-chromanol (**4**). A stirred solution of 2.06 g (10.0 mmol) of **1a** in 25 ml of moist methanol was treated with 380 mg (10.0 mmol) of sodium borohydride in several portions over a few minutes at room temperature. After 1 hr the stirred solution was treated with 2.3 ml of glacial acetic acid and concentrated. The residue was treated with saturated $NaHCO_3$ solution and then extracted with $CHCl_3$. The $CHCl_3$ extract was dried (Na_2SO_4) and the solvent evaporated, giving 2.1 g (100%) of an oil: ir (neat) 3440 (OH), 1720 cm^{-1} (C=O); nmr δ 8.04 (d, 1, J = 2 Hz, H-5), 7.81 (dd, 1, J = 2, 9 Hz, H-7), 6.83 (d, 1, J = 9 Hz, H-8), 4.79 (t, 1, J = 4 Hz, H-4), 4.30 (m, 2, OCH_2CH_2), 3.83 (s, 3, OCH_3), 3.33 (br s, 1, OH), 2.00 (m, 2, CH_2CH_2CHOH). This crude material was directly hydrogenated without further purification.

Ethylene Ketal of 6-Carbomethoxy-4-chromanone (**5**).—A stirred mixture of 2.06 g (10.0 mmol) of **1a**, 2.2 ml (40.0 mmol) of ethylene glycol, 200 mg of *p*-toluenesulfonic acid, and 20 ml of benzene was refluxed under a water separator for 31 hr. The cooled mixture was poured onto 50 ml of saturated $NaHCO_3$ solution containing 50 g of ice and then extracted with ether.

(12) Extreme difficulty was encountered in trapping products.

(13) Upon Jones oxidation,[9] gas chromatographic analysis with a variety of column substrates did not suggest the presence of more than one component. This presumably cis isomer (**2c**) was converted on equilibration[11] to a different and presumably trans isomer.

(14) For an example in the decahydroquinoline series, see V. G. Zaikin, N. S. Wulfson, V. I. Zaretskii, A. A. Bakaev, A. A. Akhrem, L. I. Ukhova, and N. F. Uskova, *Org. Mass Spectrom.*, **2**, 1257 (1969).

The ethereal extract was washed with water and dried (Na_2SO_4). Evaporation gave 2.9 g of an oil. Chromatography on silica gel (Baker) using benzene–chloroform gave a clean mixture (9:1) of ketal **5** and **1a** (owing to deketalization during chromatography). Recrystallization of this mixture from methanol gave 780 mg (31%) of **5**: mp 81–84°; ir (Nujol) 1700 cm^{-1} (C=O); nmr δ 8.09 (d, 1, J = 2 Hz, H-5), 7.85 (dd, 1, J = 2, 9 Hz, H-7), 6.81 (d, 1, J = 9 Hz, H-8), 4.50–4.00 (m, 6), 3.87 (s, 3, OCH_3), 2.10 (t, 2, J = 6 Hz, CH_2CH_2C).

Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.21; H, 5.59.

General Hydrogenation Procedure in Aqueous Methanol.—Solutions of chromans in 30 ml/g of 90% aqueous methanol were hydrogenated for 18–20 hr in a stirred stainless steel autoclave at 1700–2100 psig at 100–110° using 200–300 mg/g of 5% ruthenium on carbon. The catalysts were removed by filtration and the filtrates concentrated. The moist residues were extracted with CH_2Cl_2, and the extracts washed with water, dried ($MgSO_4$), and concentrated.

Hydrogenation of 1a.—The general procedure was used for the hydrogenation of 1.00 g (4.85 mmol) of **1a**. Chromatography on silica gel (Woelm) of the 800 mg of crude product obtained gave 260 mg (27%) of 6-carbomethoxyhexahydrochroman (**7**, R = CH_3) in the 5% ethyl acetate–methylene chloride fractions as an oil: ir (neat) 1740 cm^{-1} (C=O); nmr δ 4.20–3.20 (m, 3, $CHOCH_2$), 3.68 (s, 3, OCH_3); mass spectrum m/e (rel intensity) 198 (7), 167 (8), 166 (8), 139 (3), 138 (10), 97 (100).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.62; H, 9.15. Found: C, 66.85; H, 9.05.

The 20% ethyl acetate–methylene chloride fractions contained 160 mg (17%) of methyl 3-(3-hydroxypropyl)cyclohexanecarboxylate (**9**) as an oil: ir (neat) 3420 (OH), 1740 cm^{-1} (C=O); nmr δ 3.68 (s, 3, OCH_3), 3.64 (t, 2, J = 6 Hz, CH_2CH_2OH), 1.87 (s, 1, OH); mass spectrum m/e (rel intensity) 200 (0.7), 182 (3), 169 (3), 154 (3), 141 (17), 81 (100), 59 (12), 31 (17).

Anal. Calcd for $C_{11}H_{20}O_3$: C, 65.96; H, 10.07. Found: C, 66.11; H, 10.06.

The ethyl acetate fractions contained 290 mg (28%) of a mixture of 6-carbomethoxy-4-hexahydrochromanol isomers (**8**) as an oil: ir (neat) 3420 (OH), 1735 cm^{-1} (C=O); nmr δ 3.68 (s, OCH_3), 2.45 (s, OH); mass spectrum m/e (rel intensity) 214 (4), 213 (3), 197 (8), 196 (36), 113 (32), 81 (100), 80 (100), 57 (54).

Hydrogenation of 4.—The general procedure was used for the hydrogenation of 1.9 g (9.12 mmol) of **4**. Chromatography on silica gel (Woelm) of the 1.60 g of crude product obtained gave 740 mg (42%) of **6**, 410 mg (23%) of **7** (R = CH_3), and 390 mg of mixtures of **7** (R = CH_3), **10**, and **11** (18:14:1).

6-Carbomethoxychroman (**6**) was an oil: ir (neat) 1715 cm^{-1} (C=O); nmr δ 7.71 (m, 2, H-5 and -7), 6.80 (d, 1, J = 9 Hz, H-8), 4.20 (t, 2, J = 5 Hz, OCH_2CH_2), 3.86 (s, 3, OCH_3), 2.79 (t, 2, J = 6 Hz, CH_2CH_2Ar), 1.99 (m, 2, $CH_2CH_2CH_2$).

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 68,70; H, 6.19.

6-Carbomethoxyhexahydrochroman (**7**, R = CH_3) was identified by its nmr spectrum and elemental analysis, in agreement with material previously obtained (see above).

The mixtures of **7** (R = CH_3), **10**, and **11** were resolved by gas chromatography–mass spectra and examination of the mixture nmr spectra. 6-Carbomethoxy-4-methoxychroman (**10**): nmr δ 7.89 (m, H-5 and -7), 6.83 (d, J = 9 Hz, H-8), 4.59 (t, J = 6, H-4), 4.28 (m, OCH_2CH_2), 3.88 (s, CO_2CH_3), 3.40 (s, OCH_3), 2.08 (m, $CH_2CH_2CHCOCH_3$); mass spectrum m/e (rel intensity) 222 (65), 191 (100), 163 (27). 6-Carbomethoxy-4-methoxyhexahydrochroman (**11**): mass spectrum m/e (rel intensity) 228 (4), 197 (18), 127 (100).

Hydrogenation of 1a in Aqueous Ethanol.—A solution of 1.00 g (4.85 mmol) of **1a** in 20 ml of 80% aqueous ethanol was hydrogenated for 23 hr at 1600 psig at 100° using 150 mg of 5% ruthenium on carbon. The catalyst was removed by filtration and the filtrate concentrated. The moist residue was extracted with ether and the ethereal extract dried ($MgSO_4$). Evaporation gave 830 mg of an oil. This was directly subjected to a Jones oxidation,[8] producing 550 mg of an oil. The oil was partially separated using preparative thin layer chromatography on silica gel plates. This gave 70 mg (8%) of impure **6**, identified by its nmr and mass spectrum, and 310 mg (30%) of 6-carbethoxyhexahydrochroman (**7**, R = C_2H_5) as a crude oil: nmr δ 4.10 (quartet, J = 7 Hz, OCH_2CH_3), 3.68 (m, OCH_2CH_2), 1.25 (t, J = 7 Hz, OCH_2CH_3); mass spectrum m/e (rel intensity) 212 (28), 167 (84), 139 (44), 138 (100), 97 (100).

Hydrogenation of 1b.—The general procedure was used for the hydrogenation of 1.00 g (6.16 mmol) of **1b**. Vacuum distillation of the crude product gave 540 mg of an oil: bp 90–160° (3 mm). Gas chromatography indicated six components. Mass spectra allowed identification of a minor component, 6-methylchroman (**13**): mass spectrum m/e (rel intensity) 148 (10), 147 (100).

The two major components (amounting to >65% of the distillate) were collected by preparative gas chromatography. Both appeared to be isomers of 6-methyl-4-hexahydrochromanol (**12**). Collection gave 10 mg of the first component: mass spectrum m/e (rel intensity) 170 (28), 169 (13), 153 (17), 152 (99), 113 (100), 57 (70).

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55, H, 10.65. Found: C, 70.73; H, 10.61.

Also obtained was 30 mg of the second component: ir (neat) 3340 cm^{-1} (OH); nmr δ 3.69 (m, OCH_2CH_2), 1.72 (s, OH), 0.96 (m, CH_3).

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.65. Found: C, 70.67; H, 10.79.

Hydrogenation of 1c.—The general procedure was used for the hydrogenation of 1.00 g (4.85 mmol) of **1c**. Chromatography on silica gel (Woelm) of the 830 mg of crude product obtained gave 140 mg 7-carbomethoxychroman (**14**) in the 1% ethyl acetate–methylene chloride fraction as an oil: ir (neat) 1720 cm^{-1} (C=O); nmr δ 7.54 (m, 2, H-6 and -8), 7.09 (d, 1, J = 9 Hz, H-5), 4.19 (t, 2, J = 5 Hz, OCH_2CH_2), 3.87 (s, 3, OCH_3), 2.81 (t, 2, J = 6 Hz, CH_2CH_2Ar), 2.01 (m, 2, $CH_2CH_2CH_2$).

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 68.78; H, 6.40.

The 10% ethyl acetate–methylene chloride fractions contained 190 mg (20%) of 7-carbomethoxyhexahydrochroman (**15**) as an oil: ir (neat) 1735 cm^{-1} (C=O); nmr δ 4.00 to 3.60 (m, 3, $CHOCH_2$), 3.68 (s, 3, OCH_3); mass spectrum m/e (rel intensity) 198 (8), 167 (14), 139 (13), 138 (35), 97 (100).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.62; H, 9.15; Found: C, 66.75; H, 9.26.

The 20% ethyl acetate–methylene chloride fractions contained 160 mg of a mixture of **17** and **18** (3:1) with a trace of **15** present. The mixture was resolved by gas chromatography–mass spectra and examination of the mixture nmr spectrum. 7-Carbomethoxy-4-chromanol (**18**): nmr δ 7.48 (m, Ar H), 4.75 (t, J = 5 Hz, H-4), 4.24 (t, J = 5 Hz, OCH_2CH_2), 3.84 (s, OCH_3); mass spectrum m/e (rel intensity) 208 (67), 207 (8), 190 (8), 177 (25), 149 (100). Methyl 4-(3-hydroxypropyl)-cyclohexanecarboxylate (**17**): nmr δ 3.68 (s, OCH_3), 3.55 (t, J = 6 Hz, CH_2CH_2OH), 2.23 (s, OH); mass spectrum m/e (rel intensity) 200 (3), 182 (12), 169 (13), 154 (7), 141 (38), 81 (100), 59 (30), 45 (10), 31 (33).

The ethyl acetate fractions contained 360 mg (35%) of a mixture of 7-carbomethoxy-4-hexahydrochromanol isomers (**16**) as an oil: ir (neat) 3420 (OH), 1730 cm^{-1} (C=O); nmr δ 3.68 (s, OCH_3), 2.01 (s, OH); mass spectrum m/e (rel intensity) 214 (0.6), 196 (7), 113 (9), 57 (59), 41 (100).

Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.82; H, 8.66.

Acknowledgments.—We wish to thank Dr. Robert L. Augustine for his suggestions and Mr. Regis Pellet for the mass spectra. One of us (G. S.) wishes to express appreciation to Merck and Co. for financial assistance.

Registry No.—**1a**, 41118-19-8; **1b**, 39513-75-2; **1c**, 41118-21-2; **4**, 41118-22-3; **5**, 41118-23-4; **6**, 41118-24-5; **7** (R = CH_3), 41118-25-6; **7** (R = C_2H_5), 41118-26-7; **8**, 41118-27-8; **9**, 41118-28-9; **10**, 41118-29-0; **11**, 41118-30-3; **12**, 41174-27-0; **13**, 3722-74-5; **14**, 41118-24-5; **15**, 41118-33-6; **16**, 41118-34-7; **17**, 41118-35-8; **18**, 41118-36-9.