Table II. Calculated Methyl Radical Stabilization Energies, Defined by Isodesmic Reaction 1 (in kcal/mol)

X	ROHF[a]	ROHF[b]	UHF[c]	AUHF[d]	AUMP2[d]	AUMP3[d]	AUMP4[d]
H	0.0	0.0	0	0.0	0.0	0.0	0.0
CH_3	2.3	3.3	2	2.9	2.9	3.1	3.2
F	3.4	1.8	3	2.6	4.8	3.0	5.0
CN	4.6	5.3	11	4.8	6.1	6.1	6.7
OH	6.5	5.8	6	6.4	8.8	8.0	8.9
CHO	6.7	7.7	4	8.6	9.2	9.2	9.5
NH_2	10.0	10.3	10	7.8	11.5	10.5	11.1
$CHCH_2$	6.6	7.8	21	7.9	11.0	10.6	12.6
BH_2	12.1	11.7	11	12.5	12.8	12.9	13.0

[a] 3-21G basis set. [b] 4-31G basis set (ref 2). [c] 3-21G basis set (ref 3). [d] 6-31G* basis set.

Table III. Calculated Radical Stabilization Energies for Trans 1-Substituted Allyl Radicals Defined by Isodesmic Reaction 2 (in kcal/mol)

X	UHF[a]	AUHF[b]	AUMP2[b]
H	0.0	0.0	0.0
CH_3	3.2	3.6	5.6
F	7.7	5.2	8.3
CN	8.1	4.3	9.9
CHO	15.7	4.8	11.7
OH	9.5	9.0	12.8
NH_2	10.5	8.6	13.7
BH_2	10.3	12.4	15.1

[a] 3-21G basis set. [b] 6-31G* basis set.

Table IV. Calculated Radical Stabilization Energies for 2-Substituted Allyl Radicals Defined by Isodesmic Reaction 3 (in kcal/mol)

X	UHF[a]	AUHF[d]	AUMP2[b]
H	0.0	0.0	0.0
CN	2.5	-0.6	3.0
CH_3	1.8	1.8	4.3
BH_2	5.4	3.8	5.2
NH_2	9.4	6.1	9.4
F	11.4	8.8	11.0
CHO	9.8	4.8	11.6
OH	10.9	10.1	12.6

[a] 3-21G basis set. [b] 6-31G* basis set.

kcal/mol,[12] and for amino of 9-10 kcal/mol.[13] The AUMP values compare favorably with these data. Accepting the AUMP4 values as the reference, it is seen that the ROHF method gives quite acceptable results exept for the vinyl group.

We have also calculated RSE's for allyl radicals where spin contamination is substantial for all substituents. For reaction 2 we again observe a large effect upon going from the UHF to the AUHF level for the CN and CHO substitutents (Table III). The effects for the other substitutents are smaller, which is due to the fact that RSE's are relative energies, and these species contain similar amounts of spin contamination. Adding electron correlation again increases all RSE's. Similar trends are found for reaction 3 (Table IV).

For 1-substituted allyl radicals, the stabilizing order of the substituents is the same as for the methyl system, with the exception of the switch between OH and CHO, although the effects are somewhat larger. The RSE's for the cross-conjugated 2-substituted allyl radicals show no correlation with those for the 1-substituted system. At the 2-position especially the polar substituents F and OH have large RSE's, but also CHO is a good stabilizing group.

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Enantiomerically Pure Acetals in Organic Synthesis. 3. A Synthesis of (*R*)-Mevalonic Acid Lactone

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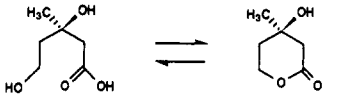
(*R*)-Mevalonic acid is the acetate-derived biosynthetic precursor of the terpene family of natural products.[1,2] The ubiquity of terpenes in nature together with the preeminent position of (*R*)-mevalonic acid in the biosynthetic pathway have prompted the development of syntheses of (*R*)-mevalonic acid lactone (1).[3]



1

Recently we reported an enantioselective approach to carbohydrates and their derivatives via a general chromatographic resolution of diastereomeric furanoside and pyranoside acetals derived from α-hydroxy esters.[4] We believed that this approach could complement the established practice of synthesizing rare or unavailable carbohydrates and their derivatives from other carbohydrates available in the "chiral pool"[5] and could be especially useful for syntheses of deoxy, branched, and heteroatom-containing sugars. Since from a synthetic perspective (*R*)-mevalonic acid lactone can be considered an example of a highly deoxygenated, branched pentopyranose, we set

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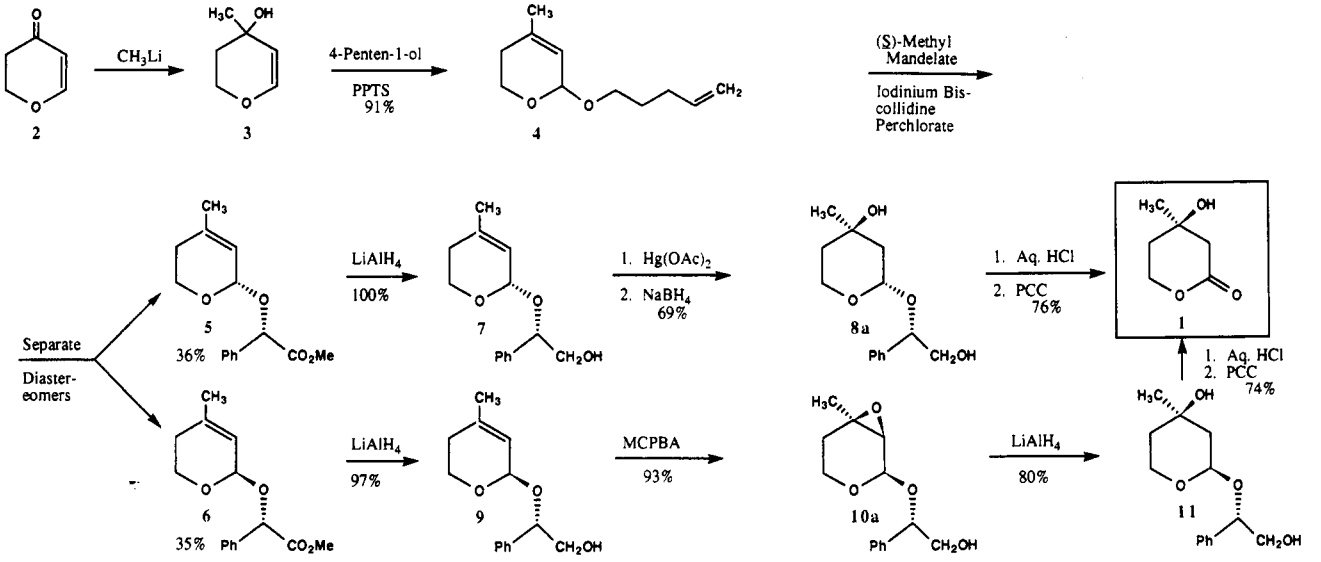
0022-3263/91/1956-0885$02.50/0

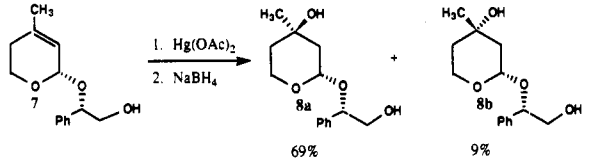
Scheme I



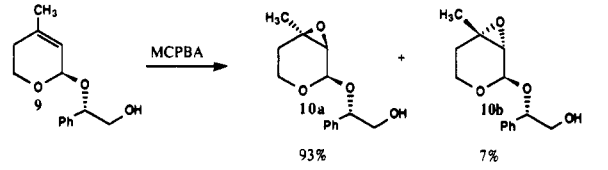
out to prepare **1** as a test of this methodology. An enantioselective synthesis of (*R*)-mevalonic acid lactone was the result (Scheme I).

Addition of methyllithium to 5,6-dihydro-4*H*-pyran-4-one (**2**)[6] gave the unstable allylic alcohol **3**, which upon treatment with pyridinium *p*-toluenesulfonate (PPTS) in the presence of 4-penten-1-ol gave "activated"[7] pentenyl pyranoside **4** in 91% yield from dihydropyrone **2**. Reaction of **4** with iodonium bis-collidine perchlorate[8] in the presence of (*S*)-(+)-methyl mandelate produced chromatographically separable diastereomers **5** and **6** in 36% and 35% yields, respectively. Attempts to convert alcohol **3** directly to a mixture of diastereomers **5** and **6** resulted in considerably lower yields. Each of the separated diastereomers **5** and **6** was converted into **1** as discussed below.

The less polar diastereomer **5** was reduced in quantitative yield to alcohol **7** by using lithium aluminum hydride in tetrahydrofuran at 0 °C. Oxymercuration–demercuration of **7** gave separable diastereomeric diols **8a** and **8b** in 69% and 9% yields, respectively.[9] Acetal **8a** was hydrolyzed to the corresponding hemiacetal, which was subsequently oxidized with use of pyridinium chlorochromate to give **1** in 76% yield from **8a**.



The more polar diastereomer **6** was reduced in 97% yield to alcohol **9**, using $LiAlH_4$ in THF at 0 °C. Treatment of **9** with *m*-chloroperoxybenzoic acid in dichloromethane at 0 °C produced separable diastereomeric epoxides **10a** and **10b** in 93% and 7% yields, respectively.[10] Reductive



epoxide ring opening using $LiAlH_4$ in THF at room temperature occurred regioselectively at C-2 to give diol **11** in 80% yield. Acetal **11** was hydrolyzed and oxidized as above to give **1** in 74% yield. The overall yield of (*R*)-mevalonic acid lactone **1** starting from 5,6-dihydro-4*H*-pyran-4-one was 34%.

The procedures described herein can provide either enantiomer of mevalonic acid and could be adapted for preparations of isotopically labeled materials[3f] and of (*R*)-3,4,5,6-tetrahydro-4-ethyl-4-hydroxy-2*H*-pyran-2-one ("homomevalonic acid lactone").[11]

Further synthetic uses of the acetals made available by this methodology will be reported in future papers.

Experimental Section

Dichloromethane was distilled from calcium hydride. Diethyl ether and tetrahydrofuran were distilled from sodium benzophenone ketyl under an inert atmosphere. Melting points were taken on a Thomas Unimelt apparatus and are uncorrected. The

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(9) Oxymercurations of esters such as **5** were exceedingly slow.

(10) Epoxidations of esters such as **6** with MCPBA were less diastereoselective and favored the anti diastereomers.

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purity of all title compounds was judged to be ≥95% by ^1H and ^{13}C NMR spectral determinations. ^1H and ^{13}C NMR spectra were recorded at 250 and 62.9 MHz, respectively. Elemental analyses were performed by Desert Analytics, Tucson, Az. Thin-layer chromatographic analyses were performed on Merck silica gel 60 plates (0.25 mm, 70–230-mesh ASTM). Column chromatography was performed on Merck silica gel 60 (gravity driven, 70–230-mesh ASTM).

5,6-Dihydro-4*H*-pyran-4-one (2). To a solution of freshly distilled *cis*-1-methoxy-1-buten-3-yne[12] (5.0 mL, 66 mmol) in THF (150 mL) at −78 °C was added a solution of *n*-BuLi in hexanes (1.6 M, 38 mL, 61 mmol) dropwise via an addition funnel. After 0.25 h, a cooled (−78 °C) solution of ethyl formate (4.9 mL, 61 mmol) in THF (30 mL) was added rapidly via cannula, and the resultant solution was allowed to stir for 0.5 h. A solution of diisobutylaluminum hydride in toluene (1.5 M, 44 mL, 66 mmol) was added dropwise. The reaction was allowed to warm to 0 °C and was quenched with 3% aqueous HCl (200 mL) and diluted with Et_2O (200 mL). The aqueous layer was extracted with ether (6 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo to give a yellow oil. The residue was taken up in 4:1 THF/H_2O (250 mL), acidified with *p*-toluenesulfonic acid monohydrate (300 mg, 1.58 mmol), and heated to reflux for 60 h. After being cooled to room temperature, the mixture was diluted with ether (200 mL) and washed with saturated aqueous $NaHCO_3$ (100 mL). The aqueous layer was extracted with ether (500 mL) in a continuous extraction apparatus. The combined organic layers were dried (Na_2SO_4) and filtered, and the solvents were removed by distillation at ambient pressure under argon. The residue was further distilled under vacuum to afford **2** (2.64 g, 26.9 mmol, 44%) as a pale yellow liquid: bp_{16} 89–92 °C, lit.[6a] bp_{15} 64 °C; R_f 0.30 (50% EtOAc/hexanes); IR ($CHCl_3$) cm^{-1} 1720, 1655; ^1H NMR ($CDCl_3$) δ 2.61 (2, t, *J* = 6.9 Hz), 4.51 (2, t, *J* = 6.9 Hz), 5.42 (1, d, *J* = 6.1 Hz), 7.37 (1, d, *J* = 6.1 Hz); ^{13}C NMR ($CDCl_3$) δ 36.37 (CH_2), 68.03 (CH_2), 107.36 (CH), 163.36 (CH), 191.66 (C).

4-Penten-1-yl 5,6-Dihydro-4-methyl-2*H*-pyran-2-yl Ether (4). To a solution of CH_3Li (14.5 mmol) in ether (30 mL) at −78 °C was added a solution of **2** (1.295 g, 13.2 mmol) in ether (50 mL) dropwise via an addition funnel. The reaction mixture was stirred for 0.25 h and then quenched with saturated aqueous NH_4Cl (50 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo to give **3** as a pale yellow liquid. The residue was taken up in CH_2Cl_2 (15 mL), 4-penten-1-ol (4.1 mL, 40 mmol) and PPTS (25 mg, 0.1 mmol) were added, and the mixture was stirred for 5 h. The mixture was then poured into saturated aqueous $NaHCO_3$ (10 mL), the aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. Chromatography of the residue on silica gel 60 (200 g) eluted with CH_2Cl_2 gave **4** (2.195 g, 12.0 mmol, 91%) as a colorless liquid, homogenous by TLC (R_f 0.30, CH_2Cl_2): IR ($CHCl_3$) cm^{-1} 3005, 2937, 1680; ^1H NMR ($CDCl_3$) δ 1.63–1.82 (6, m), 2.15 (2, q, *J* = 6.6 Hz), 2.26 (1, m), 3.45 (1, td, *J* = 6.6, 9.5 Hz), 3.68–3.85 (2, m), 3.92 (1, dt, *J* = 3.7, 11.2 Hz), 4.89 (1, s), 4.93–5.10 (2, m), 5.47 (1, s), 5.83 (1, tdd, *J* = 6.6, 10.2, 17.0 Hz); ^{13}C NMR ($CDCl_3$) δ 22.94 (CH_3), 28.98 (CH_2), 29.51 (CH_2), 30.36 (CH_2), 57.30 (CH_2), 67.09 (CH_2), 94.38 (CH), 114.64 (CH_2), 119.87 (CH), 137.44 (C), 138.19 (CH).

(*S*)-Methyl Mandelyl 4-Methyl-5,6-dihydro-2*H*-pyran-2-yl Ethers 5 and 6. To a solution of **4** (500 mg, 2.74 mmol) and (*S*)-(−)-methyl mandelate (500 mg, 3.0 mmol) in CH_2Cl_2 (30 mL) at 0 °C was added iodonium bis-collidine perchlorate[8] (1.29 g, 2.74 mmol). The mixture was stirred for 1 h and then poured into 10% aqueous $Na_2S_2O_3$ (30 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 15 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (15 mL) and brine (15 mL), then dried (Na_2SO_4), filtered, and concentrated in vacuo. Chromatography of the residue twice on silica gel 60 (200 g) with 20% Et_2O/hexanes as eluent gave the less polar product **5** (259 mg, 0.987 mmol, 36%) as a viscous oil homogenous by TLC, R_f 0.22 (20% Et_2O/hexanes): $[\alpha]^{27}_D$ +103.5° (*c* 1.15, $CHCl_3$). The more polar product **6** (252 mg, 0.961 mmol, 35%) was isolated as a viscous oil homogenous by TLC, R_f 0.16 (20% Et_2O/hexanes): $[\alpha]^{28}_D$ +52.8° (*c* 1.16, $CHCl_3$).

Spectral data for **5**: IR ($CHCl_3$) cm^{-1} 1742; ^1H NMR ($CDCl_3$) δ 1.64–1.82 (4, m), 2.26 (1, m), 3.66 (1, dt, *J* = 6.3, 11 Hz), 3.71 (3, s), 3.79 (1, dt, *J* = 3.5, 11 Hz), 5.13 (1, s), 5.36 (1, s), 5.63 (1, s), 7.26–7.52 (5, m); ^{13}C NMR ($CDCl_3$) δ 22.92 (CH_3), 29.38 (CH_2), 52.15 (CH_3), 57.67 (CH_2), 76.39 (CH), 93.65 (CH), 119.42 (CH), 127.37 (CH), 128.35 (CH), 128.49 (CH), 136.87 (C), 137.90 (C), and 171.69 (C).

Spectral data for **6**: IR ($CHCl_3$) cm^{-1} 1747; ^1H NMR ($CDCl_3$) δ 1.72–1.81 (4, m), 2.27 (1, m), 3.67–3.77 (4, m), 4.05 (1, dt, *J* = 3.5, 11 Hz), 4.93 (1, s), 5.22 (1, s), 5.46 (1, s), 7.27–7.52 (5, m); ^{13}C NMR ($CDCl_3$) δ 22.92 (CH_3), 29.36 (CH_2), 52.15 (CH_3), 57.83 (CH_2), 77.67 (CH), 93.48 (CH), 119.08 (CH), 127.28 (CH), 128.52 (CH), 136.31 (C), 138.23 (C), and 171.39 (C).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.91. Found: C, 68.45; H, 6.80.

(*S*)-1-Phenyl-2-hydroxyethyl 5,6-Dihydro-4-methyl-2*H*-pyran-2-yl Ethers 7 and 9. To a suspension of $LiAlH_4$ (35 mg, 0.92 mmol) in THF (2 mL) at 0 °C was added a solution of **5** (239 mg, 0.911 mmol) in THF (2 mL) dropwise via a syringe. The mixture was stirred for 0.5 h and then quenched by successive additions of water (35 μL), 10% aqueous NaOH (35 μL), and water (105 μL) while being stirred vigorously. The reaction mixture was filtered through Celite and concentrated in vacuo. Chromatography of the residue on silica gel 60 (75 g) eluted with 50% EtOAc/hexanes gave **7** (213 mg, 0.911 mmol, 100%) as a colorless oil, R_f 0.34 (50% EtOAc/hexanes), that crystallized upon cooling: mp 45–46 °C; $[\alpha]^{28}_D$ +97.53° (*c* 1.41, $CHCl_3$).

Similar reduction of **6** (220 mg, 0.839 mmol) gave **9** (190 mg, 0.811 mmol, 97%) as a colorless oil homogenous by TLC, R_f 0.33 (50% EtOAc/hexanes): $[\alpha]^{27}_D$ +54.85° (*c* 1.01, $CHCl_3$).

Spectral data for **7**: IR ($CHCl_3$) cm^{-1} 3590, 3458, 1678; ^1H NMR ($CDCl_3$) δ 1.65–1.80 (4, m), 2.06–2.38 (2, m), 3.30–3.39 (1, m), 3.55–3.82 (3, m), 4.71 (1, dd, *J* = 4.3, 8.0 Hz), 5.20 (1, s), 5.54 (1, s), 7.20–7.42 (5, m); ^{13}C NMR ($CDCl_3$) δ 22.94 (CH_3), 29.37 (CH_2), 57.56 (CH_2), 66.79 (CH_2), 81.38 (CH), 95.88 (CH), 119.49 (CH), 126.56 (CH), 127.53 (CH), 128.16 (CH), 138.27 (C), 140.22 (C).

Spectral data for **9**: IR ($CHCl_3$) cm^{-1} 3593, 3431, 1680; ^1H NMR ($CDCl_3$) δ 1.76 (3, s), 1.84 (1, s), 2.27 (1, m), 2.76 (1, dd, *J* = 4.8, 8.9 Hz), 3.61–3.88 (3, m), 4.03 (1, dt, *J* = 3.6, 11.3 Hz), 4.89 (2, m), 5.43 (1, s), 7.34 (5, m); ^{13}C NMR ($CDCl_3$) δ 22.93 (CH_3), 29.43 (CH_2), 57.88 (CH_2), 67.44 (CH_2), 79.99 (CH), 92.41 (CH), 119.67 (CH), 126.89 (CH), 127.99 (CH), 128.47 (CH), 137.87 (C), 138.66 (C).

(*S*)-1-Phenyl-2-hydroxyethyl (2*S*,4*R*)-4-Hydroxy-4-methyltetrahydropyran-2-yl Ether (8a). THF (2 mL) was added to a solution of $Hg(OAc)_2$ (203 mg, 0.637 mmol) in water (2 mL), and the bright yellow mixture was cooled to 0 °C. A solution of **7** (149 mg, 0.636 mmol) in THF (3 mL) was then added dropwise. The mixture was stirred at 0 °C for 18 h. The clear reaction mixture was quenched by addition of 10% aqueous NaOH (0.8 mL), followed by a solution of $NaBH_4$ (12 mg, 0.32 mmol) in 10% aqueous NaOH (0.8 mL). The aqueous layer was saturated with NaCl, the mixture was filtered, and the aqueous layer was extracted with EtOAc (5 × 10 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. Chromatography of the residue on silica gel 60 (100 g) with EtOAc as eluent gave the major product **8a** (110 mg, 0.436 mmol, 69%) as an oil that crystallized upon cooling, mp 83–85 °C: R_f 0.28 (EtOAc); $[\alpha]^{27}_D$ −7.07° (*c* 1.16, EtOH); IR ($CHCl_3$) cm^{-1} 3596, 3458, 3009, 2955; ^1H NMR ($CDCl_3$) δ 1.18–1.39 (4, m), 1.42–1.93 (4, m), 2.27 (1, m), 3.60–3.82 (4, m), 4.76 (1, t, *J* = 6 Hz), 5.02 (1, dd, *J* = 3.0, 7.5 Hz), 7.25–7.44 (5, m); ^{13}C NMR ($CDCl_3$) δ 30.54 (CH_3), 38.21 (CH_2), 43.80 (CH_2), 60.97 (CH_2), 66.53 (CH_2), 69.02 (C), 80.64 (CH), 98.89 (CH), 126.49 (CH), 127.61 (CH), 128.24 (CH), 139.48 (C).

The minor diastereomer **8b** was also isolated as a viscous oil contaminated with (*S*)-2-hydroxy-2-phenylethanol (R_f 0.40, EtOAc): yield corrected by ^1H NMR, 14 mg 0.055 mmol, 9%; ^1H NMR ($CDCl_3$) δ 1.19 (3, s), 1.24–2.07 (5, m), 3.27–3.85 (5, m), 4.10 (1, s), 4.68 (1, dd, *J* = 4.4, 7.5 Hz), 5.26 (1, m), 7.34 (5, s); ^{13}C NMR ($CDCl_3$) δ 29.89 (CH_3), 37.75 (CH_2), 40.90 (CH_2), 56.44 (CH_2), 66.30 (CH_2), 68.03 (C), 80.88 (CH), 98.79 (CH), 126.56 (CH), 128.15 (CH), 128.64 (CH), 138.97 (C).

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(S)-1-Phenyl-2-hydroxyethyl (2R,3R,4R)-3,4-Epoxy-4-methyltetrahydropyran-2-yl Ether (10a). To a solution of **9** (185 mg, 0.789 mmol) in CH_2Cl_2 (15 mL) at 0 °C was added MCPBA (200 mg, 0.9 mmol). The reaction was maintained at 0 °C for 18 h. The reactiom mixture was poured into saturated aqueous $NaHCO_3$ (15 mL), and the aqueous layer extracted was with EtOAc (3 × 15 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. Chromatography of the residue on silica gel 60 (100 g) with 50% EtOAc/hexanes as eluent gave the syn epoxide **10a** (183 mg, 0.731 mmol, 93%) as a viscous oil homogenous by TLC, R_f 0.15 (50% EtOAc/hexanes): $[\alpha]^{28}_D$ +123.01° (*c* 1.13, $CHCl_3$); IR ($CHCl_3$) cm^{-1} 3663, 3475, 3011, 2922; ^1H NMR ($CDCl_3$) δ 1.39 (3, s), 1.83–1.98 (2, m), 3.02 (1, s), 3.07 (1, d, J = 3.1 Hz), 3.46–3.94 (4, m), 4.84–4.90 (2, m), 7.27–7.40 (5, m); ^{13}C NMR ($CDCl_3$) δ 21.80 (CH_3), 29.80 (CH_2), 56.14 (C), 56.71 (CH_2), 58.30 (CH), 67.12 (CH_2), 79.32 (CH), 91.35 (CH), 127.08 (CH), 128.16 (CH), 128.51 (CH), 138.16 (C).

The anti epoxide **10b** (14 mg, 0.056 mmol, 7%) was also isolated as a viscous oil homogenous by TLC, R_f 0.20, (50% EtOAc/hexanes): ^1H NMR ($CDCl_3$) δ 1.42 (3, s), 1.75–1.89 (1, m), 1.98–2.12 (1, m), 2.95 (1, s), 3.41–3.53 (1, m), 3.66–3.88 (4, m), 4.83 (1, s), 4.87 (1, dd, J = 3.7, 8.0 Hz), 7.35 (5, m); ^{13}C NMR ($CDCl_3$) δ 23.36 (CH_3), 28.83 (CH_2), 55.98 (CH_2), 56.38 (C), 57.57 (CH), 67.23 (CH_2), 81.06 (CH), 94.29 (CH), 126.93 (CH), 128.35 (CH), 128.62 (CH), 137.75 (C).

(S)-1-Phenyl-2-hydroxyethyl (2R,4R)-4-Hydroxy-4-methyltetrahydropyran-2-yl Ether (11). To a suspension of $LiAlH_4$ (30 mg, 0.79 mmol) in THF (1.5 mL) at 0 °C was added a solution of epoxide **10a** in THF (3 mL) dropwise via syringe. The mixture was stirred at ambient temperature for 8 h and then quenched by successive additions of water (30 μL), 10% aqueous NaOH (30 μL), and water (90 μL). The mixture was filtered through Celite and concentrated in vacuo. Chromatography of the residue on silica gel 60 (100 g) with EtOAc as eluent gave the product **11** (144 mg, 0.571 mmol, 80%) as an oil that crystallized upon cooling, mp 83–84 °C: R_f 0.31 (EtOAc); $[\alpha]^{25}_D$ +184.11° (*c* 1.41, EtOH); IR ($CHCl_3$) cm^{-1} 3435, 3009, 2971, 2931; ^1H NMR ($CDCl_3$) δ 1.22 (3, s), 1.60–1.89 (4, m), 3.55–3.87 (4, m), 4.30 (1, dt, J = 3.0, 11.9 Hz), 4.49 (1, s), 4.84 (2, s), 7.33 (5, s); ^{13}C NMR ($CDCl_3$) δ 29.80 (CH_3), 37.89 (CH_2), 40.92 (CH_2), 56.38 (CH_2), 66.78 (CH_2), 67.03 (C), 78.41 (CH), 94.47 (CH), 127.10 (CH), 128.21 (CH), 128.55 (CH), and 137.58 (C).

Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.58; H, 7.88.

(4R)-4-Hydroxy-4-methyltetrahydropyran-2-one (1). To a solution of **8a** (100 mg, 0.396 mmol) in THF (5 mL) was added 10% aqueous HCl (3 mL). The mixture was stirred for 0.5 h, then poured into saturated aqueous $NaHCO_3$ (20 mL), and extracted with hot EtOAc (10 × 20 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. Chromatography of the residue on silica gel 60 (75 g) with EtOAc as eluent gave the lactol as a colorless liquid homogenous by TLC, R_f 0.25 (EtOAc). This material was subjected to oxidation without characterization.

To a suspension of PCC (215 mg, 1.00 mmol) and freshly ground 3-Å sieves (230 mg) in CH_2Cl_2 (1.5 mL) was added a solution of the above lactol in CH_2Cl_2 (2 mL). The mixture was stirred for 7 h at ambient temperature. Ether (10 mL) was added with vigorous stirring. Filtration of the mixture through silica gel 60 (15 g) with ether as eluent gave (*R*)-mevalonolactone (**1**) (39 mg, 0.30 mmol, 76%), which exhibited identical physical and spectral properties when compared to a sample of authentic racemic material (Aldrich): R_f 0.31 (EtOAc); $[\alpha]^{27}_D$ -20.0° (*c* 0.85, EtOH); lit.[3a] $[\alpha]_D$ -23° (*c* 0.32, EtOH); IR ($CHCl_3$) cm^{-1} 3431, 3013, 2973, 1729; ^1H NMR ($CDCl_3$) δ 1.39 (3, s), 1.91 (2, m), 2.50 (1, d, J = 17 Hz), 2.67 (1, d, J = 17 Hz), 2.88 (1, s), 4.30–4.42 (1, m), 4.56–4.68 (1, m); ^{13}C NMR ($CDCl_3$) δ 29.53 (CH_3), 35.68 (CH_2), 44.54 (CH_2), 66.15 (CH_2), 67.93 (C), 171.04 (C).

Similarly, hydrolysis of pyranoside **11** (130 mg, 0.515 mmol) and oxidation with PCC (275 mg, 1.25 mmol) and 3-Å sieves (300 mg) gave **1** (49 mg, 0.38 mmol, 74%), $[\alpha]^{26}_D$ -20.1° (*c* 1.0, EtOH).

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Supplementary Material Available: ^1H NMR and ^{13}C NMR spectra of all new compounds (24 pages). Ordering information is given on any current masthead page.

A Novel Reaction between Acetone and the Benzo[*c*]phenanthrene K-Region *o*-Quinone Containing a Peri-Fluoro Substituent

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Polycyclic aromatic hydrocarbons, the ubiquitous environmental pollutants, are bioactivated by cytochromes P450 and epoxide hydrolase to carcinogenic bay-region diol epoxides[1,2] but are detoxified by the same enzymes to K-region dihydrodiols. Interestingly, the weak carcinogen, 6,7-difluorobenzo[*c*]phenanthrene[3,4] (**1**), is predominantly metabolized by rat liver cytochromes P450 to the K-region quinone **2** (Scheme I).[4] In this paper, we describe a novel and surprisingly facile reaction of the fluoroquinone **2** with acetone that was discovered during our studies on the oxidative metabolism of **1**. We found that the K-region quinone **2** reacts readily with aqueous acetone[5] at 25 °C to exclusively form a pair of aralkyl acetomethyl ethers (**4**, **5**) in the absence of added catalyst or light (Scheme I). Additionally, we observed that the ether **4** converted to the regioisomer ether **5** in aqueous organic solutions under ambient conditions. Both, the formation of regioisomeric ethers (**4**, **5**) from the quinone as well as the rearrangement of one aralkyl acetomethyl ether to its regioisomer are novel reactions.

Oxidative metabolism of **1** at its K region by rat liver cytochromes P450 yielded the quinone **2** (0.1 M potassium phosphate buffer containing MeCN (5% v/v), pH 7.4, 37 °C, 20 min). When MeCN was replaced with acetone (5% v/v) as a cosolvent for the hydrocarbon substrate, two new products were formed at the expense of the quinone as indicated by HPLC analysis. Subsequently, we synthesized the quinone **2** and observed that it reacted quantitatively with aqueous acetone[5] at 25 °C to yield the same two products. The assignment of the structures **4** and **5** to the early and late eluting products (cf. Experimental Section for HPLC conditions) and the proposed mechanism of their formation are described.

High-resolution mass spectra (EI) of the ethers **4** and **5** gave molecular ions at m/z = 334.1007 and 334.1016, respectively, and established their molecular formula as $C_{21}H_{15}O_3F$ (calcd m/z = 334.1005). The molecular formula suggests addition of elements of acetone to the quinone **2**. The UV spectra of **4** and **5** in MeOH/H_2O (4/1) (HPLC mobile phase) had absorption maxima at 228 and 266 nm, respectively. The deconvoluted FTIR spectrum of each

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