to room temperature. A solution of 4-amino-3-buten-2-one[3] (0.42 g, 5.0 mmol) in DMF (4.0 mL) was added dropwise and the resultant homogeneous solution was stirred for 2 h. The solvent was removed under vacuum. The residue was dissolved in chloroform and washed with 5% Na_2CO_3 solution, and the chloroform layer was dried (Na_2SO_4), filtered, and evaporated. The crude material was chromatographed on silica gel, eluting with chloroform. The isolated product was crystallized from hexane/*n*-BuCl (6:1) to give 0.44 g (53%) of product: mp 84–86 °C; NMR ($CDCl_3$) δ 2.7 (s, 3 H), 9.0 (dd, J = 2, 3 Hz, H_4), 9.4 (d, J = 2 Hz, H_2), 9.6 (d, J = 3 Hz, H_6). Anal. Calcd for $C_7H_6N_2O_3$: C, 50.60; H, 3.64; N, 16.87. Found: C, 50.84; H, 3.36; N, 16.88.

3-Nitro-5,6,7,8-tetrahydroquinolin-5-one (1b): NMR ($CDCl_3$) δ 2.3 (m, 2 H_7), 2.8 (t, J = 6 Hz, 2 H_6), 3.3 (t, J = 8.9 Hz, 2 H_8), 8.9 (d, J = 3 Hz, H_4), 9.4 (d, J = 3 Hz, H_2). Anal. Calcd for $C_9H_8N_2O_3$: C, 56.25; H, 4.20; N, 14.58. Found: C, 56.38; H, 4.16; N, 14.36.

3-Nitro-5-oxo-6,7-dihydro-5*H*-cyclopenta[*b*]pyridine (1c): NMR ($CDCl_3$) δ 2.9 (m, 2 H_6), 3.4 (m, 2 H_7), 8.8 (d, J = 2 Hz, H_4), 9.6 (d, J = 2 Hz, H_2). Anal. Calcd for $C_8H_6N_2O_3$: C, 53.93; H, 3.39; N, 15.73. Found: C, 53.85; H, 3.41; N, 15.91.

5-Nitronicotinaldehyde (1e): NMR ($CDCl_3$) δ 8.9 (dd, J = 2 Hz, H_4), 9.4 (d, J = 2 Hz, H_2), 9.6 (d, J = 2 Hz, H_6), 10.3 (s, CHO). Anal. Calcd for $C_6H_4N_2O_3$: C, 47.37; H, 2.65; N, 18.42. Found: C, 47.38; H, 2.65; N, 18.59.

***endo*-2-Nitro-*exo*-3-chloro-5-norbornene-*exo*-2-carboxaldehyde (4a).** A solution of sodium nitromalonaldehyde monohydrate (3.14 g, 20 mmol) in DMF (18 mL) was dried over 4-Å sieves (4.0 g) for 2 h. The sieves were removed by filtration and washed with DMF (6 mL) and the combined filtrate was cooled to −5 °C. A solution of *p*-toluenesulfonyl chloride (3.81 g, 20 mmol) in DMF (18 mL) was added dropwise, while the temperature was maintained below 0 °C. After 15 min, a solution of freshly prepared cyclopentadiene (2.64 g, 40 mmol) in DMF (16 mL) was added and the solution was stirred overnight. The reaction mixture was diluted with diethyl ether (400 mL) and the precipitated sodium tosylate (2.0 g) removed by filtration. The filtrate was concentrated under high vacuum and the residue extracted with hot hexane followed by hot *n*-butyl chloride. The combined extracts were concentrated, and the residue was redissolved in diethyl ether, washed with water, dried (Na_2SO_4), and evaporated to give 1.87 g of a dark oil. This was chromatographed on E. Merck silica gel, eluting with hexane/*n*-butyl chloride (1:1), to give 0.76 g (19%) of solid product, which was recrystallized from hexane to give 0.60 g of product, which became gummy upon removal of solvent: NMR ($CDCl_3$) δ 2.03 (d, d, t, J = 10.5, 3.3, 1.6 Hz, H_{7a}), 2.37 (br d, J = 10.5 Hz, H_{7b}), 3.19 (m, H_4), 3.54 (m, H_1), 4.70 (d, d, J = 3.5, 0.5 Hz, H_3), 6.20 (d, d, J = 5.5, 3 Hz, H_5), 6.45 (d, d, J = 5.5, 3.5 Hz, H_6), 9.57 (s, CHO).

This adduct was analyzed as its (2,4-dinitrophenyl)hydrazone derivative, mp 158–161 °C. Anal. Calcd for $C_{14}H_{12}ClN_5O_6$: C, 44.04; H, 3.17; N, 18.35. Found: C, 44.21; H, 3.11; N, 18.19.

A mixture of two isomeric adducts (<5% yield) was obtained from the mother liquors of adduct **4a**. This was analyzed by NMR, and the stereochemistry as illustrated in Scheme I is based on the following assignments: adduct **4b**, δ 1.68 (br d, J = 10.5 Hz, H_{7b}), 1.98 (br d, J = 10.5 Hz, H_{7a}), 3.39 (m, H_4), 3.82 (m, H_1), 5.33 (d, J = 3.5 Hz, H_3), 6.52 (d, d, J = 5.5, 3 Hz, H_5), 6.55 (d, d, J = 5.5, 3 Hz, H_6), 9.23 (s, C*H*O); adduct **4c**, δ 2.11 (d, q, J = 10.5, 2 Hz, H_{7a}), 2.72 (br d, J = 10.5 Hz, H_{7b}), 3.18 (m, H_4), 3.60 (m, H_1), 4.58 (d, J = 3.5 Hz, H_3), 5.99 (d, d, J = 5.5, 2.8 Hz, H_6), 6.37 (obscured by overlap, H_5), 9.48 (s, CHO).

Acknowledgment. The encouragement of Dr. W. C. Lumma, Jr. during the course of this work was much appreciated. The authors are indebted to J. Stranick and J. P. Moreau for microanalytical determinations, J. S. Murphy for some spectroscopic data, and M. Banker for manuscript preparation.

Registry No. **1a**, 87883-17-8; **1b**, 87883-18-9; **1c**, 87883-19-0; **1d**, 51984-71-5; **1e**, 87883-20-3; **2**, 34461-00-2; **3a**, 2976-86-5; **3b**, 5220-49-5; **3c**, 28566-12-3; **3d**, 7318-00-5; **3e**, 25186-34-9; **4a**, 87883-21-4; **4a** 2,4-dinitrophenylhydrazone, 87883-22-5; **4b**, 87935-87-3; **4c**, 87935-88-4; tosyl chloride, 98-59-9; 3-chloro-2-nitroacrolein, 87883-23-6.

Addition-Rearrangement Reaction of 3,4-Dihydro-2*H*-pyrans and 3,4-Dihydro-2-methoxy-2*H*-pyrans with (4-Methylphenyl)sulfonyl Isocyanate[1]

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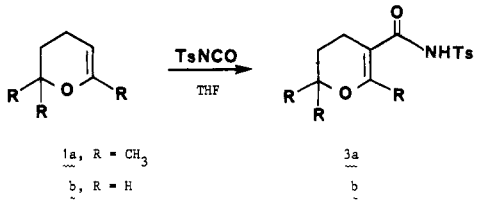
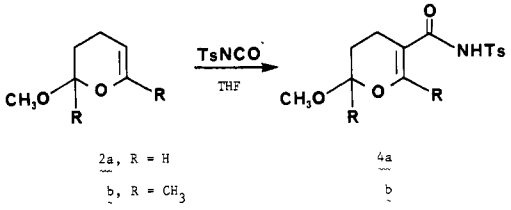
The cycloaddition and subsequent rearrangement reaction of alkyl vinyl ethers with (4-methylphenyl)sulfonyl isocyanate (TsNCO) has been extensively studied by Effenberger and his associates.[3] Herein we report the application of this reaction to a series of 3,4-dihydro-2*H*-pyrans (**1**) and 3,4-dihydro-2-methoxy-2*H*-pyrans (**2**) that results in the synthesis of a series of the corresponding 3,4-dihydro-*N*-[(4-methylphenyl)sulfonyl]-2*H*-pyran-5-carboxamides (**3**) and 3,4-dihydro-2-methoxy-*N*-[(4-methylphenyl)sulfonyl]-2*H*-pyran-5-carboxamides (**4**), respectively.

After a solution of dihydropyran **1a** and a slight excess of (4-methylphenyl)sulfonyl isocyanate in anhydrous tetrahydrofuran was stirred for 48 h, the solvent was removed and the residue crystallized to yield dihydropyran-5-carboxamide **3a** (88%). Similar treatment of dihydropyran **1b** formed dihydropyran-5-carboxamide **3b** in 83% yield.[4]



1a, R = CH_3 3a
b, R = H b

Analogous reactions with the 2-methoxydihydropyrans **2a** and **2b** yielded the corresponding 2-methoxydihydropyran-5-carboxamides **4a** and **4b** as the only condensation products in isolated yields of 74% and 58%, respectively.



2a, R = H 4a
b, R = CH_3 b

In contrast, treatment of 2-methoxy-6-methyldihydropyran (**2c**) with (4-methylphenyl)sulfonyl isocyanate in THF after 48 h yielded the expected 2-methoxy-6-methyldihydropyran-5-carboxamide **4c** (43%), as well as

(1) Part 9 in the series, "The Chemistry of 3,4-Dihydro-2-alkoxy-2*H*-pyrans". For part 8, see Weber, G. F.; Hall, S. S. *J. Org. Chem.* **1979**, *44*, 447–449.

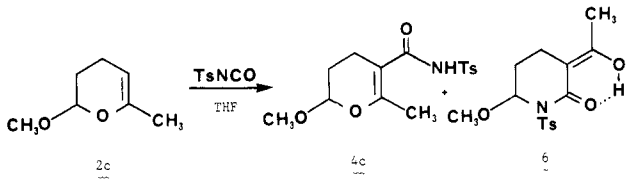
(2) Taken in part from the Ph.D. thesis of J.H.C., Rutgers University, May 1982. Present address: Burroughs Wellcome Co., Research Triangle Park, NC 27709.

(3) (a) Effenberger, F.; Prossel, G.; Fischer, P. *Chem. Ber.* **1971**, *104*, 2002–2012. (b) Effenberger, F.; Fischer, P.; Prossel, G.; Gebhard, K. *Ibid.* **1971**, *104*, 1987–2001. (c) Effenberger, F. *Angew. Chem.* **1969**, *81*, 374–391. (d) Effenberger, F.; Kiefer, G. *Ibid.* **1967**, *79*, 936–937. (e) Effenberger, F.; Gleiter, R. *Chem. Ber.* **1964**, *97*, 1576–1583.

(4) This reaction with 3,4-dihydro-2*H*-pyran (**1b**) and TsNCO in Me_2SO and in refluxing benzene has been described in ref 3e. Analogous reactions with **1b** and trifluoroacetyl, (2,2,2-trichloroethyl)sulfonyl, and (2,2,2-trichloroethoxy)sulfonyl isocyanates [(a) Barrett, A. G. M.; Fenwick, A.; Bretts, M. J. *J. Chem. Soc., Chem. Commun.* **1983**, 299–301] and trichloroacetyl isocyanate [(b) Chitwood, J. L.; Gott, P. G.; Martin, J. C. *J. Org. Chem.* **1971**, *36*, 2228–2232; (c) Smith, L. R.; Speziale, A. J.; Fedder, J. E. *J. Org. Chem.* **1969**, *34*, 633–637] have also been reported.

0022-3263/84/1949-0195$01.50/0

3-(1-hydroxyethylidene)-6-methoxy-2-piperidinone **6** (18%).



2c 4c 6

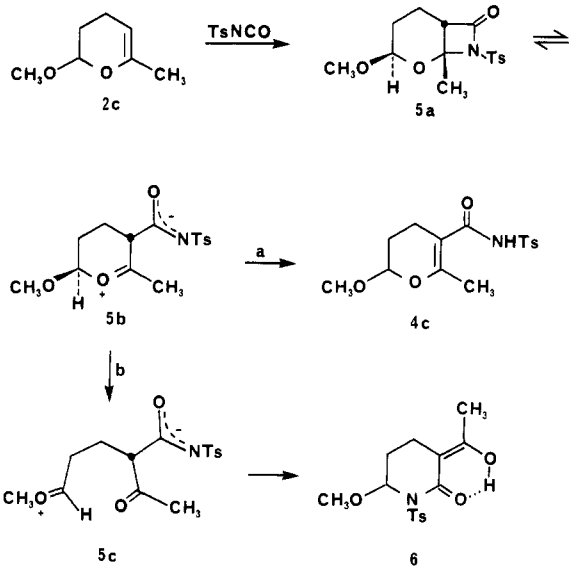
A suggested mechanism for these reactions is depicted in Scheme I, using the dihydropyran **2c** as the example. Enol ethers are known to undergo a [2 + 2] cycloaddition with isocyanates to form 4-alkoxyazetidin-2-ones that slowly but irreversibly rearrange to the corresponding β-alkoxyacrylamides via a resonance-stabilized zwitterion.[3] For the example shown, the (4-methylphenyl)sulfonyl isocyanate would be expected to add anti to the axial methoxy group[5] in **2c** to form the *cis*-azetidin-2-one **5a**. *cis*-4-Alkoxyazetidin-2-ones, which have been generated from acyclic alkyl vinyl ethers, are known to equilibrate to the trans isomer through a zwitterion analogous to **5b**,[3a,b,d] and it is such a zwitterion that can irreversibly deprotonate (prototropic shift) via pathway a to the dihydropyran-5-carboxamide **4c**. This, apparently, is the general reaction sequence followed by all of the 3,4-dihydro-2*H*-pyrans examined in this study with the exception of 2-methoxy-6-methyldihydropyran **2c** where both the stabilizing effect of the 6-methyl group on intermediate **5b** and the participation of the 2-methoxy group become important[6] and pathway b becomes competitive.

Experimental Section[7]

The syntheses of 3,4-dihydro-2,2,6-trimethyl-2*H*-pyran (**1a**),[8] 3,4-dihydro-2-methoxy-2,6-dimethyl-2*H*-pyran (**2b**), and 3,4-dihydro-2-methoxy-6-methyl-2*H*-pyran (**2c**) have been described.[5] 3,4-Dihydro-2*H*-pyran (**1b**) and 3,4-dihydro-2-methoxy-2*H*-pyran (**2a**) are available from Aldrich Chemical Co. and were distilled, bp 86 and 51 °C (80 torr), respectively, from CaH_2 prior to use. (4-Methylphenyl)sulfonyl isocyanate (TsNCO) was from Carwin Organic Chemicals, North Haven, CN. Tetrahydrofuran (THF) was distilled from $LiAlH_4$ just prior to use. Reactions were performed in oven-dried glassware under a static N_2 atmosphere. Column chromatography was executed on 70–230-mesh silica gel 60 (EM Reagents). Preparative HPLC was performed on a silica gel cartridge (PREPPAK-500/silica, Waters Associates).

3,4-Dihydro-2,2,6-trimethyl-*N*-[(4-methylphenyl)sulfonyl]-2*H*-pyran-5-carboxamide (3a). To a stirred and cooled (3–5- °C ice–water bath) solution of 433 mg (2.20 mmol) of (4-methylphenyl)sulfonyl isocyanate (TsNCO) in 5 mL of anhydrous THF was slowly added a solution of 231 mg (1.83 mmol) of 3,4-dihydro-2,2,6-trimethyl-2*H*-pyran (**1a**) in 5 mL of THF. The solution was slowly allowed to warm to ambient temperature. After 48 h the solvent was removed in vacuo

Scheme I



2c 5a 5b 4c 5c 6

(water-aspirator pressure) and the off-white semisolid residue crystallized from Et_2O–hexane to yield 520 mg (1.61 mmol, 88%) of **3a** as a white solid: mp 156–158 °C; IR (CH_2Cl_2) 3420, 2940, 1690, 1595, 1400, 1165, 1020 cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 8.30 (1 H, br s, exchanges with D_2O), 8.05 (2 H, d, J = 9 Hz), 7.30 (2 H, d, J = 9 Hz), 2.40 (3 H, s), 2.20 (3 H, s) superimposed on 2.35–2.05 (2 H, apparent t, J = ca. 6 Hz), 1.60 (2 H, apparent t, J = ca. 6 Hz), 1.20 (6 H, s); mass spectrum, m/z (relative intensity) 323 (M^+, 4), 268 (5), 155 (44), 151 (23), 108 (22), 97 (24), 91 (100), 65 (25), 43 (97). Anal. ($C_{16}H_{21}NO_4S$) C, H, N, S.[9]

3,4-Dihydro-*N*-[(4-methylphenyl)sulfonyl]-2*H*-pyran-5-carboxamide (3b). Similar treatment of 879 mg (4.46 mmol) of TsNCO and 312 mg (3.71 mmol) of **1b** in 15 mL of THF, as described for **3a**, produced an off-white solid that after crystallization from absolute EtOH yielded 870 mg (3.09 mmol, 83%) of **3b** as a white solid: mp 202–204 °C (lit.[3e] mp 204–205 °C); IR (CH_2Cl_2) 3400, 1690, 1630, 1610, 1160, 1030 cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 8.8–8.4 (1 H, br s, $W_{1/2}$ = 14 Hz, exchanges with D_2O), 8.00 (2 H, d, J = 9 Hz), 7.53 (1 H, s), 7.33 (2 H, d, J = 9 Hz), 4.00 (2 H, t, J = 5 Hz), 2.41 (3 H, s), 2.14 (2 H, q, J = 5 Hz), 1.83 (2 H, t, J = 5 Hz); mass spectrum, m/z (relative intensity) 281 (M^+, 2), 217 (5), 197 (2), 171 (4), 155 (10), 126 (100), 111 (75), 108 (81), 91 (67), 65 (31). Anal. ($C_{13}H_{15}NO_4S$) C, H, N, S.

3,4-Dihydro-2-methoxy-*N*-[(4-methylphenyl)sulfonyl]-2*H*-pyran-5-carboxamide (4a). Similar treatment of 997 mg (5.05 mmol) of TsNCO and 481 mg (4.21 mmol) of **2a** in 15 mL of THF, as described for **3a**, produced a brown oily residue that was column chromatographed on 60 g of silica gel and eluted with CH_2Cl_2–EtOAc (95:5) to yield 972 mg (3.12 mmol, 74%) of **4a** as a white foamy solid, which crystallized from Et_2O–hexane as white crystals (856 mg, 2.75 mmol, 65%): mp 104–106 °C; IR (CH_2Cl_2) 3400, 3290, 2940, 1690, 1615, 1160, 1025 cm^{-1}; NMR (79.5 MHz, Me_2SO-d_6) δ 11.51 (1 H, br s, exchanges with D_2O), 7.82 (2 H, d, J = 8.4 Hz), 7.55 (1 H, s), 7.40 (2 H, d, J = 8.2 Hz), 5.07 (1 H, t, J = ca. 2.9 Hz), 3.38 (3 H, s), 2.39 (3 H, s), 2.12–1.94 (2 H, m), 1.82–1.65 (2 H, m); mass spectrum, m/z (relative intensity) 311 (M^+, 1), 279 (3), 247 (2), 197 (2), 171 (9), 156 (35), 139 (87), 91 (100), 58 (95). Anal. ($C_{14}H_{17}NO_5S$) C, H, N, S.

3,4-Dihydro-2-methoxy-2,6-dimethyl-*N*-[(4-methylphenyl)sulfonyl]-2*H*-pyran-5-carboxamide (4b). Similar treatment of 1.43 g (7.25 mmol) of TsNCO and 858 mg (6.03 mmol) of **2b** in 20 mL of THF, as described for **3a**, produced a brown foamy residue that was purified on preparative HPLC with CH_2Cl_2–EtOAc (95:5) as eluant to yield 1.18 g (3.48 mmol, 58%) of **4b** as white crystals: mp 128–130 °C; IR (Nujol) 3300, 1690, 1610, 1465, 1380, 1165, 1150, 1050 cm^{-1}; NMR (79.5 MHz, Me_2SO-d_6) δ 11.28 (1 H, br s, exchanges with D_2O), 7.84 (2 H, d, J = 8.3 Hz), 7.41 (2 H, d, J = 8.1 Hz), 3.17 (3 H, s), 2.39 (3 H,

(5) As has been previously discussed, the C-2 methoxy group should be axial in the preferential conformation of the 3,4-dihydro-2-methoxy-2*H*-pyrans **2a–c**. See: Hall, S. S.; Weber, G. F.; Duggan, A. J. *J. Org. Chem.* **1978**, *43*, 667–672.

(6) The influence of both the 6-methyl group and the 2-methoxy group has been previously observed. See ref 5 and the following: (a) Duggan, A. J.; Hall, S. S. *J. Org. Chem.* **1977**, *42*, 1057–1062. (b) *Ibid.* **1974**, *39*, 3432–3433. (c) Hall, S. S.; Chernoff, H. C. *Chem. Ind.* **1970**, 896–897.

(7) Melting points (uncorrected) were determined with a Büchi apparatus. Preparative HPLC was performed on a Waters Associates Model 500A liquid chromatograph. The IR spectra were determined with a Perkin-Elmer Model 727B infrared spectrometer. All NMR spectra were determined in $CDCl_3$ or Me_2SO-d_6, and the chemical shifts are expressed in δ values (ppm) relative to Me_4Si internal standard. The NMR spectra were determined at 200, 80, and 60 MHz with IBM Instruments Model WP200SY, Varian Associates Model FT-80, and Hitachi/Perkin-Elmer Model R-24B NMR spectrometers, respectively. The mass spectra were determined at 70 eV with a Varian Associates Model CH-5 DF double-focusing mass spectrometer with a VG Model 2200 data system attachment.

(8) Albisetti, Jr., C. J. U.S. Patent 2628252, 1953.

(9) Satisfactory combustion analysis data were reported for **3a**, **3b**, **4a–c**, and **6**.

s), ca. 2.35–2.05 (2 H, m), 1.91 (3 H, s), ca. 1.9–1.4 (2 H, m), 1.37 (3 H, s); mass spectrum, m/z (relative intensity) 339 (M^+, 0.4), 308 (1), 184 (12), 167 (28), 91 (28), 72 (100), 43 (53). Anal. ($C_{16}H_{21}NO_5S$) C, H, N, S.

3-(1-Hydroxyethylidene)-6-methoxy-1-[(4-methylphenyl)sulfonyl]-2-piperidinone (6) and 3,4-Dihydro-2-methoxy-6-methyl-*N*-[(4-methylphenyl)sulfonyl]-2*H*-pyran-5-carboxamide (4c). Similar treatment of 740 mg (3.75 mmol) of TsNCO and 400 mg (3.12 mmol) of **2c** in 10 mL of THF, as described for **3a**, produced a brown foamy residue that was column chromatographed on 60 g of silica gel and eluted with CH_2Cl_2–MeOH (99.5:0.5) to yield 180 mg (0.55 mmol, 18%) of **6** as a colorless oil, which crystallized from Et_2O–hexane as white crystals, followed by 440 mg (1.35 mmol, 43%) of **4c** as a colorless oil. Compound **6**: mp 93–94 °C; IR (CH_2Cl_2) 3050–2450, 2940, 1625, 1600, 1350, 1165, 1085 cm^{-1}; IR (film) 3300–2300, 2950, 1600, 1405, 1350, 1260, 1160, 1080, 880, 800 cm^{-1}; NMR (200 MHz, $CDCl_3$) δ 13.80 (1 H, s, exchanges with D_2O), 7.90 (2 H, d, J = 8.4 Hz), 7.30 (2 H, d, J = 8.2 Hz), 5.70 (1 H, t, J = 2.9 Hz), 3.54 (3 H, s), 2.57 (1 H, apparent td, J = ca. 14, 5 Hz), 2.43 (3 H, s), 2.25 (2 H, apparent dd with further splitting, J = ca. 14, 5 Hz), 1.95 (3 H, s), 1.73 (1 H, apparent tdd, J = ca. 14, 5, 2.5 Hz); mass spectrum, m/z (relative intensity) 325 (M^+, 12), 293 (6), 265 (6), 261 (5), 218 (12), 155 (28), 153 (30), 138 (17), 128 (20), 111 (20), 108 (26), 96 (16), 91 (100), 71 (82), 65 (32), 58 (69), 43 (92). Anal. ($C_{15}H_{19}NO_5S$) C, H, N, S. Compound **4c**: IR (CH_2Cl_2) 3400, 2940, 1690, 1605, 1400, 1165, 1005 cm^{-1}; NMR (79.5 MHz, Me_2SO-d_6) δ 11.26 (1 H, br s, exchanges with D_2O), 7.80 (2 H, d, J = 8.3 Hz), 7.38 (2 H, d, J = 8.1 Hz), 4.97 (1 H, t, J = ca. 3.0 Hz), 3.33 (3 H, s), 2.36 (3 H, s), 2.3–2.0 (2 H, m), 1.88 (3 H, s), 1.8–1.5 (2 H, m); mass spectrum, m/z (relative intensity) 325 (M^+, 4), 293 (5), 170 (13), 153 (58), 111 (28), 91 (43), 58 (100), 43 (68). Anal. ($C_{15}H_{19}NO_5S$) C, H, N, S.

Acknowledgment. We thank the Ciba-Geigy Corp. (Pharmaceuticals Division), the Charles and Johanna Busch Memorial Fund, the Research Council (Rutgers University), and the NIH (Biomedical Sciences Support Grant) for supporting our synthetic programs. W also thank Dr. D. Brent, Dr. S. Hurlbert, R. Johnson, J. Miller, and A. Ragouzeous, Burroughs Wellcome Co., for the mass spectra and the 80-MHz NMR spectra; J. R. Flisak for the 200-MHz NMR spectra; and Dr. G. F. Weber, Hoffmann-La Roche Inc., for preparing large quantities of the dihydropyrans **1a**, **2b**, and **2c**, while a member of this research group.

Registry No. **1a**, 37642-94-7; **1b**, 110-87-2; **2a**, 4454-05-1; **2b**, 64331-95-9; **2c**, 28194-35-6; **3a**, 87937-93-7; **3b**, 87937-94-8; **4a**, 87937-95-9; **4b**, 87937-96-0; **4c**, 87937-97-1; **6**, 87937-98-2; TsNCO, 4083-64-1.

Ascorbic Acid. 2. Nucleophilic Reactivity of Ascorbate Anion toward Acyl Carbon and Phosphorus

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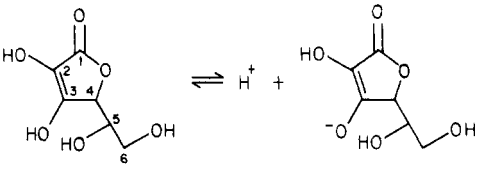
Received March 30, 1983

There has been great attention to the nutritional value of ascorbic acid (vitamin C).[1] However, biochemists have not been able to find clear evidence of essential roles. The commonly cited role of ascorbate in prolyl hydroxylase may be due to the need for a reducing agent in order to keep the essential iron atom in the Fe^{II} state, not due to direct involvement in the mechanism of action of this enzyme.[1-3] Ascorbic acid (**1**) and the anion **2** are interesting, polyfunctional species.[4] Ultimately, we should be able to understand the molecular basis of the function of ascorbate as we now understand thiamin, niacin, pyridoxal, and other vitamins.

Table I. Data for Reaction of 2,4-Dinitrophenyl Acetate by Several Nucleophiles at 30 °C

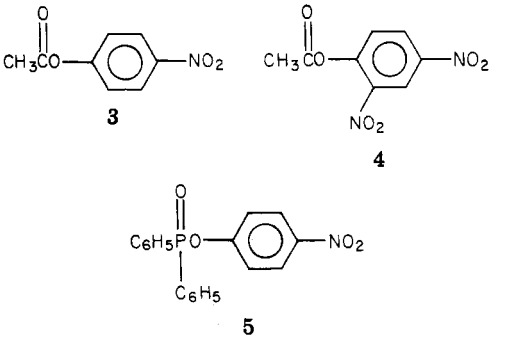
nucleophile[a]	pH	10^2k_2,[b] min^{-1} M^{-1}
$ClCH_2CO_2^-$	4.2	0.251
HCO_2^-	4.5	6.17
$CH_3CO_2^-$	5. 7	4.63
ascorbic acid anion	5.3	70

[a] In all cases a 10:1 ratio of anion to acid provided buffering. [b] Based upon three runs for the carboxylates and four runs for ascorbate.



1 2

Ascorbic acid (**1**), pK_a 4.2, will be present predominantly as the anion **2** at pH 7. The anion is stabilized by delocalization of charge over both the 1- and 3-oxygens.[5,6] We anticipated that **2** might be unusually reactive since both the 2-OH and the side chain at C-4 could potentially solvate certain transition states. For example, on the basis of its structure, the anion might be effective as an acyl transfer agent. Therefore, we have examined the nucleophilic reactivity of ascorbate monoanion **2** toward acyl carbon and acyl phosphorus centers **3–5**.



3 4 5

Experimental Section

p-Nitrophenyl acetate (**3**) was recrystallized from hexanes; mp 76.8 °C. 2,4-Dinitrophenyl acetate (**4**) was prepared by adding 1 equiv of 2,6-lutidine to 2,4-dinitrophenol, crushing the orange solid to a powder, and slowly adding 1 equiv of acetyl chloride. After cooling, the yellow-white solid was brought to a melt and allowed to recool. The solid was then crushed and removed with water, filtered, washed with 0.1 M bicarbonate, and recrystallized in acetone–heptane; mp 71–71.5 °C. *p*-Nitrophenyl diphenylphosphinate (**5**) was prepared by our method.[7]

All reactions were followed on a Cary 16 spectrophotometer with the cell compartment temperature maintained at 30 °C.

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