Addition−Rearrangement of Aryl- and Alkoxysulfonyl Isocyanates with 5-Methyl-Substituted 3,4-Dihydro-2-methoxy-*2H*-pyrans. Selective Synthesis of Functionalized 2-Piperidones[1]

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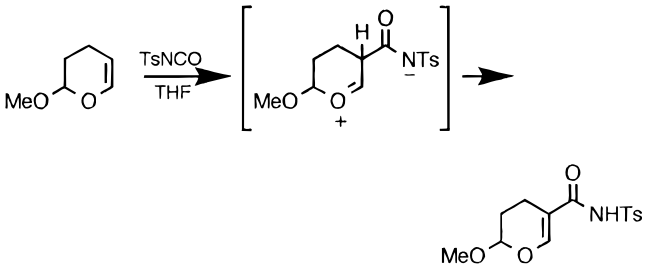
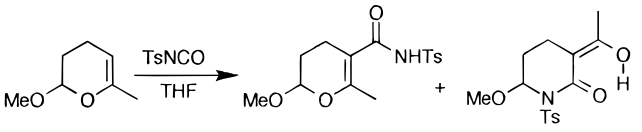
3,4-Dihydro-2-methoxy-5-methyl-*2H*-pyran and 3,4-dihydro-2-methoxy-5,6-dimethyl-*2H*-pyran undergo addition−rearrangement reactions with arylsulfonyl isocyanates to generate the corresponding 3-formyl- and 3-acetyl-6-methoxy-3-methyl-1-(arylsulfonyl)-2-piperidones. For example, 3,4-dihydro-2-methoxy-5-methyl-*2H*-pyran and phenylsulfonyl isocyanate afforded 3-formyl-6-methoxy-3-methyl-1-(phenylsulfonyl)-2-piperidone as a separable trans/cis mixture in high yield. The more reactive phenoxysulfonyl and alkoxysulfonyl isocyanates provided analogous results.

In a preliminary study of the addition of (4-methylphenyl)sulfonyl isocyanate with 3,4-dihydro-2-methoxy-*2H*-pyran and 3,4-dihydro-2-methoxy-2,6-dimethyl-*2H*-pyran, the corresponding C-5 substitution products, the 3,4-dihydro-2-methoxy-*2H*-pyran-5-carboxamides, were formed exclusively.[1a] It was assumed that such a product arose by addition of the isocyanate to the vinyl ether, followed by elimination of the C-5 proton to regenerate the 3,4-dihydro-2-methoxy-*2H*-pyran ring system. Similar chemistry has been reported for the parent 3,4-dihydro-*2H*-pyran[3a,b] and its derivative 3,4-di-*O*-acetylrhamnal.[3c]

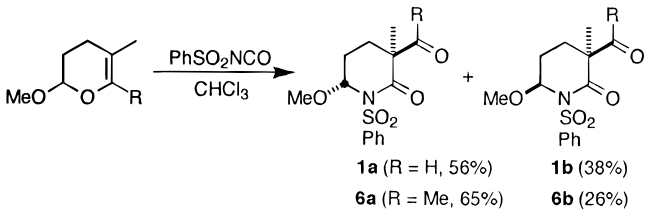


With 3,4-dihydro-2-methoxy-6-methyl-*2H*-pyran, in addition to the expected 3,4-dihydro-2-methoxy-6-methyl-*2H*-pyran-5-carboxamide, which was the major product, a 3-(1-hydroxyethylidene)-6-methoxy-2-piperidone product emerged, which was of interest.



By replacing the C-5 hydrogen with an alkyl or aryl group that could not eliminate, it was envisioned that the addition−elimination pathway would be shutdown and the substituted 2-piperidone, formed by addition−rearrangement (cycloaddition), might become the sole product. Herein is described these results using 5-methyl-substituted 3,4-dihydro-2-methoxy-*2H*-pyrans.

Stirring an equimolar solution of 3,4-dihydro-2-methoxy-5-methyl-*2H*-pyran and phenylsulfonyl isocyanate in chloroform for 19 days afforded *trans*-3-formyl-6-methoxy-3-methyl-1-(phenylsulfonyl)-2-piperidone (**1a**, 56%) and *cis*-3-formyl-6-methoxy-3-methyl-1-(phenylsulfonyl)-2-piperidone (**1b**, 38%), both as colorless crystals. The more reactive 3,4-dihydro-2-methoxy-5,6-dimethyl-*2H*-pyran produced an analogous mixture of *trans*-**6a** (65%) and *cis*-**6b** (26%) after only 27 h.[4]



X-ray crystallographic analyses of both *trans*-3-acetyl-6-methoxy-3-methyl-1-(phenylsulfonyl)-2-piperidone (**6a**) and *cis*-3-acetyl-6-methoxy-3-methyl-1-(phenylsulfonyl)-2-piperidone (**6b**) display the functionalized 2-piperidone ring as a slightly twisted chair conformation with the 6-methoxy group in an axial position and the 3-acetyl group axial in *trans*-**6a** and equatorial in *cis*-**6b**.[2b]

3,4-Dihydro-2-methoxy-5-methyl-*2H*-pyran and 4-(methylphenyl)sulfonyl isocyanate, after 17 days, afforded

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(1) (a) Chemistry of 3,4-Dihydro-2-alkoxy-*2H*-pyrans. 10. For part 9, see: Chan, J. H.; Hall, S. S. *J. Org. Chem.* **1984**, *49*, 195−197. (b) Taken from the Ph.D. Thesis of E. J. Rutgers, The State University of New Jersey, May 1990, which received the H. Martin Friedman Thesis Award. (c) Initially disclosed at the 198th National Meeting of the American Chemical Society, Miami Beach, FL, Sept 1989, paper ORGN 222, and at the 4th Ischia Advanced School of Organic Chemistry of the Societa' Chimica Italiana, Divisione Di Chimica Organica, Ischia Porto, Italy, Sept 1990, poster 11.

(2) (a) Address: Schering-Plough Research Institute, 2015 Galloping Hill Road, Kenilworth, NJ 07033-0539; where much of this research was executed. (b) Author from whom X-ray data can be obtained. The authors have also deposited atomic cordinates for *cis*-**3b**, *trans*-**6a**, and *cis*-**6b** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(3) (a) Effenberger, F.; Gleiter, R. *Chem Ber.* **1964**, *97*, 1576−1583. (b) Chitwood, J. L.; Gott, P. G.; Martin, J. C. *J. Org. Chem.* **1971**, *36*, 2228−2232. (c) Chemielewski, M.; Kaxuza, Z.; Mostowicz, D.; Bexzecki, C.; Baranowska, E.; Jacobsen, J. P.; Salanski, P.; Jurczak, J. *Tetrahedron* **1987**, *43*, 4555−4563.

(4) It has been previously demonstrated that alkyl substitutents increase the reactivity of the 3,4-dihydro-2-methoxy-2*H*-pyran ring system toward electrophiles. For example, a C-5 methyl group increases the reactivity by a factor of ca. 6 and a C-6 methyl group by a factor of ca. 14. Thus it was not unexpected that the 3,4-dihydro-2-methoxy-5,6-dimethyl-2*H*-pyran proved to be much more reactive than the 3,4-dihydro-2-methoxy-5-methyl-2*H*-pyran throughout this study. Hall, S. S.; Weber, G. F.; Duggan, A. J. *J. Org. Chem.* **1978**, *43*, 667−672.

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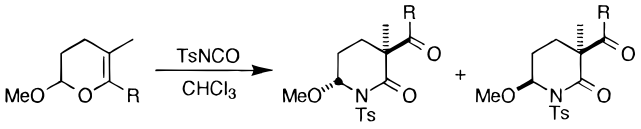
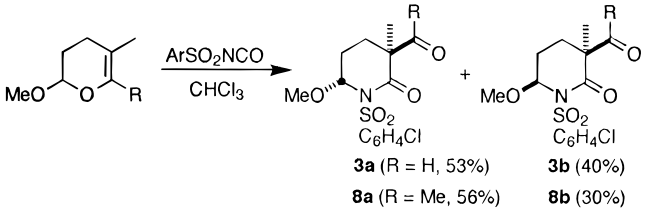
trans-3-formyl-6-methoxy-3-methyl-1-[(4-methylphenyl)-sulfonyl]-2-piperidone (**2a**, 50%) and *cis*-3-formyl-6-methoxy-3-methyl-1-[(4-methylphenyl)sulfonyl]-2-piperidone (**2b**, 37%), both as colorless crystals. 3,4-Dihydro-2-methoxy-5,6-dimethyl-*2H*-pyran assembled an allied mixture of *trans*-**7a** (63%) and *cis*-**7b** (30%) after 27 h.

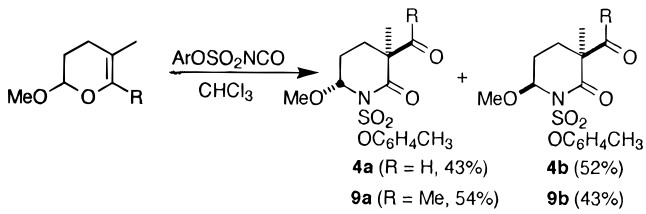


In a parallel manner, a solution of 3,4-dihydro-2-methoxy-5-methyl-*2H*-pyran and (4-chlorophenyl)sulfonyl isocyanate, after 26 days, afforded *trans*-1-[(4-chlorophenyl)sulfonyl]-3-formyl-6-methoxy-3-methyl-2-piperidone (**3a**, 53%) and *cis*-1-[(4-chlorophenyl)sulfonyl]-3-formyl-6-methoxy-3-methyl-2-piperidone (**3b**, 40%), both as colorless crystals. With 3,4-dihydro-2-methoxy-5,6-dimethyl-*2H*-pyran, an equivalent mixture of *trans*-**8a** (56%) and *cis*-**8b** (30%) was created after 21 h.



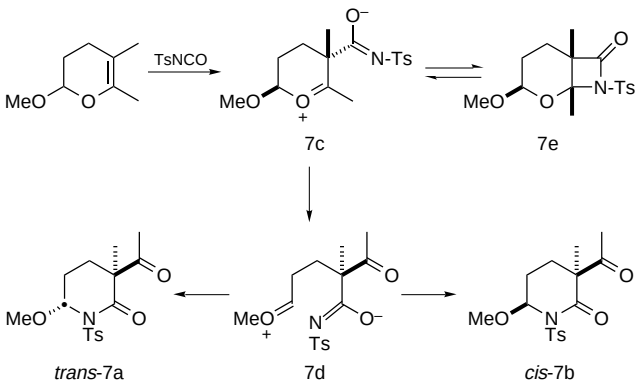
X-ray crystallographic analysis of *cis*-1-[(4-chlorophenyl)sulfonyl]-3-formyl-6-methoxy-3-methyl-2-piperidone (**3b**) revealed the functionalized 2-piperidone ring as a slightly twisted boat conformation with the 6-methoxy and the 3-formyl group in a 1,4-diaxial, cis relationship.[2b]

The much more reactive aroxysulfonyl and alkoxysulfonyl isocyanates afforded similar addition−rearrangement results. After only 27 h, 3,4-dihydro-2-methoxy-5-methyl-*2H*-pyran and 4-methylphenyl isocyanatosulfate yielded 4-methylphenyl *trans*-3-formyl-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (**4a**, 43%) and 4-methylphenyl *cis*-3-formyl-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (**4b**, 52%), both as colorless crystals.[5] The more reactive 3,4-dihydro-2-methoxy-5,6-dimethyl-*2H*-pyran produced an analogous mixture of *trans*-**9a** (54%) and *cis*-**9b** (43%) after only 5 h.

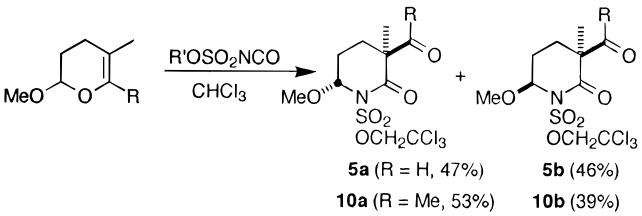


Similarly, 3,4-dihydro-2-methoxy-5-methyl-*2H*-pyran and 2,2,2-trichloroethyl isocyanatosulfate, after only 27 h, afforded 2,2,2-trichloroethyl *trans*-3-formyl-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (**5a**, 47%) and 2,2,2-trichloroethyl *cis*-3-formyl-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (**5b**, 46%), both as colorless crystals. 3,4-Dihydro-2-methoxy-5,6-dimethyl-*2H*-pyran produced

Scheme 1



a comparable mixture of *trans*-**10a** (53%) and *cis*-**10b** (39%) after only 4 h.



Scheme 1 depicts a plausible mechanism for the formation of these functionalized 2-piperidones. Infrared monitoring of these reactions, which were performed in chloroform, revealed initially a β-lactam carbonyl absorbance, which slowly disappeared with the concurrent appearance of the 3-acetyl- or 3-formyl-2-piperidone carbonyl absorbances.[6] Perhaps the powerful electron-withdrawing properties of the sulfonyl group destabilizes the β-lactam **7e** (in favor of 2-piperidones **7a/b**), which through zwitterion **7c** could rupture to the acyclic zwitterion **7d** and then ring close again to the *trans*/*cis* 2-piperidone product mixture **7a**/**b** in an irreversible process. Control experiments established that the *trans*/*cis* 2-piperidone product mixtures, such as **7a**/**b**, are not equilibrating during these reaction conditions.[7]

Experimental Section[8]

While in a dry, inert atmosphere in a glovebag, the 3,4-dihydro-2-methoxy-2*H*-pyrans and isocyanates were weighed in loaded syringes and injected into oven-dried, 5-mL Wheaton vials (with a Teflon-faced rubber septum and magnetic stirrer)

(5) The 3-formyl group of the 4-methylphenyl *trans*-3-formyl-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (**4a**) and 4-methylphenyl *cis*-3-formyl-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (**4b**) was extremely labile. For example, when the same crude reaction mixture was flash chromatographed on triethylamine-treated silica gel (pretreated with a solution of 1% Et_3N in hexane), in addition to the expected *trans*-**4a** (15%) and *cis*-**4b** (15%), 4-methylphenyl *trans*-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (**4c**, 9%) and 4-methylphenyl *cis*-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (**4d**, 45%) were also formed. See the Experimental Section for details.

(6) For example, the following observations were made with the reaction between 3,4-dihydro-2-methoxy-5-methyl-*2H*-pyran and (4-methylphenyl)sulfonyl isocyanate in chloroform when monitored by infrared spectroscopy. After the first day (24 h) there was only an intense β-lactam carbonyl absorbance at 1800 cm^{-1}. After 7 days, there were three equally intense carbonyl absorbances at 1800 cm^{-1} for the β-lactam and at 1735 and 1695 cm^{-1} for the 3-formyl-2-piperidones **2a**/**b**. After 16 days, the β-lactam absorbance (1800 cm^{-1}) had almost disappeared and the product **2a**/**b** carbonyl absorbances (1735 and 1695 cm^{-1}) were among the most intense in the spectrum.

(7) Resubjecting either pure *trans*- or *cis*-2-piperidone to these reaction conditions, or even after adding a drop of concentrated DCl to this solution in an NMR tube, indicated no evidence (NMR) of isomerization.

under nitrogen or argon. When necessary, the reaction solvents were removed at reduced pressure (house vacuum, ca. 200 Torr) on a rotary evaporator. Flash chromatography refers to the method described by Still *et al*. using Baker silica gel−flash (40 μm, 60 Å).[9] Preparative TLC separation was performed on ANALTECH 1000-μm silica precoated plates. Chloroform-*d* ($CDCl_3$) obtained from MSD Isotopes was passed through activated (120 °C, 3 days), basic Al_2O_3 (Aldrich Chemical Co.) before use. Anhydrous Gold Label tetrahydrofuran and toluene were from Aldrich Chemical Co. Methyl vinyl ether (Aldrich), methacrolein (Aldrich), 3-methyl-3-buten-2-one (MTM Research Chemicals, Lancaster Synthesis Inc.), phenylsulfonyl isocyanate (Aldrich), (4-methylphenyl)sulfonyl isocyanate (Trans World Chemical Co.), and (4-chlorophenyl)-sulfonyl isocyanate (Johnson Matthey, Alfa Products) were used without purification. 4-Methylphenyl isocyanatosulfate and 2,2,2-trichloroethyl isocyanatosulfate were prepared as described in the literature.[10] The purities (%) of all isocyanates were determined by ^{1}H NMR just prior to use.

3,4-Dihydro-2-methoxy-5-methyl-2*H*-pyran.[4,11] A sealed, 125-mL Teflon-lined acid digestion bomb (Parr Instruments) containing 0.36 g (2.65 mmol) of anhydrous zinc chloride, 0.11 g (1 mmol) of hydroquinone, 15.45 g (266 mmol) of methyl vinyl ether, and 8.74 g (125 mmol) of methacrolein was heated at 60 °C for 1 h, then at 70 °C for 1 h, and finally at 80 °C for 3 h. Fractional distillation at reduced pressure provided 10.3 g (80.47 mmol, 64%) of 3,4-dihydro-2-methoxy-5-methyl-2*H*-pyran as a colorless oil: bp 55 °C (18 Torr); ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.03 (1 H, br s), 4.80 (1 H, t, J = 2.6 Hz), 3.42 (3 H, s), 2.18−1.95 (1 H, m), 1.85−1.70 (3 H, overlapping m), 1.54 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 134.6 (−), 109.6 (+), 97.3 (−), 55.6 (−), 26.4 (+), 21.5 (+), 18.5 (−) ppm; mass spectrum (CI), m/z (relative intensity) 129 (MH^+, 100).

3,4-Dihydro-2-methoxy-5,6-dimethyl-2*H*-pyran. A sealed, 125-mL Teflon-lined acid digestion bomb containing 0.55 g (4.04 mmol) of anhydrous zinc chloride, 0.092 g (0.836 mmol) of hydroquinone, 23.18 g (400 mmol) of methyl vinyl ether, and 15.00 g (179 mmol) of 3-methyl-3-buten-2-one was heated at 60 °C for 1 h, then at 70 °C for 1 h, and finally at 85 °C for 3 h. Fractional distillation at reduced pressure provided 14.5 g (102 mmol, 57%) of 3,4-dihydro-2-methoxy-5,6-dimethyl-2*H*-pyran as a colorless oil: bp 66 °C (20 Torr); IR (film) 1695 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.83 (1 H, t, J = 2.9 Hz), 3.45 (3 H, s), 2.05 (1 H, apparent dd, J = ca. 18, 8 Hz), 1.82 (3 H, apparent ddd, J = 8.9, 5.1, 2.5 Hz), 1.75 (3 H, s), 1.59 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 142.4 (+), 104.4 (+), 99.8 (−), 57.5 (−), 29.0 (+), 24.9 (+), 19.9 (−), 18.2 (−) ppm; mass spectrum (CI), m/z (relative intensity) 143 (MH^+, 100), 142 (M^+, 28), 128 (36), 111 (65); exact mass calcd for $C_8H_{14}O_2$ (EI, M^+) 142.0994, found 142.0979.

***trans*- (1a) and *cis*-6-Methoxy-3-methyl-2-oxo-1-(phenylsulfonyl)-3-piperidinecarboxaldehyde (1b).** After addition of 717 mg (3.61 mmol) of phenylsulfonyl isocyanate (92%) to a cold (−20 °C) solution of 512 mg (4.00 mmol) of 3,4-dihydro-2-methoxy-5-methyl-2*H*-pyran in 3.5 mL of $CDCl_3$ under an N_2 atmosphere, the solution was allowed to stir at ambient temperature for 19 days, during which time the progress of the reaction was monitored (TLC, IR, and ^{1}H NMR). Gradient flash chromatography of the solution (3:7 to 1:1, ether−hexane) afforded 629 mg (2.02 mmol, 56%) of **1a** as a white solid that crystallized from CH_2Cl_2−hexane as colorless crystals, followed by 428 mg (1.38 mmol, 38%) of **1b** as a white solid that crystallized from CH_2Cl_2−hexane as colorless crystals. ***trans*-3-Formyl-2-piperidone 1a:** mp 108−109 °C; IR (Nujol) 1735, 1705 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.18 (1 H, s), 7.97 (2 H, d, J = 7.6 Hz), 7.47 (1 H, d, J = 8.0 Hz) superimposed on 7.50 (2 H, m, apparent 6-line pattern, J = 6.6 Hz), 5.53 (1 H, apparent t, J = 2.5 Hz), 3.44 (3 H, s), 2.15−1.60 (4 H, overlapping m), 1.20 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 197.9 (−), 169.9 (+), 138.8 (+), 133.8 (−), 128.8 (−), 128.6 (−), 85.9 (−), 57.3 (+), 56.2 (−), 25.0 (+), 22.7 (+), 20.5 (−) ppm; mass spectrum (FAB), m/z (relative intensity) 312 (MH^+, 30), 281 (31), 280 (100); exact mass calcd for $C_{14}H_{17}NSO_5$ (FAB, MH^+) 312.0906, found 312.0926. ***cis*-3-Formyl-2-piperidone 1b:** mp 109−110 °C; IR (Nujol) 1725, 1685 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.47 (1 H, s), 8.03 (2 H, dd, J = 8.8, 1.6 Hz), 7.52 (2 H, td, J = 7.6, 2.0 Hz) superimposed on 7.57 (1 H, m, apparent 6-line pattern, J = ca. 7 Hz), 5.64 (1 H, t, J = 2.6 Hz), 3.43 (3 H, s), 2.39 (1 H, td, J = 13.2, 5.4 Hz), 2.19 (1 H, apparent d of quintets, J = 14.2, 2.7 Hz), 1.86 (1 H, apparent tq, J = 13.6, 2.7 Hz), 1.44 (1 H, dq, J = 14.2, 2.7 Hz), 1.27 (3 H, s); homonuclear decoupling, irradiation at δ 5.64 sharpened the signal at δ 2.19 to a dq and collapsed the signal at δ 1.86 to a td; ^{13}C NMR (50 MHz, $CDCl_3$) 197.7 (−), 170.7 (+), 138.6 (+), 133.9 (2 C, −), 128.8 (2 C, −), 128.7 (−), 85.8 (−), 55.7 (−), 55.4 (+), 24.8 (+), 23.0 (+), 20.8 (−) ppm; mass spectrum (FAB), m/z (relative intensity) 312 (MH^+, 28), 281 (27), 280 (100). Anal. Calcd for $C_{14}H_{17}NSO_5$: C, 54.02; H, 5.47; N, 4.50; S, 10.29. Found: C, 54.18; H, 5.51; N, 4.50; S, 10.17.

***trans*- (6a) and *cis*-3-Acetyl-6-methoxy-3-methyl-1-(phenylsulfonyl)-2-piperidone (6b).** Similar treatment of 726 mg (3.65 mmol) of phenylsulfonyl isocyanate (92%) and 540 mg (3.82 mmol) of 3,4-dihydro-2-methoxy-5,6-dimethyl-2*H*-pyran, as described for **1a**,**b** except that the reactants were mixed at −60 °C and allowed to warm slowly to ambient temperature (3 h) and then stirred for 1 day, after chromatography of the reaction solution (3:7, ether−hexane) afforded 766 mg (2.36 mmol, 65%) of **6a** as white solid, followed by 303 mg (0.93 mmol, 26%) of **6b** as white solid, both of which crystallized from CH_2Cl_2−hexane as colorless crystals. ***trans*-3-Acetyl-2-piperidone 6a:** mp 100 °C; IR (Nujol) 1720, 1690 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.92 (2 H, dd, J = 7.0, 1.4 Hz), 7.5−7.3 (3 H, overlapping m), 5.44 (1 H, apparent t, J = 1.8 Hz), 3.31 (3 H, s), 2.1−1.5 (4 H, overlapping m) on which is superimposed 1.84 (3 H, s), 1.13 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 204.9 (+), 171.6 (+), 139.0 (+), 133.6 (−), 128.9 (2 C, −), 128.4 (2 C, −), 86.4 (−), 58.4 (+), 56.0 (−), 25.8 (+), 25.7 (−), 24.9 (+), 22.4 (−) ppm; mass spectrum (FAB), m/z (relative intensity) 294 (80), 191 (47), 175 (23), 169 (22), 141 (28), 111 (100); exact mass calcd for $C_{15}H_{19}NSO_5$ 326.1062, found 326.1072. ***cis*-3-Acetyl-2-piperidone 6b:** mp 101−102 °C; IR (Nujol) 1725, 1690, 1585 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.97 (2 H, dd, J = 7.2, 1.4 Hz), 7.60−7.37 (3 H, overlapping m), 5.58 (1 H, apparent t, J = 2.8 Hz), 3.40 (3 H, s), 2.41 (1 H, ddd, J = 13.7, 11.4, 5.5 Hz), 2.15 (1 H, apparent d of quintets, J = ca. 14 and 3 Hz), 1.95−1.80 (1 H, m), 1.80 (3 H, m), 1.34 (1 H, ddd, J = 13.6, 5.8, 3.6 Hz), 1.16 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 203.4 (+), 171.8 (+), 138.4 (+), 133.8 (−), 128.8 (2 C, −), 128.5 (2 C, −), 85.6 (−), 57.9 (+), 56.0 (−), 25.7 (−), 25.3 (+), 24.7 (+), 21.8 (−); mass spectrum (FAB), m/z (relative intensity) 326 (MH^+, 12), 295 (22), 294 (100). Anal. Calcd for $C_{15}H_{19}NSO_5$: C, 55.38; H, 5.85; N, 4.31; S, 9.85. Found: C, 55.25; H, 5.81; N, 4.31; S, 9.94.

***trans*- (2a) and *cis*-6-Methoxy-3-methyl-1-[(4-methylphenyl)sulfonyl]-2-oxo-3-piperidinecarboxaldehyde (2b).** Similar treatment of 798 mg (3.65 mmol) of (4-methylphenyl)sulfonyl isocyanate (90%) and 520 mg (4.06 mmol) of 3,4-dihydro-2-methoxy-5-methyl-2*H*-pyran, as described for **1a**,**b** except the solution was stirred for 17 days, after gradient chromatography (3:7 to 2:3, ether−hexane) of the reaction solution afforded 590 mg (1.82 mmol, 50%) of **2a** as an opaque gum, followed by 440 mg (1.35 mmol, 37%) of **2b** as a white solid that crystallized from ether−hexane as colorless crystals. ***trans*-3-Formyl-2-piperidone 2a:** IR (Nujol) 1735, 1695,

(8) The 300 MHz ^{1}H NMR spectra were determined with a Varian Model Gemini-300 or a Varian Model XL-300 Fourier transform spectrometer, and certain selected proton assignments were confirmed by homonuclear decoupling studies. The ^{13}C NMR spectra included broad-band proton-decoupled spectra and attached proton test spectra. In the latter, the CH and CH_3 carbon resonances were negative phases (−) and the C and CH_2 carbon resonances were positive phases (+). Exact mass spectra measurements were performed on a VG Analytical Model ZAB-SE spectrometer. In the fast atom bombardment (FAB) technique thioglycerol or 3-nitrobenzyl alcohol were used as the matrix. In the chemical ionization (CI) technique, ammonia was used as the carrying gas. Additional information has been described: Flisak, J. R.; Hall, S. S. *J. Am. Chem. Soc.* **1990**, *112*, 7299−7305.

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1600, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.19 (1 H, s), 7.84 (2 H, d, J = 8.0 Hz), 7.25 (2 H, d, J = 8.0 Hz), 5.52 (1 H, apparent t, J = 2.6 Hz), 3.44 (3 H, s), 2.35 (3 H, s), 2.10−1.67 (4 H, overlapping m), 1.21 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 198.0 (−), 169.9 (+), 144.8 (+), 135.8 (+), 129.2 (2 C, −), 128.9 (2 C, −), 85.9 (−), 57.3 (+), 56.2 (−), 25.1 (+), 22.7 (+), 21.6 (−), 20.5 (−) ppm; mass spectrum (FAB), *m/z* (relative intensity) 326 (MH^+, 17), 294 (100), 169 (53); exact mass calcd for $C_{15}H_{19}NO_5S$ (FAB, MH^+) 312.0906, found: 312.0926. ***cis*-3-Formyl-2-piperidone 2b:** mp 128 °C; IR (Nujol) 1735, 1685, 1595 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.41 (1 H, s), 7.86 (2 H, d, J = 8.4 Hz), 7.26 (2 H, d, J = 8.4 Hz), 5.59 (1 H, t, J = 2.7 Hz), 3.37 (3 H, s), 2.37 (3 H, s) superimposed on 2.5−2.3 (1 H, m), 2.19 (1 H, apparent d of quintets, J = 14.2, 2.8 Hz), 1.87 (1 H, apparent tq, J = 13.7, 2.6 Hz), 1.45 (1 H, dq, J = 13.8, 2.0 Hz), 1.21 (3 H, s); homonuclear decoupling, irradiation at δ 5.59 collapsed the signal at δ 2.19 to a dq, irradiation at δ 1.88 collapsed the signal at δ 5.59 to an apparent s; ^{13}C NMR (50 MHz, $CDCl_3$) 197.8 (−), 170.8 (+), 145.0 (+), 135.7 (+), 129.3 (2 C, −), 128.9 (2 C, −), 85.7 (−), 55.7 (−), 55.3 (+), 24.7 (+), 22.9 (+), 21.6 (−), 20.8 (−) ppm; mass spectrum (FAB), *m/z* (relative intensity) 326 (MH^+, 24), 294 (100), 219 (29), 191 (33), 169 (24), 157 (25). Anal. Calcd for $C_{15}H_{19}NSO_5$: C, 55.38; H, 5.85; N, 4.31; S, 9.85. Found: C, 55.05; H, 5.74; N, 4.24; S, 9.92.

***trans*- (7a) and *cis*-3-Acetyl-6-methoxy-3-methyl-1-[(4-methylphenyl)sulfonyl]-2-piperidone (7b).** Similar treatment of 718 mg (3.28 mmol) of (4-methylphenyl)sulfonyl isocyanate (90%) and 517 mg (3.64 mmol) of 3,4-dihydro-2-methoxy-5,6-dimethyl-2*H*-pyran, as described for **1a**,**b** except that the reactants were mixed at −60 °C and allowed to warm slowly to ambient temperature (3 h) and then stirred for 1 day, after gradient chromatography (1:4 to 35:65, ether−hexane) afforded 706 mg (2.08 mmol, 63%) of **7a** as a white solid that crystallized from CH_2Cl_2−isopropyl ether as colorless crystals, followed by 333 mg (0.98 mmol, 30%) of **7b** as a colorless oil that crystallized from isopropyl ether−hexane as colorless crystals. ***trans*-3-Acetyl-2-piperidone 7a:** mp 110 °C; IR (Nujol) 1720, 1700, 1595 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.91 (2 H, d, J = 8.4 Hz), 7.28 (2 H, d, J = 8.2 Hz), 5.54 (1 H, apparent quintet, J = ca. 3 Hz), 3.43 (3 H, s), 2.39 (3 H, s), 2.20−1.65 (4 H, overlapping m) on which is superimposed 2.00 (3 H, s), 1.26 (3 H, s); homonuclear decoupling, irradiation at δ 5.54 sharpened the overlapping m at δ 2.20−1.65; ^{13}C NMR (50 MHz, $CDCl_3$) 205.3 (+), 171.9 (+), 144.8 (+), 136.1 (+), 129.2 (2 C, −), 129.2 (2 C, −), 86.7 (−), 58.7 (+), 56.2 (−), 26.0 (−), 25.9 (+), 25.1 (+), 22.7 (−), 21.9 (−) ppm; mass spectrum (FAB), *m/z* (relative intensity) 340 (MH^+, 5), 308 (100), 270 (35); exact mass calcd for $C_{16}H_{21}NSO_5$ (FAB, MH^+) 340.1219, found 340.1232. ***cis*-3-Acetyl-2-piperidone 7b:** mp 98 °C; IR (film) 1730, 1695, 1605, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.90 (2 H, d, J = 8.4 Hz), 7.30 (2 H, d, J = 8.4 Hz), 5.64 (1 H, t, J = 2.9 Hz), 3.46 (3 H, s), 2.50 (1 H, ddd, J = 13.6, 10.8, 5.8 Hz), 2.41 (3 H, s), 2.21 (1 H, apparent d of quintets, J = ca. 14 and 3 Hz), 2.02−1.81 (1 H, m), superimposed on 1.90 (3 H, s), 1.41 (1 H, ddd, J = 13.8, 6.0, 3.8 Hz), 1.23 (3 H, s); homonuclear decoupling, irradiation at δ 5.64 collapsed the signals at δ 2.21 and 2.02−1.81 to ddd; ^{13}C NMR (50 MHz, $CDCl_3$) 203.7 (+), 172.0 (+), 145.0 (+), 135.6 (+), 129.3 (−), 129.2 (−), 129.2 (−), 129.1 (−), 85.8 (−), 58.1 (+), 56.2 (−), 25.9 (−), 25.5 (+), 25.1 (+), 22.1 (−), 21.9 (−) ppm; mass spectrum (FAB), *m/z* (relative intensity) 340 (MH^+, 7), 309 (46), 308 (100), 270 (24), 266 (37), 264 (37), 191 (33). Anal. Calcd for $C_{16}H_{21}NSO_5$: C, 56.63; H, 6.19; N, 4.13; S, 9.44. Found: C, 56.64; H, 6.34; N, 4.05; S, 9.76.

***trans*- (3a) and *cis*-1-[(4-Chlorophenyl)sulfonyl]-6-methoxy-3-methyl-2-oxo-3-piperidinecarboxaldehyde (3b).** Similar treatment of 850 mg (3.52 mmol) of (4-chlorophenyl)-sulfonyl isocyanate (90%) and 520 mg (4.06 mmol) of 3,4-dihydro-2-methoxy-5-methyl-2*H*-pyran, as described for **1a,b** except that the reactants were mixed at −10 °C and then stirred at ambient temperature for 26 days, after gradient chromatography of the reaction solution (3:7 to 35:65, ether−hexane) afforded 644 mg (1.86 mmol, 53%) of **3a** as a white solid, followed by 474 mg (1.37 mmol, 40%) of **3b** as a white solid, both of which crystallized from CH_2Cl_2−hexane as colorless crystals. ***trans*-3-Formyl-2-piperidone 3a:** mp 94−95 °C; IR (Nujol) 1735, 1695, 1585 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.27 (1 H, d, J = 8 Hz), 7.96 (2 H, dd, J = 8.6, ca. 2 Hz), 7.49 (2 H, dd, J = 8.8, ca. 2 Hz), 5.55 (1 H, apparent t, J = ca. 2 Hz), 3.50 (3 H, s), 2.20−2.05 (2 H, m), 2.05−1.90 (1 H, m), 1.90−1.65 (1 H, M), 1.29 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 197.5 (−), 169.7 (+), 140.1 (+), 137.2 (+), 130.4 (2 C, −), 128.7 (2 C, −), 85.9 (−), 57.3 (+), 56.1 (−), 24.7 (+), 22.8 (+), 20.3 (−) ppm; mass spectrum (FAB), *m/z* (relative intensity) 348 (MH^+, 15), 346 (MH^+, 38), 316 (49), 314 (100), 177 (28), 175 (66). Anal. Calcd for $C_{14}H_{16}NSClO_5$: C, 48.63; H, 4.63; N, 4.05; S, 9.26; Cl, 10.28. Found: C, 4.66; H, 4.66; N, 3.92; S, 9.25; Cl, 10.34. ***cis*-3-Formyl-2-piperidone 3b:** mp 115−116 °C; IR (Nujol) 1735, 1695, 1585 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.38 (1 H, s), 7.92 (2 H, d, J = 8.4 Hz), 7.43 (2 H, d, J = 8.4 Hz), 5.56 (1 H, apparent t, J = ca. 2.8 Hz), 3.34 (3 H, s), 2.37 (1 H, td, J = 13.4, 5.4 Hz), 2.19 (1 H, d of quintet, J = 14.2, 2.6 Hz), 1.87 (1 H, tq, J = 13.4, 2.6 Hz), 1.44 (1 H, dq, J = 13.7, 2.4 Hz), 1.22 (3 H, s); ^{13}C NMR (50 NMR, $CDCl_3$) 197.5 (−), 170.8 (+), 140.4 (+), 137.2 (+), 130.5 (2 C, −), 129.0 (2 C, −), 86.0 (−), 55.7 (−), 55.3 (+), 24.5 (+), 22.9 (+), 20.8 (−); mass spectrum (FAB), *m/z* (relative intensity) 348 (MH^+, 12), 346 (MH^+, 24), 316 (37), 314 (100), 177 (40), 175 (100), 169 (75). Anal. Calcd for $C_{14}H_{16}NSClO_5$: C, 48.63; H, 4.63; N, 4.05; S, 9.26; Cl, 10.28. Found: C, 48.75; H, 4.67; N, 3.95; S, 9.36; Cl, 10.34.

***trans*- (8a) and *cis*-3-Acetyl-1-[(4-chlorophenyl)sulfonyl]-6-methoxy-3-methyl-2-piperidone (8b).** Similar treatment of 780 mg (3.23 mmol) of (4-chlorophenyl)sulfonyl isocyanate (90%) and 517 mg (3.64 mmol) of 3,4-dihydro-2-methoxy-5,6-dimethyl-2*H*-pyran, as described for **1a**,**b** except that the reactants were mixed at −60 °C and allowed to warm slowly to ambient temperature (3 h) and then stirred for 18 h, after chromatography (3:7, ether−hexane) afforded 655 mg (1.82 mmol, 56%) of **8a** as a white solid that crystallized from CH_2Cl_2−hexane as colorless crystals, followed by 333 mg (0.93 mmol, 30%) of **8b** as a white solid that crystallized from isopropyl ether−hexane as colorless crystals. ***trans*-3-Acetyl-2-piperidone 8a:** mp 121−122 °C; IR (Nujol) 1725, 1695, 1575 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.91 (2 H, d, J = 8.6 Hz), 7.38 (2 H, d, J = 8.6 Hz), 5.43 (1 H, br s), 3.33 (3 H, s), 2.1−1.6 (4 H, overlapping m) on which is superimposed 1.98 (3 H, s), 1.18 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 204.9 (+), 171.8 (+), 140.0 (+), 137.6 (+), 130.6 (2 C, −), 128.7 (2 C, −), 86.7 (−), 58.6 (+), 56.0 (−), 25.8 (+), 25.7 (−), 24.5 (+), 22.3 (−) ppm; mass spectrum (FAB), *m/z* (relative intensity) 330 (34), 328 (100), 286 (25), 177 (26), 175 (74), 154 (41); exact mass calcd for $C_{15}H_{18}NSClO_5$ (FAB, MH^+) 360.0672, found 360.0665. Anal. Calcd for $C_{15}H_{18}NSClO_5$: C, 50.07; H, 5.01; N, 3.89; S, 8.90; Cl, 9.87. Found: C, 50.16; H, 5.13; N, 3.84; S, 8.90; Cl, 9.80. ***cis*-3-Acetyl-2-piperidone 8b:** mp 91 °C; IR (Nujol) 1725, 1690, 1580 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.91 (2 H, d, J = 8.8 Hz), 7.41 (2 H, d, J = 8.6 Hz), 5.55 (1 H, apparent t, J = 2.2 Hz), 3.37 (3 H, s), 2.40 (1 H, ddd), 2.17 (1 H, apparent d of quintets), 1.95−1.75 (1 H, m) on which is superimposed 1.82 (3 H, s), 1.35 (1 H, ddd), 1.18 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 203.2 (+), 171.9 (+), 140.3 (+), 136.9 (+), 130.4 (2 C, −), 128.8 (2 C, −), 85.8 (−), 57.9 (+), 5.0 (−), 25.7 (−), 25.3 (+), 24.5 (+), 21.8 (−) ppm; mass spectrum (FAB), *m/z* (relative intensity) 330 (36), 328 (100), 177 (32), 175 (84), 154 (41). Anal. Calcd for $C_{15}H_{18}NSClO_5$: C, 50.07; H, 5.01; N, 3.89; S, 8.90; Cl, 9.87. Found: C, 50.00; H, 4.98; N, 3.82; S, 9.07; Cl, 9.83.

4-Methylphenyl *trans*- (4a) and *cis*-3-Formyl-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (4b). To a cold solution (−60 °C) of 416 mg (3.25 mmol) of 3,4-dihydro-2-methoxy-5-methyl-2*H*-pyran in $CDCl_3$ was added 692 mg (3.09 mmol) of 4-methylphenyl isocyanatosulfate (95%) under N_2. The solution was allowed to warm to ambient temperature with stirring in 3 h and then stirred for 1 day. Removal of the solvent and gradient chromatography (1:9 to 4:6, ether−hexane) provided 450 mg (1.32 mmol, 43%) of **4a** as a colorless oil, followed by 550 mg (1.61 mmol, 52%) of **4b** as a white solid that crystallized from ether−hexane as colorless crystals. ***trans*-3-Formyl-2-piperidone 4a:** IR (Nujol) 1735, 1700, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.46 (1 H, s), 7.15 (4

H, superficial t, J = ca. 6.6 Hz), 5.15 (1 H, t, J = 2.4 Hz), 3.36 (3 H, s), 2.34 (3 H, s), 2.20−2.00 (2 H, two overlapping m), 1.92 (1 H, dq, J = 14.3, 3.1 Hz), 1.48 (3 H, s) superimposed on 1.58−1.38 (1 H, m); homonuclear decoupling, irradiation at δ 5.15 collapsed the signal at δ 1.92 to an apparent dt and simplified the m at δ 1.58−1.38; ^{13}C NMR (50 MHz, $CDCl_3$) 197.8 (−), 169.7 (+), 147.7 (+), 137.8 (+), 130.3 (2 C, −), 121.4 (2 C, −), 88.9 (−), 57.7 (+), 56.8 (−), 25.9 (+), 22.4 (+), 21.5 (−), 20.9 (−) ppm; mass spectrum (FAB), m/z (relative intensity) 342 (MH^+, 39), 324 (11), 311 (15), 310 (100), 266 (35); exact mass calcd for $C_{15}H_{19}NSO_6$ (FAB, MH^+) 342.1011, found 342.1012. ***cis*-3-Formyl-2-piperidone 4b:** mp 74−75 °C; IR (Nujol) 1735, 1705, 1595, 1500 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.47 (1 H, s), 7.16 (4 H, superficial t, J = ca. 4.2 Hz), 5.22 (1 H, t, J = 2.6 Hz), 3.18 (3 H, s), 2.50−2.40 (1 H, m), 2.32 (3 H, s), 2.08−1.90 (1 H, m), 1.64−1.35 (2 H, m), 1.34 (3 H, s); homonuclear decoupling, irradiation at δ 5.22 simplified the signals at δ 2.08−1.90 and 1.64−1.35; ^{13}C NMR (50 MHz, $CDCl_3$) 197.0 (−), 170.0 (+), 147.6 (+), 137.9 (+), 130.3 (2 C, −), 121.5 (2 C, −), 89.0 (−), 55.9 (+), 55.7 (−), 25.8 (+), 23.6 (+), 21.3 (−), 21.0 (−) ppm; mass spectrum (FAB), m/z (relative intensity) 342 (MH^+, 29), 324 (20), 311 (23), 310 (86), 282 (100), 266 (42), 226 (41), 191 (46), 140 (57). Anal. Calcd for $C_{15}H_{19}NSO_6$: C, 52.79; H, 5.57; N, 4.11; S, 9.38. Found: C, 52.72; H, 5.51; N, 4.03; S, 9.43.

4-Methylphenyl *trans*- (4c) and *cis*-6-Methoxy-3-methyl-2-oxo-1-piperidinesulfonate (4d) and 4a and 4b.[5] This reaction was exactly the same as described for **4a**,**b** except that the silica gel for flash chromatography was pretreated with 1% Et_3N in hexane. Flash chromatography provided 78 mg (0.25 mmol, 9%) of **4c** as a white solid followed by 410 mg (1.31 mmol, 45%) of **4d** as a white solid, then 150 mg (0.44 mmol, 15%) of **4a** as a colorless oil, and finally 150 mg (0.44 mmol, 15%) of **4b** as a white solid. *trans*-2-Piperidone **4c** was crystallized from isopropyl ether−hexane as colorless crystals: mp 79 °C; IR (Nujol) 1735, 1595, 1500 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.17 (4 H, apparent s), 5.24 (1 H, dd, J = 4.2, 1.8 Hz), 3.35 (3 H, s), 3.02−2.81 (1 H, m), 2.34 (3 H, s), 2.18−1.96 (1 H, m), 1.95−1.76 (1 H, m), 1.46−1.10 (2 H) on which is superimposed 1.19 (3 H, d, J = 6.8 Hz); homonuclear decoupling, irradiation at δ 5.24 simplified the m at δ 1.95−1.76 and 1.46−1.10, irradiation at δ 2.92 simplified the m at δ 2.18−1.96 and 1.46−1.10 and also collapsed the signal at δ 1.19 to a s, irradiation at δ 1.28 collapsed the signal at δ 5.24 to a s and simplified the m at δ 3.02−2.81, 2.18−1.96, and 1.95−1.76; ^{13}C NMR (50 MHz, $CDCl_3$) 173.9 (+), 147.9 (+), 138.0 (+), 130.5 (2 C, −), 121.8 (2 C, −), 90.0 (−), 56.3 (−), 36.1 (−), 26.7 (+), 24.0 (+), 21.1 (−), 15.7 (−) ppm; mass spectrum (FAB), m/z (relative intensity) 314 (MH^+, 13), 283 (19), 282 (100), 171 (52), 126 (31). Anal. Calcd for $C_{14}H_{19}NSO_5$: C, 53.67; H, 6.07; N, 4.47; S, 10.22. Found: C, 53.63; H, 6.20; N, 4.37; S, 10.27. *cis*-2-Piperidone **4d** was crystallized from ether−isopropyl ether as colorless crystals: mp 101−102 °C; IR (Nujol) 1720, 1595, 1500 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.13 (4 H, apparent s), 5.16 (1 H, apparent t, J = ca. 2.0 Hz), 3.27 (3 H, s), 2.44 (1 H, apparent quintet, J = 7.0 Hz), 2.31 (3 H, s), 2.06−1.90 (1 H, m), 1.90−1.64 (2 H, m), 1.64−1.46 (1 H, m), 1.27 (3 H, d, J = 7.0 Hz); homonuclear decoupling, irradiation at δ 2.44 simplified the m at δ 1.90−1.64; ^{13}C NMR (50 MHz, $CDCl_3$) 173.0 (+), 147.8 (+), 137.5 (+), 130.2 (2 C, −), 121.6 (2 C, −), 89.3 (−), 56.4 (−), 39.7 (−), 27.8 (+), 23.8 (+), 20.9 (−), 16.6 (−) ppm; mass spectrum (FAB), m/z (relative intensity) 314 (MH^+, 17), 283 (19), 282 (100), 126 (26), 112 (32), 108 (33), 107 (52); exact mass calcd for $C_{14}H_{19}NSO_5$ (FAB, MH^+) 314.1062, found 314.1072.

4-Methylphenyl *trans*- (9a) and *cis*-3-Acetyl-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (9b). Similar treatment of 813 mg (3.63 mmol) of 4-methylphenyl isocyanatosulfate (95%) and 517 mg (3.64 mmol) of 3,4-dihydro-2-methoxy-5,6-dimethyl-2*H*-pyran, as described for **1a**,**b** except that the reactants were mixed at −60 °C and allowed to warm slowly to ambient temperature (3 h) and then stirred for 2 h, after chromatography (3:7, ether−hexane) afforded 702 mg (1.98 mmol, 54%) of **9a** as a white solid that crystallized from CH_2Cl_2−isopropyl ether as colorless crystals, followed by 560 mg (1.58 mmol, 43%) of **9b** as a white solid that crystallized from CH_2Cl_2−hexane as colorless crystals. ***trans*-3-Acetyl-2-piperidone 9a:** mp 80 °C; IR (Nujol) 1730, 1710, 1600, 1505 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.13 (4 H, apparent AB pattern), 5.13 (1 H, apparent t, J = 2.6 Hz), 3.20 (3 H, s), 2.26 (3 H, s), 2.14 (3 H, s), 2.10−1.98 (2 H, m), 1.98-1.80 (1 H, m), 1.76−1.56 (1 H, m), 1.41 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 205.1 (+), 171.2 (+), 147.6 (+), 137.3 (+), 130.0 (2 C, −), 121.6 (2 C, −), 89.2 (−), 58.9 (+), 56.5 (−), 25.9 (+), 25.7 (−), 25.4 (+), 22.8 (−), 20.8 (−) ppm; mass spectrum (FAB), m/z (relative intensity) 356 (MH^+, 2), 324 (100), 275 (22), 226 (20); exact mass calcd for $C_{16}H_{21}NSO_6$ (FAB, MH^+): 356.1168, found 356.1181. ***cis*-3-Acetyl-2-piperidone 9b:** mp 76 °C; IR (Nujol) 1730, 1710, 1595, 1505 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.10 (4 H, apparent AB pattern), 5.16 (1 H, apparent t, J = 2.9 Hz), 3.23 (3 H, s), 2.48 (1 H, ddd, J = 13.6, 9.6, 6.7 Hz), 2.27 (3 H, s), 2.11 (3 H, s), 1.92 (1 H, apparent d of quintets, J = ca. 14 and 3 Hz), 1.48 (1 H, apparent ddd, J = 13.6, 7.2, 3.4 Hz), 1.31 (1 H, ddd, J = 20.6, 8.1, 3.4 Hz) on which is superimposed 1.29 (3 H, s); homonuclear decoupling, irradiation at δ 5.16 simplified the signals at δ 1.92 and 1.48; ^{13}C NMR (50 MHz, $CDCl_3$) 203.0 (+), 171.5 (+), 147.5 (+), 137.8 (+), 130.2 (2 C, −), 121.2 (2 C, −), 89.0 (−), 58.3 (+), 56.0 (−), 25.7 (−), 25.4 (2 C, +), 22.6 (−), 20.8 (−); mass spectrum (FAB), m/z (relative intensity) 356 (MH^+, 2), 324 (100), 275 (12), 226 (21), 221 (20). Anal. Calcd for $C_{16}H_{21}NSO_6$: C, 54.08; H, 5.92; N, 3.94; S, 9.01. Found: C, 54.17; H, 5.99; N, 3.90; S, 9.26.

2,2,2-Trichloroethyl *trans*- (5a) and *cis*-3-Formyl-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (5b). Similar treatment of 900 mg (3.36 mmol) of 2,2,2-trichloroethyl isocyanatosulfate (95%) and 400 mg (3.13 mmol) of 3,4-dihydro-2-methoxy-5-methyl-2*H*-pyran, as described for **1a,b** except that the reactants were mixed at −60 °C and allowed to warm slowly to ambient temperature (3 h) and then stirred for 1 day, after gradient chromatography of the reaction solution (1:9 to 3:7, ether−hexane) afforded 561 mg (1.47 mmol, 47%) of **5a** as a white solid, followed by 550 mg (1.44 mmol, 46%) of **5b** as a colorless oil, both of which crystallized from isopropyl ether−hexane as colorless crystals. ***trans*-3-Formyl-2-piperidone 5a:** mp 83 °C; IR (Nujol) 1735, 1705 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.43 (1 H, d, J = 0.8 Hz), 5.44 (1 H, dd, J = 1.8, 1.6 Hz), 5.05 (1 H, AB pattern, J = 11.7 Hz), 5.04 (1 H, AB pattern, J = 11.7 Hz), 3.52 (3 H, s), 2.25−2.05 (3 H, overlapping m), 1.85 (1 H, apparent tq, J = 9.0, 1.4 Hz), 1.46 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 197.2 (−), 170.8 (+), 93.3 (+), 89.1 (−), 81.9 (+), 57.7 (+), 56.9 (−), 25.9 (+), 23.1 (+), 20.4 (−); mass spectrum (FAB), m/z (relative intensity) 386 (MH^+, 6), 384 (MH^+, 17), 382 (MH^+, 17), 352 (41), 350 (35), 219 (23), 172 (27), 171 (100). Anal. Calcd for $C_{10}H_{14}NSCl_3O_6$: C, 31.37; H, 3.66; N, 3.66; S, 8.37; Cl, 27.84. Found: C, 31.44; H, 3.67; N, 3.58; S, 8.46; Cl, 27.57. ***cis*-3-Formyl-2-piperidone 5b:** mp 43 °C; IR (Nujol) 1740, 1700 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.51 (1 H, s), 5.45 (1 H, t, J = 2.7 Hz), 4.99 (2 H, apparent s), 3.38 (3 H, s), 2.51 (1 H, dq, J = 14.0, 6.0 Hz), 2.24−1.94 (2 H, two overlapping m), 1.58 (1 H, dq, J = 14.0, 3.0 Hz), 1.37 (3 H, s); homonuclear decoupling, irradiation at δ 5.45 simplified the multiplets at δ 2.24−1.94; ^{13}C NMR (50 MHz, $CDCl_3$) 197.0 (−), 171.5 (+), 93.3 (+), 88.9 (−), 82.1 (+), 56.1 (−), 55.6 (+), 25.8 (+), 23.4 (+), 21.0 (−) ppm; mass spectrum (FAB), m/z (relative intensity) 386 (MH^+, 6), 384 (MH^+, 14), 382 (MH^+, 16), 352 (54), 350 (57), 219 (34), 172 (39), 171 (55), 170 (63), 169 (100), 159 (44); exact mass calcd for $C_{10}H_{14}NSCl_3O_6$ (FAB, MH^+) 381.9686, found 381.9667. Anal. Calcd for $C_{10}H_{14}NCl_3SO_6$: C, 31.37; H, 3.66; N, 3.66; S, 8.37; Cl, 27.84. Found: C, 31.48; H, 3.62; N, 3.63; S, 8.60; Cl, 27.84.

2,2,2-Trichloroethyl *trans*- (10a) and *cis*-3-Acetyl-6-methoxy-3-methyl-2-oxo-1-piperidinesulfonate (10b). Similar treatment of 850 mg (3.18 mmol) of 2,2,2-trichloroethyl isocyanatosulfate (95%) and 517 mg (3.64 mmol) of 3,4-dihydro-2-methoxy-5,6-dimethyl-2*H*-pyran, as described for **1a**,**b** except that the reactants were mixed at −60 °C and then the temperature was slowly raised to 0 °C over 4 h with stirring, after chromatography (3:7, ether−hexane) afforded 665 mg (1.68 mmol, 53%) of **10a** as a colorless oil, followed by 496 mg (1.26 mmol, 39%) of **10b** as a colorless oil that crystallized from isopropyl ether−hexane as colorless crystals.

***trans*-3-Acetyl-2-piperidone 10a:** IR (Nujol) 1725, 1705 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.39 (1 H, apparent t, J = ca. 2.4 Hz), 5.01 (2 H, s), 3.48 (3 H, s), 2.30−2.15 (1 H, m) on which is superimposed 2.20 (3 H, s), 2.14−1.93 (2 H, overlapping m), 1.86 (1 H, apparent qt, J = 14.0, 3.3 Hz), 1.41 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 204.5 (+), 172.8 (+), 93.4 (+), 89.9 (−), 81.6 (+), 59.1 (+), 57.0 (−), 26.2 (+), 26.0 (+), 25.7 (−), 22.4 (−) ppm; mass spectrum (FAB), m/z (relative intensity) 396 (MH^+, 6), 394 (5), 368 (37), 366 (92), 364 (100), 184 (32). Anal. Calcd for $C_{11}H_{16}NSCl_3O_6$: C, 33.29; H, 4.03; N, 3.53; S, 8.07; Cl, 26.86. Found: C, 33.57; H, 4.01; N, 3.53; S, 7.95; Cl, 26.76. ***cis*-3-Acetyl-2-piperidone 10b:** mp 75 °C; IR (Nujol) 1735, 1720 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.52 (1 H, t, J = 3.0 Hz), 5.06 (1 H, AB pattern, J = 11.6 Hz), 5.01 (1 H, AB pattern, J = 11.6 Hz), 3.47 (3 H, s), 2.61 (1 H, ddd, J = 14.0, 10.2, 6.4 Hz), 2.26−1.95 (2 H, overlapping m) on which is superimposed 2.18 (3 H, s), 1.54 (1 H, ddd, J = 13.8, 6.0, 4.8 Hz), 1.41 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) 203.0 (+), 173.0 (+), 93.3 (+), 89.0 (−), 82.0 (+), 58.2 (+), 56.4 (−), 26.0 (−), 25.9 (+), 25.6 (+), 22.3 (−); mass spectrum (FAB), m/z (relative intensity) 396 (MH^+, 6), 394 (5), 368 (27), 366 (100), 364 (89), 184 (39). Anal. Calcd for $C_{11}H_{16}NSCl_3O_6$: C, 33.29; H, 4.03; N, 3.53; S, 8.07; Cl, 26.86. Found: C, 33.20; H, 4.04; N, 3.40; S, 8.17; Cl, 26.60.

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