Found: C, 53.64; H, 7.63; N, 6.94.

(+)-*N*-Methylpseudoconhydrine Hydrochloride [(+)-1·HCl]. To a stirred suspension of LAH (0.078 g, 2.05 mmol) in dry ether (10 mL) was added dropwise a solution of **8a** (0.29 g, 1.19 mmol) in dry ether (10 mL). The mixture was refluxed for 2 h and then cooled to room temperature. Usual workup followed by treatment with HCl gas gave a crude solid (0.245 g). After the solid was washed with AcOEt, (+)-**1**·HCl was crystallized from methanol–acetone (1:9) at −20 °C in 95% optical purity[5] (0.137 g, 0.7 mmol, 59% yield): mp 169–170 °C; $[\alpha]^{25}_D$ +23.8° (*c* 0.7, MeOH). The free base: liquid; MS, *m/e* 157 (M^+), 128, 115, 114 (base), 96; IR ($CHCl_3$) 3602, 2965, 2945, 2875, 2800, 1467, 1382, 1098, 1060, 1008, 968, 888 cm^{-1}; NMR ($CDCl_3$) δ 0.90 (t, J = 7 Hz, 3 H), 1.00–2.33 (m, 11 H), 2.24 (s, 3 H), 2.95 (ddd, J = 10, 4, and 2 Hz, 1 H), 3.35–3.93 (m, 1 H).

Anodic oxidation of 3[2] in acetic acid was carried out according to a procedure similar to the anodic oxidation of **6** described above. 2,3-Diacetoxy-1,2-bis(methoxycarbonyl)piperidine (**16**)[9] was obtained in 76% yield (8 F/mol).

Reduction of 16. Into a solution of **16** (1.828 g, 5.77 mmol) in formic acid (20 mL) was added, in portions, 90% $NaBH_4$ (1.21 g, 28.9 mmol). After stirring at room temperature for 1 h, the solution was worked up by a similar method described above to give *trans*-5-acetoxy-1,2-bis(methoxycarbonyl)piperidine (**17a**) and cis isomer **17b** in 80% (1.200 g, 4.63 mmol) and 6% (0.096 g, 0.37 mmol) yields, respectively.

17a (polar isomer): IR (neat) 2965, 1740, 1710, 1452, 1374, 1236, 1158, 1124, 1024 cm^{-1}; NMR (CCl_4) δ 1.38–2.21 (m, 4 H), 2.04 (s, 3 H), 3.11–3.41 (m, 1 H), 3.75 (s, 3 H), 3.79 (s, 3 H), 3.96–4.37 (m, 1 H), 4.92 (br s, 2 H). Anal. Calcd for $C_{11}H_{17}NO_6$: C, 50.96; H, 6.61; N, 5.40. Found: C, 51.18; H, 6.75; N, 5.30.

17b (less polar isomer): IR (neat) 2965, 1740, 1710, 1450, 1370, 1242, 1232, 1162, 1048 cm^{-1}; NMR (CCl_4) δ 1.40–2.30 (m, 4 H), 1.98 (s, 3 H), 2.57–3.00 (m, 1 H), 3.71 (s, 3 H), 3.77 (s, 3 H), 3.95–4.33 (m, 1 H), 4.47–4.97 (m, 2 H); MS, *m/e* 258 (M^+ − H), 230, 200, 140 (base). Anal. Calcd for $C_{11}H_{17}NO_6$: C, 50.96; H, 6.61; N, 5.40. Found: C, 51.25; H, 6.66; N, 5.26.

Preparation of 5-Hydroxy-2-methoxy-1-(methoxycarbonyl)piperidine (19). Carboxylic acid **18** was obtained as a white solid by hydrolysis of **17a** (1.988 g, 7.68 mmol) carried out as described above (1.56 g). Into an electrolysis cell as described above was added a solution of the crude **18** (1.56 g) and AcOK (2 g, 20 mmol) in methanol (20 mL) and acetic acid (2 mL). After 5 F/mol of electricity was passed at a constant current of 0.2 A (5.1 h, terminal voltage ca. 10 V) through the solution cooled with water, water (20 mL) was poured into the resulting reaction mixture. The organic portion was extracted with CH_2Cl_2 (3 × 20 mL) and the combined organic layer was dried over $MgSO_4$. The solvent was removed in vacuo to give a residue, which was chromatographed on silica gel (AcOEt–hexane = 1:2) to afford **19** (0.900 g, 4.76 mmol) in 62% yield: IR (neat) 3450, 2948, 1695, 1260, 1155, 1070, 1001 cm^{-1}; NMR (CCl_4) δ 1.30–2.06 (m, 4 H), 2.30–4.20 (m, 4 H), 3.14 (s, 3 H), 3.62 (s, 3 H), 5.10 (br s, 1 H); MS, *m/e* 172 (M^+ − OH), 157 (M^+ − MeOH), 140, 114 (base); exact mass calcd *m/e* 157.0739 (M^+ − MeOH), found 157.0722 (M^+ − MeOH). Anal. Calcd for $C_8H_{15}NO_4$: C, 50.78; H, 7.99; N, 7.40. Found: C, 51.05; H, 8.13; N, 7.10.

(2*R*,5*R*)- and (2*S*,5*R*)-Acetoxy-2-propyl-1-(methoxycarbonyl)piperidine (21a and 21b). To a stirred solution of $TiCl_4$ (0.42 mL, 3.83 mmol) in CH_2Cl_2 (7 mL) was added dropwise a solution of **19** (0.723 g, 3.83 mmol) and allyltrimethylsilane (0.91 mL, 5.75 mmol) in CH_2Cl_2 (17 mL) at −70 °C under an atmosphere of nitrogen. The mixture was gradually warmed to room temperature. Water (25 mL) was added to the solution and the organic portion was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layer was dried over $MgSO_4$ and the solvent was removed. A mixture of the residue and a catalytic amount of PtO_2 in acetic acid (10 mL) was stirred overnight at room temperature under an atmosphere of hydrogen (1 atm). After the catalyst and solvent were removed, the residue was dissolved in a mixed solvent of acetic anhydride (1.08 mL, 11.5 mmol) and pyridine (0.93 mL, 11.5 mmol). After the solution was stirred for 2 h, dilute HCl (20 mL) was added into the reaction mixture. The organic portion was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic layer was dried over $MgSO_4$. After the solvent was removed in vacuo, the residue was chromatographed on silica gel (AcOEt–hexane = 1:4) to afford 2*R*,5*R* isomer **21a** and 2*S*,5*R* isomer **21b** in 69% (0.635 g, 2.64 mmol) and 5% (0.050 g, 0.21 mmol) yields, respectively. Their spectroscopic data were consistent with those of **8a**,**b**.

(−)-*N*-Methylpseudoconhydrine Hydrochloride [(−)-1·HCl]. Treatment of **21a** with LAH in a way similar to the synthesis of (+)-**1** from **8a** gave (−)-**1** in more than 70% yield. IR, NMR, and MS spectrum of (−)-**1** were consistent with those of (+)-**1**. The optical purity of synthesized (−)-**1** was determined as its HCl salt (60% yield from **21a**, 90% optical purity):[5] mp 157–158 °C; $[\alpha]^{25}_D$ −22.6° (*c* 1.0, MeOH).

A Novel Reaction of Benzoyl Chlorides in Dimethyl Sulfoxide

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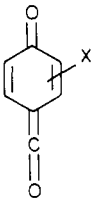
Received January 29, 1988

Previous research from this laboratory has shown that acyl-group transfer from substituted aryl 4-hydroxybenzoates to water or other acceptors takes place through either the "usual" $B_{Ac}2$ mechanism[1] or an unprecedented E1cB mechanism involving *p*-oxo ketenes **1** as reactive intermediates.[2]



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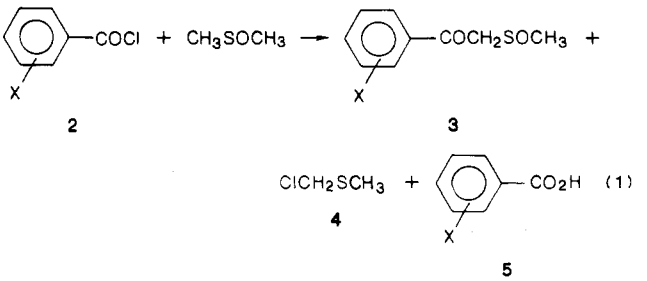
We are currently attempting to generate and characterize compounds **1** in nonaqueous solvents from substituted 4-hydroxybenzoyl chlorides in the presence of bases, and in the course of this work we have discovered a novel reaction between benzoyl chlorides and dimethyl sulfoxide (DMSO).

Careful addition of 3,5-di-*tert*-butyl-4-hydroxybenzoyl chloride (**2a**) to excess DMSO at room temperature afforded not only the expected chloromethyl methyl sulfide **4** and the carboxylic acid **5a**,[3-5] but also a significant amount of the β-keto sulfoxide **3a** (eq 1 and Table I, entry



2 **3**

4 **5** (1)

1). Formation of a deeply red compound was noticed as well, whose spectroscopic and elemental analysis data were consistent with those reported in the literature[6] for

(1) See, for example: Euranto, E. K. In *The Chemistry of Carboxylic Acids and Esters*; Patai, S., Ed.; Interscience, London, 1974; Chapter 11.
(2) Cevasco, G.; Guanti, G.; Hopkins, A. R.; Thea, S.; Williams, A. *J. Org. Chem.* **1985**, *50*, 479. Thea, S.; Cevasco, G.; Guanti, G.; Kashefi-Naini, N.; Williams, A. *J. Org. Chem.* **1985**, *50*, 1867.
(3) Michelot, R.; Tchoubar, R. *Bull. Soc. Chim. Fr.* **1966**, 3039.
(4) Amonoo-Neizer, E. H.; Ray, S. R.; Shaw, R. A.; Smith, B. C. *J. Chem. Soc.* **1965**, 6250.
(5) Bordwell, F. G.; Pitt, B. M. *J. Am. Chem. Soc.* **1955**, *77*, 572.

0022-3263/88/1953-4121$01.50/0

Table I

entry	benzoyl halide/mmol	% yield of 3
1	**2a**/1.9	16[a]
2	**2a**/1.9	15.6[a,b]
3	**2a**/1.9	16.1[c]
4	**2a**/1.9	18.2[d]
5	**2b**/3.5	6.2
6	**2c**/2.8	4.8
7	**2d**/3.2	5.5

[a] Acid **5a** was recovered in 74% yield. [b] Experiment carried out in the presence of TEA equimolar with respect to the acyl chloride. [c] Experiment performed in the presence of anhydrous *p*-toluenesulfonic acid (ca. 1.5 mmol). [d] Experiment carried out in CH_2Cl_2 solvent (20 mL) at −20 °C.

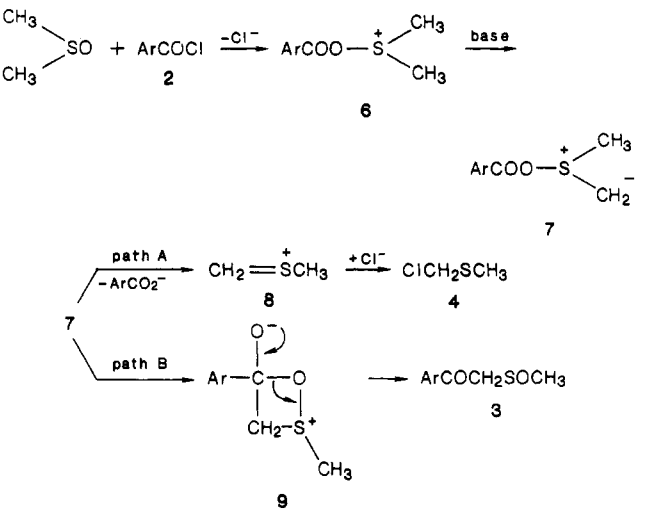
3,3′,5,5′-tetra-*tert*-butyldiphenoquinone. Owing to the very low yield obtained (<1%, estimated spectrophotometrically at 425 nm), this reaction was not further investigated. Yields of **3a** did not vary significantly as a result of addition of triethylamine (TEA) (entry 2) or anhydrous *p*-toluenesulfonic acid (PTSA) (entry 3). TEA would promote the ionization of the hydroxyl group of **2a**; PTSA would inhibit it. Therefore, it is likely that ionization of the hydroxyl group is not important in the process leading to **3a**. Experiments carried out on benzoyl chlorides **2b–d** seem to confirm that the presence of the OH function in the acyl is not prerequisite to formation of β-keto sulfoxides **3b–d**, as these were formed in all cases, although in smaller amounts (entries 5–7).

An attempt to improve the yield of **3a** by changing the experimental conditions adopted (CH_2Cl_2 solvent, −20 °C) was of little benefit (entry 4).

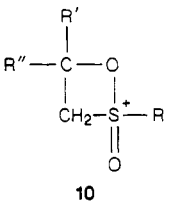
It has long been known that carboxylic acid halides react with stoichiometric DMSO either in the absence or in the presence of inert solvents (e.g., dichloromethane, benzene) to afford, as the only reaction products described, chloromethyl methyl sulfide (**4**) and the carboxylic acid **5**,[3-5] whose formation was postulated[4] to take place through a reaction pathway where the nucleophilic attack by DMSO oxygen on the acyl chloride occurs initially leading to the acyloxysulfonium chloride **6** (Scheme I). Subsequently, hydrogen abstraction from a methyl group (by an added base, a second DMSO molecule, or Cl^- itself) yields the ylide **7**. Expulsion of a carboxylate ion followed by addition of Cl^- to cation **8** finally yields chloromethyl methyl sulfide **4** (path A). Previously, Bordwell and Pitt had proposed a mechanism differing slightly from the one illustrated in path A in that an extra step is included where Cl^- displaces $ArCO_2^-$ from **6**, yielding a chlorosulfonium ion ($MeS^+(Cl)Me$), which undergoes base ($ArCO_2^-$) promoted dehydrochlorination to furnish **8**.[5]

As far as the process leading to compounds **3** is concerned, although we have no definitive evidence of the mechanism involved, the simplest rationalization is that β-keto sulfoxides are formed from the intermediary ylide **7** via the intramolecular rearrangement depicted as path B in the scheme. Actually, an alternative route to **3** could be envisaged, i.e. nucleophilic attack of the DMSO conjugate base (generated by self-ionization of DMSO) on the acyl chloride. Such a hypothesis, however, is regarded as unlikely on account of the exceedingly small autoprotolysis constant of DMSO (5×10^{-18} M).[7] The reaction mechanism proposed here to account for the formation of β-keto sulfoxides represent, to our knowledge, the first example of rearrangement in which the unusual four-membered cyclic intermediates **9** are involved. Four-membered cyclic oxosulfonium ions **10** somewhat similar to **9** have been

Scheme I



postulated recently in the reaction of (aryloxy)oxosulfonium ylides with carbonyl compounds, which yields unsaturated sulfones.[8]



10

It is likely that the β-keto sulfoxide formation was passed unnoticed to previous workers[4,5] since "simple" benzoyl chlorides (i.e. **3b**) give poor yields in **3**. Furthermore, different experimental conditions (equimolar instead of excess DMSO with respect to the acyl chloride) perhaps could have made it even lower.

Experimental Section

Materials. DMSO (Fluka Puriss, PA) was stored over molecular sieves (4 Å). Benzoyl, 3-chlorobenzoyl, and *p*-toluoyl chlorides were commercial products (Aldrich) and were distilled prior to use. 3,5-Di-*tert*-butyl-4-hydroxybenzoyl chloride was prepared as described in the literature.[9]

ω-(Methylsulfinyl)-4-hydroxy-3,5-di-*tert*-butylacetophenone (3a): mp 61–2 °C (from ethanol); ^1H NMR (deuterioacetone) δ 1.46 (s, 18 H), 2.30 (s, 3 H), 5.39 (s, 2 H), 7.91 (s, 2 H); IR (Nujol) 3545, 1690, 1220 cm^{-1}. Anal. Calcd for $C_{17}H_{26}O_3S$: C, 65.8; H, 8.4; S, 10.3. Found: C, 65.6; H, 8.4; S, 10.1. Spectroscopic and analytical data for compounds **3b–d** were consistent with the proposed structures and agreed with those reported in the literature.[10]

Methods. Composition of the final reaction mixtures was routinely assessed by TLC on Merck silica gel precoated plates, generally by using CH_2Cl_2 or CH_2Cl_2/ethyl ether mixtures for elution. The same technique was used to check the reaction products for purity after isolation. In all cases, the acyl chlorides (0.5 g) were dissolved cautiously in DMSO (2 mL, 28 mmol) at room temperature under efficient stirring. As soon as the exothermic reaction had subsided, the reaction mixture was column chromatographed (silica gel, CH_2Cl_2 eluent). Finally, the recovered β-keto sulfoxides **3** (pure by TLC) were weighed to evaluate the yield.

Registry No. **2a**, 40056-43-7; **2b**, 98-88-4; **2c**, 618-46-2; **2d**, 874-60-2; **3a**, 115207-18-6; **3b**, 2813-22-1; **3c**, 87974-10-5; **3d**, 13581-83-4; DMSO, 67-68-5.

(6) Pastor, S. D. *J. Org. Chem.* **1984**, *49*, 5260.
(7) Kolthoff, I. M.; Reddy, T. B. *Inorg. Chem.* **1962**, *1*, 189.
(8) Okuma, K.; Nakanishi, K.; Ohta, H. *J. Org. Chem.* **1983**, *49*, 1402.
(9) Mueller, E.; Rieker, A.; Mayer, R.; Scheffler, K. *Liebigs Ann. Chem.* **1961**, *645*, 36.
(10) Russell, G. A.; Mikol, G. J. *J. Am. Chem. Soc.* **1966**, *88*, 5498.