$$R_2CHOH + OH^- \rightleftarrows R_2CHO^- + H_2O \quad (8)$$

Acknowledgment. Thanks are due to Prof. R. C. Kapoor for his keen interest.

Registry No. Propan-2-ol, 67-63-0; butan-2-ol, 78-92-2; pentan-2-ol, 6032-29-7; pentan-3-ol, 584-02-1; 1-chloropropan-2-ol, 127-00-4; 1-methoxypropan-2-ol, 107-98-2; benzhydrol, 91-01-0; *N*-bromoacetamide, 79-15-2; sodium hypobromite, 13824-96-9.

Notes

A Facile Intramolecular Tertiary Amine Displacement Reaction

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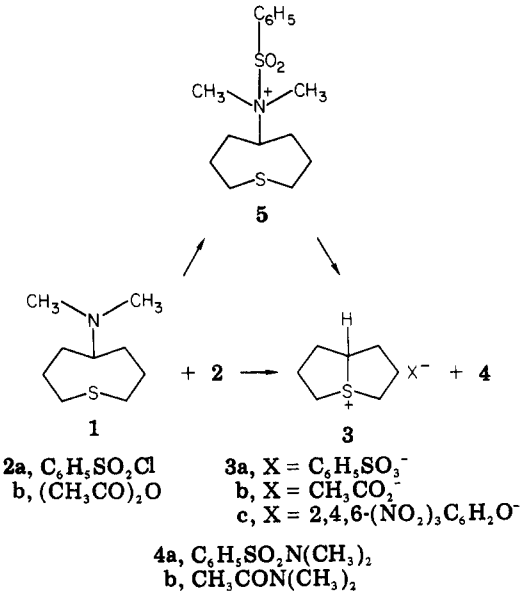
Facile carbon–nitrogen bond-cleavage reactions of tertiary amines are rare. Common exceptions are the reaction between a tertiary amine and cyanogen bromide (the Von Braun reaction)[1] and the nitrous acid dealkylation reaction.[2] When the leaving group is either benzylic or an otherwise stabilized carbocation, the C–N bond can be cleaved by acetic anhydride after lengthy refluxing.[3,4]

Tertiary amines are normally stable when treated with benzenesulfonyl chloride under the conditions of the Hinsberg test[5] although some C–N bond cleavage can occur.[6] We have seen no examples of an intramolecular displacement reaction that causes C–N bond cleavage in amines in contrast to those causing C–O bond cleavage in alcohols.

For these reasons we are reporting the surprisingly exothermic C–N bond cleavage reaction of 5-(dimethylamino)-1-thiacyclooctane (**1**) with benzenesulfonyl chloride under the conditions of the Hinsberg test. A similar reaction occurs with acetic anhydride to give *N,N*-dimethylacetamide and **3b** (NMR experiment).

Treatment of pure **1** with excess benzenesulfonyl chloride (**2a**) produces a vigorous exothermic reaction accompanied by the immediate formation of a solid material. Subsequent separation and identification confirmed the products as 1-thioniabicyclo[3.3.0]octane benzenesulfonate (**3a**) and *N,N*-dimethylbenzenesulfonamide (**4a**) in nearly quantitative yields. The reaction is initiated by a nucleophilic displacement by the amine on the sulfonyl chloride to form the intermediate $C_6H_5SO_2NR_3^+$ salt **5** (Scheme I). Subsequent displacement at C-5 by the transannular thioether leads to formation of **3a** and **4a**. Precedence for such a mechanism was deduced from a similar C–O bond-cleavage reaction of 5-hydroxy-1-thiacyclooctane with phosphoric anhydride[7] to give **3**.

Scheme I



2a, $C_6H_5SO_2Cl$
b, $(CH_3CO)_2O$

3a, X = $C_6H_5SO_3^-$
b, X = $CH_3CO_2^-$
c, X = 2,4,6-$(NO_2)_3C_6H_2O^-$

4a, $C_6H_5SO_2N(CH_3)_2$
b, $CH_3CON(CH_3)_2$

In this C–N cleavage reaction neither a stabilized carbocationic center nor a good leaving group is present so this reaction must proceed via direct displacement of *N,N*-dimethylbenzenesulfonamide by attack of the strongly nucleophilic thioether group on the transannular carbon.

Experimental Section

Reaction of 5-(Dimethylamino)-1-thiacyclooctane with Benzenesulfonyl Chloride. To 0.110 g (0.637 mmol) of **1** was added 0.281 g (1.59 mmol) of **2a**. A rapid exothermic reaction ensued accompanied by the formation of a white solid. Aqueous sodium hydroxide (4 mL of 5% solution) was added and the mixture agitated for 1 h to produce an oily layer. Extraction with ether (5 × 10 mL) provided 0.123 g (0.661 mmol, 104%) of **4a** as white crystals, mp 43.0–45.0 °C (compared with authentic **4a**).

The aqueous layer was saturated with potassium carbonate and extracted with chloroform (5 × 10 mL). Removal of the chloroform produced a pale yellow oil, which crystallized rapidly on cooling to give 0.174 g (0.608 mmol, 95%) of **3a** as an off white, very hygroscopic solid: ^1H NMR ($CDCl_3/Me_4Si$) δ 7.8 (m, 2 H, *o*-H), 7.3 (m, 3 H, *m*- and *p*-H), 4.68 (p, 1 H, CH), 3.60 (t, 4 H, CH_2S), 2.1 (m, 8 H, CH_2); IR (KBr) 3060 (w), 1440 (m), 1230 (s), 1220 (vs), 1202 (vs), 1185 (s), 1125 (s), 1035 (m), 1015 (m), 1000 (m), 760 (m), 730 (s), 695 (m), 615 (s), 656 (m) cm^{-1}. On addition of **3a** in water to a saturated aqueous picric acid solution, yellow needles of **3c** precipitated: mp 256.0–258.0 °C (lit.[8] mp 257–258 °C); ^1H NMR (CD_3COCD_3/Me_4Si) δ 8.58 (s, 2 H, Ar H), 4.90 (p, 1 H, CH), 3.7 (m, 4 H, CH_2S), 2.5 (m, 8 H, CH_2).

Reaction of 1 with 2b. A solution of 3 drops each of **1** and **2b** in 0.5 mL of $CDCl_3$ was monitored by ^1H NMR. After warming

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of the sample for 8 h at 50–60 °C, characteristic peaks of *N,N*-dimethylacetamide (**4b**) were observed at δ 3.01 (s, NCH_3), 2.93 (s, NCH_3), and 1.97 (s, CH_3CO) along with the multiplet at 4.05 (H–5) consistent with the formation of **3b** (reaction 27% complete). After additional heating at 90 °C for 6 h, the reaction was about 75% complete.

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Registry No. 1, 85939-88-4; **2a**, 98-09-9; **2b**, 108-24-7; **3a**, 86669-27-4; **3b**, 86669-28-5; **3c**, 86669-29-6; **4a**, 14417-01-7; **4b**, 127-19-5.

Unusual Reduction of an α-Oxo Ester by Lithium Diisopropylamide

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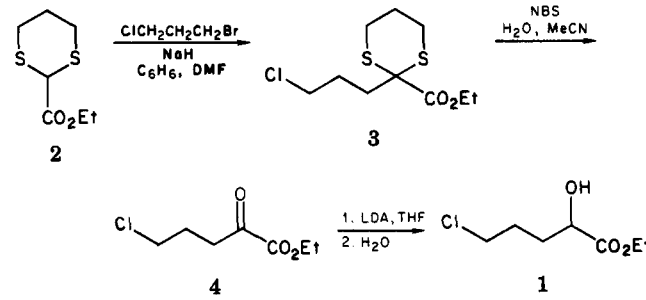
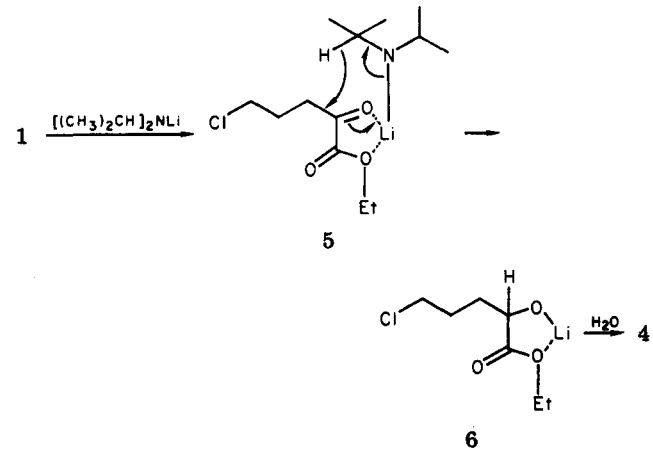
In the course of another investigation, we had occasion to attempt to generate the enolate ion of ethyl 5-chloro-2-oxopentanoate (1) by treatment of lithium diisopropylamide (LDA). We report here as a caveat to others our unexpected observation that such treatment brings about reduction of 1. The α-oxo ester 1 was prepared by the route shown in Scheme I: alkylation of ethyl 1,3-dithiane-2-carboxylate (2) with 1-bromo-3-chloropropane by the general procedure of Eliel and Hartmann[1] gave 3, which on treatment with *N*-bromosuccinimide in aqueous acetonitrile[2] gave 1. Reaction of 1 with LDA in tetrahydrofuran at −78 °C resulted in its reduction to ethyl 5-chloro-2-hydroxypentanoate (4). The structural assignment is based on the elemental composition and IR, ^1H NMR, and ^{13}C NMR spectra of the product (see Experimental Section). Although the yield of 4 after purification was low, the ^1H NMR spectrum of the crude reaction product showed it to consist of 4 and ~5% of starting material 1 with no significant amount of other products.

Lithium diisopropylamide has previously been reported to reduce α-methoxy and α-halo ketones[3] and nonenolizable ketones,[3-5] but this is the first case to our knowledge where reduction occurs of a ketone that belongs to none of these categories.[6] We suggest that the presence of the carboxylic ester group leads to strong complexation with lithium as in 5; the LDA then delivers a hydride ion to give 6 via a six-membered transition state (Scheme II), as postulated previously.[3,7] Similar complexation could account for the efficient reduction of α-oxo esters to α-hydroxy esters by halomagnesium alkoxides.[8] It is also possible that analogous complexation involving the α substituent facilitates the reduction of α-methoxy and α-halo ketones by LDA.

Scheme I



Scheme II



Experimental Section

Ethyl 5-Chloro-2-oxopentanoate (1). Ethyl 1,3-dithiane-2-carboxylate (2) (10.0 g, 52 mmol) was alkylated with 1-bromo-3-chloropropane (24.6 g, 157 mmol) and sodium hydride (50% oil dispersion; 2.68 g, 55.8 mmol) in 3:1 benzene–dimethylformamide (88 mL). After workup, the crude product was distilled at 116–117 °C (0.025 torr) to give 2-carbethoxy-2-(2-chloropropyl)-1,3-dithiane (3) (12.1 g, 86%): IR λ_{max} ($CHCl_3$) 5.82 μm; ^1H NMR ($CDCl_3$) δ 4.25 (q, J = 7 Hz, 2 H), 1.7–3.8 (m, 12 H), 1.33 (t, J = 7 Hz, 3 H).

A solution of 2 (8.06 g, 30.0 mmol) in acetonitrile (10 mL) was added quickly, dropwise, to a solution of *N*-bromosuccinimide (32.1 g, 180 mmol), silver perchlorate (24.9 g, 120 mmol), and 2,6-lutidine (6.42 g, 60 mmol) in aqueous 80% acetonitrile (150 mL) that was cooled in an ice bath. The ice bath was removed, and the mixture was stirred for 15 min at room temperature. The solution was poured into 1:1 methylene chloride–hexanes (150 mL), washed with saturated aqueous NH_4Cl, saturated aqueous Na_2SO_3, and saturated aqueous NaCl, dried, filtered, and concentrated. The crude product was distilled at 76–77 °C (1.25 torr) to give ethyl 5-chloro-2-oxopentanoate (1) (2.41 g, 45%); IR λ_{max} ($CHCl_3$) 5.78 μm; ^1H NMR ($CDCl_3$) δ 4.30 (q, J = 7 Hz, 2 H), 3.68 (t, J = 6 Hz, 2 H), 3.12 (t, J = 6 Hz, 2 H), 1.9–2.4 (m, 2 H), 1.37 (t, J = 7 Hz, 3 H); MS, m/e (relative intensity) 142 (14), 107 (3), 105 (9), 69 (100); exact mass calcd for $C_7H_{10}O_3$ (M − HCl) 142.0630, found 142.0641; calcd for $C_4H_6{}^{35}ClO$ (M − $CO_2C_2H_5$) 105.0088, found 105.0102.

Reaction of Ethyl 5-Chloro-2-oxopentanoate (1) with Lithium Diisopropylamide: Formation of Ethyl 5-Chloro-2-hydroxypentanoate (4). Ethyl 5-chloro-2-oxopentanoate (1) (2.00 g, 11.2 mmol) in dry tetrahydrofuran (4 mL) was syringed dropwise with stirring into a solution of lithium diisopropylamide (4.86 mL of 2.30 M *n*-BuLi in hexane, 1.75 mL of diisopropylamine; 11.1 mmol) in dry tetrahydrofuran (50 mL) under nitrogen

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(6) See, however, footnote 24 in ref 3. Since the submission of this note, we have observed that methyl pyruvate and ethyl 2-oxopentanoate are reduced by LDA under similar conditions to methyl lactate (22%) and ethyl 2-hydroxypentanoate (69%), respectively, indicating that reduction of 1 by LDA is not dependent on the presence of the γ-chloro substituent.
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