On the Mechanism of the Oxidation of Tropan-3α-ol with Benzoyl Chloride

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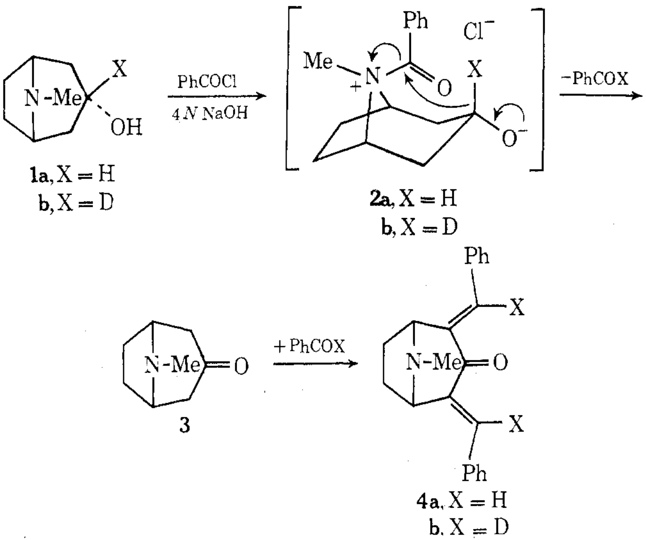
Polycyclic molecules having sterically proximate alcohol and keto functions have been occasionally observed to undergo base-catalyzed redox reactions under mild conditions.[1] However, postulated hydride transfer mechanisms have seldom been verified by isotopic labeling experiments. A case in point is the reaction of tropan-3α-ol[2] (**1a**) with benzoyl chloride under Schotten–Baumann conditions to give *trans,trans*-dibenzylidenetropinone (**4a**), for which Calvert and Hobson[3] proposed the mechanism abbreviated in Scheme I. Although circumstantial evidence is in accord with the proposed mechanism, we have reinvestigated this reaction employing deuterium-labeled precursors and the results of this study fully corroborate the mechanism of Calvert and Hobson.

Scheme I



Reduction of tropinone with $LiAlD_4$ in ether[4] afforded an 89% yield of a 1:1 mixture of the deuterated 3α- and 3β-tropanols which can be separated by fractional crystallization of the picrates.[5] Reaction of a well-stirred solution of 3β-deuteriotropan-3α-ol (**1b**) in 4 *N* NaOH with excess benzoyl chloride at ambient temperature for 15 hr gave the dideuterated dienone **4b** in ca. 80% yield. The presence of the label was readily determined by comparison of the mass spectra of **4b** and its undeuterated counterpart **4a**, which revealed that the molecular ion at *m/e* 315 and the major peaks at *m/e* 287 and 259 in **4a** were shifted two mass units higher in **4b**. Furthermore, the 100-MHz NMR spectra of **4a** and **4b** were superimposable except for the absence of the sharp singlet at δ 7.81 in **4b** corresponding to the benzylidene hydrogens.

These experimental results provide additional conclusive evidence in support of the proposed mechanism the key feature of which is the intramolecular transfer of a 3β-hydride to the strongly electrophilic carbonyl of the *N*-benzoylammonium ion **2** to afford tropinone and benzaldehyde.[6,7] The subsequent stereospecific aldol condensation of **3** with benzaldehyde is well precedented.[8] The fact that cyclohexanol, *N*-benzoylnortropine, and 3α-deuteriotropan-3β-ol are all recovered unchanged under the reaction conditions further implies the intermediacy of **2**.

Experimental Section[9]

Reaction of Tropan-3α-ol with Benzoyl Chloride. To a rapidly stirred solution of 0.426 g (3.38 mmol) of 3β-deuteriotropan-3α-ol in 65 ml of 4 *N* NaOH was added dropwise over a 30-min period 7.10 g (50.7 mmol) of freshly distilled benzoyl chloride. After addition was complete, the mixture was allowed to stir under nitrogen at ambient temperature for 15 hr. The pale yellow precipitate was collected by suction filtration, washed with 25 ml of water, and recrystallized from 10 ml of boiling methanol to afford 0.427 g (1.35 mmol, 80% yield) of the dideuterated *trans*-dibenzylidenetropinone as pale yellow needles: mp 151–153° (lit.[7] mp of undeuterated compound 153°); ir ($CHCl_3$) 1666, 1605, 1495, 1445, 1090, and 1070 cm^{-1}; 100-MHz NMR ($CDCl_3$) δ 7.36 (s, 10 H), 4.40 (m 2 H), 2.60 (m, 2 H), 2.26 (s, 3 H), 2.00 (m, 2 H); MS *m/e* (rel intensity) 317 (M^+, 41), 289 (100), and 261 (29).

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Registry No.—1b, 56292-47-8; **4b,** 56290-48-9; benzoyl chloride, 98-88-4.

References and Notes

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(2) The nomenclature used to designate the stereochemistry of the tropines in that of Fodor: G. Fodor in "Chemistry of the Alkaloids", S. W. Pelletier, Ed., Van Nostrand-Reinhold, Princeton, N.J., 1970, pp 536–538.

(3) B. J. Calvert and J. D. Hobson, *J. Chem. Soc.*, 2723 (1965).

(4) A. H. Beckett, N. J. Harper, A. D. J. Balon, and T. H. E. Watts, *Tetrahedron*, **6**, 319 (1959).

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(6) Deuterated benzaldehyde can be isolated by extraction after 3 hr reaction time.

(7) The *N*-benzoyl group must be situated syn relative to the 3β-hydride in order for the intramolecular transfer of hydride to occur as shown in structure **2**. However, Fodor has recently reviewed a body of evidence which indicates that irreversible N-quaternization and N-oxidation reactions of tropines occur preferentially anti. These data suggest that formation of the *N*-benzoylammonium ion is reversible, leading to both the syn and anti isomers, but only the syn isomer is reduced. See G. Fodor in "The Alkaloids", Vol. XIII, R. H. F. Manske, Ed., Academic Press, New York, N.Y., 1971, pp 359–365, for a discussion of the configuration of quaternary tropanium salts.

(8) R. Willstätter, *Ber.*, **30**, 731, 2679 (1897).

(9) The tropan-3α-ol, tropinone, and lithium aluminum deuteride were obtained from Sigma Chemical Co., Aldrich Chemical Co., and Merck Sharp and Dohme, Inc., respectively. The NMR spectra were recorded on a Varian HA-100 spectrometer, the ir spectra on a Perkin-Elmer 457 spectrometer, and mass spectra on a Du Pont 21-497B spectrometer.

Low-Melting Nematic Phenyl 4-Benzoyloxybenzoate Liquid Crystals[1]

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The preparation of nematic liquid crystals with specific physical properties for use in electrooptical applications has been the subject of many recent investigations.[2–5] The initial work on materials for use in these applications emphasized the preparation of liquid crystals that were either