Equilibration of Cryptone and Its β,γ-Unsaturated Isomer

Milton D. Soffer and Anne C. Williston

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One of the two recently reported[1] synthetic routes to *dl*-cryptone proceeds through the collidine dehydrobromination of 2-bromo-4-isopropylcyclohexanone, which gives a roughly equal mixture, separable by fractionation, of the α,β- and the β,γ-unsaturated ketones.

The formation of the β,γ-derivative under these conditions is of special interest since the method is in general use for the preparation of α,β-unsaturated ketones, and the apparent equilibration is an interesting example of favorable competition between conjugation and hyperconjugation effects.[2] That the ketones themselves form the same equilibrium mixture under the conditions of the dehydrohalogenation has now been demonstrated by treating the conjugated isomer with collidine and collidine hydrobromide. The distilled product appeared (λ_{max} 227 mμ, ϵ 7,620) to be a mixture comparable with that obtained from the collidine dehydrobromination (λ_{max} 227 mμ, ϵ 6,670) and this was confirmed by separating the pure isomers[1] (Δ^2 isomer, λ_{max} 227 mμ, ϵ 12,370; Δ^3isomer, no maximum at 210–360 mμ) which were converted in good yield to their characteristic dinitrophenylhydrazones.

We are indebted to the National Science Foundation for a grant in support of this work.

EXPERIMENTAL[3]

DL-*Cryptone* was regenerated[4] from a highly purified sample (9.50 g.) of the synthetic semicarbazone[1] (m.p. 194°).[5] Air was excluded with nitrogen, and an efficient steam distillation apparatus was used to effect a rapid continuous separation of the free ketone as it was formed in the acidic hydrolysis mixture. The colorless fragrant product was extracted with ether, dried over sodium sulfate, and distilled; 5.23 g. (78%), b.p. 76–80° (5 mm.), $n_{\rm D}^{20}$ 1.4815, λ_{max} 227 mμ, ϵ 11,100.

Equilibrium of DL-*cryptone.* Repeating as closely as possible the dehydrobromination conditions,[1] a mixture of 5.00 g. of cryptone, 7.3 g. of washed and dried collidine hydrobromide (from collidine in ether), and 18.9 g. of collidine, was refluxed under nitrogen for 20 min. The neutral fraction was extracted with ether, washed well in the cold with dilute hydrochloric acid, sodium bicarbonate solution, and water, dried over sodium sulfate, and distilled; 3.22 g. b.p. 60–68° (2 mm.), $n_{\rm D}^{20}$ 1.4776, λ_{max} 227 mμ, ϵ 7,620. Fractionation at 0.5 mm. through a sixty-plate Podbielniak Miniature Hypercal column[1] gave three fractions as follows: (I) 0.66 g. of *4-isopropyl-3-cyclohexenone*, b.p. 46–50°, $n_{\rm D}^{20}$ 1.4738, no maximum at 210–360 mμ (reported $n_{\rm D}^{20}$ 1.4710[1]). (II) 0.97 g. of an intermediate fraction, b.p. 51–55°, $n_{\rm D}^{20}$ 1.4824, λ_{max} 227 mμ, ϵ 9,540; and (III) 0.94 g. of *4-isopropyl-2-cyclohexenone*, b.p. 55–60°, $n_{\rm D}^{20}$ 1.4828, λ_{max} 227 mμ, ϵ 12,370 (reported for natural *l*-cryptone $n_{\rm D}^{20}$ 1.4810,[6] λ_{max} 226.3 mμ, ϵ 12,600[4]).

Treatment in the manner described previously[1] gave from fraction I the orange-yellow 4-isopropyl-3-cyclohexenone 2,4-dinitrophenylhydrazone, m.p. 105–106°.[1,7]

Similarly, from fraction III there was obtained[1] a 90% yield of the orange-red isopropyl-2-cyclohexenone 2,4-dinitrophenylhydrazone, m.p. 126–129°, which after recrystallization from ethanol had m.p. and mixed m.p. 134–135°.[1]

Department of Chemistry
Smith College
Northampton, Mass.

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[1] M. D. Soffer and M. A. Jevnik, *J. Am. Chem. Soc.*, **77**, 1003 (1955).

[2] *Cf.* W. C. Wildman, R. B. Wildman, W. T. Norton, and J. B. Fine, *J. Am. Chem. Soc.*, **75**, 1912 (1953).

[3] Melting points are corrected and boiling points uncorrected. Ultraviolet absorption spectra were determined in 95% ethanol.

[4] R. G. Cooke and A. K. Macbeth, *J. Chem. Soc.*, 1408 (1938).

[5] The reported melting points of the racemic product vary from 183° to 192° (*cf.* ref. 1), probably due to traces of the Δ^3 isomer.

[6] D. T. C. Gillespie and A. K. Macbeth, *J. Chem. Soc.*, 1531 (1939).

[7] This derivative tends to isomerize to the Δ^2 derivative and to decompose, if heated slowly, and it also shows a "double" melting point; the melt resolidifies and melts again at a temperature intermediate between the melting points of the derivatives of the two isomeric ketones. The temperature recorded represents the initial fusion.

Isolation of a Thiosulfonate from Reaction of Lithium Aluminum Hydride and a Sulfonyl Chloride

Erwin A. Lehto[1] and David A. Shirley

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Field and Grunwald[2] postulate that reduction of sulfonyl chlorides to mercaptans by lithium aluminum hydride may occur *via* two routes, one of which involves the reaction of a sulfinate salt with a sulfonyl chloride giving a disulfone, or with a metal mercaptide to give a thiosulfonate. Either of these intermediates then goes to the mercaptan *via* the disulfide. Apparently no one has isolated a thiosulfonate, although disulfides have been obtained.[2,3] The authors would like to report the isolation in 23% yield of *p-tert*-butylphenyl *p-tert*-butylbenzenethiosulfonate from the action of lithium aluminum hydride on *p-tert*-butylbenzenesulfonyl chloride. Structure of the thiosulfonate was indicated by its independent preparation from reduction of *p-tert*-butylbenzenesulfonyl chloride with zinc and hydrochloric acid by a procedure known to give the thiosulfonate.[4]

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[1] Present address: The Koppers Co., Monaca, Pa.

[2] L. Field and F. A. Grunwald, *J. Org. Chem.*, **16**, 949 (1951).

[3] J. Strating and H. J. Backer, *Rec. trav. chim.*, **69**, 638 (1950).

[4] E. Vinkler and F. Klivenyi, *Acta Chim. Acad. Sci. Hung.*, **1**, 319 (1951); *Chem. Abstr.*, **49**, 2346 (1955).

EXPERIMENTAL

Reaction of lithium aluminum hydride and p-tert-butylbenzenesulfonyl chloride. Strating and Backer[3] have reported the formation of *p-tert*-butylthiophenol in 76% yield by the treatment of an ethereal solution of *p-tert*-butylbenzenesulfonyl chloride with an ethereal solution of lithium aluminum hydride. A reverse order of addition is used here.

p-tert-Butylbenzenesulfonyl chloride was prepared by the general procedure of Huntress and Carten.[5] A solution of 18.6 g. (0.08 mole) of the sulfonyl chloride in 75 ml. of ether was added slowly with stirring to a suspension of 4.56 g. (0.12 mole) of powdered lithium aluminum hydride in 225 ml. of ether. A nitrogen atmosphere was used. The mixture was stirred for 12 hr. and hydrolyzed with water, followed by dilute hydrochloric acid, and the mixture was then extracted with ether. The ethereal extract was dried and the ether evaporated. The solid residue was extracted with dilute aqueous sodium hydroxide solution and the residue from this recrystallized from absolute ethanol. There was obtained 7.0 g. of solid, m.p. 86–135°. This solid was washed thoroughly with petroleum ether and recrystallized once more from absolute ethanol to yield 3.3 g. (23%) of colorless crystals, m.p. 150–151°.

Anal. Calcd. for $C_{20}H_{26}O_2S_2$: C, 66.30; H, 7.18; S, 17.68. Found: C, 66.14; H, 7.19; S, 17.72.[6]

Preparation of p-tert-butylphenyl p-tert-butylbenzenethiosulfonate. A mixture of 11.6 g. (0.05 mole) of *p-tert*-butylbenzenesulfonyl chloride, 100 ml. of ether, and 4.9 g. of zinc dust was treated dropwise with 32 ml. of concentrated hydrochloric acid, according to the procedure described by Vinkler and Klivenyi[4] for the preparation of the phenyl ester of benzenethiosulfonic acid (thiosulfone) by reduction of benzenesulfonyl chloride. The reaction mixture was stirred at room temperature until all the zinc had dissolved. It was then poured into an excess of cold water and, after the removal of the ether, the precipitated solid was collected by filtration. The solid was washed thoroughly with petroleum ether and recrystallized twice from absolute ethanol, resulting in the isolation of a crystalline solid melting at 150–151°. A mixture melting point with the crystalline solid obtained from the lithium aluminum hydride reduction of *p-tert*-butylbenzenesulfonyl chloride, melting at 150–151°, was 150–151°.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF TENNESSEE
KNOXVILLE, TENN.

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(5) E. H. Huntress and F. H. Carten, *J. Am. Chem. Soc.*, 62, 511 (1940).

(6) Galbraith Microanalytical Laboratories, Knoxville, Tenn.

Facile Synthesis of Dihydroisoindole

JOSEPH BORNSTEIN, SHERMAN C. LASHUA, AND ARMAND P. BOISSELLE

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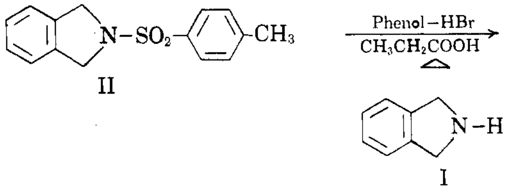
In connection with the synthesis of compounds related to isoindole, it was necessary to prepare gram-quantities of dihydroisoindole (isoindoline) (I). In an effort to avoid the preparation of I by the electrolytic reduction of phthalimide,[1] because of the special apparatus and careful control required, we examined a number of the other methods[2] which have been described. All of them were found to be poor; particularly disappointing was the newest method involving the reduction of phthalimide with lithium aluminum hydride.[3] As a result, a new two-step synthesis of dihydroisoindole was devised, which is based on recent reports[4] that sulfonamides are cleaved rapidly to amines by treatment with hydrobromic acid in the presence of phenol.

When 2-(*p*-tolylsulfonyl)dihydroisoindole (II),[5] which is readily prepared from the easily obtainable substances *o*-xylylene dibromide and *p*-toluenesulfonamide, was heated with a mixture of phenol and hydrobromic acid in propionic acid, dihydroisoindole was obtained in a high state of purity and in yields of 70–78%. This method makes dihydroisoindole easily accessible and appears to be more convenient for small-scale preparations than the electrolytic reduction of phthalimide, which has been, heretofore, the only satisfactory source of dihydroisoindole.



EXPERIMENTAL[6]

2-(p-Tolylsulfonyl)dihydroisoindole (II). This compound was obtained in slightly better yield and in a higher state of purity by modification of the procedure of Fenton and Ingold.[5] The solution, prepared by dissolving 17.0 g. (0.1 mole) of *p*-toluenesulfonamide in a solution of 5.0 g. (0.22 g.-atom) of sodium in 220 ml. of methanol, was added in the course of 40 min. to a stirred and refluxing solution of 26.4 g. (0.1 mole) of *o*-xylylene dibromide in 150 ml. of commercial ethanol. After completion of the addition, the reaction mixture was refluxed and stirred for 2 hr. The suspension was cooled, treated with 100 ml. of water, and neutralized with glacial acetic acid. Refrigeration overnight afforded white needles which, after recrystallization from 95% ethanol, weighed 13.0 g. (48%), and had m.p. 175–176° (dec.) (lit.[5] 176°).

Dihydroisoindole (I). A mixture of 12.0 g. (0.044 mole) of II, 12.0 g. (0.13 mole) of phenol, 90 ml. of 48% hydrobromic acid (freshly distilled from stannous chloride), and 15 ml. of propionic acid was heated under reflux for 2 hr.

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(1) A. Dunet, J. Rollet, and A. Willemart, *Bull. soc. chim. France*, 877 (1950).

(2) S. Gabriel and A. Neumann, *Ber.*, 26, 521 (1893); R. E. Rose and W. Scott, *J. Am. Chem. Soc.*, 39, 273 (1917).

(3) A. Uffer and E. Schlittler, *Helv. Chim. Acta*, **31**, 1397 (1948). The authors were able to obtain I in yields of only 3%; A. Dunet, J. Rollet, and A. Willemart (ref. 1) reported a 5% yield from this procedure.

(4) H. R. Snyder and R. E. Heckert, *J. Am. Chem. Soc.*, **74**, 2006 (1952); H. R. Snyder and H. C. Geller, *J. Am. Chem. Soc.*, **74**, 4864 (1952); D. I. Weisblat, B. J. Magerlein, and D. R. Myers, *J. Am. Chem. Soc.*, **75**, 3630 (1953).

(5) G. W. Fenton and C. K. Ingold, *J. Chem. Soc.*, 3295 (1928).

(6) Melting points are corrected and boiling points are uncorrected. Analyses were performed by Dr. Carol K. Fitz, Needham Heights, Mass., and Schwarzkopf Microanalytical Laboratories, Woodside, N. Y.