100 ml of water was added a supernatant layer of 50 ml of ether. The two-phase system was vigorously stirred at 0° for 15 min. The yellow organic layer was separated, and 50 ml of fresh ether was added to the aqueous layer. The extractions were continued in this manner until the ether layer remained colorless. The combined ether extracts were washed successively with 5% Na_2CO_3 solution and water, and then dried over anhydrous Na_2SO_4.

Triphenylphosphine Adduct of 1,1,1-Trifluoro-2-diazopropane (II).—To a solution of 1,1,1-trifluoro-2-diazopropane in ether, prepared by diazotization of 14.9 g (0.10 mole) of the amine hydrochloride, was added 2.6 g (0.01 mole) of triphenylphosphine. There was a loss of all yellow color within 30 min, with no gas evolution. Removal of all volatiles under aspirator vacuum yielded 3.8 g (10%, based on amine hydrochloride) of the crude phosphazine. Separation of the phosphazine from a small amount of unreacted triphenylphosphine proved difficult, but repeated recrystallization of the tan solid from hexane yielded the white phosphazine, fairly pure, mp 127–128.5°.

Anal. Calcd for $C_{21}H_{18}F_3N_2P$: C, 65.29; H, 4.70; F, 14.76. Found: C, 66.24; H, 5.02; F, 14.08.

1-Methyl-2,2,2-trifluoroethyl Benzoate.—To a solution of 1,1,1-trifluoro-2-diazopropane in ether, prepared by diazotization of 14.9 g (0.10 mole) of the amine hydrochloride, were added 12.2 g (0.10 mole) of benzoic acid and 1.4 g (0.01 mole) of boron trifluoride etherate in ether, with stirring. There was an immediate evolution of a colorless gas, and loss of all yellow color within 1 min. The reaction mixture was washed successively with saturated $NaHCO_3$ solution and water, dried over anhydrous Na_2SO_4, and distilled to yield 1.7 g (8%, based on amine hydrochloride) of the ester, bp 78° (8 mm), $n^{25}D$ 1.4452 [lit.[8] bp 88° (20 mm), $n^{17}D$ 1.4476], identical in infrared spectrum with the ester as prepared from 1,1,1-trifluoro-2-propanol and benzoyl chloride.

Oxidation of 1,1,1-Trifluoropropanone Hydrazone.—To a solution of 12.6 g (0.10 mole) of 1,1,1-trifluoropropanone hydrazone in 200 ml of anhydrous ether were added 23.2 g (0.10 mole) of silver oxide and 10 ml of a saturated solution of KOH in absolute ethanol. The reaction mixture was stirred vigorously for 1 hr at room temperature and filtered to yield a deep yellowish orange solution of the diazo compound.

This oxidation was also carried out in pentane; the filtrate was distilled into a chilled receiver until the condensate was colorless, to yield a yellow distillate containing only the diazo compound in pentane, as shown by comparison of its infrared spectrum with that of the solution prepared from the neat diazo compound in pentane.

1-Methyl-2,2,2-trifluoroethyl *p*-Toluenesulfonate. A. From 1,1,1-Trifluoro-2-diazopropane and *p*-Toluenesulfonic Acid.—To a solution of 1,1,1-trifluoro-2-diazopropane in ether, prepared by oxidation of 12.6 g (0.10 mole) of the hydrazone, was added 19.0 g (0.10 mole) of *p*-toluenesulfonic acid monohydrate in anhydrous ether, with stirring. There was an immediate evolution of a colorless gas and loss of all color within 2 min. The reaction mixture was washed successively with saturated $NaHCO_3$ solution and water, dried over anhydrous Na_2SO_4, and distilled to yield 4.8 g (18%, based on the hydrazone) of the ester, identical in boiling point, index of refraction, and infrared spectrum with the ester as prepared from 1,1,1-trifluoro-2-propanol and *p*-toluenesulfonyl chloride.

B. From 1,1,1-Trifluoro-2-propanol and *p*-Toluenesulfonyl Chloride.—To a solution of 43.4 g (0.38 mole) of 1,1,1-trifluoro-2-propanol and 74.3 g (0.39 mole) of *p*-toluenesulfonyl chloride in 350 ml of acetone at 50° was added, with stirring, a solution of 16.0 g (0.40 mole) of sodium hydroxide in 50 ml of water. The reaction mixture was stirred at room temperature for 10 days.

The mixture was concentrated to approximately 250 ml on the steam bath, poured into 100 ml of water, and extracted with petroleum ether (bp 30–60°). The combined petroleum ether extracts were washed successively with concentrated aqueous NH_3 and water, dried over anhydrous $MgSO_4$, and distilled to yield 44.8 g (43%) of the ester, bp 123–124° (2.8 mm), $n^{25}D$ 1.4619.

Anal. Calcd for $C_{10}H_{11}F_3O_3S$: F, 21.25. Found: F, 21.34.

Isolation of 1,1,1-Trifluoro-2-diazopropane.—A solution of 1,1,1-trifluoro-2-diazopropane in di-*n*-butyl ether was prepared by oxidation of 1.26 g (0.01 mole) of the hydrazone. Using the technique described by Gilman and Jones,[9] the diazo compound was isolated as a volatile, orange liquid. An approximate boiling point determination was made by allowing a small amount of the neat diazo compound to warm up from −80° at a constant pressure of 67 mm. The compound boiled at −10° (67 mm). Infrared spectra of the compound were taken in several solvents and showed strong absorptions at 4.78 μ for the diazo function and at 8.5 and 9.0 μ for the trifluoromethyl group.

When a small amount (approximately 0.2 g) of the neat diazo compound was allowed to warm to room temperature at atmospheric pressure, its temperature continued to rise above room temperature, and it detonated at 32° with a loud report.

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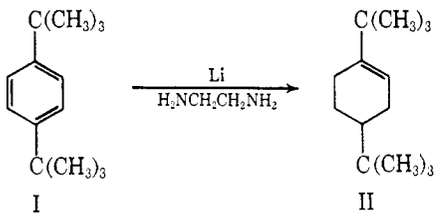
1,4-Di-*t*-butylcyclohexene

R. D. STOLOW AND JEANNE A. WARD

Department of Chemistry, Tufts University, Medford, Massachusetts 02155

Received October 4, 1965

Garbisch has reported preparation in low yield of 1,4-di-*t*-butylcyclohexene (II), a compound of interest for use in studies of steric effects upon addition reactions to the carbon–carbon double bond.[1] Assured that a better procedure for the synthesis of II would find immediate use, we wish to report the direct preparation of II from *p*-di-*t*-butylbenzene (I),[2] by reduction with lithium in ethylenediamine.[3]



I II

The procedure was adapted from an experiment of Reggel, *et al.*, which gave 97% of octalin by reduction of tetralin with lithium in ethylenediamine.[4] *t*-Butylbenzene, under similar conditions, was reported to give 1-*t*-butylcyclohexene and 3-*t*-butylcyclohexene in the ratio 7:3.[5]

p-Di-*t*-butylbenzene (I) can be reduced readily by catalytic hydrogenation to give a mixture of *cis*- and *trans*-1,4-di-*t*-butylcyclohexane[6] (*cis* III and *trans* III), but no previous direct reduction of I to give products intermediate between I and III has come to our attention. One attempted partial reduction has been noted. Whereas *p*-xylene is reduced to 2,5-dihydro-*p*-xylene in 96% yield with lithium–ammonia–ethanol, under the same conditions, *p*-di-*t*-butylbenzene (I) gives negligible reaction.[7]

(1) E. W. Garbisch, Jr., S. M. Schildcrout, D. B. Patterson, and C. M. Sprecher, *J. Am. Chem. Soc.*, **87**, 2932 (1965).

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(4) L. Reggel, R. A. Friedel, and I. Wender, *J. Org. Chem.*, **22**, 891 (1957), Table I, expt 5.

(5) R. A. Benkeser, R. K. Agnihotri, and M. L. Burrous, *Tetrahedron Letters*, **No. 16**, 1 (1960).

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Experimental Section[8]

1,4-Di-*t*-butylcyclohexene (II).—To a solution of 41.4 g (0.217 mole) of *p*-di-*t*-butylbenzene (I), mp 75–76.5°, in 760 ml of ethylenediamine (Matheson Coleman and Bell) at 100° in a nitrogen atmosphere was added 12.2 g (1.74 g-atoms) of lithium during 1.5 hr. The blue mixture was then heated under reflux for 2 hr and cooled, and water was added with cooling, dropwise at first, until 1500 ml had been added. A white solid remained which was soluble in ether. The mixture was extracted with eight 200-ml portions of ether. The total ether extract was washed with five 200-ml portions of 5% ammonium chloride, and was dried over anhydrous sodium sulfate. Removal of the ether gave 38.9 g (93%) of product containing 18% of starting material (ultraviolet analysis for *p*-di-*t*-butylbenzene). Recrystallization from methanol gave a first crop of 18.7 g (44%) of needle-like crystals, mp 53.5–54°, containing 12% of I (ultraviolet analysis). The analytical sample, prepared by further recrystallization from methanol, contained an upper limit of 4% of I (ultraviolet analysis) and had mp 54–54.5°.

Anal. Calcd for $C_{14}H_{26}$: C, 86.51; H, 13.49. Found: C, 86.72; H, 13.32.

Gas chromatography on a 300-cm, 0.25-in. o.d., column packed with 20% silicone gum rubber on Chromosorb P at 130° with 70-cc/min helium flow gave retention times as follows (in min): I, 45.5; II, 50.8; *cis* III, 53.4; *trans* III, 53.4.[9] The recrystallized samples of II contained small amounts (3–12%) of I, but no components other than I and II were detected by gas chromatography.[10]

The nmr spectrum of I shows a singlet at 1.29 ppm (18.0 protons) and a second singlet at 7.18 ppm (4.1 protons). The nmr spectrum of a sample of II containing 12% of I showed the two singlets of I with integrated intensity consistent with the presence of 13 ± 2% of I. In addition, the absorption attributable to II gave sharp singlets at 0.86 ppm (9.0 protons) and 1.00 ppm (9.0 protons), assigned to the *t*-butyl groups at C-4 and C-1, respectively, a multiplet at 5.38 ppm (1.0 proton), assigned to the olefinic proton at C-2, and broad absorption in the region 1.0–2.3 ppm (6.3 protons), assigned to the protons at C-3–C-6.

Acknowledgment.—We wish to thank the National Science Foundation for support of this work.

(8) Nmr spectra were recorded by Don C. Wiley. A Varian A-60 spectrometer was used with solutions in carbon tetrachloride containing 3% tetramethylsilane as internal standard. The infrared spectrum of II has been reproduced in ref 3. Microanalysis was performed by Dr. S. M. Nagy.

(9) It is interesting to note that the *cis*- and *trans*-1,4-di-*t*-butylcyclohexanes (*cis* III and *trans* III) were not separated from one another under these conditions or under any other conditions of gas chromatography yet tried in this laboratory.

(10) NOTE ADDED IN PROOF.—Professor Daniel J. Pasto (private communication, Dec 30, 1965) has suggested the following method for purification of II. Alumina coated with silver nitrate, when used in chromatography as described by R. Wolovsky [*J. Am. Chem. Soc.*, **87**, 3638 (1965)] gave II of 98–99% purity.

Purine N-Oxides. XVIII. Deamination of Adenine N-Oxide Derivatives[1]

JAMES C. PARHAM, JENNIFER FISSEKIS, AND GEORGE BOSWORTH BROWN

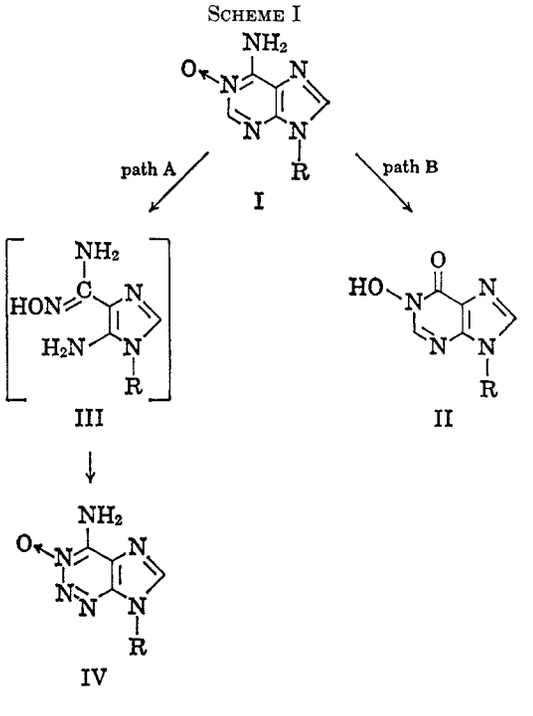
Division of Biological Chemistry, Sloan-Kettering Institute for Cancer Research, and Sloan-Kettering Division, Graduate School of Medical Sciences, Cornell University Medical College, New York, New York 10021

Received October 25, 1965

It was recently demonstrated[2] that xanthine 7-N-oxide and guanine 7-N-oxide, which may well exist as the 7-N-hydroxy derivatives,[3] can induce a variety of tumors in rats. This has stimulated interest in evaluating the N-oxides of other naturally occurring purines and their ribosyl derivatives for similar oncogenic behavior. Adenine 1-N-oxide (Ia) (6-aminopurine 1-N-oxide) showed no such activity[2] under the assay conditions employed. In considering the structural requirements for oncogenicity in purine N-oxides, it becomes of particular interest to test the structurally analogous hypoxanthine derivative, the neutral molecule of which should exist largely as 1-hydroxy-6-purinone or 1-hydroxyhypoxanthine (IIa).

The preparation of "hypoxanthine 1-N-oxide" (IIa) from methyl 4-nitroimidazole-5-carboxylate has been reported,[4] but the synthesis is laborious and does not lend itself to the quantities needed for biological studies. Since hypoxanthine is inert to direct oxidation by peroxy acids, the 1-N-oxide must be prepared either by total synthesis or by modification of a related purine 1-N-oxide. We now report procedures for obtaining 1-hydroxyhypoxanthine and its nucleoside, by deamination of the corresponding adenine 1-N-oxide derivatives. Earlier attempts at diazotization of Ia produced 2-azaadenine 1-N-oxide (IVa).[5] Since the starting material is readily hydrolyzed to 4-aminoimidazole-5-carboxamidoxime (IIIa) even in dilute mineral acid,[6] the 2-aza derivative IVa results[5] from diazotization of the imidazole intermediate and ring closure of the diazonium salt (path A, Scheme I). Previous attempts in this laboratory to obtain only deamination (path B) produced mixtures containing material similar to that obtained by Taylor, Cheng, and Vogl,[4] along with 2-azaadenine 1-N-oxide and other

SCHEME I



a series, R = H
b series, R = β-D-ribofuranosyl

(1) This investigation was supported in part by funds from the Atomic Energy Commission (Contract No. AT[30-1],910) and from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service (Grant No. CA-03190-09).

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