Reduction of *o*-Bromoanisole by Lithium Dineopentylamide

Harry S. Mosher and Erwin J. Blanz, Jr.

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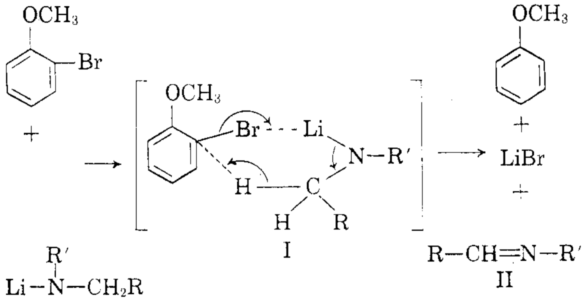
Benkeser and DeBoer[1] recently reported that *o*-bromoanisole was reduced by various lithium dialkylamides to anisole. A cyclic mechanism was proposed in which a hydrogen atom is transferred with its pair of electrons from the lithium dialkylamide to the *o*-bromoanisole as indicated by I. This mechanism requires the formation of an imine (II) from the lithium dialkylamide, but these authors were unable to isolate an aldimine from any of their reactions. They were able to obtain substituted pyrazines and nitrogenous residues which they postulated arose from the aldimines which were not isolable. Evidence that the aldimines were not stable under these conditions and that they could be converted to pyrazines was presented.



In connection with another investigation the aldimine, III, from trimethylacetaldehyde and neopentylamine was found to be unusually stable

$$(CH_3)_3CCH{=}NCH_2C(CH_3)_3 \qquad \text{III}$$

for an aliphatic imine. This stable imine, therefore, offered a means of checking this theory. Accordingly, *o*-bromoanisole was treated with lithium dineopentylamide. There was isolated from the reaction mixture a 32% theoretical yield of anisole, a 10% theoretical yield of the aldimine 2,2-dimethylpropylidene-2′,2′-dimethylpropylamine (III), and a small amount of unidentifiable basic material; 34% of the *o*-bromoanisole and 49% of the dineopentylamine were recovered. The isolation of the aldimine as a primary reaction product is added evidence in favor of the mechanism postulated by Benkeser and DeBoer.[1]

The infrared spectrum of the aldimine isolated from this reduction was identical with that of 2,2-dimethylpropylidene - 2′,2′ - dimethylpropylamine (III) prepared from trimethylacetaldehyde and neopentylamine. Additional proof of the structure of this imine is found in its hydrolysis to trimethylacetaldehyde and neopentylamine and its hydrogenation to dineopentylamine. An absorption band at 5.98μ in the infrared spectrum is additional evidence for the presence of the C=N— group.

The previously unreported dineopentylamine was prepared by the reductive alkylation of ammonia with trimethylacetaldehyde.

EXPERIMENTAL[2]

Dineopentylamine. To 4 g. (0.23 mole) of anhydrous ammonia dissolved in 100 ml. of ice cold, absolute ethanol was added 45 g. (0.52 mole) of trimethylacetaldehyde. The resulting ethanolic solution of ammonia and trimethylacetaldehyde was hydrogenated in the presence of 500 mg. of pre-reduced Adams platinum oxide catalyst in a Parr hydrogenation apparatus at approximately 40 p.s.i. After the hydrogen uptake was complete, the catalyst was removed by filtration. When the filtrate was acidified with 6*N* hydrochloric acid, a white, neutral, solid precipitated. This solid, which was probably a polymer of trimethylacetaldehyde, was removed by filtration and the acid solution was then made basic with sodium hydroxide. The amine, which separated as an oil, was extracted with ether. The ether extracts were dried over sodium hydroxide pellets, and fractionated. The material that boiled at 153–154° was collected; 21 g. (57%), n_D^{21} 1.4088. The actual yield was probably greater since 3.1 g., n_D^{20} 1.4029, b.p. 150–153°, of slightly less pure material was obtained. No other basic material was isolated and the hold up of the column was fairly large, about 12 cc.

Anal. Calcd. for $C_{10}H_{23}N$: C, 76.35; H, 14.74; N, 8.90. Found: C, 76.45; H, 14.73; N, 8.99.

The phenyl thiourethane was prepared in the usual manner from phenyl isothiocyanate, m.p. 138–140°. The *N*-nitroso derivative decomposed sharply at 214–215°.

2,2-Dimethylpropylidene-2′,2′-dimethylpropylamine (III). To a 125-ml. Erlenmeyer flask was added 17 g. (0.20 mole) of trimethylacetaldehyde. The flask was immersed into an ice bath until the temperature of the aldehyde was 0°. Seventeen grams (0.20 mole) of neopentylamine[3] (prepared from the reduction of trimethylacetonitrile with lithium aluminum hydride) was added dropwise in such a manner so that the temperature did not rise above 4°. The reaction mixture was allowed to stand for 4 hr. in the ice bath. The water from the reaction was separated from the aldimine and the aldimine was dried over anhydrous sodium sulfate. Distillation from a column of approximately 30 plate efficiency gave 21.2 g. (68%) of the aldimine boiling at 89–90° (104 mm.). n_D^{20} 1.4113.

Anal. Calcd. for $C_{10}H_{21}N$: C, 77.36; H, 13.63; N, 9.02. Found: C, 77.38, 77.49; H, 13.47, 13.57; N, 9.06, 9.13.

An infrared spectrum of the aldimine showed a narrow, very pronounced absorption in the region of 5.98 μ characteristic of C=N— in aliphatic imines and no absorption in the region of 3.0 μ characteristic of the NH group.

Hydrogenation of 2,2-dimethylpropylidene-2′,2′-dimethylpropylamine. The aldimine, 434 mg., methanol, 15 ml., and Raney nickel catalyst, approximately 150 mg., were stirred under 1 atmosphere of hydrogen in a microhydrogenation apparatus for 36 hr. The catalyst was removed by filtration, the filtrate acidified and evaporated to dryness.

The *N*-nitroso derivative was prepared from the amine hydrochloride in the usual manner. The compound decomposed sharply at 214–215°. A mixed melting point de-

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(1) R. A. Benkeser and C. E. DeBoer, *J. Org. Chem.*, 21, 281 (1956).

(2) Boiling points and melting points are uncorrected. Microanalyses were carried out by Microchemical Specialties Co., Berkeley, Calif.

(3) Attempts to prepare neopentylamine from the reductive alkylation of ammonia with trimethylacetaldehyde in 1:1 mole ratio were unsuccessful; dineopentylamine was the only basic compound isolated.

termination with a sample of *N*-nitrosodineopentylamine showed no depression of the decomposition point.

Hydrolysis of 2,2-dimethylpropylidene-2′,2′-dimethylpropylamine. To 10 ml. of 6*N* hydrochloric acid was added 500 mg. of the aldimine. An immediate reaction occurred between the aldimine and the acid. The acid phase was extracted with 10 ml. of ether. The ether extract was then poured into 5 ml. of ethanol which contained 400 mg. of 2,4-dinitrophenylhydrazine and 1 ml. of 6*N* hydrochloric acid. The resulting 2,4-dinitrophenylhydrazone, after two crystallizations from ethanol, melted at 205–206°, mixture melting point with an authentic sample of trimethylacetaldehyde, 205–206°.

The acid phase was evaporated to dryness and the resulting amine hydrochloride added to 3 ml. saturated sodium hydroxide. The amine was then separated from the sodium hydroxide solution and converted into the phenyl thiourethane, m.p. 133–134°. The phenyl thiourethane of neopentylamine was prepared, m.p. 134–135°; mixture melting point with the above sample, 134–135°.

Reduction of o-bromoanisole by lithium dineopentylamide. Lithium dineopentylamide was prepared by the reaction of 15.7 g. (0.10 mole) of *n*-butyl lithium[4] in 200 ml. of ether. After stirring for 1 hr., 18.7 (0.10 mole) of *o*-bromoanisole was added at once to the reaction mixture and it was allowed to reflux for 20 hr. As soon as the reaction mixture was decomposed with water, the ether layer was dried over anhydrous sodium sulfate and fractionally distilled. All the material that boiled between 138–158° was collected (14.1 g.). Since the unreacted dineopentylamine (b.p. 153–154°), 2,2-dimethylpropylidene-2′,2′-dimethylpropylamine (b.p. 89–90° at 104 mm.) and anisole (b.p. 155°) all boiled within ten degrees of each other, further separation was accomplished by means of gas-liquid partition chromatography. The aldimine, 115 mg. (n^{20}_{D} 1.4110), was separated from a total of 1.65 g. of the mixture (b.p. 138–158°) containing dineopentylamine and anusiole. This corresponds to a 7% yield of imine actually isolated. The infrared spectrum of the aldimine was identical to that of 2,2-dimethylpropylidene-2′,2′-dimethylpropylamine prepared from trimethylacetaldehyde and neopentylamine.

The remainder of the 138–158° fraction was then treated with 25 ml. of 6*N* hydrochloric acid and extracted with ether. The amount of anisole recovered was 3.0 g. (32% theoretical). After alkaline treatment of the acid solution and extraction with ether, 8.1 g. (49%) of unreacted dineopentylamine was recovered. Since the aldimine was decomposed by the acid hydrolysis, the remaining difference in weight, 1.3 g., corresponds to a 10% yield of the aldimine. From the distillation residue was recovered 6.3 g. (34%) of *o*-bromoanisole. A small amount of unidentified basic material, 1.2 g. (b.p. 200–215°) was obtained. A residue of dark purple, basic material (3.4 g.) remained which could not be identified.

Department of Chemistry and Chemical Engineering
Stanford University
Stanford, Calif.

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[4] H. Gilman, J. A. Beel, C. G. Brannen, M. W. Bullock, G. E. Dunn, and L. S. Miller, *J. Am. Chem. Soc.*, **71**, 1499 (1949).

Some Derivatives of *p*-Terphenyl[1]

Henry Gilman and Eugene A. Weipert

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Approaches to direct substitution in the *p*-terphenyl molecule in the past have invariably been complicated by the high order of reactivity of both terminal positions, and to a lesser extent the 2′-position.[2,3] Preparations involving the Gomberg synthesis lead to random mixtures of isomers which can only be separated by systematic fractional crystallization.[3,4]

We have found that 4-bromo-*p*-terphenyl is readily converted to the lithium reagent by the halogen-metal interconversion reaction[5] with *n*-butyllithium. Reported herein are a few examples of 4-substituted-*p*-terphenyl derivatives prepared from this lithium reagent. Also included are the 2- and 3-methyl derivatives, prepared by condensation of *p*-biphenylyllithium with the appropriately substituted cyclohexanones, followed by dehydration and aromatization.

By coupling of *N*-nitroso-4-acetamidobiphenyl with toluene only small amounts of any particular isomeric methyl-*p*-terphenyl could be recovered by earlier workers. The direct preparation of the 4-methyl isomer from the corresponding lithium reagent is clearly the ideal approach to this isomer in view of the yield obtained (67%). Although the three-step preparation of the other two isomers results in considerably lower yields, this method has the advantages of wide scope, direct approach, and the apparent lack of need for isolation and purification of the intermediate carbinol or olefin. The purification of the final product from this series of reactions can surely be simplified by application of a more suitable dehydrogenating agent. Although the use of selenium by von Braun, Irmisch, and Nelles[2] gave poor results, dehydrogenation by chloranil in xylene according to Arnold, Collins, and Zenk[6] appears promising with this type of compound.

The compounds described at this time were prepared incidental to a study concerned with organic liquid solution scintillators. Evaluation of the compounds for this purpose is being made by Drs. Wright H. Langham, F. N. Hayes, and D. G. Ott of the Los Alamos Laboratories who will report the results later.

EXPERIMENTAL[7]

4-Carboxy-p-terphenyl. Into a three necked flask, fitted with stirrer, dropping funnel, and condenser, were placed

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[1] This work was supported by the United States Atomic Energy Commission under Contract No. AT(11-1)-59.

[2] J. v. Braun, G. Irmisch, and J. Nelles, *Ber.*, **66B**, 1471 (1933).

[3] H. France, I. M. Heilbron, and D. H. Hey, *J. Chem. Soc.*, 1364 (1938).

[4] H. France, I. M. Heilbron, and D. H. Hey, *J. Chem. Soc.*, 1283 (1939).

[5] R. G. Jones and H. Gilman, *Org. Reactions, VI*, 339 (1951).

[6] R. T. Arnold, C. Collins, and W. Zenk, *J. Am. Chem. Soc.*, **62**, 983 (1940).

[7] All melting points are uncorrected. Reactions involving organolithium reagents were carried out under an atmosphere of dry, oxygen-free nitrogen in sodium dried solvents.