

in chloroform (200 ml.) and purified by filtration through an alumina column. Evaporation of the chloroform yielded crude IV (70 g., 81%), m.p. 162–164°.

Recrystallization from ethanol gave the pure compound as white crystals, m.p. 165–166°.

Anal. Calcd. for  $C_{15}H_{15}N_3$ : C, 75.88; H, 6.37; N, 17.71. Found: C, 75.68; H, 6.56; N, 17.67.

Absorption in the nitrile region occurred at 4.49  $\mu$  (KBr wafer).

## Reaction of *trans*-2-Aminocyclohexanol and Formaldehyde

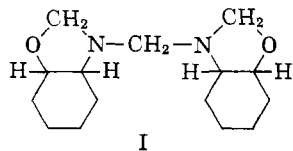
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Blaha and Kovar<sup>3</sup> have suggested that the product from the reaction of *trans*-2-aminocyclohexanol and formaldehyde is bis(4,5-tetramethylene-oxazolid-3-yl)methane (I). Gil-Av<sup>4</sup> obtained a product from the same reagents, having a molecular weight of 300 and showing no oxazolidine triplet in the infrared. On this basis Gil-Av concluded that 2-aminocyclohexanols do not form oxazolidines.

Because of the discrepancy between these two reports we have studied this reaction further. Blaha and Kovar obtained their product by treating the aminocyclohexanol and formaldehyde in alcoholic potassium carbonate for 24 hours. We have found that the reaction can be carried out by treating *trans*-2-aminocyclohexanol with 37% aqueous formaldehyde at 25°. The reaction was complete after one-half hour to give a white crystalline product melting at 157–158° as compared to 148–150° for the product of Blaha and Kovar. This product was found to have a molecular weight of 266 and elemental analysis gave a molecular formula of  $C_{15}H_{26}O_2N_2$ .



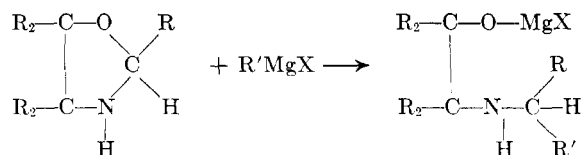
The infrared spectrum of I shows no bands for  $C=N$  ( $1630\text{--}1670\text{ cm.}^{-1}$  or  $OH$  ( $3650\text{ cm.}^{-1}$ ).<sup>5</sup> Neither is there an oxazolidine triplet at 1100, 1155, and  $1190\text{ cm.}^{-1}$ .<sup>6</sup> An aliphatic ether band is present at  $1125\text{ cm.}^{-1}$ . The absence of  $OH$  and

$C=N$  bands would eliminate a Schiff base as a possible structure.

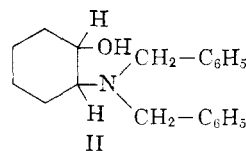
Because of lack of definite evidence for the structure of I by infrared, we have determined the n.m.r. spectrum for this compound.<sup>7</sup> This spectrum shows five singlet bands at  $\tau$  values of 5.47, 5.67, 5.76, 5.87, and 6.07 as compared to the protons of tetramethylsilane at a  $\tau$  value of 10.00. In addition there are two low intensity, broad multiplets with the highest peaks at 6.67 and 7.22, respectively, and a higher intensity broad multiplet with its most intense peaks at 8.26 and 8.73. The four bands at  $\tau$  values of 5.47, 5.67, 5.87, and 6.07 can be assigned to the hydrogens of a  $O-CH_2-N$  structure in which the chemical difference of the two protons gives two resonance lines which are further split by spin-spin coupling. Integration of the area under the curve shows four hydrogens of this type.

The singlet at 5.76 can be assigned to the protons of a  $N-CH_2-N$  structure and integrates as two protons. The multiplet at 6.67 and 7.22 can be assigned to the protons of the tertiary carbons in the cyclohexyl ring, the low field multiplet is the signal from the proton adjacent to the oxygen of the oxazolidine ring and the high field multiplet is due to the proton adjacent to the nitrogen. The broad multiplet with the most intense band at 8.73 is assigned to the remaining protons of the two cyclohexyl rings.<sup>8</sup> These values are in good agreement with the proposed structure I.

Because of the possible oxazolidine structure in I, it was subjected to ring opening by means of Grignard reagent. Senkus<sup>9</sup> has shown that Grignard reagents will cause ring openings of the following type



Compound I was treated with phenylmagnesium bromide and gave an 86% yield of *N,N*-dibenzyl-2-aminocyclohexanol (II), based on the formation of one mole of II from one mole of I.



### Experimental

**The Reaction of *trans*-2-Aminocyclohexanol with Formaldehyde.**—A solution of 21.4 g. of *trans*-2-aminocyclohexanol in 150 ml. of water was stirred with 22.6 ml. of 37%

(7) The authors wish to express their appreciation to Dr. P. W. K. Flanagan of Continental Oil Co., Ponca City, Oklahoma, for the preparation and interpretation of the n.m.r. spectrum of I.

(8) A. C. Huitric and J. B. Carr, *J. Org. Chem.*, **26**, 2648 (1961).

(9) M. Senkus, *J. Am. Chem. Soc.*, **67**, 1515 (1945).

(1) Present address: Continental Oil Co., Ponca City, Oklahoma.

(2) From the M.S. thesis of William R. Van Hoozer.

(3) R. Blaha and J. Kovar, *Chem. Vesty*, **52**, 77 (1958).

(4) E. Gil-Av, *J. Am. Chem. Soc.*, **81**, 1602 (1959).

(5) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, New York, 1954.

(6) E. D. Bergmann, E. Zimkin, and S. Pinchas, *Rec. trav. chim.*, **71**, 168 (1952).

aqueous formaldehyde at room temperature. Crystals formed within 5 min. and the reaction was complete after 0.5 hr. The solid was removed by filtration and dried at 110°. Crystallization from ethanol gave 25.8 g. of material which melted at 157–158°. Infrared spectrum (C—O—C) 1125 cm.<sup>-1</sup>, (C—N—C) 1190 and 1050 cm.<sup>-1</sup>.

*Anal.* Calcd. for C<sub>15</sub>H<sub>20</sub>O<sub>2</sub>N<sub>2</sub>: C, 67.63; H, 9.83; N, 10.52; mol. wt., 266. Found: C, 67.62; H, 9.89; N, 10.43; mol. wt.: Rast, 265.1; perchloric acid titration,<sup>10</sup> 266.2.

**The Reaction of the Oxazolidine with Phenylmagnesium Bromide.**—Twenty milliliters of 3 M phenylmagnesium bromide in ether was added to 3.1 g. of the oxazolidine in 250 ml.

(10) R. Belcher and A. Godbert, "Semi-Micro Quantitative Organic Analysis" Longmans, Green and Co., New York, 1954, pp. 152–154.

of ether over a period of 10 min. The mixture was stirred for 30 min. Water (25 ml.) was added and after thorough mixing, the ether layer was removed. The residue was washed with ether and combined with the first ether layer. Evaporation of the ether and crystallization from ethanol gave a solid melting at 90–91° (3.0 g.). The melting point of N,N-dibenzyl-2-aminocyclohexanol is given as 89.5–91°. Infrared spectrum (bonded OH) 3440 cm.<sup>-1</sup> (aromatic C=C) 1590 cm.<sup>-1</sup>, 1480 cm.<sup>-1</sup> (monosubstituted benzene) 755 cm.<sup>-1</sup>, 700 cm.<sup>-1</sup>.

*Anal.* Calcd. for C<sub>20</sub>H<sub>25</sub>ON: C, 81.45; H, 8.53; N, 4.74; mol. wt., 295. Found: C, 81.33; H, 8.40; N, 4.78; mol. wt.: perchloric acid titration, 296.

(11) F. Winternitz and R. M. Thakkar *Bull. soc. chim. France*, 646 (1952).

## Communications TO THE EDITOR

### Palladium-Catalyzed Hydrogenation of Pyridines

Sir:

Platinum<sup>1,2</sup> and nickel<sup>3</sup> in various forms have been used extensively in hydrogenation of pyridines (salts or bases, respectively), and currently the search for catalysts for the same purpose, less susceptible to inhibition by organic bases, is being extended to ruthenium<sup>4</sup> and rhodium.<sup>5</sup> General or practical use of palladium catalysts in hydrogenating pyridines, quinolines, and like compounds has not been made, the impression perhaps having been that palladium is more easily "poisoned" than platinum by such heterocyclic bases. We wish to report, in contrast to what may be a fairly well established misconception, that supported palladium *can* be employed, often more successfully than platinum oxide,<sup>1c</sup> in convenient low pressure hydrogenation of the acetate salts of

many compounds incorporating the pyridine nucleus, to corresponding piperidines. What is more, the new technique is ideally adapted to *selective* reduction of the pyridine ring without any attack upon other, more or less nickel- or platinum-reducible, functional groups (appended oxyphenyl, cyclopropyl, aldehyde, acetal, ester, amide, and so forth) appropriately located in various molecules,<sup>6</sup> and has now facilitated the synthesis, in uniformly high yields, of a number of new compounds closely related to the profoundly useful central stimulants, pipradrol<sup>2d,2e</sup> and methylpheniate,<sup>2j,2k</sup> as well as novel piperidylalkyloxindoles,<sup>2l,2m</sup> dipiperidyl compounds, and many others.

In reductions of pyridines to corresponding piperidines described below as the more interesting, selected examples, a *ca.* 0.3–0.5 (by weight) ratio of 10% palladium-charcoal to compound, glacial

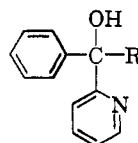
(1) (a) A. Skita and W. Brunner, *Ber.*, **49**, 1597 (1916); (b) S. M. McElvain and R. Adams, *J. Am. Chem. Soc.*, **45**, 2738 (1923); (c) T. S. Hamilton and R. Adams, *ibid.*, **50**, 2260 (1928).

(2) (a) G. Scheuing and L. Winterhalder, *Ann.*, **473**, 126 (1929); (b) K. E. Crook and S. M. McElvain, *J. Am. Chem. Soc.*, **52**, 4006 (1930); (c) R. R. Burtner and J. M. Brown, *ibid.*, **69**, 630 (1947); (d) C. H. Tilford, R. S. Shelton, and M. G. Van Campen, *ibid.*, **70**, 4001 (1948); (e) H. W. Werner and C. H. Tilford, U. S. Patent 2 624, 739 (1953); (f) C. H. Tilford and M. G. Van Campen, *J. Am. Chem. Soc.*, **76**, 2431 (1954); (g) F. J. McCarthy, C. H. Tilford, and M. G. Van Campen, *ibid.*, **79**, 472 (1957); (h) E. L. Schumann, M. G. Van Campen, and R. C. Pogge, U. S. Patent 2,804,422 (1957); (i) N. Sperber, *et al.*, U. S. Patents 2,739,968 and 2,739,969 (1956); (j) L. Pannizzon, *Helv. Chim. Acta*, **27**, 1748 (1944); (k) K. Scholz and L. Pannizzon, *ibid.*, **37**, 1605 (1954). (l) H. Bader and W. Oroshnik, *J. Am. Chem. Soc.*, **79**, 5686 (1957); (m) A. P. Gray, *J. Org. Chem.*, **23**, 1453 (1958).

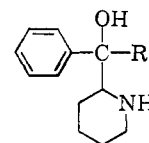
(3) H. Adkins, L. F. Kuick, M. Farlow, and B. Wojcik, *J. Am. Chem. Soc.*, **56**, 2425 (1934); H. Adkins and H. R. Billica, *ibid.*, **70**, 695 (1948).

(4) M. Freifelder and G. R. Stone, *J. Org. Chem.*, **26**, 3805 (1961).

(5) M. Freifelder, R. M. Robinson, and G. R. Stone, *ibid.*, **27**, 284 (1962).



- Ia. R = CH(OEt)<sub>2</sub>  
 b. R = CHO  
 c. R = CH=NOH  
 d. R = CH<sub>2</sub>NH<sub>2</sub>  
 e. R = CH<sub>2</sub>OH  
 f. R = CH<sub>2</sub>-



- IIa. R = CH(OEt)<sub>2</sub>  
 b. R = CH<sub>2</sub>NH<sub>2</sub>  
 c. R = CH<sub>2</sub>OH  
 d. R = -CH<sub>2</sub>-

(6) The sole, presently evident disadvantage of the new method is that primary and secondary (but ordinarily *not tertiary*) alcohol and oxo groups on carbon atoms adjacent to aromatic rings are hydrogenolyzed under the conditions necessarily used to promote reduction of the heterocyclic moiety. However, this as well as other side reactions also may occur with other catalysts, especially rhodium [see E. Breitner, E. Roginski, and P. N. Rylander, *ibid.*, **24**, 1855 (1959); M. Freifelder, *J. Am. Chem. Soc.*, **82**, 2386 (1960)], ruthenium [E. Breitner, E. Roginski, and P. N. Rylander, *J. Chem. Soc.*, 2918 (1959)], and rhenium [H. S. Broadbent, *et al.*, *J. Org. Chem.*, **24**, 1847 (1959)].