

For comparative purposes the melting points of some related compounds were redetermined. *p*-Phenylphenacyl chloride, reported to melt at 122–123°,² was obtained after many recrystallizations from ethanol as colorless needles melting sharply at 129.0°. Calcd. for C₁₄H₁₁OCl: Cl, 15.42. Found¹: Cl, 15.40; 15.16. The melting points of the *p*-phenylphenacyl halides decrease consequently from the chloride to the bromide, m. p. 127.0°,³ and iodide as in the series of the phenacyl halides.

Phenacyl chloride, reported as melting at 52–55°,⁴ 54°,⁵ 56.5°,⁶ 57–58°,⁷ 58–59°⁸ and 59°⁹ was prepared according to the procedure of Korten and Scholl^{8b}; treated in ethanol with active charcoal, crystallized from alcohol, distilled and finally recrystallized from carbon tetrachloride, it melts sharply at 56.5°.

(2) A. Collet, *Bull. soc. chim.*, [3] 17, 510 (1897); S. L. Silver and A. Lowy, *THIS JOURNAL*, 56, 2430 (1934).

(3) Crystallized first many times from ethanol (m. p. 125°) and then twice from carbon tetrachloride. Reported melting points are 125.5°, N. L. Drake and J. Bronitsky, *THIS JOURNAL*, 52, 3719 (1930), and 126–127°, B. R. Carpenter and E. E. Turner, *J. Chem. Soc.*, 869 (1934).

(4) Ch. St. Gibson, J. D. A. Johnson and D. C. Vining, *Rec. trav. chim.*, 49, 1006 (1930).

(5) N. Puschin and K. S. Hrutanovic, *Ber.*, 71, 798 (1938).

(6) A. P. J. Hooegeveen, *Rec. trav. chim.*, 50, 669 (1931).

(7) A. Collet, *Bull. soc. chim.*, [3] 17, 506 (1897).

(8) (a) W. Staedel, *Ber.*, 10, 1830 (1877); (b) H. Korten and R. Scholl, *ibid.*, 34, 1902 (1901); (c) D. A. Clibbens and M. Nierenstein, *J. Chem. Soc.*, 107, 1492 (1915).

(9) F. Tutin, *ibid.*, 97, 2500 (1910).

Phenacyl iodide, reported to melt at 28,¹⁰ 29.5–30¹¹ and 30°¹², was apparently never crystallized from a solvent, evidently being considered too soluble in common solvents for this purpose.¹³ We obtained it in 95.4% yield by mixing solutions of phenacyl bromide and sodium iodide in dry acetone. The precipitate of sodium bromide, immediately formed, was separated and washed with dry acetone. The acetone solutions, *quickly* evaporated at room temperature, left as residue a reddish oil which was extracted with ether. The ethereal solutions, decolorized with sodium thiosulfate, dried with anhydrous sodium sulfate and *quickly* evaporated gave an oil that, poured over ice, crystallized immediately. This crude product treated with active charcoal in ethanol was recrystallized from very dilute alcohol using the following technique: The product is dissolved in a small amount of slightly heated ethanol, small pieces of ice added and the flask kept in ice water; the substance separates in crystalline form. By repeating this process a few times the phenacyl iodide was obtained in colorless crystals melting sharply at 34.4°.

Anal. Calcd. for C₈H₇OI: I, 51.58. Found¹: I, 51.68, 51.81.

(10) A. Lucas, *Ber.*, 32, 601 (1899).

(11) A. Collet, *Compt. rend.*, 128, 312 (1899).

(12) J. U. Nef, *Ann.*, 308, 294 (1899).

(13) C. Paal and H. Stern, *Ber.*, 32, 532 (1899).

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COMMUNICATIONS TO THE EDITOR

QUINOLIZIDINE

Sir:

Recently it became of interest to us to find a simple and convenient method of preparing quinolizidine (norlupinane) and various related compounds. It was found that diethyl β -(2-pyridyl)-ethylmalonate, prepared by the Michael addition of diethyl malonate to 2-vinylpyridine, could be hydrogenated directly to quinolizidine in 65% yield.

The addition of various nucleophilic reagents to 2-vinylpyridine was recently reported to *THIS JOURNAL* in an interesting article by Doering and Weil.¹ Our experiments on the addition of diethyl malonate to 2-vinylpyridine, which were carried out independently and prior to their publication, are in good agreement with their results. When 2-vinylpyridine was treated with an excess of diethyl malonate, there was obtained yields of 42 to 43% of diethyl β -(2-pyridyl)-ethylmalonate; b. p. 162–164° at 2 mm. *Anal.* Calcd. for C₁₄H₁₉O₄N: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.35; H, 7.26; N, 5.27. When diethyl malonate and 2-vinylpyridine were employed in equivalent amounts, the major product was a high-boiling viscous oil whose composition as indicated by analysis of the picrate, is presumed to be

(1) W. E. Doering and R. A. N. Weil, *THIS JOURNAL*, 69, 2461 (1947).

diethyl di-(β -(2-pyridyl)-ethyl)-malonate. *Anal.* Calcd. for C₃₃H₃₂O₁₈N₈: C, 47.77; H, 3.89. Found: C, 47.95; H, 3.77.

Catalytic reduction of diethyl β -(2-pyridyl)-ethylmalonate using copper chromite as catalyst at 250° gave a 65% yield of quinolizidine; b. p. 84° at 21 mm.²; *n*²⁰_D 1.4796. The quinolizidine was identified through formation of its picrate²; m. p. 198–199°; methiodide,² dec. 309–311° (*Anal.* Calcd. for C₁₀H₂₀NI: C, 42.71; H, 7.17. Found: C, 42.50; H, 7.09); and hydrochloride, indefinite m. p. (*Anal.* Calcd. for C₉H₁₉NCl: C, 61.53; H, 10.32. Found: C, 61.20; H, 10.01). Catalytic reduction of diethyl β -(2-pyridyl)-ethylmalonate using Raney Ni at 140° gave 3-carbethoxy-4-ketoquinolizidine in 90% yield; b. p. 149° at 0.15 mm. *Anal.* Calcd. for C₁₂H₁₉O₃N: C, 63.97; H, 8.50; N, 6.22. Found: C, 63.92; H, 8.47; N, 5.97. The structure of the 3-carbethoxy-4-ketoquinolizidine was established by its conversion, via hydrolysis and decarboxylation, to 4-ketoquinolizidine (α -norlupinone). The 4-ketoquinolizidine formed a hydrochloride, m. p.

(2) The following physical constants have been recorded for quinolizidine and its derivatives. Prelog and Bozicevic (*Ber.*, 72, 1103 (1939)) give b. p. 69–70° at 11 mm.; picrate, m. p. 196°; methiodide, dec. 333°. Clemo, Ramage and Raper (*J. Chem. Soc.*, 2959 (1932)) give b. p. 72° at 16 mm.; picrate 194°; methiodide, dec. 335°. Galinovsky and Stern (*Ber.*, 76, 1034 (1943)) give 70° at 10 mm.; picrate, m. p. 199–200°; and methiodide, dec. 333°.

143–145° (lit.,³ m. p. 146–147°) and was readily converted by copper chromite reduction to quinolizidine which was identified as before.

Details of the synthesis of quinolizidine and various derivatives will be reported in a subsequent publication.

(3) Ochiai, Tsuda and Yokoyama, *Ber.*, **68**, 2291 (1935).

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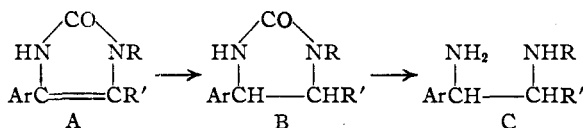
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DIAMINES. I. THE SYNTHESIS OF AMINO ANALOGS OF ADRENALINE, ARTERENOL AND EPHEDRINE

Sir:

Diamines C (R and R' = H or CH₃) wherein the alcoholic hydroxy group of arylalkanolamines, such as adrenaline, arterenol and ephedrine, is replaced by an amino group (III, IV and V) have attracted interest,¹ but only I² and II³ have been described adequately. Recently Funke and Bovet reported that a group of diamines including I and IV are sympathomimetics.⁴ Methods of preparation, physical and chemical properties of the new diamines were not reported.

Prior to that, we had investigated numerous α,β -diamines. Thus, α -aminoketones ArCOCH(NHR)R' were cyclized to imidazolones (A) which, due to labilization of the double bond by aryl,⁵ could be selectively hydrogenated to imidazolidones (B). Hydrolysis (for the adrenaline analog after protective benzylation) afforded C.



I, Ar = Ph; R = R' = H.—II, Ar = Ph; R = H; R' = CH₃.—III, Ar = 3,4-(HO)₂C₆H₃; R = CH₃; R' = H.—IV, Ar = 3,4-(HO)₂C₆H₃; R = R' = H.—V, Ar = Ph; R = R' = CH₃.

Refluxing adrenalone hydrochloride with 2 moles of potassium cyanate in water and neutralizing with hydrochloric acid gave almost 100% of A (III), m. p. 276–277° (*Anal.* Calcd. for C₁₀H₁₀O₃N₂: C, 58.25; H, 4.89. Found: C, 58.14; H, 5.02). Hydrogenation in acetic acid with palladium charcoal at 3 atm. pressure yielded almost 100% of B (III), m. p. 167–169° (*Anal.* Calcd. for C₁₀H₁₂O₃N₂: C, 57.68; H, 5.81. Found: C, 57.85; H, 5.93). Benzylation⁶ of B (III) gave 90% of 1-methyl-4-(3,4-dibenzyloxy-

phenyl)-2-imidazolidone, m. p. 128–130° (*Anal.* Calcd. for C₂₄H₂₄O₃N₂: C, 74.20; H, 6.23. Found: C, 74.54; H, 6.39). This compound was heated for forty-eight hours at 120° with ca. 4 N aqueous ethanolic sodium hydroxide. After extraction with ether, 72% of 3,4-dibenzyloxyphenyl-N²-methyl-ethylenediamine was isolated as dihydrochloride, m. p. 184–185° (*Anal.* Calcd. for C₂₃H₂₆O₂N₂·2HCl: C, 63.44; H, 6.48. Found: C, 63.68; H, 6.46). The latter, by palladium catalyzed hydrogenation, gave 91% of 3,4-dihydroxyphenyl-N²-methyl-ethylenediamine dihydrochloride (C III), m. p. 202–203° (*Anal.* Calcd. for C₉H₁₄O₂N₂·2HCl: C, 42.36; H, 6.32. Found: C, 42.55; H, 6.49).

The dihydrochlorides of C (IV), m. p. ca. 245° (dec.) (*Anal.* Calcd. for C₈H₁₂O₂N₂·2HCl: C, 39.85; H, 5.85. Found: C, 40.09; H, 5.71), and of C (V), m. p. ca. 249° (dec.) (*Anal.* Calcd. for C₁₀H₁₆N₂·2HCl: C, 50.64; H, 7.65. Found: C, 50.69; H, 7.82) were obtained from B (IV) and B (V) by acid hydrolysis.

Diamines of type C are sympathomimetics of relatively low toxicity. When administered intravenously in dogs and cats III and IV showed one-tenth of the pressor activity of adrenaline, I only 1/900. IV is therefore more potent than it appears from published data.⁴ As a bronchodilator III was ten times stronger than IV.

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RAMAN SPECTRUM AND NORMAL MODES OF VIBRATION OF BUTADIENE-1,2¹

Sir:

We have recently redetermined the Raman spectrum of butadiene-1,2 in an effort to improve the assignment of the normal modes of vibration. A very pure sample of butadiene-1,2 was obtained from the Cryogenic Laboratory of this College. This sample is identical with the one used in obtaining the thermodynamic properties of this molecule.² The Raman spectrum was obtained in two different spectrographs,^{3,4} up to 2000 cm.⁻¹ shifts. The spectrum obtained generally agrees with the previous one of Bourguet and Piaux⁵; there were, however, a few important differences, which warrant a reassignment. The polarizations of the strong lines were also obtained and were useful guides in making the new assignment.

The following assignment has been made for the normal modes of vibration of butadiene-1,2.

- (1) Review by Hartung, *Ind. Eng. Chem.*, **37**, 128 (1945).
- (2) Feist and Arnstein, *Ber.*, **28**, 425, 3172 (1895).
- (3) Jaeger and van Dijk, *Proc. Acad. Sci. Amsterdam*, **44**, 26 (1941).
- (4) Funke and Bovet, *Compt. rend. soc. biol.*, **141**, 327 (1947). I and IV appear to have equal pressor activity.
- (5) Cf. Duschinsky and Dolan, *THIS JOURNAL*, **67**, 2079 (1945); "E. C. Borell-Jubilee Volume," Basle, 1946, p. 164.
- (6) Cf. Suter and Ruddy, *THIS JOURNAL*, **66**, 747 (1944).

- (1) The work described in this communication was carried out under Contract N60nr-269 Task Order V between the office of Naval Research and the Pennsylvania State College.
- (2) Aston and Szasz, *THIS JOURNAL*, **69**, 3108 (1947).
- (3) Rank and Wiegand, *J. Opt. Soc. Am.*, **36**, 325 (1946).
- (4) Rank, Scott and Fenske, *Ind. Eng. Chem., Anal. Ed.*, **14**, 816 (1942).
- (5) Bourguet and Piaux, *Bull. soc. chim.*, **51**, 1041 (1932).