

$C_{32}H_{26}O$: C, 90.11; H, 6.14. Found: C, 90.24; H, 5.90.

Infrared absorption spectra in nujol mull were taken using a Baird split beam recording spectrophotometer. The above compound showed very strong absorption at 6 microns, the carbonyl absorption band, and no absorption at 2.9 microns, the hydroxyl band. The compound was unsaturated to bromine and to potassium permanganate.

Dehydrogenation of Pentaphenylethanol.—The above material (0.2 g.) heated at 170–180° with 0.02 g. of palladium on charcoal catalyst⁸ yielded *o*-biphenyl triphenylmethyl ketone, m.p. and mixed m.p. 175–176°,⁷ and a small amount of an unidentified product.

Isolation of the Enol Form.—When the crude, ether-insoluble material from the Grignard reaction above, filtered after hydrolysis, was carefully washed with dilute hydrochloric acid (about 2 *M*) and chloroform and then ether, the residue gave an infrared spectrum with absorption at 2.9 μ , indicative of hydroxyl. Tests with bromine in carbon tetrachloride and potassium permanganate in acetone indicated unsaturation. All attempts to recrystallize this material yielded either the unsaturated ketone described above, m.p. 175–176°, or *o*-biphenyl triphenylmethyl ketone.

(8) R. P. Linstead and S. L. S. Thomas, *J. Chem. Soc.*, 1130 (1940).
NEWARK, DELAWARE

2,2-Dimethyl-3-aminopentane and its Reaction with Nitrosyl Chloride

BY WILLIAM A. MOSHER, JAMES C. COX, JR., AND
JAMES KREITZER

RECEIVED FEBRUARY 21, 1953

Although rearrangement was expected, we undertook the reaction of 2,2-dimethyl-3-aminopentane with nitrosyl chloride as a possible method of preparing 2,2-dimethyl-3-chloropentane. The amine was prepared by the reduction of the corresponding ketoxime. On treatment of the amine in ether solution with gaseous nitrosyl chloride as employed by Bartlett and Knox¹ the only product isolated was identical with the nitrosochloride from 2,3-dimethyl-2-pentene.

Markownikoff² reported the preparation of 2,2-dimethyl-3-aminopentane by reduction of the secondary nitro compound formed by the nitration of 2,2-dimethylpentane. This nitro compound gave on hydrolysis with alkali a ketone erroneously identified as ethyl *t*-butyl ketone on the basis of correspondence with reported physical constants.³ Markownikoff's ketone must actually have been methyl neopentyl ketone since it gave a semicarbazone of m.p. 175°; the reported values for this derivative from ethyl *t*-butyl ketone⁴ and methyl neopentyl ketone⁵ are, respectively, 144 and 176°.

Apparently 2,2-dimethyl-3-aminopentane has not been previously reported. The following physical properties were determined in the present study: b.p. 128.0° (760 mm.), n_D^{25} 0.7615, n_D^{15} 1.4306, n_D^{20} 1.4287, n_D^{30} 1.4249, viscosity at 25°, 24.86 millipoises; surface tension, capillary rise 23.3 dynes/cm. The phenylthiourea melts at 151° and the 3,5-dinitrobenzoate at 149–151°.

Experimental

Preparation of Ethyl-*t*-butylcarbinol.—This compound was prepared from *t*-butylmagnesium chloride and pro-

pionaldehyde in the usual manner; yield 45%, b.p. 135° (757 mm.), n_D^{25} 1.4180, phenylurethan m.p. 83°. A 45% recovery of propionaldehyde, presumably through enolization, was observed.

Oxidation of Ethyl-*t*-butylcarbinol.—The oxidation was carried out as described by Mosher and Langerak⁷ with chromic anhydride in aqueous acetic acid. The ketone was distilled through a column of 15 theoretical plates; yield 88–90%, b.p. 125°, n_D^{25} 1.4013, m.p. of semicarbazone 144°,^{4,8} of 2,4-dinitrophenylhydrazone 143°,⁸ and oxime 84–85°.⁸

Reduction of the Ketoxime.—A total of 190 g. of ketoxime was reduced in the following manner: ethyl *t*-butyl ketoxime, 16.3 g. (0.13 mole), was dissolved in 300 ml. of *n*-amyl alcohol and heated to boiling under reflux; 21 g. of metallic sodium, cut into thin strips, was added slowly. Refluxing was continued for three hours. The reaction mixture was allowed to cool and then poured into 500 ml. of water. The amyl alcohol layer, containing most of the amine, was separated and acidified with concd. hydrochloric acid, the acidified washings were combined, made basic with 10% sodium hydroxide and extracted with several portions of ether. The ether extracts were dried over solid potassium hydroxide, the ether distilled and the amine purified by fractionation. The yields were 75–90% of theory. Chloroplatinate salt: calcd. for $(C_7H_{13}NCl)_2PtCl_4$: Pt, 30.49. Found: Pt, 30.45. Hydrochloride m.p. 221: calcd. for $C_7H_{13}NCl$: Cl, 23.38. Found: Cl, 23.35. Phenylthiourea m.p. 151°: calcd. for $C_{14}H_{23}N_2S$: N, 11.19. Found: N, 11.30. 3,5-Dinitrobenzoate m.p. 149–151°: calcd. for $C_{14}H_{19}O_6N_3$: N, 12.87. Found: N, 12.77.

Reaction of 2,2-Dimethyl-3-aminopentane with Nitrosyl Chloride.—This reaction, including the preparation of nitrosyl chloride, was carried out as described by Bartlett and Knox.¹ The reaction temperature was –10° and ether was employed as solvent. Gaseous nitrosyl chloride was added until the persistence of a brown color indicated that an excess had been added. The ether solution was washed with water, dried with sodium sulfate, and evaporated. The solution was blue-green, indicating the presence of a completely substituted double bond,⁹ the recrystallized product melted at 124°. For comparison purposes, methyl ethylisopropylcarbinol was prepared by the reaction of ethylmagnesium bromide on methyl isopropyl ketone and the alcohol formed was dehydrated with potassium acid sulfate. Fractionation gave 2,3-dimethyl-2-pentene, b.p. 97–98°, n_D^{20} 1.4212,¹⁰ confirmed by ozonolysis into acetone and methyl ethyl ketone and only a trace of acetaldehyde. The nitrosochloride of 2,3-dimethyl-2-pentene was prepared as above: m.p. and mixed m.p. with the product from 2,2-dimethyl-3-aminopentane, 124°. *Anal.* Calcd. for $C_7H_{14}ONCl$: Cl, 21.67. Found: Cl, 21.80.

(6) J. Leroide, *Ann. chim. phys.*, [9] 16, 366 (1921); F. C. Whitmore and W. S. Forster, *THIS JOURNAL*, 64, 2966 (1942).

(7) W. A. Mosher and E. O. Langerak, *ibid.*, 71, 286 (1949).

(8) F. C. Whitmore, C. I. Noll and V. C. Meunier, *ibid.*, 61, 684 (1939).

(9) Cf. J. L. Simonsen, "The Terpenes," Vol. I, Second Edition, Cambridge Univ. Press, Cambridge, 1947, p. 168.

(10) M. P. Doss, "Physical Constants of the Principal Hydrocarbons," Third Edition, The Texas Co., New York, N. Y., 1942, p. 24.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF DELAWARE
NEWARK, DELAWARE

A Synthesis of 3,2'-Nornicotyrine¹

BY HENRY RAPOPORT AND MELVIN LOOK

RECEIVED MAY 25, 1953

Recently² it has been shown that the use of *N*-nitroso-*N*-(3-pyridyl)-isobutyramide (I) in the Gomberg (or diazo) reaction affords a reasonable method for introducing the 3-pyridyl radical into

(1) Reported in part in *Abstracts Papers Am. Chem. Soc.*, 122, 14M (1952).

(2) H. Rapoport, M. Look and G. J. Kelly, *THIS JOURNAL*, 74, 6293 (1952).

(1) P. D. Bartlett and L. H. Knox, *THIS JOURNAL*, 61, 3184 (1939).

(2) B. V. Markownikoff, *Ber.*, 33, 1906 (1900).

(3) A. Wischnegradsky, *Ann.*, 178, 103 (1875).

(4) A. Favorskii, *J. Russ. Phys. Chem. Soc.*, 44, 1339 (1912).

(5) R. J. McCubbin and H. Adkins, *THIS JOURNAL*, 52, 2647 (1930).

an aromatic system, the specific example being the preparation of 3-phenylpyridine. An interesting extension of this method has now been found in the introduction of the 3-pyridyl radical into a pyrrole nucleus, thus providing a convenient synthesis of 3,2'-nornicotyrine (III).

In considering the applicability of such an approach to the synthesis of a pyridylpyrrole, two essential questions had to be answered, *viz.*, can the pyrrole nucleus be substituted employing this reaction and, if so, at what position(s) does substitution occur.

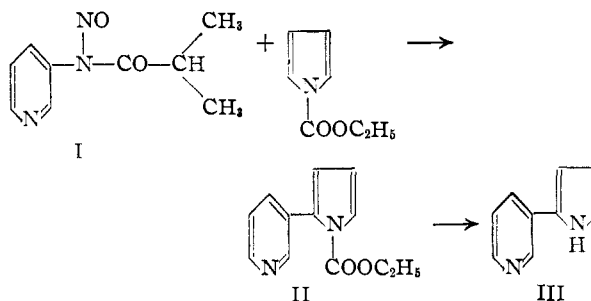
A search of the literature revealed only one instance in which a pyrrole compound had been successfully employed in the Gomberg reaction. This was the work of Rinke,⁸ who prepared 2-phenylpyrrole from the reaction of N-nitrosoacetanilide with 1-carboxypyrrole followed by hydrolysis of the carbethoxyl group. We have confirmed his results and obtained a parallel reaction with 3,3-dimethyl-1-phenyltriazeno in place of N-nitrosoacetanilide. The 2-phenylpyrrole thus obtained melts at 129–130° and is apparently the pure 2-isomer.

Whether any of the 3-isomer is an accompanying impurity in the original reaction mixture is difficult to say since 3-phenylpyrrole has not been reported. Although the preparation of 2-phenylpyrrole by thermal rearrangement of 1-phenylpyrrole⁴ admits to the possibility (and probability) of some of the 3-isomer as a side-product, synthesis from ethyl benzoylacetate, ammonia and α,β -dichloroethyl ethyl ether must give only the 2-isomer.⁵ In each case^{3,4,5} the melting points are identical, and we are led to the conclusion that the Gomberg reaction apparently gave exclusive (or overwhelming) substitution of the pyrrole nucleus at the 2-position. This is surprising in view of the fact that with substituted benzenes⁶ and pyridine,⁷ all possible isomers are formed.

Attempts were next made to replace 1-carboxypyrrole with 1-methylpyrrole in the Gomberg reaction. However, coupling took place without nitrogen elimination and the product was 1-methyl-2-phenylazopyrrole. This is not too surprising when one considers that 1-methylpyrrole readily forms azo compounds with diazonium salts, whereas 1-carboxypyrrole does not. Parallel results were obtained in the benzene series where phenols and naphthols in the Gomberg reaction give azo compounds rather than nitrogen elimination.⁸

These observations indicated that the pyrrole nucleus could be substituted in the Gomberg reaction if 1-carboxypyrrole was used and that the entering substituent took the 2-position. To apply this reaction to the synthesis of a pyridyl-

pyrrole related to the nicotine series, N-nitroso-N-(3-pyridyl)-isobutyramide (I) was allowed to react with 1-carboxypyrrole. The product, isolated by distillation in 23% yield, was N-carboxy-3,2'-nornicotyrine (II), which was hydrolyzed with alkali to 3,2'-nornicotyrine (III),



m.p. 98–100°. Again in this reaction apparently none (or extremely little) of the isomeric 3-substituted pyrrole was formed. Since 3,3'-nornicotyrine is the higher melting and less soluble of the two isomers,⁹ its presence in even small amount would be detectable.^{9a}

This reaction thus appears to offer an interesting alternative method, with some possibility of variation, for the synthesis of certain compounds related to nicotine.

Experimental¹⁰

2-Phenylpyrrole.—A mixture of 11.6 g. (0.08 mole) of 3,3-dimethyl-1-phenyltriazeno¹¹ and 50 ml. of N-carboxypyrrole¹² were warmed on the steam-bath (protected from atmospheric moisture) until gas evolution ceased. The solution was then steam distilled (four liters of distillate collected), the distillate was extracted with four 250-ml. portions of ether, the combined ether extracts were washed with sodium carbonate and dried over magnesium sulfate, and the ether was evaporated. Distillation of the residue gave 5.1 g., 30% yield, of 1-carboxy-2-phenylpyrrole, b.p. 150–155° (12 mm.). Hydrolysis by the procedure of Rinke⁸ gave a quantitative yield of 2-phenylpyrrole, m.p. 129–130° (reported^{3,4,5} m.p. 129–130°).

1-Methyl-2-phenylazopyrrole.—Using N-nitrosoacetanilide¹³ or the triazene¹¹ and N-methylpyrrole (du Pont, redistilled) and the same coupling and isolation procedure as given above, 1-methyl-2-phenylazopyrrole, an orange liquid, was the only isolable product, b.p. 120–130° (3 mm.).¹⁴

Anal. Calcd. for C₁₁H₁₁N₃: C, 71.4; H, 6.0; N, 22.6. Found: C, 71.6; H, 6.4; N, 22.1.

The picrate was prepared with ethanolic picric acid and recrystallized from absolute ethanol, m.p. 148–149°.

Anal. Calcd. for C₁₇H₁₄O₇N₆: C, 49.3; H, 3.4; N, 20.3. Found: C, 49.0; H, 3.3; N, 20.6.

N-Carboxy-3,2'-nornicotyrine.—N-Nitroso-N-(3-pyridyl)-isobutyramide was prepared from 10 g. (0.06 mole) of N-(3-pyridyl)-isobutyramide and nitrosyl chloride as described previously,³ except that the extraction of the aqueous solution was made with three 100-ml. portions of cold, peroxide-free ether. The combined extracts, after washing with 100 ml. of 2% sodium hydroxide and 100 ml. of saturated sodium chloride solution, were dried over magnesium sulfate, and evaporated at reduced pressure and room tem-

(3) I. J. Rinke, *Rec. trav. chim.*, **62**, 116 (1943).
 (4) A. Pictet and P. Crepieux, *Ber.*, **28**, 1904 (1895); G. Plancher and E. Ghigi, *Gazz. chim. ital.*, **55**, 757 (1925); C. F. H. Allen, M. R. Gilbert and D. M. Young, *J. Org. Chem.*, **2**, 227 (1937); H. Adkins and H. L. Coonradt, *THIS JOURNAL*, **63**, 1563 (1941).
 (5) A. Fujita, *J. Pharm. Soc. Japan*, No. 519, 4 (1925); *Chem. Zentr.*, **96**, II, 1753 (1925).
 (6) D. P. De Tar and H. J. Scheifele, Jr., *THIS JOURNAL*, **73**, 1442 (1951).
 (7) W. J. Adams, D. H. Hey, P. Mamalis and R. E. Parker, *J. Chem. Soc.*, 3181 (1949).
 (8) R. Huisgen and R. Horeld, *Ann.*, **562**, 137 (1949).

(9) (a) J. P. Wibaut and H. P. L. Gitsels, *Rec. trav. chim.*, **57**, 755 (1938); (b) E. Späth and P. Kainrath, *Ber.*, **71**, 1276 (1938).
 (10) All melting points are corrected; microanalyses were performed by the Microchemical Laboratory, University of California.
 (11) J. Elks and D. H. Hey, *J. Chem. Soc.*, 441 (1943).
 (12) W. Tschelinzeff and B. Maxaroff, *Ber.*, **60**, 194 (1927).
 (13) H. France, I. M. Heilbron and D. H. Hey, *J. Chem. Soc.*, 369 (1940).
 (14) This compound, prepared by methylation of 2-phenylazopyrrole, has been reported as boiling at 140° (21 mm.) and forming a picrate, m.p. 151° [G. Plancher and E. Soncini, *Gazz. chim. ital.*, **32**, II, 464 (1902)].

perature. To the residue was added 51 g. (0.37 mole) of N-carbethoxypyrrole and the mixture was allowed to stand at 0° for three days and room temperature for an additional day, at which time gas evolution had ceased. Ether was added, the solution was washed with dilute sodium carbonate and then steam distilled until four liters of distillate was collected. The distillate was extracted with four 250-ml. portions of ether and the ether extracts were dried and distilled giving recovered N-carbethoxypyrrole at 100° (50–55 mm.) and 2.5 g. of N-carbethoxy-3,2'-nornicotyrine at 141–143° (2 mm.). Similar extraction of the steam distillation residue gave an additional 0.5 g.; total, 3.0 g., 23% yield.

The picrate was prepared with ethanolic picric acid and recrystallized from ethanol, m.p. 146–147°.

Anal. Calcd. for $C_{18}H_{15}O_9N_2$: C, 48.5; H, 3.4; N, 15.7. Found: C, 48.6; H, 3.3; N, 15.7.

3,2'-Nornicotyrine.—To a solution of 1.3 g. of sodium hydroxide in 2.6 ml. of water was added 2.7 g. of the N-carbethoxy compound and sufficient ethanol to make a homogeneous solution. After standing at room temperature overnight, the solution was freed from ethanol by concentration at reduced pressure, the residue was extracted with three 50-ml. portions of ether, and the combined ether extracts were dried over magnesium sulfate and evaporated. Distillation of the residue gave 0.9 g. (50%) of 3,2'-nornicotyrine, b.p. 146–147° (1 mm.), which solidified in the receiver and melted at 98–100° on crystallization from benzene (5 ml.)–petroleum ether (1 ml.) (m.p. variously reported^{9,15} from 99 to 101°).

Addition of saturated ethanolic picric acid gave a picrate which was crystallized from ethanol, m.p. 203–205° dec. (reported^{9,15} m.p. from 202 to 204°).

(15) M. L. Swain, A. Eisner, C. F. Woodward and B. A. Brice, *THIS JOURNAL*, **71**, 1841 (1949); F. Lions and E. Ritchie, *J. Proc. Roy. Soc. N. S. Wales*, **74**, 110 (1940).

DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA

An Anomalous Result of an Attempted Dakin Reaction

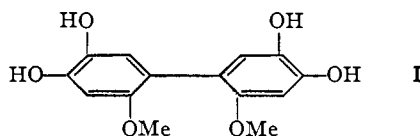
BY DAVID H. ROSENBLATT AND ROBERT W. ROSENTHAL

RECEIVED MAY 7, 1953

In connection with some studies being made in these laboratories, the synthesis of 4-methoxycatechol was undertaken. Kvalnes¹ reported, without giving any details of the synthesis, that he had obtained 4-methoxycatechol, m.p. 48–50°, in good yield by means of the Dakin² reaction, *i.e.*, replacement of the aldehyde or aceto group in ortho or para phenolic aldehydes or ketones with a hydroxyl group by means of hydrogen peroxide. When we added hydrogen peroxide to an aqueous solution of 2-hydroxy-5-methoxybenzaldehyde and sodium hydroxide, a precipitate was formed which softened at 200° and carbonized at 300°. Changing the reaction temperature from room temperature to 45°, and providing a nitrogen atmosphere to exclude oxygen, did not affect the results. The experiment was repeated twice, using lithium hydroxide and potassium hydroxide, respectively, and it was observed that, regardless of the hydroxide used, if the reaction mixture were allowed to stand for several days, the same precipitate was the only isolable product. Its solubility in hot water is compatible with the assumption that it is a polyhydroxy compound, but the high melting point of the material (m.p. 267–270° dec.) and its insolubility

in ether suggest that it is not a simple nuclearily substituted catechol.

Raudnitz³ has reported that the reaction between potassium persulfate and *p*-cresol yields 2,2'-dimethyl-5,5'-dihydroxydiphenyl, and Burton and Hopkins⁴ have found that the oxidation of 4-methylcatechol by ferric acetate or silver oxide yields 4,5,4',5'-tetrahydroxy-2,2'-dimethyldiphenyl and further oxidation products. These two analogous reactions suggest that the substance is a bis-(4-methoxycatechol) such as I or an isomer.



In an attempt to isolate the previously reported 4-methoxycatechol, a large quantity of the sodium salt of 2-hydroxy-5-methoxybenzaldehyde was treated with hydrogen peroxide according to Surrey's⁵ procedure for making 3-methoxycatechol. Only a trace of a compound having the m.p. (48–50°) of 4-methoxycatechol¹ was found.

Experimental

2-Hydroxy-5-methoxybenzaldehyde.—This compound (b.p. 129° (12 mm.), lit. 124° (12 mm.)) was prepared by the Reimer-Tiemann reaction from *p*-methoxyphenol, as reported by Rubenstein.⁶ The semicarbazone melted at 224–225°.

Bis-(4-methoxycatechol).—To a solution of 3.04 g. (0.02 mole) of 2-hydroxy-5-methoxybenzaldehyde in 20 ml. of 1 *N* KOH at room temperature was added in one portion 3.3 g. of 26% hydrogen peroxide in 30 ml. of water. The mixture became gradually brown, then cherry red, and was then heated for 15 minutes on a water-bath at 60°. The mixture was allowed to cool and stand overnight, whereupon 0.83 g. of precipitate was obtained. The precipitate was recrystallized three times from water slightly acidified with hydrochloric acid, m.p. 267–270°. When the mother liquor was allowed to stand several more days additional precipitate was isolated.

Anal. Calcd. for $C_{12}H_{14}(OCH_3)_2(OH)_4$: C, 60.4; H, 5.04; OCH_3 , 22.3; mol. wt., 278; active H, 1.44. Found: C, 60.3, 59.8; H, 5.1, 5.1; OCH_3 , 21.9; mol. wt.,⁷ 279.6; active H, 1.46.

The same procedure with 1 *N* lithium hydroxide solution gave a similar result and a cleaner product.

4-Methoxycatechol.—To a mixture of 25 g. of 2-hydroxy-5-methoxybenzaldehyde and 83 ml. of 2 *N* sodium hydroxide at room temperature, 25 g. of 26% hydrogen peroxide in 145 ml. of water was added dropwise. The solution darkened and by the end of the addition, the temperature had risen to 60°. After the reaction mixture cooled, sodium chloride was added and the solution was extracted with chloroform. On standing the aqueous layer yielded several crops of the high-melting compound reported in this work. The solvent was removed from the chloroform extract and the residue was extracted with boiling water. A white precipitate, melting at 258–262°, which was evidently more of the biphenyl compound, formed from the extract overnight. The mother liquor was stored in the refrigerator and after several weeks a few large translucent crystals formed. This precipitate was filtered, dissolved in hot benzene, and reprecipitated with petroleum ether. The compound was yellow and melted at 49–51° (lit. 48–50°).

(3) H. Raudnitz, *Ber.*, **63B**, 517 (1930).

(4) H. Burton and H. Hopkins, *J. Chem. Soc.*, 2445 (1952).

(5) A. Surrey, *Org. Syntheses*, **26**, 90 (1946).

(6) L. Rubenstein, *J. Chem. Soc.*, **127**, 1998 (1925).

(7) Determined by modification of the method of Signer (*Ann.*, **478**, 246 (1930)), the details of which were reported by the Analytical Branch of the Chemical Corps Chemical and Radiological Laboratories, Army Chemical Center, Maryland (Abstracts of Papers, 123rd Meeting American Chemical Society, March, 1953, p. 5B).

(1) D. Kvalnes, *THIS JOURNAL*, **56**, 2487 (1934).

(2) H. Dakin, *Am. Chem. J.*, **42**, 477 (1909).