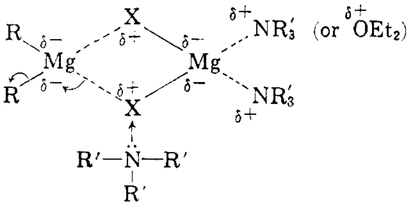
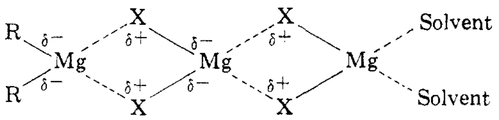


Through a concerted action the carbon in R^- would be released more readily. Since triethylamine was found to be without affect on the reactivity of halogen-free diethylmagnesium,[1] the mechanism involving the halogen is favored inspite of an apparent weakness. The attack of the amine on the halogen should be a function of the steric factor on the amine and the size of the halogen (reference acid). Thus, when changing the halogen from bromine to iodine, one would expect differences in the order of reactivities with the change in the structure of the amine (Table I). However none were observed, and the maximum reactivity occurred in both cases in the presence of dimethyl-*t*-butylamine.

The addition of magnesium bromide to ethylmagnesium bromide would shift the position of equilibrium in equation (1) to the right. Further coordination is possible by forming bridged chains or polymers:[17]



The amine presumably could coordinate with the magnesium, but whether electronic effects would be transmitted through the "bridged" halogens to the alkyl group is uncertain.

The sharp increase in reactivity of ethylmagnesium bromide in the presence of a mixture of tertiary amine and magnesium bromide may explain in part why the triethylamine reversed the order of reactivity of methyl- and ethylmagnesium halides.[1] In the absence of amine the order of reactivity was[18] Cl>>Br>I while in the presence of "catalytic" amounts of triethylamine the order of reactivity was I>Br>Cl.[1] In the preparation of Grignard reagents, the alkyl iodides lead to side reactions, Wurtz-type of coupling. The alkyl chlorides have the least tendency to undergo Wurtz-type coupling. This was evident from the determinations of halogen to basic-magnesium ratios of the three ethyl-magnesium halides used in the present study; iodide 1.15, bromide 1.08, and chloride 0.67.[19] Thus the iodide containing the highest magnesium halide content was effected to the greatest extent by the addition of tertiary amine.

$$\mathrm{RI} + \mathrm{Mg} \longrightarrow \mathrm{RMgI} \xrightarrow{\mathrm{RI}} \mathrm{R{-}R} + \mathrm{MgI_2}$$

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[18] J. H. Wotiz, C. A. Hollingsworth, and R. E. Dessy, *J. Am. Chem. Soc.* **77**, 103 (1955).

[19] The much lower value is caused in part by the low solubility of the $MgCl_2$ in ether.

[COMMUNICATION NO. 2003 FROM THE KODAK RESEARCH LABORATORIES, EASTMAN KODAK COMPANY]

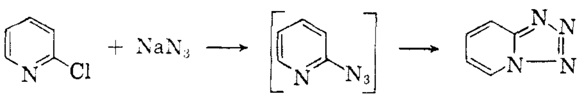
Cyclization of Certain Heterocyclic Azides

GEORGE A. REYNOLDS, JAMES A. VANALLAN, AND JOHN F. TINKER

Received February 5, 1959

The synthesis and properties of certain heterocyclic azides are described. A theory is proposed to account for the isomerization of azides to tetrazoles.

Introduction. In view of the discrepancies in the literature regarding the structure of certain azides, a number of these compounds were synthesized. In many cases, the azide function is adjacent to a ring nitrogen atom and cyclization to form the isomeric bicyclic tetrazole may take place, as in the well known example of 1,2,3,3a-tetrazaindene (III).



I II III

The proximity of the azide group to a ring nitrogen does not necessarily result in cyclization. In fact, it has been pointed out that there are no known examples of the cyclization of an azide group attached to a five-membered heterocyclic ring.[1] This statement was proved to be no longer true since at least three examples of ring closure into a five-membered ring were found; these will be discussed in a later section.

The azides and isomeric tetrazoles described in this paper were prepared by two methods: (1) treatment of a hydrazine with nitrous acid, and (2) reaction of a halide with sodium azide in aqueous alcohol. The course of the reaction (azide formation of cyclization) appeared to be independ-

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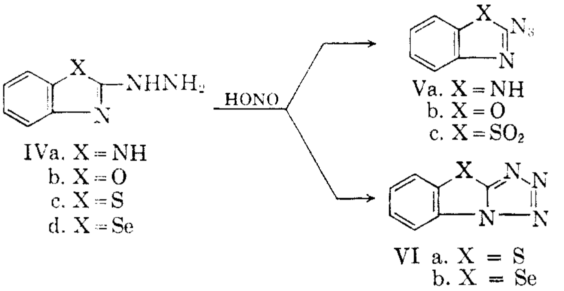
[1] J. H. Boyer and F. C. Canter, *Chem. Revs.*, **54**, 22 (1954).

ent of the method employed in the cases that were studied; therefore, the choice of method depended only on the availability of the starting materials.

Many of the examples described in the literature were assigned either the azide or the tetrazole structure, with no proof or even consideration of the alternate possibility. Therefore, the structures of certain compounds which had not been proved were checked, and several were found to be incorrectly formulated. The structures were determined by means of infrared and ultraviolet absorption curves, since azides show a characteristic absorption band at about $4.6\ \mu$ and $280\ m\mu$.

Azides attached to five-membered rings. Nearly all of the examples of five-membered heterocyclic azides were recorded in the literature as being linear azides. Many compounds, such as azidobenzimidazole (Va) and azidobenzoxazole (Vb), are true azides since they have a characteristic band in the infrared region at $4.6\ \mu$; others, such as those obtained from 2-hydrazinobenzothiazole (IVc) and from the corresponding selenazole (IVd), have cyclized to VIa and VIb, respectively.

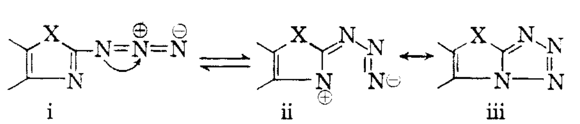


IVa. X = NH
b. X = O
c. X = S
d. X = Se

Va. X = NH
b. X = O
c. X = SO_2

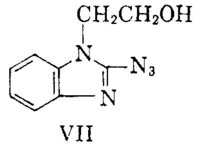
VI a. X = S
b. X = Se

Experimentally, the identity of X has an important influence on the ability of the azide to cyclize. The origin of the effect is clear from the resonance contributor that grows in importance as the azide bends. As the three nitrogens bend away from the linear arrangement, the hybridization changes[2] to that indicated. Here, the ordinarily poorly contributing form, ii, becomes an important contributor, until the fourth nitrogen comes within bonding distance. The stability of the partly bent state depends on the ability of the hetero-nitrogen to supply an electron pair to the azide. The electronegative character of X is in competition with this process; the more electronegative this atom is, the more energetic the transition state. The examples are in excellent agreement with this view: oxygen (Vb) and nitrogen (Va) atoms prevent the ring closure; sulfur (VIa) allows it, but the sulfone group (Vc), of enhanced electronegativity, prevents the reaction.

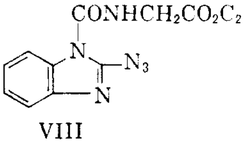


i ii iii

The data do not support the alternative possibility that the physical size of the hetero atom, X, influences the ease of cyclization. The difference in the size of N and S would not be expected to be great enough to influence the course of the reaction. Also the fact that Vc, VII, and VIII fail to form a ring demonstrates the fact that a bulky group at X is of little importance.

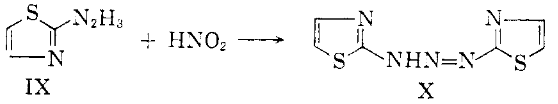


VII



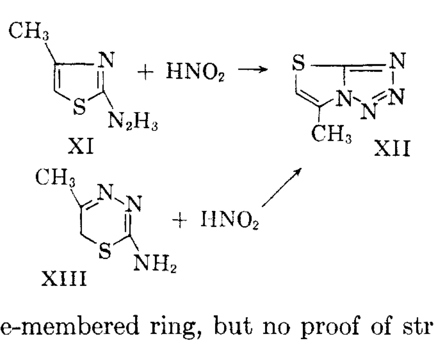
VIII

The presence of a six-membered ring attached to the heterocyclic five-membered ring also contributes to the ease of cyclization. The reason may be that the 6–5–5 ring system is more stable than the 5–5 system. This effect is illustrated by the reaction of 2-hydrazinobenzothiazole (IVc) and 2-hydrazinothiazole (IX) with nitrous acid. The former gave the ring-closed product (VIa) in excellent yield, while the only product isolated from the latter was a light-sensitive material which analyzed for a triazene (X). It is claimed[3] that 2-hydrazino-4-methylthiazole (XI) and nitrous acid gave a 5% yield of the ring-closed material (XII) and a large amount of red material which was not identified but probably has an azoamino structure like X. The amine (XIII) also gave (XII) but in much better yield.



IX X

These reactions were of interest because they were one of two examples found in the literature in which it was claimed that a cyclized product is derived from the cyclization of an azide attached to a five-membered ring, but no proof of structure was included. The following year, it was shown[4] that the starting materials XI and XIII should have interchanged structures and the reaction



XI XII XIII

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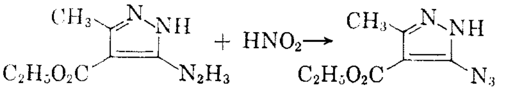
(2) D. F. Heath and J. W. Linnett, *Trans. Faraday Soc.*, **45**, 264 (1949). D. F. Heath and J. W. Linnett, *J. Chem. Phys.*, **18**, 147 (1950).

(3) H. Beyer, W. Lässig, and G. Ruhlig, *Ber.*, **86**, 765 (1953).

(4) H. Beyer, W. Lässig, and E. Bulka, *Ber.*, **87**, 1385 (1954).

product with nitrous acid was now assigned the azide structure. No data for the assignment of the azide structure were given but were promised at a future date. It has now been shown that XIII with nitrous acid gives a 25% yield of ring-closed XII, along with quite a bit of material thought to be a mixture of XII and the azoamine.

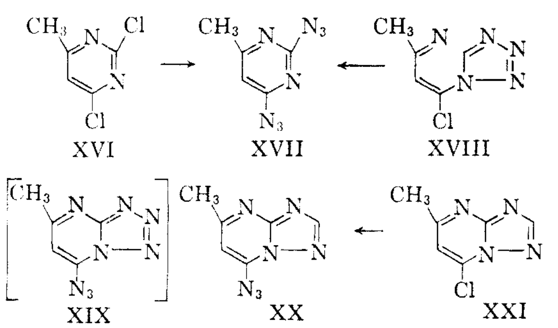
A second example of ring closure was reported to take place when 4-carbethoxy-3-hydrazino-5-methylpyrazole (XIV) was treated with nitrous acid, but again no proof was presented.[5] The reaction product has been found to be the azide (XV), rather than the ring-closed tetrazole as claimed.[5]



XIV XV

Azides attached to six-membered rings. The ring closure of an azide group into a six-membered ring takes place more readily than into the corresponding five-membered ring, a fact that has been demonstrated in other types of cyclization. There are numerous examples of this ring closure in the literature.

An attempt was made to cyclize both azide groups of several six-membered ring diazides containing suitable cyclization centers. Thus, it has been stated,[6] on the basis of spectral evidence, that 2,4-dichloro-6-methylpyrimidine (XVI) gave the diazide (XVII) when treated with sodium azide. This conclusion has been substantiated in the following manner: When 4-chloro-6-methyl-1,2,3,-3a,7-pentaziandene (XVIII) was treated with sodium azide, the product appeared to have the structure (XVII), rather than the isomeric (XIX), because its ultraviolet absorption curve (Fig. 1) was very different from that of 4-azido-6-methyl-1,3,3a,7-tetrazaindene (XX) which was prepared from 4 - chloro - 6 - methyl - 1,3,3a,7 - tetrazaindene (XXI) and sodium azide.



XVI XVII XVIII

XIX XX XXI

One is forced to conclude that ring fission has occurred to give (XVII) during the reaction of (XVIII) with sodium azide. This indicates that the tetrazole ring may be unstable even in the case of the more stable 6–5 ring combination.

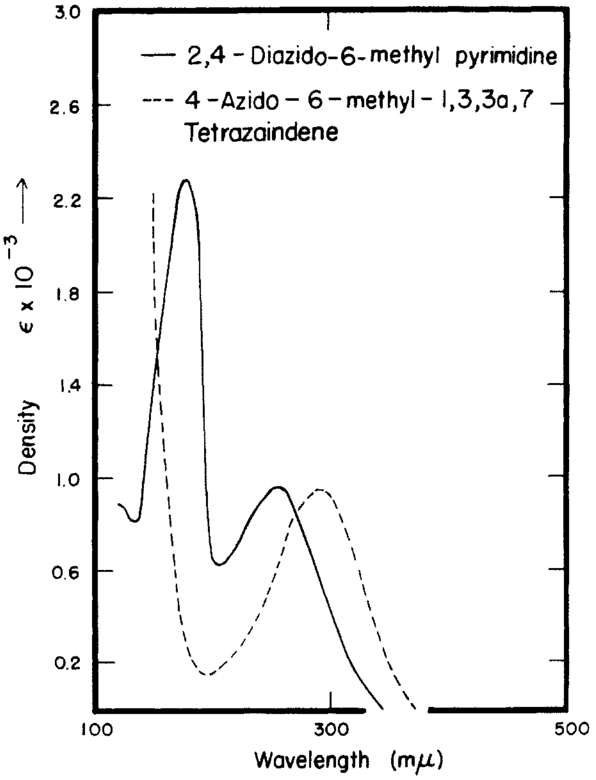
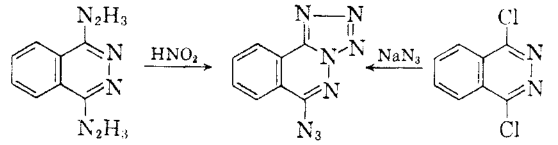


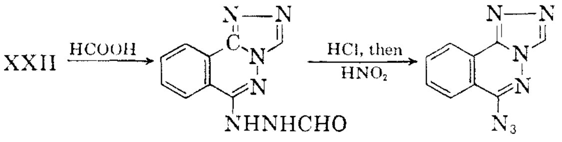
Fig. 1. Ultraviolet absorption spectra of XVII and XX in methanol

The analogous 1,4-dihydrazino-phthalazine (XXII), on treatment with nitrous acid, gave 5 - azido - 1,2,3,3a,4 - pentazacyclopent[*e*]indene (XXIII) which was identical with the product obtained from 1,4-dichlorophthalazine (XXIV) and sodium azide.[7]



XXII XXIII XXIV

This series was investigated further by reaction of XXII with formic acid to give 5-(2-formylhydrazino) - 1,2,3a,4 - tetrazabenz[*e*]indene (XXV), which was deformylated and treated with nitrous acid to give 5-azido-1,2,3a,4-tetrazabenz[*e*]indene (XXVI).



XXV XXVI

All attempts to ring-close the second azido group in these examples were unsuccessful.

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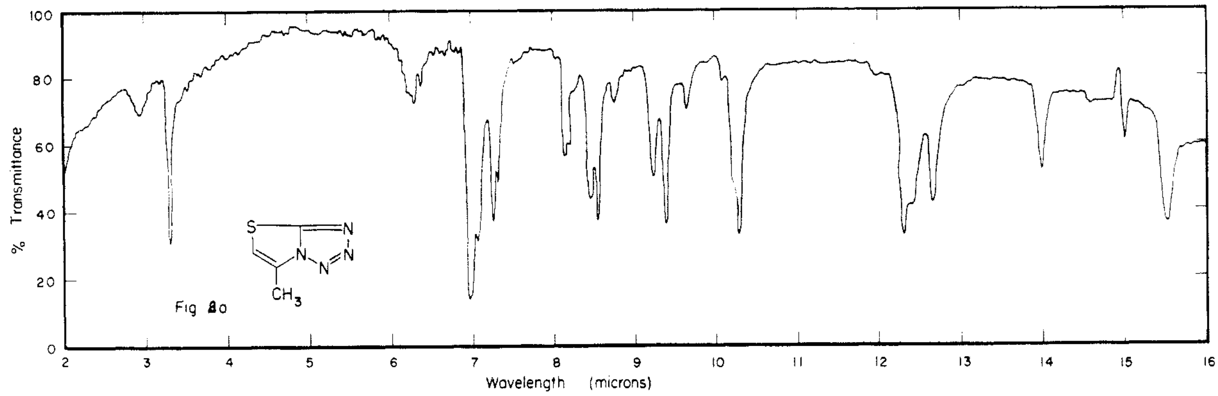
[5] H. Beyer, G. Wolter, and H. Lemke, *Ber.*, **89**, 2554 (1956).

[6] C. Benson, L. Hartzel, and E. Otten, *J. Am. Chem. Soc.*, **76**, 1859 (1954).

[7] R. Stolle and H. Storch, *J. prakt. Chem.*, **135**, 128 (1932).



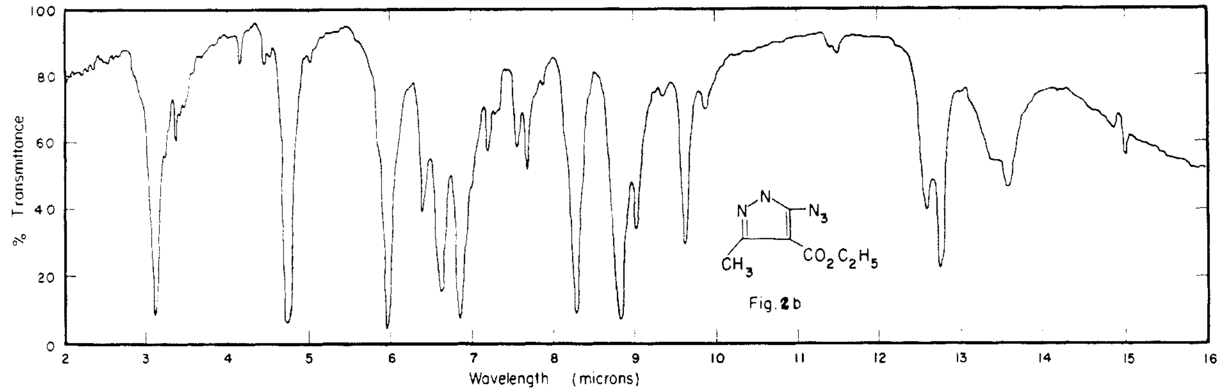


Fig. 2a. Infrared spectrum of XII; Fig. 2b. Infrared spectrum of XV

Proof of structure from spectral evidence. It has been shown[6] that azides have a strong, distinct band at 4.6 μ in the infrared, and at about 280 mμ in the ultraviolet. This latter band may be masked by other absorptions. Compound XII has no absorption in the 4–5 μ region of the infrared (Fig. 2a) and has a single peak at 252 mμ (ϵ = 7,300) in the ultraviolet, which indicates that an azide function is absent. In contrast, XV shows the strong absorption at 4.6 μ (Fig. 2b) in the infrared and at 280 mμ in the ultraviolet, typical of an azide grouping.

EXPERIMENTAL

The following compounds were prepared by previously described methods: 2-hydrazinobenzimidazole (IVa);[8] 2-azidobenzimidazole (Va);[9] 2-hydrazinobenzoxazole (IVb);[8] 2-azidobenzoxazole (Vb);[9] 2-hydrazinobenzothiazole (IVc);[8] 8-thia-1,2,3,3a-tetrazacyclopent[*a*]indene (VIa);[9] 2-hydrazinobenzoselenazole (IVd);[9] 8-seleno-1,2,3,3a-tetrazacyclopent[*a*]indene (VIb);[9] 2-azidobenzothiazole-1,1-dioxide (Vc);[10] 2-azido-1-β-hydroxyethylbenzimidazole (VII);[9] 2-hydrazinothiazole (IX);[11] 2-hydrazino-4-methylthiazole (XI);[3] 6-methyl-4-thia-1,2,3,6a-tetrazapentalene (XII);[3] 2-amino-5-methyl-1,3,4-thiadiazine (XIII);[3] 4-carbethoxy-3-hydrazino-5-methylpyrazole (XIV);[5] 3-azido-4-carbethoxy-5-methylpyrazole (XV);[5] 2,4-diazido-6-methylpyrimidine (XVII);[1] 1,4-dichlorophthalazine (XXIV).[7]

2-Azido-1-carbethoxymethylcarbamylbenzimidazole (VIII). A mixture of 3.9 g. of 2-azidobenzimidazole and 3.3 g. of ethyl isocyanatoacetate in 30 ml. of acetonitrile was refluxed for 4 hr., then cooled to 12–15°, and the crystals which had separated were collected by filtration, and dried. (Yield, 5.5 g.; m.p., 105–106°.) A sample was recrystallized from acetonitrile to give white crystals, m.p. 108°.

Anal. Calcd. for $C_{12}H_{11}N_6O_3$: C, 50.2; H, 3.8. Found: C, 50.2; H, 4.3.

2-Thiazolylaminoazo-2-thiazole (X). To a solution of 1.5 g. (0.01 mole) of 2-hydrazinothiazole hydrochloride in 75 ml. of water was slowly added an aqueous solution containing 0.7 g. of sodium nitrite. The brown-yellow solid that separated was collected and washed with water, m.p. above 300°. All attempts to recrystallize this material resulted in extreme darkening, and allowing the material to stand in the light for a day caused the color to become a deep red-brown.

Anal. of the crude material: Calcd. for $C_6H_5N_5S_2$: C, 34.0; H, 2.4; N, 33.1. Found: C, 33.2; H, 2.1; N, 32.6.

2,4-Diazido-6-methylpyrimidine (XVII) *from* XVIII.[12] A solution of 3.0 g. of sodium azide in 10 ml. of water was treated with 4.0 g. of XVIII. The suspension was shaken well and 20 ml. of methanol added. This mixture was refluxed for 1.5 hr., then 20 ml. of water was added, and the mixture was chilled. The product which separated was filtered off and crystallized from aqueous ethanol to give XVII, m.p. 127–128°. This material, on admixture with a sample prepared as in Ref. 6, gave no melting-point depression. The ultraviolet absorption curves of these two samples were also identical.

4-Azido-6-methyl-1,3,3a,7-tetrazaindene (XX) was pre-

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(8) O. Bayer, U. S. Patent **2,073,600** (1937).

(9) G. A. Reynolds and J. A. VanAllan, *J. Org. Chem.* in press.

(10) E. Schrader, *J. prakt. Chem.*, **95**, 312 (1917).

(11) H. Beyer, H. Höhn, and W. Lässig, *Ber.*, **85**, 1125 (1952).

(12) S. Gabriel and J. Colman, *Ber.*, **32**, 1533 (1899).

pared from XXI[13] and sodium azide in the same way, to give an 84% yield of XX, m.p. 120° dec. from water.

Anal. Calcd. for $C_6H_5N_7$: N, 56.1. Found: N, 56.4.

1,4-Dihydrazinophthalazine (XXII). A mixture of 52 g. of phthalonitrile, 200 ml. of dioxane, and 100 ml. of 95% hydrazine was treated with 18 ml. of acetic acid below 30°, then heated on the steam bath for 3 hr. The orange-colored solid was broken up, filtered and washed with ethanol, and dried; yield, 69 g.; m.p. 185–190° dec. A sample was recrystallized from water, m.p. 190° dec., to a red liquid.

Anal. Calcd. for $C_8H_{10}N_6$: C, 50.5; H, 5.3; N, 44.2. Found: C, 51.6; H, 5.3; N, 43.6.

5-(2-Formylhydrazino)-1,2,3a,4-tetrazabenz[e]indene (XXV). A solution of 5 g. of XXII in 25 ml. of formic acid was refluxed for 3 hr.; water (50 ml.) was added and the solution was chilled. The product separated in the form of white crystals which were crystallized first from dimethylformamide, then from water, to give 4.0 g. of XXV, m.p. 300° dec.

Anal. Calcd. for $C_{10}H_8ON_6$: C, 52.5; H, 3.5; N, 36.8. Found: C, 52.5; H, 3.5; N, 36.6.

5-Azido-1,2,3a,4-tetrazabenz[e]indene (XXVI). A suspension of 4 g. of XXV in 25 ml. of concentrated hydrochloric acid, and 25 ml. of water was refluxed for 1 hr. Complete solution ensued. The solution was concentrated to about 15 ml., filtered with Norit, and the filtrate made alkaline with sodium carbonate solution. The precipitate, 5-hydrazino-1,2,3a,4-tetrazabenz[*e*]indene (XXVa), m.p. >298°, weighed 3.0 g.

Anal. Calcd. for $C_9H_7N_6$: N, 42.1. Found: N, 41.8.

A solution of 4 g. of XXVa in 35 ml. of water containing 4 ml. of concentrated hydrochloric acid and 8 ml. of acetic acid was treated with 4 g. of sodium nitrite in 20 ml. of water at 10°. A precipitate which formed was filtered off and crystallized from alcohol to give 3.1 g. of XXVI, m.p. 195°.

Anal. Calcd. for $C_9H_4N_7$: C, 51.4; H, 1.9; N, 46.7. Found: C, 51.5; H, 2.5; N, 46.8.

5-Azido-1,2,3,3a,4-pentazacyclopent[e]indene (XXIII). This was prepared by treatment of XXII with nitrous acid as just described. It melted at 152° and showed no depression of melting point when mixed with a sample prepared according to the directions given in Ref. 7.

ROCHESTER, N. Y.

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(13) C. F. H. Allen, H. R. Beilfuss, D. M. Burness, G. A. Reynolds, J. F. Tinker, and J. A. VanAllan, *J. Org. Chem.* **24,** 790 (1959).

[CONTRIBUTION FROM THE TECHNICAL RESEARCH DEPARTMENT OF MATSUSHITA ELECTRIC WORKS, LTD.]

N,N-Bis(2-hydroxybenzyl)arylamines: Condensation of Saligenin with Primary Aromatic Amines[1]

MIYOSHI NODA

Received February 9, 1959

Condensation of saligenin with primary aromatic amines and formaldehyde resulted in *N*-(2-hydroxybenzyl)arylamines. Nitroso and formaldehyde derivatives were obtained from *N*-(2-hydroxybenzyl)arylamines on treatment with sodium nitrite and formaldehyde, respectively. *N,N*-Bis(2-hydroxybenzyl)arylamines were also prepared by reaction with equimolar quantities of saligenin and *N*-(2-hydroxybenzyl)arylamines and they were also obtained from direct reaction of saligenin and aromatic amines. Eleven new compounds were synthesized and their properties were studied.

Burke and his collaborators, in a recent paper, described the preparation of several *N,N*-bis-(hydroxybenzyl)alkylamines[2] and new types of 3,4-dihydro-3-*p*-tolyl-6-substituted-1,3,2*H*-benzoxazines[2,3] by the direct condensation of *p*-substituted phenols with paraformaldehyde and *p*-toluidine under various conditions. Compounds of *N*-(2-hydroxybenzyl)-*p*-bromoaniline,[4(a)] *N*-(2-hydroxybenzyl)aniline,[4(b)] *N*-(2-hydroxybenzyl)-*p*-anisidine,[4(a),4(d)] *N*-(2-hydroxybenzyl)-*p*-toluidine,[4b] and *N*-(2-hydroxybenzyl)-*p*-chloroaniline[4(a)] were synthesized by heating saligenin and appropriate aromatic amines disolved in a small amount of alcohol in a sealed tube. *N*-(2-Hydroxybenzyl)aniline was also obtained by treatment of salicylal-aniline with sodium amalgam.[4(c)] Some nitroso compounds of *N*-nitroso-*N*-(2-hydroxybenzyl)arylamines were also synthesized by nitrosation of *N*-(2-hydroxybenzyl)arylamines in ordinary method by pioneers.[5]

In the previous reports it was shown that *N*-(2-hydroxybenzyl)arylamines were obtained through condensation reaction of 2,6-dimethylol-*p*-cresol with primary aromatic amines, 3,4-dihydro-3,6-substituted-1,3,2*H*-benzoxazines were prepared from reaction of *N*-(2-hydroxybenzyl)-arylamines with formaldehyde, and *N*-nitroso-*N*-(2-hydroxybenzyl)-arylamines were formed from treatment of *N*-(2-hydroxybenzyl)arylamines with sodium nitrite.[6(a)] Each type of

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(1) Given in part at the 10th Annual Meeting at the Chemical Society of Japan, April 6, 1957.

(2) W. J. Burke, R. P. Smith and C. Weatherbee, *J. Am. Chem. Soc.*, **74,** 602 (1952).

(3) (a) W. J. Burke, K. C. Murdock, and Grace Ec, *J. Am. Chem. Soc.*, **76,** 1677 (1954). (b) W. J. Burke, *J. Am. Chem. Soc.*, **71,** 609 (1949). (c) W. J. Burke, C. W. Stephens, *J. Am. Chem. Soc.*, **74,** 1518 (1952).

(4) (a) C. Paal, *Arch. Pharm.*, **240,** 681, 684, 685 (1902). (b) C. Paal, H. Senninger, *Ber.*, **27,** 1802, 1804 (1894). (c) O. Emmerich, *Ann.*, **241,** 344 (1887). (d) von H. Euler and H. Nystöm; *cf.* N. J. L. Megson, *Phenolic Resin Chemistry*, Butterworths Publication Ltd., London, 1958, p. 133.

(5) (a) E. Banberger and J. Müller, *Ann.*, **313,** 105, 116 (1900). (b) A. Hantzsch and E. Wechsler, *Ann.*, **325,** 248 (1902).

(6) (a) M. Noda, H. Shimaoka, and S. Nagase, *J. Org. Chem.*, **24,** 512 (1959). (b) M. Noda, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, **62,** 744, 747 (1959). (c) M. Noda, *J. Chem. Soc. Japan, Pure Chem. Sect.*, **80,** 101, 104 (1959).