This material had an optical rotation of $[\alpha]^{24}D$ $+33°$ (c 0.5, 0.1 N NaOH) compared to the Swiss authors' value of $[\alpha]^{20}D$ $+29.3$ in 0.1 N NaOH. The amount of the 6-isomer in this material was less than 1% measured by the growth stimulation of *C. fasciculata*, and after oxidation with permanganate the only major product observed by paper chromatography was 2-amino-4-hydroxypteridine-7-carboxylic acid.[2,4]

It is of interest to note the relationship between the optical configuration about the asymmetric carbon atoms in the polyhydroxyalkyl side chain of these pteridines and their activity in supporting the growth of *C. fasciculata*. Only the compounds containing two adjacent carbon atoms with the L-configuration are highly active—namely, biopterin,[3] I and V. It is not required that one of these carbon atoms be attached to the pyrazine ring, and the presence of other carbinols, either primary or secondary, is without appreciable effect. The biological significance of this configurational specificity is not understood at this time.

Acknowledgment.—The authors are indebted to Mr. L. Brancone and staff for the microanalyses.

Pearl River, N. Y.

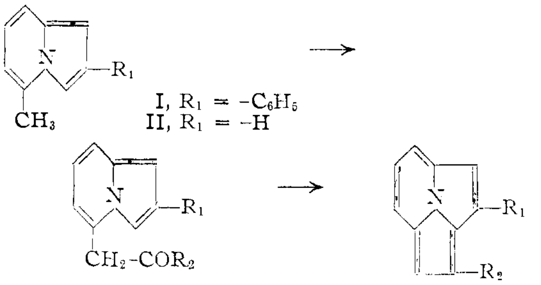
COMMUNICATIONS TO THE EDITOR

CYCLAZINES. THE SYNTHESIS OF A NEW CLASS OF AROMATIC COMPOUNDS[1]

Sir:

We wish to report the synthesis of a new class of aromatic compounds having the general structure shown by IX, for which we propose the trivial name, cycl[3,2,2]azine.[2] The general procedure employed in these syntheses is illustrated below.

When 2-phenyl-5-methylpyrrocoline, I (m.p. 83–83.5°. Found: C, 87.16; H, 6.65), prepared by the Chichibabin procedure,[3] was treated with n-butyllithium followed by N,N-dimethylbenzamide, ketone III (m.p. 125–127°. Found: C, 84.92; H, 5.83) resulted. Heating III in glacial acetic acid gave VII (yellow crystals, m.p. 143.5–144°. Found: C, 90.09; H, 5.22; N, 4.79; mol. wt., 295). Similarly, substitution of dimethyl formamide for dimethylbenzamide in the reaction sequence gave the aldehyde IV, which was cyclized directly to give VIII (yellow crystals, m.p. 98–99°. Found: C, 88.12; H, 5.27). As evidence for the proposed structures, it was found that treatment of 5-methylpyrrocoline,[4] II (b.p. 124° at 34 mm. Found: C, 82.00, H, 7.15, N, 10.93) with n-butyllithium and dimethylbenzamide gave V (m.p. 111–112°. Found: C, 82.15; H, 5.73) which cyclized to give VIII, identical in all respects with the sample previously described. Finally, repetition of the reaction sequence using 5-methylpyrrocoline and dimethylformamide gave VI, which on cyclization yielded the parent cycl[3,2,2]azine, IX (yellow crystals, m.p. 65–66°. Found: C, 84.93; H, 5.30; N, 9.87).



I, $R_1 = -C_6H_5$
II, $R_1 = -H$

III, $R_1 = R_2 = -C_6H_5$
IV, $R_1 = -C_6H_5$; $R_2 = -H$
V, $R_1 = -H$; $R_2 = -C_6H_5$
VI, $R_1 = R_2 = -H$

VII, $R_1 = R_2 = -C_6H_5$
VIII, $R_1 = -H$; $R_2 = -C_6H_5$
or
$R_1 = -C_6H_5$; $R_2 = -H$
IX, $R_1 = R_2 = -H$

In contrast to the behavior of pyrrocolines, the cyclazines show unusual stability toward air, light and heat. Also, they show a complete lack of basicity; the ultraviolet absorption spectrum, characteristic of the system, is unaffected by added acid. These observations are in general accord with the predictions of simple molecular orbital theory.[5]

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(1) Aided in part by the Office of Ordnance Research, Army Ordnance Contract No. DA-30-115-ORD-723.

(2) In this proposal of nomenclature, the word cyclazine would be reserved for the general case of a conjugate, unsaturated cycle held planar by three covalent bonds to an internal nitrogen atom. The various possible cyclazines which then arise through having cycles of different size or different points of attachment to nitrogen can be distinguished by placing in brackets numerals which correspond to the number of atoms on the cycle between points of fusion, *i.e.*, IX becomes cycl[3,2,2]azine.

(3) A. E. Chichibabin, *Ber.*, **60**, 1607 (1927).

(4) The preparation of 5-methylpyrrocoline, which has been accomplished by two independent routes, will be described in the full publication.

(5) These calculations will be presented in the full publication.

(6) National Science Foundation Predoctoral Fellow, 1956–1958.

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Received March 21, 1958

A ONE-STEP TRANSFORMATION OF ACETOPHENONE INTO BENZALDEHYDE[1]

Sir:

By means of a new method, acetophenone has been transformed in one step into benzaldehyde. There does not appear to be another known method for a one-step degradation of an acyl substituent

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(1) Financial assistance under a National Institutes of Health Grant No. H-2295(c) and Contract No. DA-01-009-ORD-428 with Office of Ordnance Research, U. S. Army, is gratefully acknowledged.

attached to a carbon atom of an aromatic nucleus into a formyl group.

To a mixture of 0.05 mole of acetophenone and 6 ml. of concentrated sulfuric acid in 50 ml. of either benzene or nitrobenzene preheated to 60°, 0.05 mole of an alkyl azide is added at such a rate that the reaction temperature maintains itself at 75°. Separation of the layers after dilution with ice-water allows the isolation of benzaldehyde from the benzene layer by distillation. Upon making the aqueous acid layer basic using sodium carbonate and then sodium hydroxide, amines, corresponding to the azides, are isolated by ether extraction. Formaldehyde is detected in the aqueous acid layer as its dimethone derivative by the addition of a methanolic solution of methone.

Four alkyl azides and phenyl azide have been investigated. The best yield (85%) of benzaldehyde is obtained using cyclohexyl azide[2] and good yields (70–80%) are obtained using *n*-butyl,[2] *n*-hexyl[2] or *n*-octyl[3] azides. Phenyl azide[4] is unsuccessful in transforming acetophenone into benzaldehyde. Benzaldehyde, b.p. 35° (2 mm.), n^{23}_{D} 1.5423, was further identified by a mixture m.p. determination (156°) of its phenylhydrazone derivative with a known sample. Apparently the methyl group of acetophenone is transformed into formaldehyde, isolated in 80–85% yield as its dimethone derivative, m.p. and mixture m.p. 191.4°, as an alkyl azide is reduced to an amine. From the corresponding azides, *n*-butyl, *n*-hexyl, *n*-octyl and cyclohexylamines are obtained in yields, respectively, of 60, 65, 52 and 50%. Identification of the amines was indicated by b.p. and confirmed using m.p. determinations of hydrochloride, picrate and chloroplatinate derivatives: *n*-butylamine, b.p. 78° hydrochloride m.p. 195°, picrate m.p. 195°[5]; *n*-hexylamine, b.p. 129–130°, hydrochloride m.p. 219°, chloroplatinate 263–268° dec.[6]; *n*-octylamine, b.p. 175–177°, picrate m.p. 111.5–112.5°[6,7]; cyclohexylamine, b.p. 134°, n^{20}_{D} 1.4371, hydrochloride m.p. 205–207°.[8]

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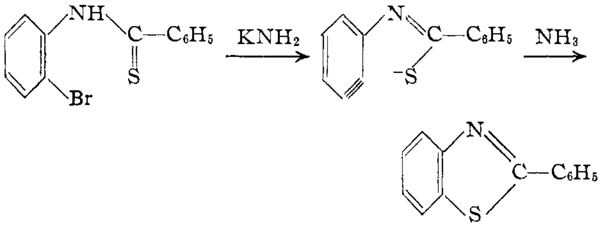
RECEIVED FEBRUARY 8, 1958

A GENERAL PRINCIPLE FOR THE SYNTHESIS OF HETEROCYCLIC AND HOMOCYCLIC COMPOUNDS[1]

Sir:

We wish to report a new general principle for the synthesis of heterocyclic and homocyclic compounds. This principle involves the creation of an intermediate species which is of the benzyne[2] type and which has a nucleophilic center located so that it can add, intramolecularly, to the "triple bond" of the benzyne structure. This method is illustrated by the conversion of thiobenz-*o*-bromoanilide to 2-phenylbenzothiazole in 90% yield through the action of potassium amide in liquid ammonia



As expected from the mechanism, the same product is obtained from thiobenz-*m*-bromoanilide (in 68% yield).

Through the action of potassium amide in liquid ammonia, we have also accomplished the synthesis of benzoxazole, phenothiazine, indole and indane ring systems. The examples studied include conversion of benz-*o*-chloroanilide to 2-phenylbenzoxazole (69% yield), of acetoacet-*o*-chloroanilide to 2-hydroxy-3-acetylindole (57%), of 2-amino-2′-bromodiphenyl sulfide to phenothiazine (35%) and of *o*-chlorophenylacetone to indan-2-one (6%). These cases illustrate intramolecular addition of nucleophilic sulfur, oxygen, nitrogen and carbon reagents; the formation of 2-phenylbenzoxazole is of further interest as the first instance of addition of an oxygen reagent to a benzyne derivative in ammonia solution in substantial yield. In these examples the formation of both five- and six-membered rings and of both heterocyclic and homocyclic systems are also illustrated.

To this list of examples should be added the preparation of N-methyl-2,3-dihydroindole (58%) and of N-methyl-1,2,3,4-tetrahydroquinoline (28%) from treatment of appropriate N-methyl-ω-(chlorophenyl)-alkylamines with phenyllithium. These were reported by Huisgen and König[3] without comment on the generality of the method.

One can visualize application of this principle of ring closure to the synthesis of countless heterocyclic and homocyclic systems both known and unknown. We expect that this soon will be recognized as a major method for the synthesis of cyclic compounds.

Some new compounds are involved in the work reported here. Thiobenz-*o*-bromoanilide, m.p. 85–86°, was prepared by thiation[4] of benz-*o*-bromoanilide.[5] (*Anal.* Calcd. for $C_{13}H_{10}BrNS$: Br, 27.35; N, 4.79. Found: Br, 27.50; N, 4.78.) Thiobenz-*m*-bromoanilide, m.p. 106–108°, was similarly prepared. (*Anal.* Found: Br, 27.50; N, 4.78). Condensation of sodium *o*-bromothiophenoxide with *o*-chloronitrobenzene gave 2-nitro-2′-bromodiphenyl sulfide, m.p. 116–117°. (*Anal.*

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[1] Research supported in part by the Office of Ordnance Research, U. S. Army.

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