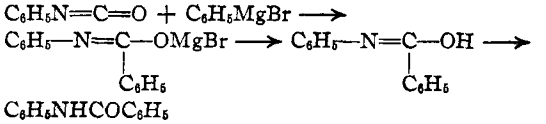
[CONTRIBUTION FROM THE LABORATORIES OF THE MOUNT SINAI HOSPITAL]

Studies on Triazines. I. Reaction of Isocyanuric Ester with Organomagnesium Compounds

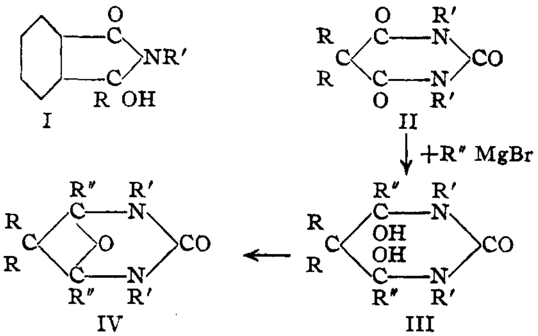
BY HARRY SOBOTKA AND EDITH BLOCH[1]

The behavior of CO-groups, attached to nitrogen or situated between two nitrogen atoms in heterocyclic nuclei, toward Grignard reagent has been studied in a number of cases. The reaction of isocyanic esters with phenylmagnesium bromide yields benzoyl substituted amines, probably under primary addition of the Grignard reagent to the oxygen atom.[2] Kapfhammer and Matthes[3] investigated the reaction of sarcosine anhydride (N,N′-dimethyldiketopiperazine) with phenylmagnesium bromide and obtained minor amounts of methylaminoacetophenone in addition to other products not further identified. Béis[4] and Sachs and Ludwig[5] prepared numerous compounds of the general formula (I) by the reaction of organomagnesium compounds with phthalimide or its N-substituted derivatives. Lukeš[6] obtained N-methyl-2-hydroxy-2-phenylpyrrolone-5 and several 2-alkyl homologs from N-methyl succinimide, and corresponding pyrrolidones from N-methylglutarimide. The reaction of the group —CO—NH—CO— with the Grignard reagent has been studied by several investigators. A. W. Dox[7] studied the reaction of substituted barbituric acids; two of the three oxo groups reacted with excess Grignard reagent and the resulting dicarbinols lost the elements of water to form an internal ether (Formulas II, III, IV). H. Schulze[8] studied the reaction of caffeine and methylcaffeine with phenylmagnesium bromide and introduced two phenyl groups into the molecule; the yield was poor, triphenylcarbinol being the main product of the reaction.

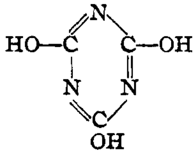


$$C_6H_5N{=}C{=}O + C_6H_5MgBr \longrightarrow$$
$$C_6H_5{-}N{=}\underset{C_6H_5}{\underset{|}{C}}{-}OMgBr \longrightarrow C_6H_5{-}N{=}\underset{C_6H_5}{\underset{|}{C}}{-}OH \longrightarrow$$
$$C_6H_5NHCOC_6H_5$$

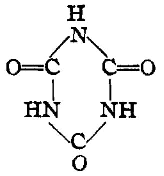
It seemed of interest to study the reactions of oxo triazines with organomagnesium compounds.



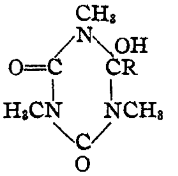
I II III IV



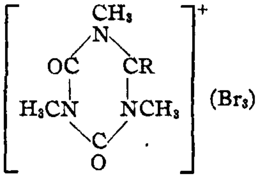
V



VI



VIIA, R = Phenyl
VIIB, R = Ethyl
VIIC, R = Propyl



VIIIA, R = Phenyl
VIIIB, R = Ethyl
VIIIC, R = Propyl

Whereas cyanuric acid may be considered as trihydroxytriazine (V), isocyanuric esters are to be regarded as trioxo hexahydrotriazine derivatives (VI). One of the three carbonyl groups of trimethyl isocyanurate reacts with organomagnesium compounds to form substituted monohydroxydioxohexahydrotriazines (VII). This reaction requires a multiple excess of the Grignard reagent, since three equivalents are taken up by the tertiary nitrogen atoms. Even a large excess of the Grignard reagent, beyond a fourth equivalent, fails to combine with more than one of the carbonyl groups, whereas more strenuous conditions result in ring cleavage and formation of triphenylcarbinol (*cf.* Schulze[8]) in the case of phenylmagnesium bromide. The new product obtained by hydrolysis of the Grignard addition product reacts no further with phenylmagnesium bromide except for the loose addition of three molecules to the three tertiary nitrogens referred to above. The newly formed hydroxyl group

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[1] Isidore Hernsheim Fellow.

[2] Gilman and Kinney, THIS JOURNAL, **46**, 493 (1924).

[3] Kapfhammer and Matthes, *Z. physiol. Chem.*, **223**, 43 (1933).

[4] Béis, *Compt. rend.*, **138**, 987; **139**, 61 (1904).

[5] Sachs and Ludwig, *Ber.*, **37**, 385 (1904).

[6] Lukeš, *Chem. Listy*, **22**, 1, 26 (1928); *Collection Czechoslov. Chem. Commun.*, **1**, 334 (1929); *ibid.*, **7**, 476 (1935); *ibid.*, **8**, 223 (1936).

[7] Dox, THIS JOURNAL, **49**, 2275 (1927).

[8] Schulze, *Ber.*, **40**, 1744 (1907).

lacks phenolic and alcoholic character; it proves inert toward diazomethane and phenyl isocyanate. The substance is unusually stable against concentrated acids and may be recovered in unaltered state from a solution in concentrated sulfuric acid.

It seems unlikely that the decomposition of the Grignard addition compound is accompanied by ring cleavage, yielding benzoyltrimethylbiuret. The neutral character of the reaction product as well as the strong general tendency for cyclization in this group favors the present formulation. The related substituted dihydroxytetrahydrotriazines of Ostrogovich[9] are formed by dilute alkali from acetyl or benzoyl biuret, and trigenic acid, the interesting methyldihydroxyhexahydrotriazine of Liebig and Woehler[10] is obtained easily from acetaldehyde and cyanic acid. In the above example for the reaction of organomagnesium compounds with phthalimide Sachs and Ludwig[5] likewise favor the cyclic formulation for the reaction product.

The present formula was corroborated by the formation of halogen derivatives. The hydroxydiketo substances (VII) react readily with bromine in chloroform or glacial acetic acid and red bromo derivatives precipitate instantaneously in brilliant crystals whose deep color, upon removal of the solvent, changes to orange yellow with loss of hydrogen bromide. The resulting products are quite stable; they may be recrystallized from boiling glacial acetic acid and do not change on prolonged storage. Their molecule contains three bromine atoms and has lost one oxygen and one hydrogen atom during bromination. The tribromo derivatives are completely debrominated by 0.1 *N* aqueous alkali, by silver nitrate in aqueous solution and by alcoholic or ethereal suspensions of silver acetate or silver nitrite. Debromination to the original product also may be achieved by treatment with aqueous sodium thiosulfate or with zinc dust in ethanol or glacial acetic acid. All three bromine atoms are removed simultaneously with any of the methods enumerated; hence formulation as a perbromide of a quaternary base is suggested (VIII). Iodination of VIIC in chloroform leads to the corresponding triiodo derivative, composed of large dichroitic platelets of blackish green color with red metallic luster. The same product was obtained by treatment of the tribromo derivative with concentrated aqueous potassium iodide solution.

Similar halogenated derivatives of triazines obtained from benzoylbiuret by the synthesis of Ostrogovich[9] will be described in a subsequent communication. On the other hand, the acyclic derivatives, as benzoylbiuret and trimethylbiuret, failed to react with bromine under the above conditions.

Experimental

Trimethyl Isocyanuric Ester (VI).—Cyanuric acid was methylated with diazomethane in etheric suspension[11] to obtain the starting material for the present investigation; yield 90%; m. p. 174° (all melting points corrected).

1,3,5 - Trimethyl - 2 - phenyl - 2 - hydroxy - 4,6 - dioxohexahydrotriazine (VIIA).—Six hundredth mole of phenylmagnesium bromide was prepared from 9.6 g. of bromobenzene and 1.44 g. of magnesium in 150 cc. of dry ether and 0.01 mole (1.71 g.) of trimethylisocyanurate (VI) in 200 cc. of dry ether was added, causing the formation of a white precipitate. The mixture was refluxed for two hours on the water-bath and kept overnight at room temperature. The Grignard addition product was decomposed by addition of saturated ammonium chloride solution under cooling. The ethereal fractions were dried and evaporated and the resulting yellow oil crystallized upon addition of a few drops of petrolic ether. Recrystallization from benzene–petrolic ether, yield 1.68 g. (69% of calcd.), m. p. (dec.) 158–159°, gave white prisms, very soluble in methanol, ethanol, chloroform, dioxane, ether, hot glacial acetic acid and benzene; insoluble in cold water and in petrolic ether.

Anal. Calcd. for $C_{12}H_{15}O_3N_3$: C, 57.80; H, 6.08; N, 16.78; mol. wt., 249.14. Found: C, 57.44; H, 6.47; N, 16.89.

1,3,5 - Trimethyl - 2 - ethyl - 2 - hydroxy - 4,6 - dioxohexahydrotriazine (VIIB).—The ethyl derivative was obtained by analogous procedure. The substance, recrystallized from ether, melted at 112–113° and was very soluble in all organic solvents, except petrolic ether; soluble in water.

Anal. Calcd. for $C_8H_{15}O_3N_3$: C, 47.73; H, 7.52; N, 20.89; mol. wt., 201.14. Found: C, 48.38; H, 7.45; N, 20.64.

1,3,5 - Trimethyl - 2 - propyl - 2 - hydroxy - 4,6 - dioxohexahydrotriazine (VIIC).—This was also prepared and melted after recrystallization from ether at 129°; solubilities like the ethyl compound.

Anal. Calcd. for $C_9H_{17}O_3N_3$: C, 50.19; H, 7.96; N, 19.53; mol. wt., 216.16. Found: C, 50.45; H, 7.78; N, 20.00.

Reaction of Trimethyl Isocyanurate with C_6H_5MgBr in Benzene Solution.—C_6H_5MgBr was prepared as above from 1.44 g. of magnesium and 9.6 g. of bromobenzene and

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[9] A. Ostrogovich, *Gazz. chim. ital.*, **39**, 540 (1909); **44**, 562 (1914); **65**, 229 (1935); *Bul. Soc. Stiinte Cluj*, **4**, 521, 528 (1929).

[10] Liebig and Woehler, *Ann.*, **59**, 296 (1846); *cf.* Herzig, *Monatsh.*, **2**, 398 (1881).

[11] Palazzo and Scelsi, *Gazz. chim. ital.*, **38**, 659 (1908).

a solution of 0.85 g. of trimethyl isocyanurate in 200 cc. of benzene (dried over sodium) added slowly. The mixture was heated on a boiling water-bath for four hours, the ether gradually being distilled off on a descending condenser and the remaining solution finally refluxed. The material was decomposed and extracted as above. The residue crystallized on prolonged standing in the ice-box. It was recrystallized from benzene and from methanol; m. p. 161°, mixed m. p. with substance VIIA, 135°; with triphenylcarbinol, 161°.

Anal. Calcd. for $C_{19}H_{16}O$: C, 87.66; H, 6.19; mol. wt., 260.1. Found: C, 87.46; H, 6.36.

Reaction of Substance VIIA with Grignard Reagent.—C_6H_5MgBr was prepared from 0.48 g. of magnesium and 3.2 g. of bromobenzene in 100 cc. of dry ether and a solution of 0.8 g. of substance VIIA in 100 cc. of ether slowly added. After refluxing for two hours, the material was worked up as above. The oily ether residue crystallized on addition of petrolic ether and was recrystallized from benzene; m. p. and mixed m. p. with substance VIIA, 159°. From the mother liquors a small amount of triphenylcarbinol could be obtained.

Bromination of VIIA.—To 250 mg. of substance dissolved in 1 cc. of glacial acetic acid, 4.0 cc. of an 8% bromine solution in glacial acetic acid was added slowly. A red crystalline precipitate formed, which was filtered and washed with ether. During this procedure hydrogen bromide is lost and the color changes to dark yellow. Recrystallization from glacial acetic acid; yield 80%; m. p. 196°. The substance is very soluble in methanol, ethanol, soluble in hot glacial acetic acid and chloroform; insoluble in ether, petrolic ether, water.

Anal. Calcd. for $C_{12}H_{14}O_2N_3Br_3$: C, 30.52; H, 2.99; N, 8.90; Br, 50.81; mol. wt., 471.88. Found: C, 30.79; H, 3.09; N, 8.62; Br, 50.63.

Bromination of the Ethyl Derivative VIIB, as above.—The resulting tribromo derivative is soluble in water and organic solvents, except ether and petrolic ether, m. p. 128°.

Anal. Calcd. for $C_8H_{14}O_2N_3Br_3$: Br, 56.56; mol. wt., 423.88. Found: Br, 56.42.

Bromination of the Propyl Derivative VIIC.—Preparation and solubilities were as above, m. p. 151°.

Anal. Calcd. for $C_9H_{16}O_2N_3Br_3$: Br, 54.75; mol. wt., 437.90. Found: Br, 54.52.

Iodination of 1,3,5-Trimethyl-2-propyl-2-hydroxy-4,6-dioxohexahydrotriazine, VIIC.—Fifty milligrams of substance VIIC was dissolved in a few drops of chloroform and 2 cc. of a 12% solution of iodine in chloroform was added. On standing overnight the triiodo compound crystallized. The same substance was also obtained with better yield (90%) from the corresponding tribromo derivative VIIIC by shaking 50 mg. with a solution of 1 g. of potassium iodide in 3 cc. of water. Recrystallization from hot glacial acetic acid; m. p. 112–115°; soluble in methanol and ethanol.

Anal. Calcd. for $C_9H_{16}O_2N_3I_3$: I, 65.75; mol. wt., 578.90. Found: I, 64.92.

Summary

Trimethyl isocyanurate reacts with Grignard compounds to form 1,3,5-trimethyl-2-alkyl-(or aryl)-2-hydroxy-4,6-dioxohexahydrotriazines, into which three atoms of bromine or iodine may be introduced.

NEW YORK, N. Y. RECEIVED JULY 15, 1937

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

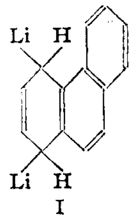
The Addition of Alkali Metals to Phenanthrene

BY ALLENE JEANES[1] AND ROGER ADAMS

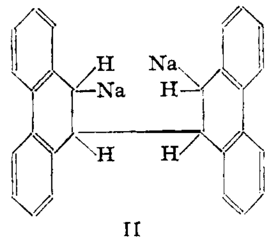
The addition of alkali metals to aromatic compounds was first studied intensively by Schlenk and Bergmann.[2] Since 1928 much interest has been shown in such compounds and they have proved to be valuable intermediates in synthetic work not only from a scientific but also from a practical standpoint.[3]

This communication contains a discussion of Schlenk's results on the addition of alkali metals to phenanthrene and a description of a detailed study of dialkaliphenanthrenes and their derivatives made in this Laboratory.

Schlenk[2] reported that lithium added to phenanthrene in the 1,4-positions (I). On the other hand, he showed that sodium reacted to form a substance reported as the 9,9′-biphenanthryl (II).



I



II

Ziegler[3a] obtained a compound corresponding to Schlenk's biphenanthryl (II) by the reaction

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(1) Abstract of a thesis submitted in partial fulfilment of the requirement for the degree of Doctor of Philosophy in Chemistry.

(2) Schlenk and Bergmann, *Ann.*, **463**, 84 (1928); see also Berthelot, *Ann. chim.*, [4] **12**, 155 (1867).

(3) (a) Ziegler and Bäher, *Ber.*, **61**, 253 (1928); (b) Ziegler and Crössmann, *ibid.*, **62**, 1768 (1929); (c) Ziegler and Wollschitt, *Ann.*, **479**, 123 (1930); (d) Ziegler, *Angew. Chem.*, **49**, 455 (1936); (e) N. D. Scott, U. S. Patents, 2,054,303, 2,019,832, 2,023,793, 2,027,000; (f) N. D. Scott, Walker and Hansley, THIS JOURNAL, **58**, 2442 (1936).