[Contribution from the Chemical Laboratory, Case School of Applied Science]

THE INTERACTION OF ISOCYANIC ACID AND ISOCYANATES WITH SOME ALKYL AND ARYL SCHIFF BASES AND WITH HYDRAZONES. ADDITION TO THE CH:N LINKAGE

By N. A. Lange

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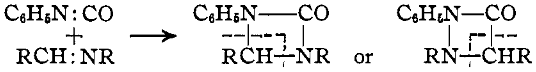
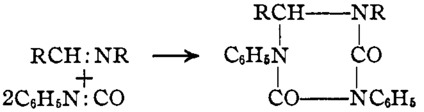
In previous communications[1] it has been shown that the addition of two molecular proportions of isocyanic acid to a Schiff base, where the alkyl groups ethyl, propyl, butyl and amyl are attached to the nitrogen atom of the C:N complex, resulted in the formation of a diketocyanidine. This reaction is analogous to the polymerization of cyanic acid to cyanuric acid and to the addition of two molecular proportions of a ketene to one of Schiff base.[2] As a continuation of this reaction, a further study has been made of the addition of phenylisocyanate to the same Schiff bases. The theoretical possibilities for such a condensation are few; reaction between the hydrogen attached to the carbon atom of the Schiff base and the oxygen atom of the isocyanate would be most unlikely, thus leaving direct addition at the double linkage between the carbon and the nitrogen atoms of the Schiff base as the expected point of attack. Equimolecular additions would then give 4-membered rings of two possible structures.



I II

The result could be distinguished easily, since such 4-membered rings are readily hydrolyzed as indicated by the dotted lines, I giving C_6H_5NHCO-NHR and RCHO while II would yield $RNH.N(C_6H_5)CHO$ and RCHO. Additions of two molecular proportions of isocyanate for one of Schiff base would give 6-membered rings containing three nitrogen atoms.



III

A 6-membered ring of this type would be expected to show the stability of cyanuric acid and, having no free amino or imino hydrogen, should not acetylate. The results of the experiments show that phenylisocyanate reacts with N-alkyl Schiff bases in the same manner as isocyanic acid, giving 6-membered diketocyanidines (III) which are stable, crystalline compounds, not affected by conditions likely to produce hydrolysis and not affected by acetylating agents. As compared with isocyanic acid, however, phenylisocyanate is not so reactive; whereas with the former,

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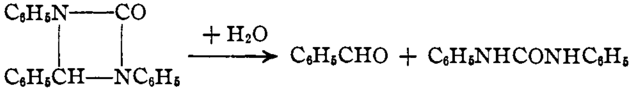
[1] Hale and Lange, This Journal, **41**, 379 (1919); **42**, 107 (1920).

[2] Staudinger, *Ann.*, **374**, 11 (1911); *Ber.*, **50**, 1042 (1917).

reaction takes place below room temperature, with the latter it is necessary to use temperatures above 150°; moreover, with phenylisocyanate the butyl and *iso*-amyl derivatives were never obtained in the many experiments under various conditions of time and temperature. Attempts to prepare the methyl derivatives from benzylidene-methylamine by the action of isocyanic acid in cold glacial acetic acid solution or by the action of phenylisocyanate at elevated temperatures were not successful. Molecular-weight determinations of the phenylisocyanate-benzylidene-ethylamine addition compound show conclusively that the compound is monomolecular.

All attempts to obtain addition compounds with phenylisocyanate and N-aryl Schiff bases were unsuccessful. Experiments with benzylidene-aniline or benzylidene-*p*-toluidine using one or two molecular proportions of phenylisocyanate for one of Schiff base gave results showing 6-membered rings are not produced. The reaction products had a decided odor of phenylisocyanate and when steam distilled gave the corresponding *sym.*-disubstituted ureas, the formation[3] of which can be accounted for by 4-membered ring formation or by hydrolysis of unchanged Schiff base and subsequent reaction of the liberated amine with the unchanged isocyanate.



or

(1) $C_6H_5CH{:}NC_6H_5 + H_2O \longrightarrow C_6H_5CHO + C_6H_5NH_2$

(2) $C_6H_5NH_2 + C_6H_5NCO \longrightarrow C_6H_5NHCONHC_6H_5$

Similar results were obtained in the interaction of isocyanic acid with N-aryl Schiff bases in glacial acetic acid, although in these cases the ureas condensed further with the aldehyde set free, giving white, highly insoluble ureides which probably are polymerized forms of the simple compound $C_6H_5CH(NHCONHR)_2$. These same insoluble ureides were obtained by direct condensation of the aldehyde and the substituted urea.

Attempts were made to bring about the addition of phenylisocyanate to the CH:N group in benzylidene and ethylidene *asym.*-diphenylhydrazones, compounds having no imino hydrogen. Numerous experiments under various conditions failed to bring about the addition; this failure to add to the CH:N group of phenylhydrazones finds its counterpart in the chemistry of the ketenes where such attempted additions met with failure.[4] Previous work of others has shown that hydrazones having imino hydrogen do add isocyanates. Benzylidene-phenylhydrazone is reported as adding phenylisocyanate to the imino nitrogen when warmed to 170° forming 1-benzylidene-2,4-diphenylsemicarbazone; likewise, benzylidene-benzylhydrazone with isocyanic acid gives 1-benzylidene-2-benzylsemicarbazone.[5]

[3] Senier and Shepheard, *J. Chem. Soc.*, **95**, 504 (1909).

[4] Staudinger, "Die Ketene," F. Enke, Stuttgart, **1912**, p. 71.

[5] Busch and Walter, *Ber.*, **36**, 1360 (1903).

Experimental Part

The Schiff bases employed in this investigation were prepared by adding an equimolecular quantity of freshly distilled benzaldehyde to the amine in question (ethyl, propyl, phenyl, etc.), at 5–10°, extracting the solution with ether, washing with water and drying the ether solution over anhydrous potassium carbonate. After evaporation of the ether, the Schiff base remaining was distilled, if a liquid or, if a solid, recrystallized from alcohol.

1-Ethyl-3,5,6-triphenyl-2,4-diketo-hexahydrocyanidine, $C_2H_5.C_3HO_2N_3(C_6H_5)_3$.—A mixture of two molecular proportions of phenylisocyanate and one of benzylidene-ethylamine was sealed in a glass tube and heated to 180–200° for about four days; after the tube had cooled it was opened. The viscous reaction product was treated in the tube with an equal volume of alcohol and a few drops of ether. The crystals which usually separated after a short time were filtered off, washed with ether and recrystallized from alcohol. If no separation of crystals occurred after the addition of alcohol and ether to the original reaction mixture, overheating was indicated, in which case a low yield of the product could be obtained by steam-distilling the viscous material for several hours, decanting the water from the non-volatile residue and adding ether to this to remove the resinous impurities, leaving the insoluble crystalline cyanidine condensation product. It was found that the yield varied with the length of time of heating; the following yields of condensation product were obtained at 180–200°: after 48 hours, 21.4%; 72 hours, 36.6%; 96 hours, 39%; 120 hours, 29%; and after 168 hours at room temperature, 23.4%. The cyanidine is readily soluble in ethylene chlorohydrin or chloroform, fairly soluble in ethyl acetate, benzene, toluene, xylene, methyl alcohol, ethyl alcohol or amyl alcohol, slightly soluble in carbon tetrachloride and insoluble in water, ether or petroleum ether. It forms colorless crystals melting at 192° (corr.). When steam is passed through a suspension of the compound in hydrochloric acid or aqueous sodium hydroxide no hydrolysis occurs; the compound remains unchanged when boiled with acetic anhydride and fused sodium acetate. Molecular-weight determinations by depression of the freezing point were made with naphthalene as the solvent; the values obtained on 18 determinations of various concentrations gave a mean value of 380; the calculated value is 371.[6]

Anal. Calcd. for $C_{23}H_{21}O_2N_3$: C, 74.35; H, 5.70; N, 11.3. Found: C, 74.62; H, 5.74; N, 11.3.

1-Propyl-3,5,6-triphenyl-2,4-diketo-hexahydrocyanidine.—This compound was obtained in very poor yields by heating one molecular proportion of benzylidene-propylamine with two of phenylisocyanate in sealed tubes at 180–200°. Attempts to determine the optimum length of time of heating were unsuccessful, as in many cases tubes under supposedly identical conditions gave different yields varying from nothing to about 10% of the calculated amount. The values obtained on combustion were sufficient to identify it as the propyltriphenyldiketo-hexahydrocyanidine. It is fairly soluble in benzene, methyl alcohol, ethyl alcohol, carbon tetrachloride or acetone and insoluble in water, ether or petroleum ether. It forms colorless crystals from alcohol; m. p., 156° (corr.).

Anal. Calcd. for $C_{24}H_{23}O_2N_3$: C, 74.77; H, 6.02; N, 10.9. Found: C, 74.85; H, 6.01; N, 10.7.

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[6] The writer is indebted to Mr. Milton Zucker for these molecular-weight determinations.

1-Ethyl-6-phenyl-3,5-di(*p*-tolyl)-2,4-diketo-hexahydrocyanidine.—This compound was obtained in a 21% yield on heating one molecular proportion of benzylidene-ethylamine with two of *p*-tolylisocyanate in a sealed tube at 180–200° for 118 hours. After cooling, an equal volume of alcohol and a few drops of ether were added to the reaction mixture; after several hours, crystals of the condensation product separated; these were filtered off, washed with ether and recrystallized from alcohol. The substance formed colorless crystals which were fairly soluble in methyl alcohol, ethyl alcohol, carbon tetrachloride or acetone, slightly soluble in benzene and insoluble in water, ether or petroleum ether; m. p., 173° (corr.). It was not hydrolyzed on steam distillation in aqueous acid or alkaline suspensions and was not acetylated when boiled with acetic anhydride and fused sodium acetate.

Anal. Calcd. for $C_{25}H_{25}O_2N_3$: C, 75.15; H, 6.31; N, 10.5. Found: C, 74.62; H, 6.40; N, 10.2.

Benzylidene-bis-*p*-tolylureide; $[C_6H_5CH(NHCONHC_6H_4CH_3)_2]_x$.—A 1.2-g. yield of this ureide was obtained when 5.5 g. of benzylidene-*p*-toluidine in cold glacial acetic acid was treated with 4.6 g. of potassium cyanate and allowed to stand in the cold for 24 hours. The solid that separated was filtered off, washed successively with water, alcohol, hot acetone and then ether; the white powder thus obtained is insoluble in the common organic solvents; m. p., 206–208° (corr.).

Anal. Calcd. for $C_{23}H_{24}O_2N_4$: C, 71.10; H, 6.23; N, 14.4. Found: C, 71.16; H, 6.24; N, 14.3.

The same compound was obtained when two molecular proportions of *p*-tolyl urea and one of benzaldehyde in glacial acetic acid were warmed and then allowed to stand at room temperature; the white solid that separated was purified as described above.

Anal. Calcd. for $C_{23}H_{24}O_2N_4$: N, 14.4. Found: 14.8.

Both products hydrolyzed when steam-distilled in dil. hydrochloric acid, giving benzaldehyde and *p*-tolyl urea.

Benzylidene-bis-*o*-tolylureide, $[C_6H_5CH(NHCONHC_6H_4CH_3)_2]_x$.—This compound was obtained in a 1.8-g. yield from 6 g. of benzylidene-*o*-toluidine and 4 g. of potassium cyanate in acetic acid and was purified in the same manner as the *p*-toluidine isomer above. It formed a white powder insoluble in the common organic solvents; m. p., 199–200° (corr.).

Anal. Calcd. for $C_{23}H_{24}O_2N_4$: C, 71.10; H, 6.23; N, 14.4. Found: C, 71.29; H, 6.33; N, 13.8.

The same compound was obtained by the interaction of benzaldehyde with two molecular proportions of *o*-tolyl urea in glacial acetic acid.

Anal. Calcd. for $C_{23}H_{24}O_2N_4$: C, 71.10; H, 6.23; N, 14.4. Found: C, 70.92; H, 6.27; N, 14.1.

Both products, when steam-distilled in dil. hydrochloric acid, hydrolyzed forming benzaldehyde and *o*-tolyl urea.

Phenylisocyanate with Benzylidene-*p*-toluidine and with Benzylidene-aniline.—When benzylidene-*p*-toluidine and two molecular proportions of phenylisocyanate were heated in a sealed tube to 180–200° for 120 hours, a clear viscous liquid was obtained having a decided odor of phenylisocyanate. No crystals separated on standing nor were any obtained on treatment of the reaction mixture with various solvents. When steam distilled, benzaldehyde and *sym.*-*p*-tolylphenyl urea were obtained. When two molecular proportions of phenylisocyanate were heated with one of the same Schiff base the same results were obtained. Similar results were obtained when benzylidene-aniline replaced the benzylidene-toluidine; the products isolated from this reaction were correspondingly benzaldehyde and *sym.*-diphenyl urea.

Phenylisocyanate with α-Benzylidene-β,β-diphenylhydrazone and with α-Ethylidene-β,β-diphenylhydrazone.—Sealed tubes containing one molecular proportion of benzylidene-diphenylhydrazone with one of phenylisocyanate and with two of phenylisocyanate were heated for various periods of time at 180–200°. A light brown, viscous liquid was obtained which solidified to a transparent resin on cooling; benzylidene-phenylhydrazone was the only crystalline material that could be obtained from a solution of this resin in alcohol. The mother liquors on evaporation left a resin from which no crystalline substances could be isolated either before or after steam-distillation. Ethylidene-diphenylhydrazone, when heated with one and with two molecular proportions of phenylisocyanate, similarly gave resinous products from which phenylcyanurate was the only crystalline product isolated.

Summary

Phenylisocyanate resembles the ketenes in the addition compounds that it forms with some alkyl Schiff bases, two molecular proportions adding to yield a 6-membered ring; aryl Schiff bases, on the other hand, do not give similar compounds, probably adding but one molecular proportion of the isocyanate to form unstable 4-membered rings which could not be isolated; attempts to add phenylisocyanate to the CH:N linking in hydrazones were not successful.

Cleveland, Ohio

[Contribution from the Chemical Laboratory of the University of Illinois]

SYNTHESIS OF A HOMOLOG OF CHAULMOOGRIC ACID. Δ²-CYCLOPENTENYLACETIC ACID. VII

By C. R. Noller[1] with Roger Adams

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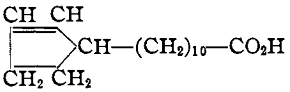
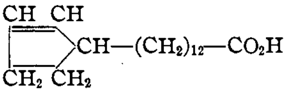
The successful syntheses of dihydrohydnocarpic and dihydrochaulmoogric acids[2c] and many of their homologs[2g] has led us to determine whether a similar procedure might not be employed to obtain hydnocarpic acid (I) and chaulmoogric acid (II) and their homologs.



I



II

Although the preparation of hydnocarpic acid itself,[2a] the immediate goal, has not yet been reached, nevertheless a very important step forward has been made by finding a most satisfactory method for preparing certain Δ²-cyclopentenyl compounds which may be used as intermediates in syn-

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[1] This communication is an abstract of a portion of a thesis submitted by C. R. Noller in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry at the University of Illinois.

[2] (a) Shriner with Adams, This Journal, **47**, 2727 (1925). (b) Noller with Adams, *ibid.*, **48**, 1074; (c) 1080 (1926). (d) Hiers with Adams, *ibid.*, **48**, 1089 (1926). (e) VanDyke and Adams, *ibid.*, **48**, 2393 (1926). (f) Sacks with Adams, *ibid.*, **48**, 2395 (1926). (g) Hiers with Adams, *ibid.*, **48**, 2385 (1926).