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THE REACTION OF 1,1-DIPHENYLHYDRAZINE WITH DICHLOROCARBENE

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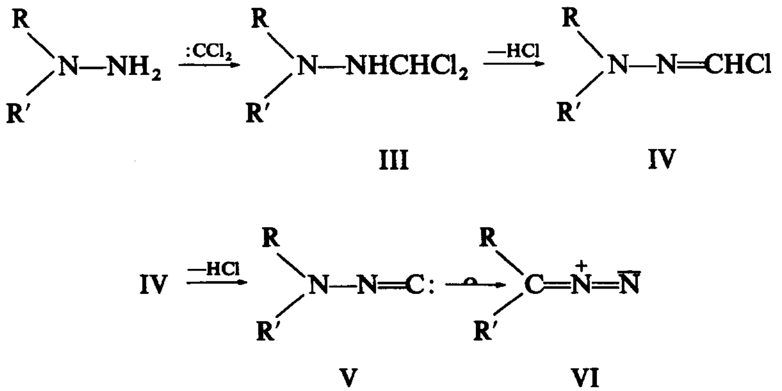
Abstract—The reaction of 1,1-diphenylhydrazine with chloroform in the presence of potassium hydroxide gives diphenylamine as the major product and *not* benzophenone as originally reported. This seems to be the favored path regardless of the source of dichlorocarbene. Diphenylcyanamide (but not the isomeric isonitrile) was identified in trace amounts. The reaction of phenylhydrazine under similar conditions has been also reinvestigated and gave N,N'-diphenylformazan; aniline and phenyl isonitrile have also been identified. A mechanism for the rationalization of these results is presented.

INTRODUCTION

MORE than fifty years ago, Staudinger and Kupfer[2] obtained diazomethane (II) in 30% yield by treatment of hydrazine with chloroform in the presence of potassium hydroxide. The expected product diisonitrile (I) which would have resulted from a double Hofmann reaction[3] of hydrazine could not be detected.

$$\underset{\text{I}}{:C{=}N{-}N{=}C:} \xleftarrow[OH^-]{2CHCl_3} H_2NNH_2 \xrightarrow[OH^-]{CHCl_3} \underset{\text{II}}{CH_2{=}\overset{+}{N}{=}\overline{N}} \tag{1}$$

Presumably, the initial adduct (III) of dichlorocarbene (generated by the reaction of potassium hydroxide on chloroform) with hydrazine lost two molecules of hydrogen chloride and gave N-amino isonitrile (V). At this point, V was apparently diverted to an unexpected path (to give diazomethane) before the attack of a second dichlorocarbene. Although Staudinger and Kupfer proposed V(R = R' = H) as the intermediate which underwent rearrangement to II (VI, R = R' = H), no evidence for its existence was adduced nor was a path for this double migration suggested.

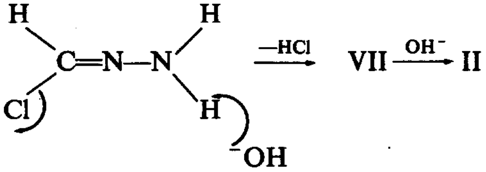


(2)

No further investigations of this reaction have been reported since the initial work in Germany.[4] The study of the chemistry of isodiazomethane, formulated up to 1968[11] as VII, had shown that it could be converted by the action of potassium hydroxide to diazomethane presumably *via* the diazomethyl anion (VIII) as depicted in reaction 3.[5,6] Müller viewed the formation of diazomethane from hydrazine and dichlorocarbene as arising from the 1,3-elimination of hydrogen chloride from IV (R,R′ = H) to give VII[5,7] followed by the conversion of VII to II (reaction 4).

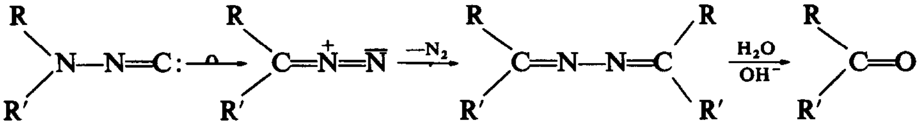
$$H\bar{C}{=}\overset{+}{N}{=}N{-}H \underset{H_2PO_4^-}{\overset{OH^-}{\rightleftharpoons}} H{-}\bar{C}{=}\overset{+}{N}{=}\bar{N} \underset{CH_3Li}{\overset{H_2O,\,OH^-}{\rightleftharpoons}} H_2C{=}\overset{+}{N}{=}\bar{N} \qquad (3)$$

VII VIII II



(4)

Although Müller's mechanism can reasonably account for the formation of diazomethane, Staudinger and Kupfer also reported that 1,1-diphenylhydrazine treated under the same conditions[2a] gave benzophenone in 60% yield! Evidently, in this case, the participation of the N-amino isonitrile V(R = R′ = Ph) would seem unavoidable in rationalizing the formation of benzophenone. Presumably, the ketone arose *via* hydrolysis of benzophenone azine (X, R = R′ = Ph), itself generated from diphenyldiazomethane (IX, R = R′ = Ph). The formation of diphenyldiazomethane would require the astounding *double* migration of the phenyl groups from nitrogen to carbon (VI → IX).



(5)

VI IX X XI

RESULTS

The intriguing and far-reaching implications of this putative double migration spurred our interest in the reaction. The formation of diazomethane has been well established experimentally by Staudinger and Kupfer[2a] and confirmed more recently by McManus and his students.[2b] The initial purpose of our investigation was to duplicate and confirm the results[2a] obtained with 1,1-diphenylhydrazine. It was our intention next to modify the experimental conditions so as to perhaps isolate the intermediate N-amino isonitrile (VI) and have it undergo the rearrangement in a separate step.

The reaction of 1,1-diphenylhydrazine with chloroform in the presence of potassium hydroxide yielded a compound, m.p. 48–49°, apparently benzophenone, in the same yield (59%) and with the same m.p. as previously reported.[8] However, its IR spectrum was devoid of *any* absorption in the carbonyl region but displayed a band at 3400 cm^{-1}; the compound contained nitrogen and was identified as diphenylamine by its m.p. and the comparison of its IR spectrum with that of an authentic sample.

The surprising discovery that diphenylamine and *not* benzophenone was formed, prompted a thorough study of all the parameters of the reaction. Commercial absolute ethanol was dried over magnesium ethoxide and distilled; distilled *spectro* grade chloroform previously dried over calcium chloride and *pure, colorless* 1,1-diphenylhydrazine[9] were used. Again, the original conditions of Staudinger and Kupfer were duplicated as closely as the details given allowed; the ethanolic solution of chloroform was added over a period of 3 hr at 40° (the literature indicates "in der Warme"). Again, diphenylamine was obtained in the same yield; its identity was further confirmed by the preparation of its benzoyl derivative which was identical in all respects with authentic N-benzoyl diphenylamine. In order to insure that benzophenone was not being overlooked, the reaction mixture was worked up very carefully; an 82·5% yield of diphenylamine was obtained by distillation. Chromatographic separation of the residue gave an additional amount of diphenylamine whose total yield amounted to 90%. In addition, 5% of a carbonyl containing compound, identified as 2,2-diphenylformylhydrazine and trace amounts (0·1 g, 2·3 %) of a material, m.p. 65–67°, containing a moderately strong band at 2205 cm^{-1}, subsequently identified as diphenylcyanamide (XII) were isolated. These results confirmed that *no* benzophenone was being formed in the reaction since better than 97% of the starting hydrazine was accounted for!

Even though it was clear that the original report was in error, the reaction of 1,1-diphenylhydrazine with dichlorocarbene generated from different sources and under varying conditions, was investigated further. In all the cases (Table 1) studied, diphenylamine was isolated as the principal product.*

TABLE 1 REACTION OF 1,1-DIPHENYLHYDRAZINE WITH DICHLOROCARBENE

Conditions (solvent, temp)	Carbene source	Products (%) Ph_2NH	Ph_2NCN	others
Ethanol, 40°	$CHCl_3$, KOH	90	2·3	*a*
Cyclohexane, 0–10°	$CHCl_3$, t-BuOK	50	0·2	*b*
Cyclohexane, 0–5°	$Cl_3CCOCCl_3$, $NaOCH_3$	60	traces	
Benzene, 80°	Cl_3CO_2Na	30	traces	*c*

[a] $Ph_2NNHCHO$ (5%).

[b] Ph_2NCONH_2 (0·3%); $Ph_2NCONPh_2$ (0·3%).

[c] Reaction not complete; unidentified carbonyl containing compounds formed.

The reaction of phenylhydrazine with chloroform in the presence of potassium hydroxide[2a] was also investigated. Aniline and phenyl isonitrile were identified among the volatile products by comparison of their IR spectra with those of authentic samples. In addition to unidentified carbonyl containing compounds, an unstable compound

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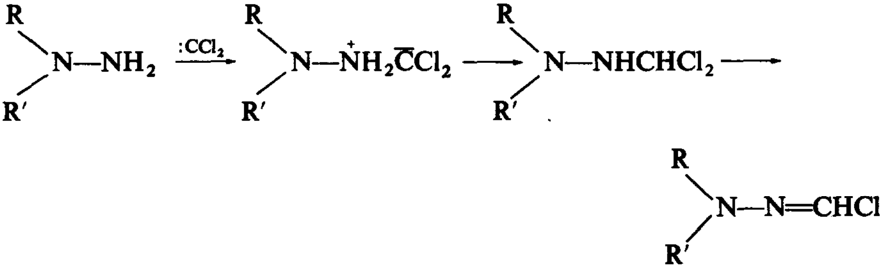
* Diphenylamine has also been obtained as an inevitable product in several attempts to prepare diphenylamino isonitrile by other routes, N. Koga and J.-P. Anselme, Unpublished results.

having a band at 2090 cm^{-1} was also present. The only product isolated in 24% yield was identified as diphenylformazan (XIII).

DISCUSSION

The initial stages of the reaction of dichlorocarbene with hydrazine, phenylhydrazine and 1,1-diphenylhydrazine probably follow a common path to give the formhydrazonoyl chlorides (IV).

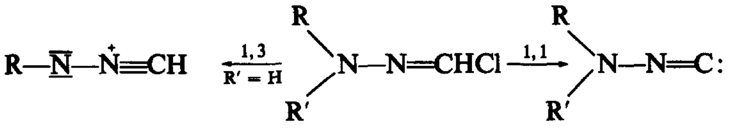


(6)

IV

Although Müller and his students[10] have recently proved that isodiazomethane is in reality the parent N-amino isonitrile (V, R,R′ = H), and *not* the nitrilimine VII, the mechanism suggested earlier by Müller (reaction 4) to explain the formation of diazomethane reported by Staudinger and Kupfer seems simpler and more reasonable than the one involving N-amino isonitrile (V). An intermediate such as VII offers one advantage over V, *viz*, only one hydrogen has to migrate from N to C to give diazomethane. However, the choice of VII over Va as an intermediate is only an intuitive one.

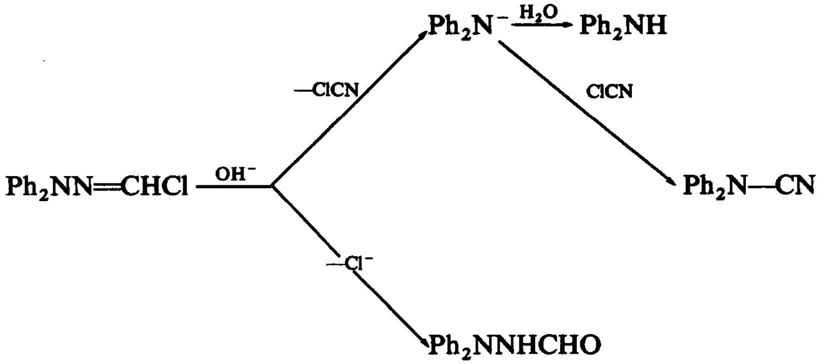
While the elimination of hydrogen chloride from formhydrazonoyl and phenylformhydrazonoyl chlorides (IV, R = R′ = H and R = Ph, R′ = H respectively) may proceed by two routes (reaction 7), diphenylformhydrazonoyl chloride (IV, R = R′ = Ph) can lose hydrogen chloride in only one way to give the N-amino isonitrile V (R = R′ = Ph). However, the formation of the products isolated can be best explained without the participation of diphenylamino isonitrile.



(7)

IV V

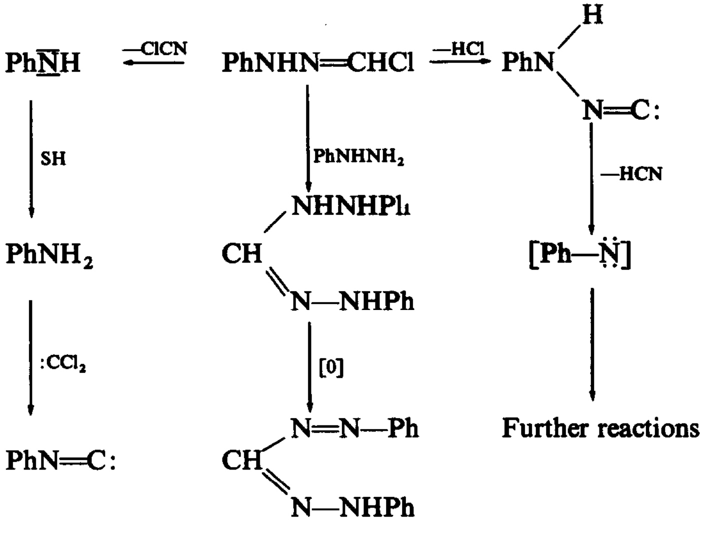
Base-induced fragmentation of IV (R = R′ = Ph) would give cyanogen chloride and the relatively stable diphenylamine anion. Recombination of these two fragments (perhaps in the solvent cage) could account for the small amount of diphenylcyanamide (XII); it seems unlikely that an isonitrile-nitrile rearrangement (V → XII) would occur under the mild conditions of our reaction in view of the high temperatures required for this rearrangement,[11] attack of hydroxide ion on IV would lead to 2,2-diphenylformylhydrazine. Similarly, IV (R = H, R′ = Ph) may fragment to cyanogen chloride and aniline (after proton abstraction from the solvent). Reaction of aniline



(8)

XII

with dichlorocarbene would give phenyl isonitrile. The reaction of phenylformhydrazonoyl chloride with phenylhydrazine presumably gave the hydrazidine which was then oxidized to N,N′-diphenylformazan (XIII). The unstable product detected by the presence of a band at 2090 cm^{-1} may be the corresponding α-elimination product, phenylamino isonitrile (V, R = H, R′ = Ph). The large amount of tars and dark materials obtained in this reaction could be rationalized *via* this compound since the elimination of hydrogen cyanide[12] would generate phenylnitrene.



XIII

The results obtained herein coupled with those of Bredereck, Föhlish and Walz[13] can help rationalize the failure of N-amino piperidine and 1,1-*bis*(*p*-chlorophenyl)-hydrazine to give the corresponding isonitriles.[14] Elimination of hydrogen cyanide, as shown by Bredereck *et al.*,[13] probably took place very readily under the strongly basic conditions used by Smith and Kalenda.[14] As for the diaryl case, the two chlorines would stabilize the diarylamine anion to an even greater extent than in the unsubstituted compound.

CONCLUSION

The results of our studies clearly show that the formation of diazomethane from hydrazine and dichlorocarbene is *not* a general reaction of hydrazines and in fact is probably restricted to hydrazine itself. Even if the presumed intermediate N-amino isonitriles were able to survive the strongly basic conditions,[13] the formation of dialkyl diazoalkanes would still require the unprecedented *double migration* of the alkyl groups from nitrogen to carbon.

The ease of fragmentation of 1,1-diphenylhydrazine suggests that this reaction may prove to be a useful deamination procedure for 1,1-diarylhydrazines which do not bear substituents sensitive to the reaction conditions.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. IR spectra were obtained either as neat liquids or as KBr pellets on a Perkin–Elmer 137 Spectrophotometer (Infracord).

1. *Reaction of* 1,1-*diphenylhydrazine with dichlorocarbene*: A. *Chloroform as source of dichlorocarbene*

(a) *In ethanol* (Staudinger and Kupfer procedure[2a])

To a soln of 10 g (0·18 mole) KOH in 100 ml EtOH, 4·4 g (0·024 mole) 1,1-diphenylhydrazine was added. To this mixture kept at 40°, a soln of 6 g (0·05 mole) CHCl$_3$ in 20 ml EtOH was added over a period of 3 hr with stirring. During the addition, a vigorous reaction took place and the mixture became orange in color. After completion of the addition, the mixture was heated under reflux for 2 hr; EtOH and excess CHCl$_3$ were removed by distillation. After the addition of 50 ml water, the residue was extracted with 200 ml ether. The ethereal extract was dried over MgSO$_4$ and evaporated. The residue was distilled *in vacuo*. The first fraction consisted of essentially pure diphenylamine (3·3 g), b.p. 135–145°/2·5 mm. The second fraction (1 g), b.p. 145–175°/2·5 mm was chromatographed (Fisher Scientific Company alumina A-540). Elution with 1:1 benzene-n-hexane gave 0·3 g diphenylamine. Diphenylcyanamide (0·11 g) and 2,2-diphenylformylhydrazine (0·25 g) were eluted next with benzene and MeOH respectively.

An aliquot from the residue of the distillation treated with 2,4-dinitrophenylhydrazine did not give a positive carbonyl test.

(b) *In cyclohexane.* 1,1-Diphenylhydrazine (16·3 g, 0·09 mole) was added to a suspension of t-BuOK, prepared from 11·7 g (0·3 g-atom) K, in 200 ml cyclohexane. To the above mixture kept at 0–10°, was added over a period of 2 hr a soln of 11·9 g (0·1 mole) CHCl$_3$ in 50 ml cyclohexane. The mixture was kept at room temp for 1·5 hr. Ice water (300 ml) was added and the mixture was extracted with two 100 ml portions ether. The ethereal extract was dried over MgSO$_4$ and the solvent evaporated. Distillation of the residue gave two fractions: the first (6 g), b.p., 120–130°/1 mm was pure diphenylamine. The second fraction (3 g), b.p. 130–180°/1 mm, was chromatographed as before and gave the following compounds (elution solvent given in parentheses).

diphenylamine	1·3 g (1:1 benzene-n-hexane)
diphenylcyanamide	0·3 g (benzene)
tetraphenylurea	0·5 g (1:1 benzene–ether)
1,1-diphenylurea	0·5 g (methanol)

All the compounds were identified by mixture m.p. and comparison of their IR spectra with those of authentic samples.

B. *Hexachloroacetone in cyclohexane*

To a cold suspension of 2·2 g (0·04 mole) NaOMe in 100 ml cyclohexane was added 1·84 g (0·01 mole) diphenylhydrazine. To this mixture kept at 0–5° was added over a period of 2 hr, 5·2 g (0·02 mole) hexachloroacetone. After the addition, the mixture was allowed to stand at room temp for 0·5 hr. Then, 100 ml ether was added and the inorganics were filtered off. The solvent was evaporated and the residue distilled *in vacuo* to give 1·05 g (60 %) diphenylamine. Examination of the IR spectrum of the residue indicated the presence of diphenylcyanamide and of carbonyl containing compounds.

The reaction of 1,1-diphenylhydrazine with dry sodium trichloroacetate as the dichlorocarbene source in boiling benzene gave essentially identical results except that the yield of diphenylamine was lower (Table 1).

2. *Reaction of phenylhydrazine with dichlorocarbene*

To a soln of 10 g (0·092 mole) phenylhydrazine in 150 ml EtOH was added over a period of 3 hr a soln of 20 g (0·185 mole) $CHCl_3$ in 50 ml EtOH. The temp was kept at 20–30°. The mixture which had become deep red in color, was kept at 25° for 1·5 hr after the completion of the addition. The inorganic solid was filtered, washed with ether and the combined organic phase was evaporated *in vacuo* at room temp. After addition of 100 ml ether, the soln was washed with water and dried. Upon evaporation of the solvent, the residue deposited 2 g (24%) red crystals, m.p. 92–93°. Two recrystallizations from n-hexane gave pure N,N'-diphenylformazan, m.p. 115–117°, identical in all respects with an authentic sample. Distillation of the residue gave 2 g phenylhydrazine and 1·8 g higher boiling liquids (C=O, —CHO). From the trap, a mixture (0·1 g) aniline, phenyl isonitrile (as shown by comparison of their IR spectra with those of authentic samples) and an unstable compound having an absorption at 2090 cm^{-1} was isolated. The band at 2090 cm^{-1} disappeared upon standing.

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