REACTION OF 1,3-DIPHENYLNITRILIMINE WITH BENZALDEHYDE PHENYLHYDRAZONE

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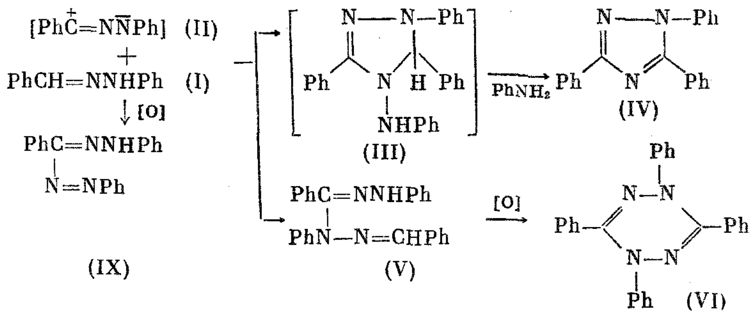
Nitrilimines, like other 1,3-dipolar reagents (1,3-DPR), are not only capable of 1,3-dipolar cycloaddition, but also of reacting with compounds of type RXH, which contain a labile hydrogen [1-8], and of entering into dimerization, rearrangement, and other reactions [1]. Although it was postulated that the 1,3-DPR react more slowly with compounds of type RXH than with dipolarophiles [3], still kinetic measurements were not made, and apparently the rates of both reactions can vary in a broad range. Consequently, for dipolarophiles of general formula d = c-f-XH, which contain both a multiple bond and a group with a labile hydrogen (unsaturated alcohols, acids and amines, enols, oximes, hydrazones, amidines, etc.), it is possible to have competing reactions of the 1,3-DPR with the XH group. For example, the reaction of N,N-unsubstituted hydrazones with nitrilimines proceeds at the NH_2 group, and the formation of the 1,3-cycloadducts at the C=N bond was not observed [7]. Taking into account the reactivity characteristics of the 1,3-DPR makes it possible to not only expand the possibilities of their use in synthesis (for example, on the basis of their reaction with RXH), but also to correctly predict the directions of the competing reactions.

When benzaldehyde phenylhydrazone (I) was reacted with 1,3-diphenylnitrilimine (II) (from 2,5-diphenyltetrazole in refluxing anisole), we isolated only 1,3,5-triphenyl-1,2,4-triazole (IV) and aniline [4], i.e., the subsequent transformation products of the initially formed 1,3-cycloadduct: 1,3,5-triphenyl-4-anilino-1,2,4-triazoline-2 (III). The competing reaction of nitrilimine (II) at the NH group of hydrazone (I) could be expected to give either 1,4-diphenyl-2-benzylidenehydrazidine (V) or its subsequent transformation products, for example, 1,3,4,6-tetraphenyl-1,4-dihydro-1,2,4,5-tetrazine (VI).



In order to check if the NH group of arylhydrazones can take part in the reaction with nitrilimines we made a detailed study of the reaction of hydrazone (I) with nitrilimine (II), which was generated from benzoyl chloride phenylhydrazone [PhC(Cl)=NNHPh (VII)] by treatment with triethylamine.

When hydrazone (I) was reacted with nitrilimine (II), generated from 2,5-diphenyltetrazole under the conditions given in [4], we unexpectedly isolated benzyl β-phenylosazone (VIII) as the main product and a small amount of hydrazidine (V). When the complex mixture of products obtained here was analyzed by TLC we were also able to record the presence of triazole (IV), dihydrotetrazine (VI), 1,3,5-triphenylformazan (IX), benzanilide (X), and the thermolysis products of hydrazidine (V), namely (XI) and (XII).

The formation of osazone (VIII) in this case is due to the thermal rearrangement of hydrazidine (V) (apparently a 1,3-sigmatropic shift, and not a radical process), since in the control experiment under the same conditions compound (V) is 70% converted to osazone

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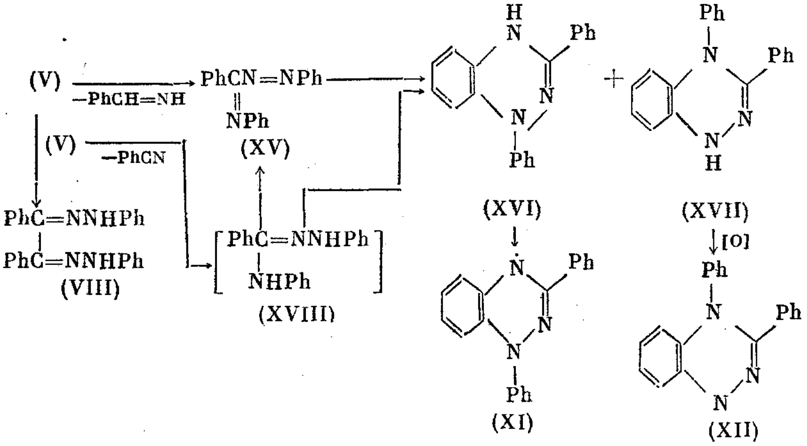
(VIII). Another direction for the thermal transformation of hydrazidine (V) is cleavage at the N—N bond. Here are formed benzonitrile, the stable radical (XI), described in [9] as being 1,3-diphenyl-1,4-dihydro-1,2,4-benzotriazinyl-4, the radical (XII), which is apparently isomeric with radical (XI), i.e., 3,4-diphenyl-1,4-dihydro-1,2,4-benzotriazinyl-1, and two products (XIII) and (XIV) of unestablished structure. The formation of several other products could be recorded only by chromatography due to their small amount in the reaction mixture. Cleavage of the N—N bond during the thermolysis of hydrazidine (V) can be depicted by two paths: by the cleavage of benzaldehyde imine with the formation of azoimine (XV) or by the cleavage of benzonitrile with the formation of benzanilide amidrazone (XVIII). The latter, either via the step of azoimine (XV) or directly, is cyclized to 1,3-(XVI) and to 3,4-diphenyl-1,4-dihydro-1,2,4-benzotriazines (XVII), which are easily converted to radicals (XI) and (XII). For example, when radical (XI) is reduced by ascorbic acid to leuco base (XVI) the latter was again converted to radical (XI) even during isolation.

Azoimine (XV) is heat unstable and in refluxing anisole it is converted within 20 min completely to radicals (XII) and predominantly (XI).



The reaction of hydrazones (I) and (VII) in the presence of triethylamine (generation of 1,3-diphenylnitrilimine under milder conditions) also proceeds unequivocally and the composition of the formed products is strongly dependent on the reaction conditions. Thus, in refluxing benzene in an argon atmosphere the products are 32.6% of hydrazidine (V) and small amounts of triazole (IV), dihydrotetrazine (VI), osazone (VIII), and formazan (IX). The yield of hydrazidine (V) increases to 40.2% when the reaction time is increased to 14 h. The yield of the hydrazidine dropped to 29.1%, and the amount of formazan (IX) increased, when this experiment was repeated in air.

The obtained results make it possible to conclude that irrespective of the method of generation, nitrilimine (II) reacts predominantly with the NH group of benzaldehyde phenylhydrazone (I) to give hydrazidine (V), and to a much lesser degree via 1,3-dipolar cycloaddition to the C=N bond, which leads in the final analysis to triazole (IV). The possibility of forming hydrazidine (V) via oxidative processes is slight and cannot be competitive with the reaction of the 1,3-dipole with the NH group of hydrazone (I). Thus, when a benzene solution of hydrazone (I) was left standing for a long time in the presence of triethylamine at 20-25°C in air we were able to record only traces of hydrazidine (V) and dihydrotetrazine (VI) (a substantially larger amount of formazan (IX) is formed here), whereas the addition of chlorohydrazone (VII) to the reaction medium leads to the formation of either 27% (6 days) or 34.5% (40 days) of hydrazidine (V), despite an intensification of the oxidative processes. The formation of other products is explained by a series of parallel and consecutive reactions. Thus, dihydrotetrazine (VI) is apparently formed only by the [3 + 3]-dimerization of nitrilimine (II) and by its reaction with the anion of chlorohydrazone (VII), as was shown in [1, 4, 10], since its formation was not observed during the thermolysis of hydrazidine (V) in refluxing anisole.

In all of the studied cases the formation of formazan (IX) was due to the secondary autooxidation of both hydrazone (I) [11] and chlorohydrazone (VII). In THF, for example, this direction predominates and only formazan (IX) can be isolated. Formazan (IX) is also formed during the separation of the reaction mixtures, especially during chromatography on

Al_2O_3 columns, and also when solutions of hydrazone (I) or chlorohydrazone (VII) in THF, benzene, alcohol, or acetone are left standing. Formazan (IX) is formed from hydrazone (I) via the step of the arylazo peroxide Ph(COOH)N = NPh and its decomposition to the diazo salt (the coupling with (I) gives (IX)) [11]. Water and PhCOOH are also formed here, which with either nitrilimine (II) or chlorohydrazone (VII) give 1-benzoyl-2-phenylhydrazine (XIX) and 1,2-dibenzoyl-2-phenylhydrazine (XX). The isolation of substantial amounts of hydrazine (XIX) in Expt. a) is apparently mainly due to hydrolysis of chlorohydrazone (VII) during isolation.

In addition, when the reaction is run in refluxing benzene the formation of osazone (VIII) is due to the thermal rearrangement of hydrazidine (V), as is evidenced by its formation (30%) when benzene solutions of (V) are refluxed for 8 h. As a result, it can be seen that the observed thermal rearrangement of hydrazidine (V) to osazone (VIII) can proceed in refluxing benzene, and this fact must be considered when interpreting the experimental data. It is not excluded that the formation of osazone (VIII), observed during the oxidation of benzaldehyde phenylhydrazone with MnO_2 in refluxing benzene [12], is also due to this rearrangement.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer, the UV spectra on a Specord UV-VIS spectrometer, and the PMR spectra on a Varian T-60 spectrometer. The melting points were determined on a Boëtius stand. The TLC was run on Silufol and Silufol UV-254 plates, and the chromatographic separation was run on Al_2O_3 (II activity) columns.

Reaction of Benzaldehyde Phenylhydrazone (I) and Benzoyl Chloride Phenylhydrazone (VII) in Presence of Triethylamine. a) Under an argon stream, to a solution of 2.3 g (0.01 mole) of (VII) and 1.96 g (0.01 mole) of (I) in 45 ml of dry benzene, freed of oxygen as described in [13], was added 2.1 ml (0.015 mole) of Et_3N in either one or three portions (0.01 mole at the start and then 0.005 mole each at 2 h intervals) and the mixture was refluxed for 6 h. The mixture was cooled and after 12 h was filtered to give 1.44 g of precipitate, which analyzed 0.1 g (5.1%) of the starting (I) and 1.34 g (98.2%) of $Et_3N \cdot HCl$ (separated by treatment with water). The benzene was removed in vacuo (under argon), and the residue was treated with 40 ml of ethanol, and after 2 h the precipitate was filtered and washed with alcohol (4 × 15 ml) and acetone (2 × 3 ml). Recrystallization of 1.21 g of the product from either a 1:1 ethanol—acetone mixture or ethanol gave 1.15 g (29.5%) of analytically pure 1,4-diphenyl-2-benzylidenebenzhydrazidine (V) with mp 203-204° [14, 15]. Ultraviolet spectrum (λ_{max}, nm (log ε): in acetonitrile 242 (4.49), 297 (4.26), 339 (4.55); in $CHCl_3$ — 300 (4.29), 348 (4.54). Infrared spectrum (Nujol, ν, cm^{-1}): 3332 (NH), 1600, 1552 (ArC=N). PMR spectrum (δ, ppm): 9.93 (DMSO), 10.61 (Hexametapol) (s, 1H, NH).

All of the solutions after washing and recrystallization were combined, the solvents were removed in vacuo, and the residue was chromatographed on an Al_2O_3 column, using as eluant first a 1:1 petroleum ether—ether mixture and then ether. Here we isolated 0.12 g (3.1%) of hydrazidine (V) and trace amounts of triazole (IV), formazan (IX), dihydrotetrazine (VI), and osazone (VIII) (identified by comparing with standards on Silufol UV-254 plates), and also 0.25 g of 1-benzoyl-2-phenylhydrazine (XIX) with mp 168-169°, which was identical with the sample obtained from phenylhydrazine and benzoyl chloride.

b) Similar to Expt. a), but using 0.02 mole of Et_3N and refluxing for 14 h. We obtained 40.2% of hydrazidine (V) and a larger amount of osazone (VIII), while the amount of the other products remained constant.

c) Similar to b), but refluxing for 20 h. We isolated 34.3% of hydrazidine (V) and 15.4% of osazone (VIII) with mp 234-235° [14, 15].

d) Similar to b), but in air. We isolated 29.1% of hydrazidine (V) and 0.15 g of formazan (IX) with mp 170°.

e) Similar to a) but using ethanol as the solvent, 0.011 mole of Et_3N, and refluxing for 2.5 h. The yield of hydrazidine (V) was 37.2%.

f) Similar to a), but using 0.011 mole of Et_3N and letting stand at 20-25° for 6 days. We isolated 30% of hydrazone (I), a small amount of chlorohydrazone (VII), and 27.0% of hydrazidine (V). When the residue from the mother liquors was separated by chromatography on an Al_2O_3 column, using a 3:1 petroleum ether—ether mixture for elution until distinct zones were obtained, followed by elution with a 1:1 mixture of the same solvents, we isolated 0.01 g of formazan (IX) and hydrazidine (V). Subsequent elution with ether gave 0.03 g of benzanilide (X), with mp 164-165° (from ethanol), and 0.025 g of 1,2-dibenzoyl-1-phenylhydrazine (XX) with mp 175.5-177.5°. Ultraviolet spectrum (λ_{max}, nm (log ε), in ethanol): 228 (4.30), 236 (3.90) (shoulder). Infrared spectrum (Nujol, ν, cm^{-1}): 1694, 1656 (C=O), 1602 (C=C). The formazan (IX), benzanilide (X), and hydrazine (XX) were identified by comparing them with authentic specimens (UV, IR, TLC). Hydrazine (XX) was obtained by the benzoylation of phenylhydrazine with benzoyl chloride [16]. Ultraviolet spectrum (λ_{max}, nm (log ε), in ethanol): 228 (4.30), 263 (3.90) (shoulder). Infrared spectrum (Nujol, ν, cm^{-1}): 3214 (NH), 1694, 1656 (C=O), 1602 (C=C). Triazole (IV) could not be isolated on the column due to indistinct separation, and the mixture of appropriate zones was separated on a Silufol UV-254 plate. Triazole (IV) was isolated and characterized by the method of standards and by the UV spectrum (λ_{max} 246 nm in ethanol). It was identical with an authentic sample, obtained from phenylhydrazine and benzonitrile in benzene in the presence of Na as described in [17].

When chromatographing the reaction mixtures that contained unreacted hydrazone (I), the separation of the products proved to be very difficult due to the constant formation of formazan (IX) during elution, which is also observed during the chromatographing of the pure hydrazone (I).

g) When the reaction is run the same as in Expt. f), but until the starting hydrazones (I) and (VII) are completely consumed (40-50 days), the yield of hydrazidine (V) is 34.5%. In addition, we isolated small amounts of formazan (IX), benzanilide (X), and hydrazine (XX), and also recorded the formation of triazole (IV) and a number of products of unestablished structure.

h) When the reaction is run in THF, we isolated only 0.11 g of formazan (IX). The formation of hydrazidine (V) could be recorded by chromatography. The other products were not identified.

Reaction of Hydrazone (I) with 1,3-Diphenylnitrilimine as Described in [4]. A solution of 0.25 g of 2,5-diphenyltetrazole and 0.44 g of benzaldehyde phenylhydrazone in 2.5 ml of anisole was refluxed for 6 h under N_2. The anisole was removed and the residue was treated with ethanol. Recrystallization gave 0.04 g of a mixture, composed of 0.01 g of hydrazidine (V) and 0.03 g of osazone (VIII), which was separated as described in [14].

The residue from removal of the alcohols was chromatographed on a 45 × 1.8 cm column, with successive elution by heptane, a 1:1 heptane—ether mixture, and ether. Here we isolated fractions that by chromatography were shown to contain hydrazidine (V), osazone (VIII), triazole (IV), formazan (IX), benzanilide (X), dihydrotetrazine (VI), radicals (XI) and (XII), and the starting hydrazone (I). The identification of these compounds without prior separation into fractions is difficult.

Thermolysis of Hydrazidine (V). A solution of 0.4 g of hydrazidine (V) in 3 ml of anisole was refluxed in an argon atmosphere for 6 h. The anisole and formed benzonitrile (identified by GLC) were removed in vacuo, and the residue was treated with 5-7 ml of ethanol. Filtration gave 0.28 g (70%) of osazone (VIII) with mp 234-235°, which was identical with that obtained from phenylhydrazine and benzil [14, 15]. The residue from removal of the alcohol was chromatographed on a column (Al_2O_3, petroleum ether, 1:1 petroleum ether—ether, ether, and 1:1 ether-methanol). Here we isolated another 0.02 g (5%) of osazone (VIII), 0.03 g of a (XIII)-(XIV) mixture (separated by fractional solution in acetone), 0.035 g of radical (XI), and 0.008 g of radical (XII).

Product (XIII) was obtained as yellow crystals (0.02 g) with mp 179-182° (ethanol). Ultraviolet spectrum (λ_{max}, nm, in ethanol): 249, 282, 344, 415. Infrared spectrum (Nujol, ν, cm^{-1}): 1600, 1500, 1311, 1293, 1278, 1100, 1070, 1032, 700. PMR spectrum (DMSO-d_6, δ, ppm): 6.90-8.11 (w. m). Found: C 80.71; H 5.46; N 14.55%.

Product (XIV) was obtained as crimson plates (0.008 g) with mp 174-176° (ethanol). Ultraviolet spectrum (λ_{max}, nm, in ethanol): 227, 243 (shoulder), 270, 310. Infrared spectrum (Nujol, ν, cm^{-1}): 1602, 1585, 1275, 1060, 1030, 690. PMR spectrum (DMSO-d_6, δ, ppm): 7.46-8.10 m.

Radical (XI) was obtained as black lustrous crystals with mp 113-115° (ethanol). It was identical with the sample obtained as described in [9] from azoimine (XV) [18] either by treatment with HBr or by short refluxing (20 min) in anisole (70% yield). Ultraviolet spectrum (λ_{max}, nm (log ε), in methanol): 260 (4.51) (shoulder), 268 (4.53), 320 (3.86), 375 (4.71), 420 (4.39), 500 (4.10), 565 (3.78) (shoulder). Mass spectrum (m/z): 286 (27), 285 (100), 284 (28), 270 (14), 269 (14), 208 (14). The intensity of the peaks in the mass spectrum with m/z 286, 270, 269, 209 increases when D_2O is added.

Radical (XII) was obtained as black lustrous crystals with mp 153-156° (ethanol). Ultraviolet spectrum (λ_{max}, nm, in ethanol): 239, 279, 294 (shoulder), 325, 385, 460, 524. The IR spectrum in Nujol fails to have any absorption bands above 1600 cm^{-1}. An identical specimen was isolated (20%) when azoimine (XV) is refluxed in anisole.

The EPR spectra of radicals (XI) and (XII) are very similar.

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CONCLUSIONS

1. Benzaldehyde phenylhydrazone reacts with 1,3-diphenylimine, generated from 2,5-diphenyltetrazole (at 160°) or from benzoyl chloride phenylhydrazone (at either 80 or 25°), mainly with involvement of the NH group to give 1,4-diphenyl-2-benzylidenebenzhydrazidine, and only partially enters into 1,3-dipolar cycloaddition involving the C=N bond.

2. It was found that 1,4-diphenyl-2-benzylidenebenzhydrazidine is thermally rearranged to benzil β-phenylosazone.

LITERATURE CITED

1. R. Huisgen, Angew. Chem., 75, 742 (1963).
2. R. Huisgen, J. Sauer, and M. Seidel, Chem. Ber., 94, 2503 (1961).
3. R. Huisgen and E. Aufderhaar, Chem. Ber., 98, 2185 (1965).
4. R. Huisgen, R. Grashey, and E. Aufderhaar, Chem. Ber., 98, 642 (1965).
5. B. I. Buzykin, L. P. Sysoeva, and Yu. P. Kitaev, Zh. Org. Khim., 10, 2200 (1974); 11, 173, 348 (1975); 12, 1557 (1976).
6. B. I. Buzykin, N. G. Gazetdinova, S. A. Flegontov, A. P. Stolyarov, and Yu. P. Kitaev, Zh. Org. Khim., 13, 1947 (1977).
7. B. I. Buzykin, G. D. Lezhnina, and Yu. P. Kitaev, Zh. Org. Khim., 11, 848, 1078 (1975).
8. M. Märky, H. Meler, A. Wunderli, H. Heimgarther, H. Schmid, and H.-J. Hansen, Helv. Chim. Acta, 61, 1477 (1978).
9. H. M. Blatter and H. Lukaszewski, Tetrahedron Lett., 1968, 2701.
10. R. Huisgen, K. Adelberger, E. Aufderhaar, H. Knupfer, and G. Wallbillich, Monatsh. Chem., 98, 1618 (1967).
11. G. E. Lewis and G. L. Spencer, Austral. J. Chem., 28, 1733 (1975).
12. I. Bhatnagar and M. V. George, J. Org. Chem., 32, 2252 (1967).
13. A. Gordon and R. Ford, Chemistry Manual [Russian translation], Mir (1976), p. 447.
14. R. B. Woodward and C. Winter, Tetrahedron Lett., 1969, 2697.
15. N. I. Christova and A. W. Spassov, Z. Chem., 18, 23 (1978).
16. H. Franzen, Ber., 42, 2467 (1909).
17. R. Engelhardt, J. Prakt. Chem., 54, 143 (1896).
18. M. Busch and R. Ruppenthal, Ber., 43, 3001 (1910).