

1087. *The Reactions of Hydrazones and Related Compounds with Strong Bases. Part II.*¹ *Nitriles from Phenylhydrazones.*

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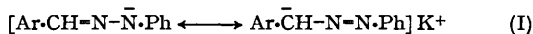
The modified Wolff-Kishner procedure¹ was applied successfully to certain aryl aldehyde hydrazones. When aryl aldehyde phenylhydrazones were heated at 110–120° in toluene or "Diglyme" with potassium t-butoxide, nitriles and aniline were formed in 24–35% yields, but only in the presence of oxygen. The reaction is believed to involve the formation of the hydrazidines (V) by homolytic oxidation, and their subsequent heterolytic decomposition.

In Part I¹ we showed that ketone hydrazones are converted into hydrocarbons with potassium t-butoxide in toluene at 110°. Application of this process to an $\alpha\beta$ -unsaturated ketone and to an α -amino-ketone gave the corresponding olefin and amine, respectively, instead of the abnormal products encountered in the traditional Wolff-Kishner reaction. We have now extended the modified procedure to aryl aldehyde derivatives.

The new method gave satisfactory results with two aryl aldehyde hydrazones. When a solution of anisaldehyde hydrazone and potassium t-butoxide in toluene was refluxed for 15 hours 4-methoxytoluene was obtained in 57% yield, and similar treatment of 3-methoxybenzaldehyde hydrazone afforded 3-methoxytoluene (66%). With vanillin hydrazone, however, vanillin azine was the principal product, and 4-hydroxy-3-methoxytoluene was isolated in only 15% yield.

The most widely accepted mechanism for the Wolff-Kishner reaction involves the successive removal of two protons attached to the terminal nitrogen atom of a hydrazone.² In accordance with this formulation, we find that phenylhydrazones and *NN*-diphenylhydrazones, do not give Wolff-Kishner products when heated with potassium t-butoxide. Other products are obtained, however, from aryl aldehyde derivatives and we now report a study of these reactions.

When potassium t-butoxide in toluene was treated with a toluene solution of the phenylhydrazone of benzophenone, benzaldehyde, anisaldehyde, or 4-formylpyridine, a coloured solid was formed rapidly. After separation, the solid was stable for a short time in air, but with water afforded the phenylhydrazone and an alkaline aqueous solution. The product is presumably a potassium salt of the following general structure:³



As expected, benzaldehyde *NN*-diphenylhydrazone, which does not contain an NH group, did not give a precipitate with potassium t-butoxide. The salts of benzaldehyde, benzophenone, and 4-formylpyridine phenylhydrazones were yellow, orange, and red, respectively; the

¹ Part I, Grundon, Henbest, and Scott, *J.*, 1963, 1855.

² Seibert, *Chem. Ber.*, 1947, **80**, 494; Cram, Sahyun, and Knox, *J. Amer. Chem. Soc.*, 1962, **84**, 1734.

³ Cf. Ragno, *Gazzetta*, 1945, **75**, 175.

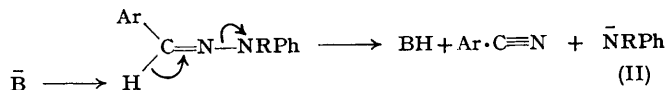
change in colour apparently reflects increasing stabilisation of the negative charge in this series.

After being heated with potassium t-butoxide in toluene or "Diglyme," the phenylhydrazones of benzaldehyde and anisaldehyde were recovered, often in good yields, but benzonitrile or anisonitrile (2–3%) and aniline were also isolated (Table; Nos. 1, 5, and 6).

Reaction of phenylhydrazones, Ar·CH=N·NH·Ph, with potassium t-butoxide.

No.	Ar	Conditions	KOBu ^t (mol.)	Temp.	Time (hr.)	Phenyl- hydra- zone re- covered (%)	Nit- rile (%)	Aniline (%)
1	Ph	"Diglyme" under N ₂	1	120°	15	28	2	14
2	Ph	"Diglyme" in air	1	120	15	—	24	38
3	Ph	Toluene in air	1	110	6	21	9	15
4	Ph	Toluene in air	1	110	17	25	15	10
5	<i>p</i> -OMeC ₆ H ₄	Toluene under N ₂	1	110	15	60	0	4
6	<i>p</i> -OMeC ₆ H ₄	"Diglyme" under N ₂	1	115	15	—	3	15
7	<i>p</i> -OMeC ₆ H ₄	"Diglyme" in air	1	115	15	—	24	46
8	<i>p</i> -OMeC ₆ H ₄	Toluene in air	1	110	15	38	28	20
9	<i>p</i> -OMeC ₆ H ₄	Xylene in air	1	140	15	30	35	35
10	<i>p</i> -OMeC ₆ H ₄	Toluene in air	2	110	15	24	17	26
11	<i>p</i> -OMeC ₆ H ₄	Toluene in air	2.5	110	15	52	0	8
12	<i>p</i> -OMeC ₆ H ₄	Toluene under N ₂ with (t-BuO) ₂	1	110	15	30	9	10
13	<i>m</i> -OMeC ₆ H ₄	"Diglyme" in air	1	120	15	—	25	28

The formation of these products is apparently due to the presence of an α -CH group, since benzophenone phenylhydrazone, which does not contain such a group, was recovered in good yield when heated with potassium t-butoxide, and gave no aniline. Nitriles and aniline may be produced by the following elimination reactions (R=H) of the aldehyde phenylhydrazones, which presumably are in equilibrium with their potassium salts (I):



Benzaldehyde *NN*-diphenylhydrazone afforded benzonitrile (8%) and diphenylamine (15%); the higher yields of cleavage products compared to those in the phenylhydrazone reactions can be attributed to the greater stability of the leaving group (II; R=Ph). Base-catalyzed elimination reactions of other derivatives of aryl aldehydes have been reported.⁴

The above experiments were carried out under nitrogen, but when air was present a dramatic change occurred, and the phenylhydrazones of benzaldehyde, anisaldehyde, and 3-methoxybenzaldehyde were converted into the corresponding nitriles and aniline in substantial yields (Table; Nos. 2, 4, 7, 8, and 13). At a higher temperature (140°) more of the cleavage products were formed from anisaldehyde phenylhydrazone (Table; No. 9).

In the reaction of benzaldehyde phenylhydrazone with potassium t-butoxide, a by-product, C₂₆H₂₂N₄, was isolated in 5% yield, and was shown to be identical with the hydrazidine (V; Ar=Ph), obtained by treating benzaldehyde phenylhydrazone with mercuric oxide. Anisaldehyde phenylhydrazone gave a by-product, C₂₈H₂₆N₄O₂, which probably is the corresponding hydrazidine (V; Ar=*p*-C₆H₄OMe). When the benzaldehyde phenylhydrazone reaction was conducted for 6 hr. instead of 17 hr. less benzonitrile was obtained (Table; No. 3), but the hydrazidine (V; Ar=Ph) was isolated in much higher yield. Furthermore, heating hydrazidine (V; Ar=Ph) with potassium t-butoxide in "Diglyme" gave benzonitrile and aniline. These observations suggest that the formation of nitriles and aniline from phenylhydrazones is a two-step process, with the hydrazidines (V) as intermediates. The two stages will now be considered separately.

⁴ Hauser and Gillaspie, *J. Amer. Chem. Soc.*, 1930, **52**, 4517; Hauser, LeMaistre, and Rainsford, *ibid.*, 1935, **57**, 1056; Smith and Walker, *J. Org. Chem.*, 1962, **27**, 4372.

petroleum gave 3-methoxytoluene as an oil (1.92 g., 66%). The infrared spectrum, which was identical with that of an authentic sample of 3-methoxytoluene, was unchanged after distillation of the compound at 168—172°/760 mm. (lit.,⁸ b. p. 177°/760 mm.).

(b) Anisaldehyde hydrazone⁹ (9 g.) was reduced by the method described in (a). Treatment of the crude product with light petroleum (b. p. 40—60°) gave a solid, which separated from water in needles (0.18 g., 2%), m. p. 184°, undepressed by admixture with an authentic sample of anisic acid. Evaporation of the light petroleum solution gave 4-methoxytoluene as an oil (4.64 g., 57%). The infrared spectrum, which was unchanged after distillation of the compound at 174—176°/760 mm., was identical with that of an authentic sample.

(c) A solution of vanillin hydrazone (9 g.) and potassium *t*-butoxide (11 g.) in toluene (450 c.c.) was refluxed under nitrogen for 15 hr., and added to dilute hydrochloric acid. After separation of the toluene, the aqueous solution was made alkaline with ammonia. Crystallization of the precipitate from ethanol gave vanillin azine in yellow needles (4.6 g., 57%), m. p. 176—178°, alone or mixed with an authentic sample prepared by the method of Noelting.¹⁰

Evaporation of the toluene solution, and distillation of the residue gave 4-hydroxy-3-methoxytoluene as an oil (1.08 g., 15%), b. p. 111—112°/15 mm. (Found: C, 69.6; H, 7.2. Calc. for C₈H₁₀O₂: C, 69.6; H, 7.3%). The picrate separated from ethanol in yellow needles, m. p. 109—111° (lit.,¹¹ 111—111.5°).

*Reaction of Benzaldehyde Phenylhydrazone with Potassium *t*-Butoxide.*—(a) A solution of benzaldehyde phenylhydrazone (20 g.) and potassium *t*-butoxide (12 g.) in toluene (1000 c.c.) was refluxed for 17 hr., and then added to water. The toluene layer was separated, and the aqueous layer was extracted with ether. The combined toluene-ether solution was washed with several portions of 2*N*-hydrochloric acid, and then concentrated to ca. 100 ml. The precipitate (5.0 g., 25%), m. p. 154—158°, was identical (mixed m. p. and infrared) with benzaldehyde phenylhydrazone. The toluene solution was evaporated, the residue was steam-distilled, and the distillate was extracted with ether. Evaporation of the ether and distillation of the residue gave an oil (1.54 g.), b. p. 70°/15 mm. This was benzonitrile containing less than 10% of benzaldehyde, as shown by comparing the infrared spectrum with spectra of authentic mixtures. A pure sample of benzonitrile was obtained by washing the product in ether with a saturated solution of sodium pyrosulphite.

The residue from the steam-distillation was extracted with ether, and a solution in benzene was chromatographed on alumina. Elution with benzene, evaporation of the solution, and crystallization of the residue from benzene-ethanol gave *N*^α*N*^β-diphenyl-*N*^β-benzylidenebenzhydrazidine in yellow needles (0.98 g., 5%), m. p. 205—207° (Found: C, 79.6; H, 5.6; N, 14.4. Calc. for C₂₆H₂₂N₄: C, 80.0; H, 5.6; N, 14.4%). The m. p. was undepressed by admixture with an authentic sample, m. p. 205—207° (lit.,⁵ 200.5—201°), prepared by the method of Minunni and Rap.¹²

The hydrochloric acid washings (see above) were made alkaline with sodium hydroxide and were extracted with ether, and the ether was evaporated off. Trituration of the residue with a mixture of ether and light petroleum (b. p. 40—60°) gave *N*-phenylbenzamidine in prisms (0.5 g., 2.5%), m. p. and mixed m. p. 114—115° (Found: C, 79.2; H, 5.9; N, 14.0. Calc. for C₁₃H₁₂N₂: C, 79.6; H, 6.1; N, 14.3%). Evaporation of the ether-light petroleum solution, and distillation of the residue gave aniline (0.94 g.), b. p. 70°/15 mm. The infrared spectrum was identical with that of an authentic sample, and reaction with benzoyl chloride gave benzanilide, m. p. and mixed m. p. 158—162°.

The aqueous alkaline solution, obtained earlier by adding the reaction mixture to water, was acidified with hydrochloric acid, and extracted with ether. Evaporation of the ether and crystallization of the residue from water gave benzoic acid (0.57 g., 5%), m. p. and mixed m. p. 119—120°.

The above procedure was used for experiments 3 and 4 (Table).

(b) A solution of benzaldehyde phenylhydrazone (10 g.) and potassium *t*-butoxide (6 g.) in "Diglyme" (250 c.c.) was stirred and heated at 120° for 15 hr., and added to water. The mixture was extracted with ether, and the ethereal solution was washed with water and then with several portions of 2*N*-hydrochloric acid. Evaporation of the ethereal solution, and distillation of the residue gave benzonitrile (1.27 g.), b. p. 70°/15 mm. The infrared spectrum was identical with that of an authentic sample.

⁸ Pinette, *Annalen*, 1888, **243**, 32.

⁹ Hinman, *J. Org. Chem.*, 1960, **25**, 1775.

¹⁰ Noelting, *Ann. Chim. (France)*, 1910, [8], **19**, 476.

¹¹ Schepss, *Ber.*, 1913, **46**, 64.

¹² Minunni and Rap, *Gazzetta*, 1896, **26**, 441.

The hydrochloric acid washings were made alkaline with sodium hydroxide and steam-distilled. By ether extraction of the distillate and subsequent distillation, aniline was obtained as an oil (1.82 g., 38%), b. p. 70°/15 mm., identical (infrared spectrum) with an authentic sample.

The above procedure was used in experiments 1 and 2 (Table).

N^αN^β-Diphenyl-N^β-benzylidenebenzhydrazidine.—A solution of benzaldehyde phenylhydrazone (7.5 g.) in "Diglyme" (250 c.c.) was heated at 120° with stirring and in the presence of air for 15 hr., and then added to water. The mixture was extracted with ether, the ether solution washed with water, and the solvent evaporated. Fractional crystallisation of the residue from ethanol gave first the hydrazidine in yellow needles (1.14 g., 16%), m. p. and mixed m. p. 205—207°, and then benzaldehyde phenylhydrazone (2.5 g., 33%), m. p. and mixed m. p. 152—155°.

When the reaction was repeated in an atmosphere of nitrogen only benzaldehyde phenylhydrazone was obtained.

The reaction of the hydrazidine (6.25 g.) with potassium *t*-butoxide in "Diglyme" was carried out as described for benzaldehyde phenylhydrazone [method (b)]. Trituration of the neutral fraction with light petroleum (b. p. 40—60°) gave a solid, separating from benzene-ethanol in yellow needles (0.1 g.), m. p. 225—230° (Found: C, 80.3; H, 5.6. Calc. for C₂₆H₂₂N₄: C, 80.0; H, 5.6). This is probably β-benzilosazone (lit.,⁵ m. p. 229—231°). Evaporation of the light petroleum solution, and distillation of the residue gave benzonitrile (0.86 g.), b. p. 70°/15 mm. The basic fraction yielded aniline (0.94 g.).

*Reaction of Anisaldehyde Phenylhydrazone with Potassium *t*-Butoxide.*—(a) A solution of anisaldehyde phenylhydrazone (10 g.) and potassium *t*-butoxide (4 g., 1 mol.) in toluene (500 ml.) was refluxed for 15 hr. The yellow precipitate was removed by filtration, washed with water, and crystallised from ethanol to give anisaldehyde phenylhydrazone (3.28 g.), m. p. and mixed m. p. 118—120°. The aqueous alkaline washings were added to the filtrate. The toluene layer was separated, was washed with 2*N*-hydrochloric acid, and was evaporated. The residue was chromatographed on neutral alumina (120 g.). Elution with benzene-light petroleum (b. p. 40—60°), evaporation of the eluate, and trituration of the residue with light petroleum (b. p. 40—60°) gave anisonitrile (1.67 g.), m. p. 50—57°, crystallising from the same solvent in prisms, m. p. 56—58° (lit.,¹³ 61°) (Found: C, 71.9; H, 5.2; N, 9.9. Calc. for C₈H₇NO: C, 72.1; H, 5.3; N, 10.5%). Elution with benzene gave anisaldehyde phenylhydrazone (0.5 g.), m. p. and mixed m. p. 118—120° (total yield, 3.78 g.). The hydrochloric acid solution was made alkaline with aqueous sodium hydroxide, and was extracted with ether. Evaporation of the ether and distillation of the residue yielded aniline as a colourless oil (0.82 g.), b. p. 72—75°/15 mm., identical (infrared spectrum) with an authentic sample. The alkaline solution, obtained after separation of the toluene solution, was acidified with hydrochloric acid, and was extracted with ether. Evaporation of the solvent gave anisic acid (0.4 g., 6%), m. p. 170—180°, identical (infrared spectrum) with an authentic sample.

This isolation procedure was used in experiments 5—12 (Table), except that in some cases, the anisonitrile was distilled before crystallisation, and the aniline steam-distilled before distillation.

(b) (Table; No. 12) Reaction (a) was repeated under nitrogen and with the addition of *t*-butyl peroxide (2.2 g., 0.1 mol.). After separation of anisonitrile, elution with benzene afforded plates (0.3 g., 0.5%) (from benzene-ethanol), m. p. 194—199° (Found: C, 74.1; H, 5.7; N, 12.7. Calc. for C₂₈H₂₆N₄O₂: C, 74.7; H, 5.8; N, 12.4%). This compound is probably *N^αN^β-diphenyl-N^β-anisylidene anishydrazidine* (lit.,¹⁴ m. p. 197—198°).

*Reaction of 3-Methoxybenzaldehyde Phenylhydrazone with Potassium *t*-Butoxide.*—A solution of 3-methoxybenzaldehyde phenylhydrazone (10 g.) and potassium *t*-butoxide (4 g., 1 mol.) in "Diglyme" (250 c.c.) was heated at 120° for 15 hr., and then added to water. The mixture was extracted with ether, and the ether solution was washed successively with water and with 2*N*-hydrochloric acid. The ether was evaporated and the residue in benzene was chromatographed on neutral alumina (200 g.). Elution with benzene, evaporation of the eluate, and distillation of the residue gave 3-methoxybenzonitrile as a colourless oil (1.41 g.), b. p. 80°/0.5 mm. (lit.,¹⁵ 112°/13 mm.); ν_{\max} . 2250 cm.⁻¹ (C=N) (Found: C, 71.7; H, 4.9; N, 10.9. Calc. for C₈H₇NO: C, 72.3; H, 5.2; N, 10.5%). The residue from the distillation was shown by vapour-phase chromatography (10% polyethylene glycol succinate on Celite at 150°, with anisonitrile as an internal standard) to contain a further 0.07 g. of 3-methoxybenzonitrile (total yield, 1.48 g., 25%). Hydrolysis of the nitrile with 30% aqueous sodium hydroxide afforded 3-methoxybenzoic acid, separating

¹³ Grignard, Bellet, and Courtet, *Ann. Chim. (France)*, 1915, [9], 4, 28.

¹⁴ Witkop and Kissman, *J. Amer. Chem. Soc.*, 1953, 75, 1975.

¹⁵ Carothers, Bickford, and Hurwitz, *J. Amer. Chem. Soc.*, 1927, 49, 2908.

from water in needles, m. p. 104—106° (lit.,¹⁶ 110°) (Found: C, 62.7; H, 5.0. Calc. for $C_8H_8O_3$: C, 63.2; H, 5.3%).

The hydrochloric acid washings were made alkaline with sodium hydroxide, and steam-distilled. Extraction of the distillate with ether, evaporation of the ether, and distillation of the residue yielded aniline (1.15 g.), b. p. 70°/15 mm., identical (infrared spectrum) with an authentic sample.

Reaction of Benzaldehyde Diphenylhydrazone with Potassium t-Butoxide.—Benzaldehyde diphenylhydrazone,¹⁷ m. p. 122—125°, (10 g.) was treated with potassium t-butoxide as described above for 3-methoxybenzaldehyde phenylhydrazone. Trituration of the crude product with benzene–light petroleum (b. p. 40—60°) afforded benzaldehyde diphenylhydrazone (5.91 g., 59%), m. p. and mixed m. p. 122—124°. Evaporation of the benzene–light petroleum solution, and distillation of the residue gave first benzonitrile (0.3 g., 9%), b. p. 68°/10 mm., identical (infrared spectrum) with an authentic sample, and then diphenylamine as a yellow oil which later solidified to brown crystals (0.94 g., 15%), m. p. and mixed m. p. 50—54°.

Treatment of Benzophenone Phenylhydrazone with Potassium t-Butoxide.—A solution of benzophenone phenylhydrazone (10 g.) in toluene was treated with a solution of potassium t-butoxide (10 g.) in toluene (500 ml.), and an orange precipitate was formed immediately. A small portion of the precipitate was obtained by filtration, and on treatment with water gave benzophenone phenylhydrazone, m. p. and mixed m. p. 135—137°, and an alkaline aqueous solution. The original toluene mixture was refluxed for 17 hr., and then added to water. The toluene layer was separated, and the aqueous solution was extracted with ether. Concentration of the combined ether and toluene solution yielded benzophenone phenylhydrazone in prisms (7.59 g., 76%), m. p. and mixed m. p. 135—137°. Washing the remaining toluene solution with dilute hydrochloric acid gave no basic product.

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¹⁶ Ullmann and Uzbachian, *Ber.*, 1903, **36**, 1797.

¹⁷ Fischer, *Annalen*, 1877, **190**, 67.
