New Rearrangement of Arylhydrazones in Polyphosphoric Acid: Formation of Diaryl Ethers. 4

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Arylhydrazones of 4-hydroxyacetophenones and benzophenones, when heated at 100 °C with a 10-fold excess by weight of polyphosphoric acid, give diaryl ethers and biphenyl derivatives. In this way, the 2,6-dimethylphenylhydrazone of 3,5-dimethyl-4-hydroxyacetophenone (**1**) gives 4-acetyl-4'-amino-2,6,3',5'-tetramethyldiphenyl ether (**2**; mp 165 °C, yield 25%), the structure of which was proved by independent synthesis. Similar treatment of the 2,6-dimethylphenylhydrazone of 4-hydroxyacetophenone (**4**, mp 173 °C) gives 4-acetyl-4'-amino-3',5'-dimethyldiphenyl ether (**5**, mp 128 °C) and 3-(4-amino-3,5-dimethylphenyl)-4-hydroxyacetophenone (**6**, mp 170 °C). The 3,5-dimethylphenylhydrazone of 3,5-dimethyl-4-hydroxyacetophenone (**7**, mp 122 °C) affords 4-acetyl-4'-amino-2,6,2',6'-tetramethyldiphenyl ether (**9**, mp 121 °C). The 2,6-dimethylphenylhydrazone of 3,5-dimethyl-4-hydroxybenzophenone (**8**) analogously gives 4-amino-4'-benzoyl-3,5,2',6'-tetramethyldiphenyl ether (**10**, mp 120 °C). The 2,6-dimethylphenylhydrazone of 4-hydroxybenzophenone (**11**, mp 141 °C) yields 3-(4-amino-3,5-dimethylphenyl)-4-hydroxybenzophenone (**12**, mp 162 °C) only. Possible mechanisms are discussed.

The results reported in this paper are part of the research line we have been developing for a few years on the behavior of arylhydrazones of aromatic and arylaliphatic carbonyl compounds toward polyphosphoric acid (PPA).[1-3]

The 2,6-dimethylphenylhydrazone of 3,5-dimethyl-4-hydroxyacetophenone (**1**), when heated at 120 °C for a short time with a large excess of PPA, gave a basic compound in about 25% yield,[4] to which the structure of 4-acetyl-4'-amino-2,6,3',5'-tetramethyldiphenyl ether (**2**) was assigned on the basis of chemical and spectroscopic evidence (Scheme I).

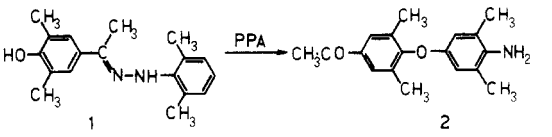
The assigned structure was confirmed by independent synthesis: nitration of 1,3-dimethyl-5-fluorobenzene gave the 2,6-dimethyl-4-fluoronitrobenzene which afforded the diaryl ether **3**, though in low yield, by condensation with 3,5-dimethyl-4-hydroxyacetophenone (Scheme II). Reduction of the latter with zinc in acetic acid solution gave **2**.

Similar treatment of the 2,6-dimethylphenylhydrazone of 4-hydroxyacetophenone (**4**) with PPA afforded two isomeric compounds (Scheme III). The first one contains a primary aromatic amino group and an acetyl group but no phenolic function. Its ^{1}H NMR data are consistent with the diaryl ether structure **5**. The second product contains the primary amino group and the carbonyl function as well, but its solubility in aqueous sodium hydroxide shows that there is a phenol group as well. In addition the ^{1}H NMR data strongly support the biphenyl structure **6**.

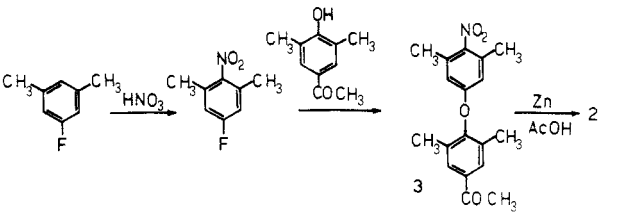
The formation of diaryl ether derivatives was also observed in the rearrangement of the 3,5-dimethylphenylhydrazone of 3,5-dimethyl-4-hydroxyacetophenone (**7**) and the 2,6-dimethylphenylhydrazone of 3,5-dimethyl-4-hydroxybenzophenone (**8**), which gave 4'-acetyl-4-amino-2,2',6,6'-tetramethyldiphenyl ether (**9**) and 4-amino-4'-benzoyl-3,5,2',6'-tetramethyldiphenyl ether (**10**), respectively (Scheme IV).

The 2,6-dimethylphenylhydrazone of 4-hydroxybenzophenone (**11**) unexpectedly gave 3-(4-amino-3,5-dimethylphenyl)-4-hydroxybenzophenone (**12**), although in modest yields (Scheme V).

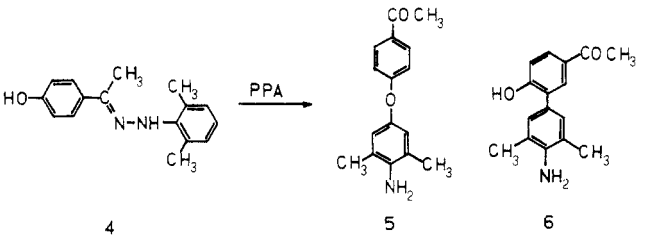
Scheme I



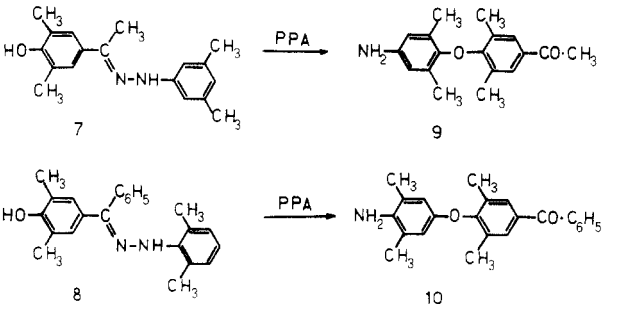
Scheme II



Scheme III



Scheme IV



Structural assignments for **9**, **10** and **12** are supported by chemical and spectroscopical evidence.

Discussion

The results reported above show that arylhydrazones of 4-hydroxyacetophenones and benzophenones can undergo

(1) R. Fusco and F. Sannicolò, *Tetrahedron Lett.*, 3163 (1977).
(2) R. Fusco and F. Sannicolò, *Tetrahedron Lett.*, 1233 (1978).
(3) R. Fusco and F. Sannicolò, *J. Org. Chem.*, previous paper in this issue; *Tetrahedron*, **36**, 161 (1980).
(4) Whenever arylhydrazones of phenolic ketones reacted with PPA, unidentified water-soluble byproducts were formed (may be phosphoric esters at phenolic OH): D. C. Ayres and R. C. Denney, *J. Chem. Soc.*, 4506 (1961).

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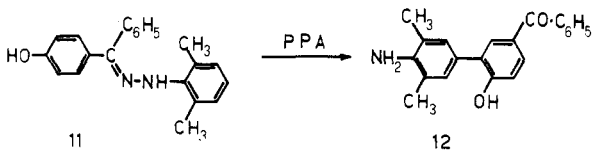
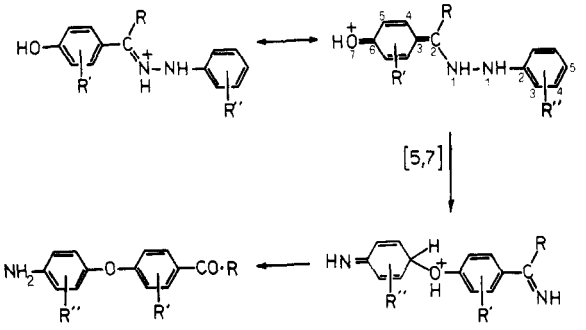
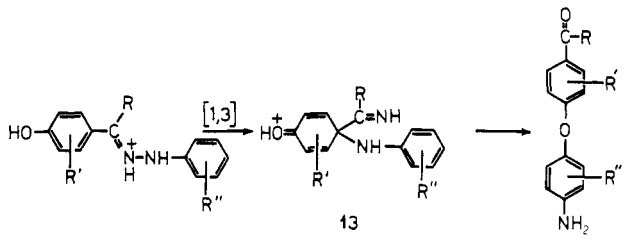
Scheme V



Scheme VI



Scheme VII



two different rearrangements in hot PPA solution. The first produces biphenyl derivatives through a [5,5] sigmatropic rearrangement very similar to that previously studied in analogous substrates.[1,2]

The second rearrangement, which gives rise to diaryl ethers is unprecedented in the literature and can be explained by two alternative mechanisms.

The first involves the single-step [5,7] sigmatropic rearrangement represented in Scheme VI.

The second mechanism involves two subsequent steps: an initial [1,3] sigmatropic rearrangement to a quinamine derivative (13) which could subsequently rearrange to a diaryl ether in accord with the known behavior of quinamines (Scheme VII).[5]

Research is in progress to determine whether this rearrangement occurs with mercapto or amino groups instead of phenolic OH in the starting arylhydrazone.

Experimental Section

All melting points were determined on a Büchi apparatus and are uncorrected. IR spectra (Nujol) were recorded on a Perkin-Elmer Model 377 spectrophotometer. ^1H NMR spectra were recorded on a Varian Associates A-60 spectrometer with $CDCl_3$ as solvent unless otherwise stated and tetramethylsilane as internal standard; chemical shifts are given in δ units and refer to the center of the signal: s = singlet; d = doublet; m = multiplet; dd = double doublet. All new products gave correct elemental analyses. Wavenumbers (ν) are given in reciprocal centimeters.

2,6-Dimethylphenylhydrazone of 3,5-Dimethyl-4-hydroxyacetophenone (1). A solution of 3,5-dimethyl-4-hydroxyacetophenone[6] (10 g), (2,6-dimethylphenyl)hydrazine[7] (8.3 g), and AcOH (0.5 mL) in EtOH (75 mL) was refluxed for 3 h. Hydrazone 1 (10 g) separated on cooling of the mixture and was reacted with PPA with no further purification due to its low stability.

Reaction of Hydrazone 1 with PPA. Hydrazone 1 (10 g) was added in portions to well-stirred PPA (100 g) preheated at 80 °C; the reaction was slightly exothermic. The mixture was then heated at 120 °C for another 30 min and then poured into H_2O; the pH was adjusted to 8 with aqueous NH_3 solution, and the product which separated was extracted with Et_2O. Removal of the solvent left an oily residue (2.14 g) which was chromatographed on a silica gel column (60 g, eluent C_6H_6-AcOEt, 9:1). 4-Acetyl-4′-amino-2,6,3′,5′-tetramethyldiphenyl ether (2) was the main product eluted: yellow crystals; mp 165 °C (*i*-PrOH); ^1H NMR 7.65 (2 H, s, aromatic in positions 3 and 5), 6.31 (2 H, s, aromatic in positions 2′ and 6′), 3.30 (2 H, br s, exchangeable with D_2O, NH_2), 2.56 (3 H, s, $COCH_3$), 2.10 and 2.16 (2 x 6 H, 2 s, 4 CH_3); IR ν_{NH_2} 3465 and 3380, $\nu_{C=O}$ 1675, $\nu_{=C-O}$ 1195.

2,6-Dimethyl-4-fluoronitrobenzene. Fuming NHO_3 (d = 1.52; 5 g) was carefully added dropwise to neat 3,5-dimethylfluorobenzene[8] (10 g) cooled to −20 °C in a $CHCl_3$–solid CO_2 bath with stirring. Care was taken to maintain a temperature below −15 °C. At the end of the addition the cooling bath was removed, and the temperature was allowed to reach room temperature. The reaction mixture was allowed to stand for 3 h and then poured into H_2O. The yellow solid which separated was extracted with Et_2O. The organic extract was washed with alkali, dried over K_2CO_3, and evaporated to dryness. The oily residue slowly crystallized on standing to give large crystals of 2,6-dimethyl-4-fluoronitrobenzene, which were pressed on a glass funnel and dried in vacuo: mp 44 °C; ^1H NMR 6.80 and 6.40 (2 × 1 H, 2 s, aromatic), 2.28 (6 H, S, 2 CH_3).

4-Acetyl-4′-nitro-2,6,3′,5′-tetramethyldiphenyl Ether (3). 3,5-Dimethyl-4-hydroxyacetophenone[6] (1.1 g) was added to a 2 M solution of MeONa in MeOH (1.5 mL). The solvent was distilled and the residual salt diluted with dry DMF (10 mL). 2,6-dimethyl-4-fluoronitrobenzene (1.0 g) was added, and the mixture was heated to 100 °C for 4 h with stirring and then poured into H_2O. The solid precipitate was extracted with Et_2O, the undissolved impurities were filtered off, and the organic layer was washed with alkali and dried. Removal of the solvent left a solid residue which was crystallized from diisopropyl ether to give 3 in a pure state: yield 0.4 g; mp 167 °C; ^1H NMR 7.89 (2 H, s, aromatic in positions 3 and 5), 6.59 (2 H, s, aromatic in positions 2′ and 6′), 2.67 (3 H, s, $COCH_3$), 2.34 and 2.25 (2 × 6 H, 2 s, 4 CH_3).

4-Acetyl-4′-amino-2,6,3′,5′-tetramethyldiphenyl Ether (2). A mixture of ether 3 (0.25 g), AcOH (5 mL), concentrated HCl (0.5 mL), and Zn powder (0.2 g) was stirred at 60 °C for 2 h, diluted with H_2O, and filtered. The clear filtrate was made strongly alkaline with concentrated NaOH solution and the precipitate extracted with ether. The residue resulting from removal of the solvent was crystallized from *i*-PrOH to give 2 (0.1 g) identical in every respect with the product obtained from rearrangement of hydrazone 1 in PPA.

2,6-Dimethylphenylhydrazone of 4-Hydroxyacetophenone (4). A solution of 4-hydroxyacetophenone[9] (3.8 g) and (2,6-dimethylphenyl)hydrazine[7] (4.6 g) in EtOH (20 mL) was refluxed for 30 min in the presence of AcOH (0.5 mL). The solvent was evaporated and the residue treated with cyclohexane to give hydrazone 4: yield 6.5 g; mp 173 °C.

Reaction of Hydrazone 4 with PPA. Hydrazone 4 (7.0 g) was added in portions to PPA (70 g) preheated at 90 °C in a an oil bath with stirring. An exothermic reaction occurred, and the temperature spontaneously rose to 110 °C; then it was increased to 170 °C for a few minutes. The mixture was then poured into H_2O (300 mL), and the light yellow precipitate was filtered by suction, suspended in H_2O, and treated with diluted NH_4OH solution. An oily product separated which was extracted with $CHCl_3$. Evaporation of the solvent left a redsidue (1.1 g) which was dissolved in Et_2O and washed with 10% NaOH solution. The organic layer gave, upon removal of the solvent, a solid residue which was crystallized from diisopropyl ether to yield 4-acetyl-4′-amino-3′,5′-dimethyldiphenyl ether (5): yield 0.30 g; mp 128

(5) B. Miller, *Tetrahedron Lett.*, 55 (1962).
(6) W. S. Ide and A. P. Phillips, *J. Am. Chem. Soc.*, **77**, 2522 (1955).
(7) R. B. Carlin and D. P. Carlson, *J. Am. Chem. Soc.*, **81**, 4673 (1959).
(8) G Valkanas, *J. Chem. Soc.*, 5554 (1963).
(9) K. W. Rosemund and W. Schnurr, *Justus Liebigs Ann. Chem.*, **460**, 88 (1927).

°C; ^{1}H NMR 7.96 (2 H, dd, aromatic in positions 3 and 5); 7.01 (2 H, dd, aromatic in positions 2 and 6), 6.77 (2 H, s, aromatic in positions 2′ and 6′), 3.59 (2 H, br s, exchangeable with D_2O, NH_2), 2.59 (3 H, s, $COCH_3$), 2.19 (6 H, s, 2 CH_3); IR ν_{NH_2} 3472 and 3370, $\nu_{C=O}$ 1670, $\nu_{=C-O}$ 1230. Alkaline extracts were acidified with concentrated HCl solution to give 3-(4-amino-3,5-dimethylphenyl)-4-hydroxyacetophenone (**6**), which was purified by crystallization from *i*-PrOH: mp 170°C; ^{1}H NMR 7.91 (2 H, m, aromatic in positions 2 and 4), 7.1 (3 H, m, aromatic in positions 5, 2′, and 6′), 3.92 (2 H, br s, exchangeable with D_2O, NH_2), 2.57 (3 H, s, $COCH_3$), 2.31 (6 H, s, 2 CH_3).

3,5-Dimethylphenylhydrazone of 3,5-Dimethyl-4-hydroxyacetophenone (7). A solution of (3,5-dimethylphenyl)hydrazine[10] (4.0 g) and 3,5-dimethyl-4-hydroxyacetophenone[6] (4.25 g) in EtOH (100 mL) was refluxed for 2 h in the presence of a trace of AcOH. The solvent was distilled, the solid residue dissolved in hot benzene (10 mL), and the resulting solution diluted with hexane (15 mL) to precipitate hydrazone **7**: mp 122 °C; 4.0 g (yield 52%).

Reaction of Hydrazone 7 with PPA. Hydrazone **7** (4.0 g) was added in portions with stirring to PPA (40 g) preheated at 80 °C in a oil bath. The reaction was exothermic. The temperature was then increased to 120 °C and kept there for 30 min. The mixture was poured into H_2O and the pH adjusted to 8 with 26% aqueous NH_3 solution. An oily product separated which was extracted with ether. The organic extract was dried (K_2CO_3) and the solvent removed to afford a residue which was dissolved in hot benzene. The resulting solution was diluted with an equal amount of hexane. 4-Acetyl-4′-amino-2,6,2′,6′-tetramethyldiphenyl ether (**9**) separated as yellow crystals: mp 121 °C (0.7 g); ^{1}H NMR 7.75 (2 H, s, aromatic in positions 3 and 5), 6.45 (2 H, s, aromatic in positions 3′ and 5′), 3.48 (2 H, br s, exchangeable with D_2O, NH_2), 2.58 (3 H, s, $COCH_3$), 2.12 and 2.0 (2 × 6 H, 2 s, 4 CH_3); IR ν_{NH_2} 3460 and 3360, $\nu_{C=O}$ 1670, $\nu_{=C-O}$ 1210.

2,6-Dimethylphenylhydrazone of 3,5-Dimethyl-4-hydroxybenzophenone (8). A solution of 3,5-dimethyl-4-hydroxybenzophenone[11] (12.2 g), (2,6-dimethylphenyl)hydrazine[7] (7.8 g), and AcOH (0.5 mL) in EtOH (50 mL) was refluxed for 4 h. The solvent was evaporated and the oily residue (18.6 g) chromatographed on a silica gel column (100 g, eluent $CHCl_3$). The first product eluted was hydrazone **8** as an orange viscous oil (9.2 g) which was used for the reaction with PPA without further purification due to its low stability.

(10) H. K. Snyder, H. R. Beilfuss, and J. K. Williams, *J. Am. Chem. Soc.*, **75**, 1873 (1953).
(11) K. von Auwers and E. Janssen, *Justus Liebigs Ann. Chem.*, **483**, 44 (1930).

Reaction of Hydrazone 8 with PPA. Hydrazone **8** (9.0 g) was added to PPA (100 g) preheated at 100 °C in a oil bath with stirring. After 1 h of additional heating, the mixture was poured into H_2O, and the crude gummy solid which separated was treated with diluted aqueous NH_3 solution and extracted with Et_2O. Removal of the solvent left an oily residue (1.9 g) which was chromatographed on a silica gel column (40 g, eluent $CHCl_3$). The main product of the reaction, 4-amino-4′-benzoyl-3,5,2′,6′-tetramethyldiphenyl ether (**10**), was collected after elution of a few minor fractions: mp 120 °C; ^{1}H NMR 7.8 (2 H, m, aromatic in position ortho of the C_6H_5CO group), 7.6 (5 H, m, aromatic in positions 3′ and 5′ and remaining aromatic of the C_6H_5CO group), 6.40 (2 H, s, aromatic in positions 2 and 6), 3.34 (2 H, br s, exchangeable with D_2O, NH_2), 2.16 and 2.13 (2 × 6 H, 2 s, 4 CH_3); IR ν_{NH_2} 3480 and 3350 $\nu_{C=O}$ 1650, $\nu_{=C-O}$ 1215.

2,6-Dimethylphenylhydrazone of 4-Hydroxybenzophenone (11). A mixture of 4-hydroxybenzophenone[9] (16.6 g) and (2,6-dimethylphenyl)hydrazine[7] (11.4 g) was heated at 120 °C on an oil bath for 1 h and then cooled and dissolved in benzene (5 mL). The solution was chromatographed through a silica gel column (250 g, eluent benzene) to remove tarry byproducts. Hydrazone **11** was rapidly eluted and purified by concentration of its benzene solution and dilution of the residue with cyclohexane: mp 141 °C; yield 6.0 g.

Reaction of Hydrazone 11 with PPA. Hydrazone **11** (6 g) was added to PPA (70 g) preheated at 80 °C with vigorous stirring. The reaction was slightly exothermic and was completed by heating the mixture at 120 °C for 1 h. The fluid mass was poured into H_2O to give a solid phosphoric acid salt, which was filtered and dissolved in a 10% NaOH solution. Impurities were removed by filtration, and the clear solution was acidified with AcOH. A solid product separated which was extracted with ether and, after the usual treatment, gave 3-(4-amino-3,5-dimethylphenyl)-4-hydroxybenzophenone (**12**): yield 1.2 g; mp 162 °C (*i*-PrOH). More **12** was obtained from the phosphoric aqueous solution: ^{1}H NMR 7.8 (7 H, m, aromatic in positions 2′ and 4′ and C_6H_5CO), 7.25 (2 H, s, aromatic in positions 2 and 6), 7.17 (1 H, d, aromatic in position 5′), 3.63 (2 H, br s, exchangeable with D_2O, NH_2), 2.23 (6 H, s, 2 CH_3).

Registry No. **1**, 75475-99-9; **2**, 75476-00-5; **3**, 75476-01-6; **4**, 75476-02-7; **5**, 75476-03-8; **6**, 75476-04-9; **7**, 75476-05-0; **8**, 75476-06-1; **9**, 75476-07-2; **10**, 75476-08-3; **11**, 75476-09-4; **12**, 75476-10-7; 3,5-dimethyl-4-hydroxyacetophenone, 5325-04-2; (2,6-dimethylphenyl)-hydrazine, 603-77-0; 2,6-dimethyl-4-fluoronitrobenzene, 315-12-8; 3,5-dimethylfluorobenzene, 461-97-2; 4-hydroxyacetophenone, 99-93-4; (3,5-dimethylphenyl)hydrazine, 39943-61-8; 3,5-dimethyl-4-hydroxybenzophenone, 5336-56-1; 4-hydroxybenzophenone, 1137-42-4.

α-Silicon- and α-Alkynyl-Substituted Vinyl Cations

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The solvolytic reactivity of a number of silicon- and alkynyl-substituted vinyl triflates was investigated in aqueous ethanol. Activation parameters and solvent *m* values were determined for all substrates. Relative rate data show that the Me_3Si group is accelerating and hence stabilizing relative to hydrogen but destabilizing relative to a *t*-Bu group. The α-ethynyl substituent causes a rate decrease compared to a methyl group despite its π-donating resonance ability. These results are discussed.

Diverse evidence suggests a dichotomous donor-acceptor behavior for trialkylsilyl groups.[1a] It is well established that an α-$(CH_3)_3Si$ group imparts considerable stability to a carbanion.[1b] The effect of silicon substitution on the

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