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Phosphoramides. XI.* Phosphoramides as Reagents in the Synthesis of Benzamidines from Benzophenone Oxime

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N,N-Dialkyl-*N'*-phenylbenzamidines were prepared by treating benzophenone oxime with hexamethylphosphoric triamide or the appropriate phenyl tetraalkylphosphorodiamidate at 235 °C. The catalytic effect of polyphosphoric acid was demonstrated.

Hot hexamethylphosphoric triamide, HMPT, has previously been observed to cause a Beckmann rearrangement of benzophenone oxime *1*.[2] *N,N*-Dimethyl-*N'*-phenylbenzamidine *9* was observed as a by-product in this reaction. The purpose of this work is to show that the yield of amidines can be increased dramatically by addition of polyphosphoric acid, PPA, to the reaction mixture.

* Part X, *cf.* Ref. 1.

RESULTS AND DISCUSSION

It was now found that the yield of *N,N*-dimethyl-*N'*-phenylbenzamidine *9* obtained from benzophenone oxime *1* in HMPT at 235 °C increased from 5 to 29 and 48 % by addition of 1/4 and 1/2 equivalent of PPA (HPO_3) respectively in regard to the oxime (see experiments 1 and 2 in Table 1). Evidently, the yield of amidine corresponds with the amount of PPA added. On the other hand excess of HMPT does not seem to have any influence on the yield, and the molar ratio of the phosphoric amide to oxime was, therefore, in the following experiments reduced to 2:1. In the experiments 3 – 9 phenyl phosphorodiamidates *4* were found to react similarly to HMPT at 235 °C, and 26 –

Table 1. Preparation of benzamidines *2* from benzophenone oxime (*1*, 10 g, 50 mmol) and a phosphoramide in the presence of PPA (HPO_3).

Exp. No.	Phosphoramide (mol)	PPA (mmol HPO_3)	Yield %
	$(Me_2N)_3PO$ (0.33)	0	5 [2]
1	$(Me_2N)_3PO$ (0.33)	12.5	29
2	$(MeN)_3PO$ (0.1)	25	48
3	$PhOP(O)(NEt_2)_2$ (0.1)	25	21
4	$PhOP(O)(NEt_2)_2$ (0.1)	50	53
5	$PhOP(O)(NEt_2)_2$ (0.1)	100	46
6	$PhOP(O)[\overline{N(CH_2)_3CH_2}]_2$ (0.1)	50	37
7	$PhOP(O)[\overline{N(CH_2)_4CH_2}]_2$ (0.1)	50	33
8	$PhOP(O)[N(CH_2CH_2)_2O]$ (0.1)	50	26
9	$PhOP(O)[N(CH_2CH_2)_2NCH_3]_2$ (0.1)	50	59

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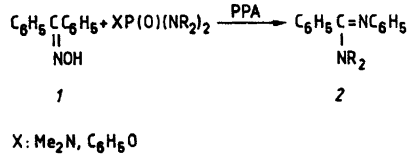
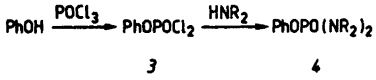
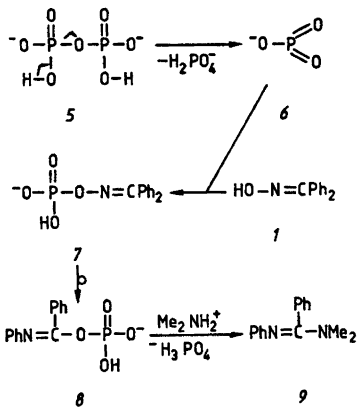
59 % yields were found of the corresponding *N'*-phenylbenzamidines *2*. Also, when *4* were



used as reagents, an obvious dependence of the yields of the amidine was found with respect to the amount of PPA added to the reaction mixture. In the experiments 3 – 5 it was found that equimolar amounts of PPA and oxime were preferable. Compounds *4* were obtained as follows, *cf.* Ref. 3.



In the reaction of benzyl alcohols with HMPT at 200 °C the metaphosphate *6* has recently been found to be a reactive intermediate



which adds the benzyl alcohol with formation of a benzyl phosphate undergoing further reactions.[4] The metaphosphate ion *6* was formed in the rate-determining step from the pyrophosphate ion *5*. Since *5* also has been observed in the reactions of oximes with HMPT,[2,5] similar reaction mechanisms can be postulated in the latter reaction. The ion *6* adds *1* with formation of the phosphate *7*, which undergoes a Beckmann type of rearrangement reaction to *8*. The imidoylphosphate *8* then yields the amidine *9*. The ion *5* is obtained from a rapid reaction between H_3PO_4 and HMPT. Assuming formation of *6* to be the rate-determining step, the reaction should be catalysed by species able to produce *6*. It is then believed that PPA is in a rapid equilibrium with the monomeric metaphosphoric acid as well as other phosphoric acid derivatives. For the reaction of *1* with *4* a similar mechanism may be proposed.

EXPERIMENTAL

Preparation of compounds *4*

General procedure (*cf.* Ref. 3). Phenyl phosphorodichloridate *3* was added dropwise to a secondary amine in toluene at 0 – 15 °C. The mixture was stirred for 3 days at room temperature and filtered to remove amine hydrochloride. The filtered solution was stirred for 24 h with powdered KOH, which was then filtered off using diatomite to avoid clogging of the filter. The title products were then obtained by distillation.

Phenyl di-1-pyrrolidinylphosphinate was prepared from pyrrolidine (120 g) and phenyl phosphorodichloridate *3* (80 g). Yield 72 g (68 %) b.p. 160 – 170 °C/0.15 mmHg, n_D^{20} 1.5362. NMR $\delta(CDCl_3)$: 1.85 (8 H), 3.24 (8 H), 7.21 (5 H). MS, *m/e* (%): 280 (M^+, 9), 279 (2), 210 (6), 187 (24), 146 (7), 118 (8), 116 (6), 71 (11), 70 (100). IR ν_{max} (film) 1260 cm^{-1} (P=O). UV, λ_{max} (96 % EtOH) (log ε): 209 (3.71), 263 (2.68), 268 (2.55) nm. Found: C 59.40; H 7.80; N 9.75. Calc. for $C_{14}H_{21}N_2O_2P$: C 59.99; H 7.55; N 9.99.

Phenyl bis(4-methyl-1-piperazinyl)phosphinate was prepared from *N*-methylpiperazine (101 g), phenyl phosphorodichloridate *3* (47 g) and triethylamine (101 g). The latter compound was added to avoid precipitation of the product hydrochloride. Distillation afforded 55 g (74 %), b.p. 180 – 205 °C/0.1 mmHg, m.p. 52 – 53 °C (light petroleum, b.p. 50 – 70 °C). NMR, $\delta(CDCl_3)$: 2.30 (14 H), 3.20 (8 H), 7.20 (5 H). MS, *m/e* (%): 56 (33), 70 (23), 71 (38), 83 (15), 97 (22), 99 (26), 239 (100), 241 (49), 268 (23), 338 (M^+, 28). IR, ν_{max} (film) 1240 cm^{-1} (P=O). UV (96 % EtOH), λ_{max} (log ε): 216 (3.34), 262 (2.68), 268 (2.57) nm. Anal. $C_{16}H_{27}N_4O_2P$: C, H, N. The title compound was very hygroscopic.

Preparation of *N'*-phenylbenzamidines

General procedure. A mixture of polyphosphoric acid (PPA), benzophenone oxime *1* and phosphorodiamidate *4* or HMPT was heated with stirring for 3 h on an oil bath (235 °C); the reaction mixture was extracted at 100 °C

with 4 M HCl, which was washed with ether and pH adjusted to about 11. The water phase was then extracted with ether, which was washed with water and distilled.

N,N-Dimethyl-N'-phenylbenzamidine, Exp. Nos. 1 and 2. M.p. 70–72 °C (light petroleum, b.p. 50–70 °C), lit. m.p. 70–72 °C.[6]

N,N-Diethyl-N'-phenylbenzamidine, Exp. Nos. 3, 4 and 5. B.p. 120–135 °C/0.3 mmHg, n_D^{25} 1.5820. Picrate m.p. 109 °C, lit.[7] m.p. 110.5 °C.

1-(N'Phenylbenzimidoyl)pyrrolidine, Exp. No. 6. B.p. 165–170 °C/0.6 mmHg, m.p. 67–68 °C (light petroleum, b.p. 50–70 °C). $\delta(CDCl_3)$: 1.90(4 H), 3.42 (4 H), 6.5–7.3 (10 H). MS, *m/e* (%): 250 (M^+, 49), 249 (69), 221 (24), 180 (68), 146 (24), 130 (46), 104 (29), 77 (100), 70 (24), 51 (20). IR, ν_{max} (KBr) 1565 cm^{-1}. UV (96 % EtOH), λ_{max} (log ε): 205 (4.38), 230 (sh) nm. Anal. $C_{17}H_{18}N_2$: C, H, N.

1-(N-Phenylbenzimidoyl)piperidine, Exp. No. 7. B.p. 150–160 °C/0.5 mmHg, m.p. 48 °C. Picrate m.p. 179–180 °C (EtOH), lit.[7] m.p. 180.5–181 °C. NMR, $\delta(CDCl_3)$: 1.64 (6 H), 3.37 (4 H), 6.5–7.3 (10 H). MS, *m/e* (%): 264 (M^+, 77), 263 (100), 235 (15), 181 (14), 180 (69), 160 (57), 104 (54), 84 (31), 77 (83), 51 (13).

4-(N-Phenylbenzimidoyl)morpholine, Exp. No. 8. B.p. 155–165 °C/0.15 mmHg, m.p. 76–77 °C (ligroin, b.p. 80–100 °C). Hydroiodide m.p. 280–285 °C, lit.[8] m.p. 288–289 °C. NMR, $\delta(CDCl_3)$: 3.50 (4 H), 3.72 (4 H), 6.4–7.3 (10 H). MS, *m/e* (%): 267 (13), 266 (M^+, 97), 265 (95), 236 (8), 235 (23), 181 (18), 180 (100), 104 (18), 77 (77), 51 (15).

1-Methyl-4-(N-phenylbenzimidoyl)piperazine, Exp. No. 9. B.p. 180–200 °C/0.5 mmHg. The title product was purified further by preparative silica gel TLC using acetone for elution, m.p. 82 °C (petroleum ether, b.p. 50–70 °C). NMR, $\delta(CDCl_3)$: 2.21 (7 H), 3.43 (4 H), 6.5–7.2 (10 H). MS, *m/e* (%): 279 (M^+, 16), 209 (68), 197 (53), 180 (97), 117 (26), 105 (24), 83 (44), 77 (100), 70 (53), 51 (32), 38 (32). IR, ν_{max} (KBr): 1598 cm^{-1}. UV (96 % EtOH), λ_{max} (log ε): 203 (4.44), 230 (sh) nm. Anal. $C_{18}H_{21}N_3$: C, H, N.

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