

THE REACTION OF α -SUBSTITUTED DEOXYBENZOINS WITH HEXAMETHYLPHOSPHORIC TRIAMIDE.
FORMATION OF A NOVEL CYCLIC ENAMIDOPHOSPHATE

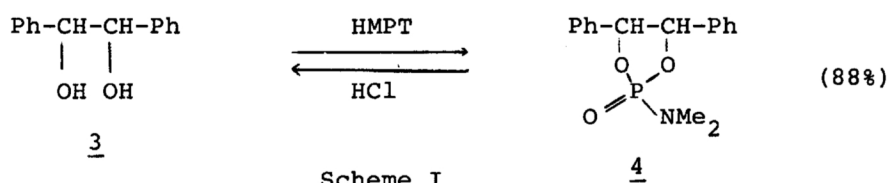
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Abstract

The reaction of benzoin and other substituted deoxybenzoins with HMPT has been investigated. Along with modest yields of tetraphenylpyridine, the major product in all cases is 2-dimethylamino-4,5-diphenyl-3-methyl-1-oxa-3-aza-2-phosphacyclopent-4-ene 2-oxide (5). meso-Hydrobenzoin similarly gives 2-dimethylamino-4,5-diphenyl-1,3-dioxo-2-phosphacyclopentane 2-oxide (4). The mechanism of formation of 5 and the pyridine is discussed.

We recently reported our findings¹ on the reaction of benzoins (1) with refluxing hexamethylphosphoric triamide (HMPT). This reaction gave the corresponding 2,3,5,6-tetraarylpyridine (2) in yields ranging from 10-19%, as well as substantial amounts of organophosphorus products.

A suggestion as to the structure of the organophosphorus product was first provided by the reaction of meso-hydrobenzoin with refluxing HMPT. This reaction gave the cyclic amidophosphate 4 in 88% yield (Scheme I). The structure of compound 4 was confirmed by spectral and analytical data², and by its hydrolysis in aqueous

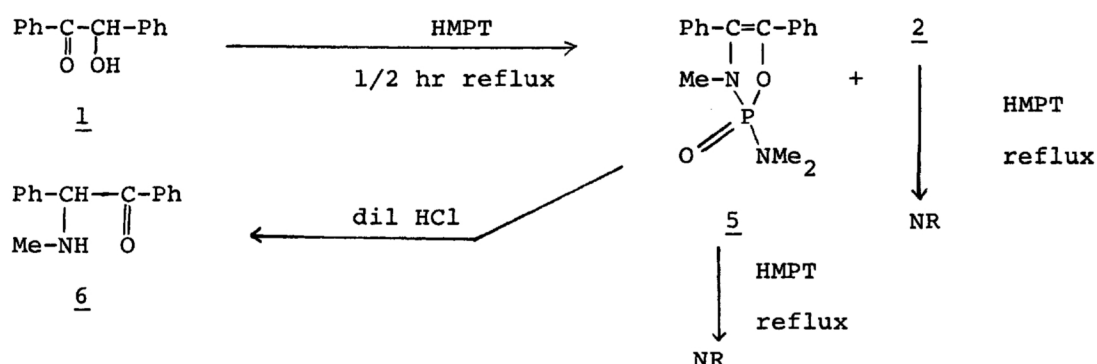


Scheme I

acid to the precursor 3. It is also analogous to the non-cyclic organophosphorus compounds isolated by Kawanisi and co-workers.³

The possibility that benzoin reacts in an analogous manner naturally followed

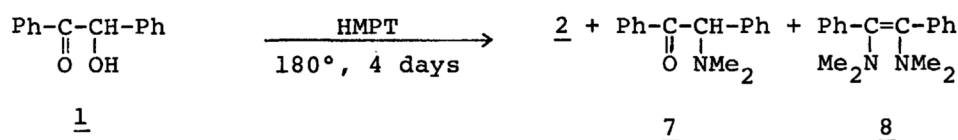
and we reexamined the reaction of benzoin with HMPT with this in mind. Benzoin and HMPT were refluxed for 30 minutes, and the tetraphenylpyridine (2) isolated as described.¹ The ethanolic filtrate remaining after this isolation was concentrated and the concentrate stored under vacuum. After several days, partial crystallization occurred. Isolation and recrystallization of this material gave a slightly hygroscopic solid which has been identified as the cyclic enamidophosphate 5 (Scheme II). Spectral and analytical data confirm the structure of 5⁴, as does the fact that it is hydrolyzed by dilute acid to α -N-methylaminodeoxybenzoin (6).



Scheme II

Infrared examination of the crude reaction mixture from benzoin and HMPT suggested that 5 constitutes 70% of the total reaction product, although only a 47% yield of it could be isolated. That 5 is not an intermediate in the formation of the pyridine was demonstrated by refluxing it with HMPT for two hours, whereupon only starting material could be isolated from the reaction mixture. Similarly, tetraphenylpyridine (2) does not react in refluxing HMPT.

The reaction between benzoin and HMPT was then carried out at a lower temperature in order to isolate possible intermediates. A run conducted at 180° for four days yielded two products after the usual work-up followed by chromatography on neutral alumina. The first product was the pyridine (2). The second product was redistilled giving a liquid which exhibited a broad infrared absorption at 6.10 μ . Its NMR spectrum (CCl₄) showed only singlets at δ 7.67 (5H) and 3.24 (6H). Further characterization of this compound has not been possible, but we have tentatively assigned it the structure of an enediamine, PhC(NMe₂)=C(NMe₂)Ph (8). A repeat of the reaction at 180° followed directly by distillation afforded the above two products, as well as α -N,N-dimethylaminodeoxybenzoin (7) which was identified by comparison with an authentic sample prepared by an independent route. These results are shown in Scheme III.



Scheme III

It had previously been demonstrated that benzyl alcohols are readily converted to the corresponding dimethylbenzylamines in refluxing HMPT⁵. Thus, the possibility existed that benzoin was initially converted to 7, thence to 8, and finally to pyridine. Accordingly, 7 was subjected to HMPT reflux resulting in an 80% (isolated) yield of 5. No pyridine could be isolated, nor could it be detected by infrared examination of the reaction mixture. Therefore, if 7 is formed in the reaction of benzoin with HMPT at reflux, it leads only to 5 and must be excluded as an intermediate in the pyridine formation.

Three additional α -substituted deoxybenzoins were subjected to HMPT reflux for varying times such that the carbonyl band in the ir was extinguished. The results of these runs and of the two mentioned above are summarized in Table I.

Table I. The Reaction of α -Substituted Deoxybenzoins with HMPT

$ \begin{array}{ccc} \text{Ph}-\text{C}-\text{CH}-\text{Ph} & \xrightarrow[\text{reflux}]{\text{HMPT}} & \text{Ph} \quad \text{Ph} \\ \parallel \quad & & \diagup \quad \diagdown \\ \text{O} \quad \text{Y} & & \text{N} \\ & & \diagdown \quad \diagup \\ & & \text{Ph} \quad \text{Ph} \\ & & \underline{2} \end{array} + \begin{array}{c} \text{Ph}-\text{C}=\text{C}-\text{Ph} \\ \quad \\ \text{Me}-\text{N} \quad \text{O} \\ \diagdown \quad \diagup \\ \text{P} \\ \diagup \quad \diagdown \\ \text{O} \quad \text{NMe}_2 \\ \underline{5} \end{array} $				
Y	Reflux Time (hr)	Yield ^a of <u>2</u> (%)	Yield ^b of <u>5</u> (%)	
-Cl	0.5	20	80	
-OH	0.5	18	70	
-NMe ₂ ·HCl	0.5	5	80	
-OMe	2.5	5	80	
-NMe ₂	1.0	0	100	

a) isolated yield

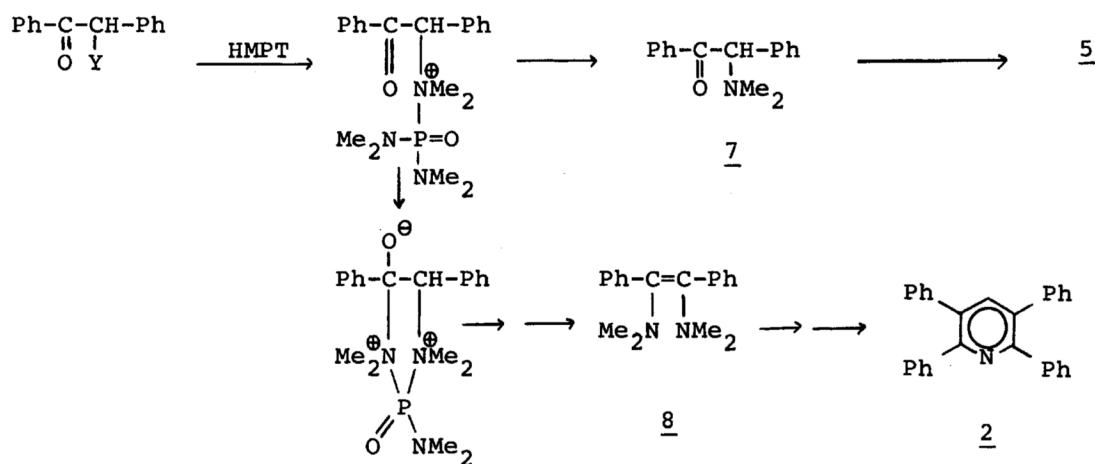
b) yield estimated by ir

The data in Table I suggest that the overall rapidity of the reaction as well as the formation of pyridine are promoted in the cases where Y, the α substituent is a good leaving group. Thus, -Cl and -OH[in the form of -OP(O)(NMe₂)₂] give the best yields of pyridine, while -OMe and -NMe₂ require greater reaction time and give little or no pyridine. In all cases, however, there is substantial formation of 5.

Discussion

The evidence so far accumulated on the reaction of benzoin derivatives with refluxing HMPT does not allow for an unequivocal mechanistic proposal. Nevertheless,

certain conclusions may be drawn. For one, the initial attack by HMPT on the benzoin derivatives is almost certainly at the α -position rather than the carbonyl position, since the reaction of deoxybenzoin itself requires five hours to be carried to the same extent.⁶ Second, it is likely that α -N,N-dimethylaminodeoxybenzoin (7) forms and is converted to 5. Third, the precursor of the pyridine must be symmetric since it has been shown¹ that non-equivalent aryl groups in the initial benzoin are scrambled in the pyridine. A reasonable candidate for this precursor is the enediamine 8. From these considerations, we are led to propose a tentative mechanism for the overall reaction which is outlined in Scheme IV.



Scheme IV

References

1. R. S. Monson and A. Baraze, *J. Org. Chem.*, **40**, 1672 (1975).
2. The crude 4 was recrystallized from ethanol, mp 192-3°; ir (film) 6.87, 7.79, and 9.75 μ ; NMR (CDCl_3) δ 7.15 (s,10), 5.90 (d,2, $J=10$ Hz), 3.00 (d,6, $J=11$ Hz).
Analysis for $\text{C}_{16}\text{H}_{18}\text{NO}_3\text{P}$ was $\pm 0.1\%$ for C,H,N, and P.
3. S. Arimatsu, R. Yamaguchi, and M. Kawanisi, *Bull. Chem. Soc. Jpn.*, **47**, 1693 (1974).
4. The reaction afforded 47% of 5, mp 140-1°; ir (film) 6.1, 7.6, 7.9 and 8.2 μ ; NMR (CDCl_3) δ 7.86(m,5), 7.54 (s,5) 3.03 (m,9).
Analysis for $\text{C}_{17}\text{H}_{19}\text{H}_2\text{O}_2\text{P}$ was $\pm 0.1\%$ for C,H,N, and P.
5. R. S. Monson and D. N. Priest, *Chem. Commun.*, 1018 (1971).
6. R. S. Monson and A. Baraze, *Tetrahedron*, **31**, 1145 (1975).

(Received March 23, 1976)