Tetrahedron Letters No. 22, pp. 1909-1912, 1971. Pergamon Press. Printed in Great Britain.

THE REACTION OF ALKYL PHOSPHITES WITH QUINONEDISULFONIMIDES [1a]

D. Levy and M. Sprecher[1b]

Department of Chemistry, Tel-Aviv University, Tel-Aviv, Israel

(Received in France 20 April 1971; received in UK for publication 22 April 1971)

In a continuation of our studies on the reactions of trivalent phosphorus nucleophiles with quinonediimides[2] we have investigated the reactions of di- and tri-alkyl phosphites with *p*-quinonedisulfonimides[3]. The latter, like *p*-quinones, react with C, N, O or S nucleophiles to give products in which the reagent has bonded to a ring carbon[3]. In contrast, *p*-quinones react with phosphite esters to yield almost only aryl phosphates by P-O bond formation[4]. This has been rationalized[4] on the basis of the large P-O bond energy (P-O 98±7;P-C 70±5 kcal/mol[5]) which current theory associates with p_π-d_π overlap. The considerably lower P-N bond energy (∿83 kcal/mol in phosphoramidates[5]) and the fact that the lone electron pair on the nitrogen of quinonedisulfonimides is presumably already involved in p_π-d_π interaction with the sulfonyl group, raise the possibility that such *p*-quinonediimides, unlike *p*-quinones, might react with alkyl phosphites exclusively at a ring carbon. In fact, a report of just such a result in the reaction of dialkyl phosphites with *p*-benzoquinonedibenzenesulfonimide(**1a**)[6] appeared while this investigation was in progress. (However, *vide infra*.) The recent publication of a note describing the products obtained from the reaction of trimethyl and triethyl phosphites with **1a** and with *p*-benzoquinonedimethanesulfonimide(**1b**)[7] prompts us to report our results in this field. These are completely at variance with those of Mustafa, Sidky *et al*[6], and, while in accord with some of the findings of Sidky and Zayed[7], differ from them in significant details and are more extensive.

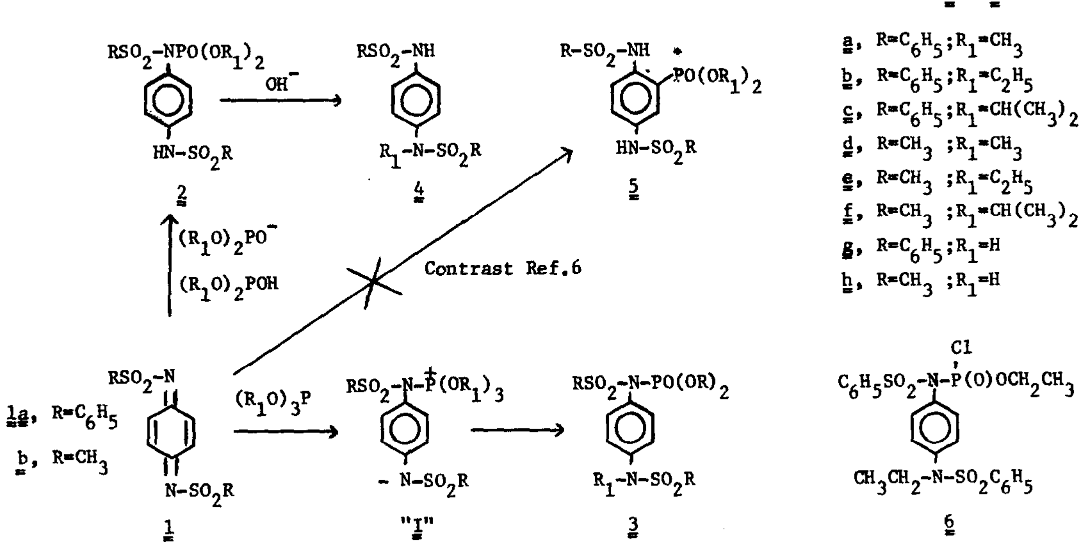
The uncatalyzed reaction of **1a** with 1.5 molar equivalents of purified dialkyl phosphites in refluxing benzene under purified N_2 atmosphere gave erratic results. In most cases no reaction took place[8a]. Occasionally (in 1 out of 10 reactions with dimethyl and 5 of 11 with diethyl phosphite) the same products as obtained under base catalysis (*vide infra*) were produced. The reason for this behaviour is not yet clear[9]. Results were comparable for reactions carried out in untreated and in silylated pyrex vessels. Neither addition of benzoyl peroxide nor admission of air nor exposure to sunlight[8a] (24 days, August) induced significant product formation from dimethyl phosphite. Addition of H_2SO_4 resulted in decomposition of **1a**. Base catalysis[10] (NaH, 0.25 molar equiv.), however, resulted in consistently successful reaction. Under these conditions **2a** and **2b** were obtained as the major porducts (>80%) from dimethyl and diethyl phosphite respectively[8a]. Minor products (<20%) **5a** and **5b** respectively, as well as traces of *p*-phenylenedibenzenesulfonamide(**4g**) were also isolated. Both **2a** and **2b** were hydrolyzed to **4g** by hot aqueous alcoholic alkali. Methylation (CH_3I, CH_3ONa, hot CH_3OH) of **2a** yielded **3a** (41%) accompanied by **4g** and its N-methyl and N,N'-dimethyl derivatives. Ethylation (CH_3CH_2I, NaH, dimethyl formamide) of **2b** yielded **3b** (58%). These chemical conversions as well as the spectral data presented in the Table (note esp. pmr in aromatic region) unequivocably establish the principal products, 2a and 2b, to be phosphoramidates as shown in Scheme.

The attempted uncatalyzed reaction of 1a with pure diisopropyl phosphite also failed, while the addition of a basic catalyst led to decomposition. However, in one attempt, when impure (by pmr) diisopropyl phosphite was refluxed with 1a in benzene for one week, a 43% yield of a product 5c having properties similar to those reported for his "2c" by Mustafa[6] was obtained.

It is probable that 5c does in fact have the diisopropyl 2,5-bis(benzenesulfonamido) phenylphosphonate structure[6] and that our minor products 5a and 5b are the respective methyl and ethyl esters; but, predictably, none of them yielded 4g upon saponification[8a]. Only starting material and a little unidentified grossly impure product were recovered[11]. Methylation (CH_3I, CH_3ONa, hot CH_3OH) of 5a gave a dimethyl derivative [no N-H in ir; pmr($CDCl_3$) δ3.10 (s,3H,NCH_3), 3.18 (s,3H,$N'CH_3$), 3.79 (d,6H,J_{PH}=11.5Hz)].

The properties of 2d and 2e, the major (∿80%) products of the reactions of dimethyl and diethyl phosphite respectively with 1b under base catalysis, are also listed in the Table. Again, it is clear from the spectral data and from the fact that both 2d and 2e were hydrolyzed to p-phenylenedimethanesulfonamide (4h), that the compounds are the phosphoramidates shown.

Scheme



2 - 5

a, R=C_6H_5;R_1=CH_3
b, R=C_6H_5;R_1=C_2H_5
c, R=C_6H_5;R_1=$CH(CH_3)_2$
d, R=CH_3 ;R_1=CH_3
e, R=CH_3 ;R_1=C_2H_5
f, R=CH_3 ;R_1=$CH(CH_3)_2$
g, R=C_6H_5;R_1=H
h, R=CH_3 ;R_1=H

The reaction of trialkyl phosphites (1.5 to 2 molar equiv.) with a solution of 1a or suspension of 1b in dry benzene was found to be rapid and complete at room temperature[8b]. However, when only one molar equiv. of phosphite was used,[8b] reaction was incomplete because part of the phosphite was converted to dialkyl phosphite and part to dialkyl alkylphosphonate ($RPO(OR)_2$; spectral evidence). Thus the alkylation of the anionic nitrogen in the intermediate "I" (see Scheme) appears to be mediated, at least in part, by trialkyl phosphite. In dilute solution the reaction of 1a was twice as fast as that of 1b.

The structures of the principal products obtained from the reactions of trimethyl phosphite and triethyl phosphite with **1b** and with **1a** have been correctly identified[7] as the N-alkyl-N'-dialkoxyphosphinyl-*p*-phenylenedimethane(or dibenzene)sulfonamides, **3d**, **3e**, **3a** and **3b**. However, the data reported[7] for the latter two are incorrect and are for evidently grossly impure samples (compare Table). We further found[8b] that the formation of **3b**, unlike that of **3a**, is accompanied by a minor product, **2b**, (~7%), lacking the N-alkyl group. This compound is probably the product of a competing elimination (E_2) reaction involving proton abstraction by the anionic nitrogen of an intermediate like "I" from the CH_3CH_2O- group of the ethylating species. This rationale is supported by our finding that the reaction of **1a** with triisopropyl phosphite yielded **3c** and **2c** in the ratio 3:1. Interestingly, the reaction of diethyl chlorophosphite with **1a** (refluxing benzene, 2.5 hr) yielded a product to which we assign structure **6** [no N-H in ir;pmr($CDCl_3$) δ1.07 (t,3H,J_{HH}=7Hz), 1.37 (t,3H,J_{HH}=7Hz),3.60 (q,2H,J_{HH}=7Hz) 4.36 (m,2H), 7.01 (4H), 7.25-7.84 (m,10H)]. On treatment with Ag_2O in absolute ethanol, **6** gave **3b**, and on base hydrolysis, **4b**.

In the reactions of **1b**, we found **3d** to be accompanied by very small amounts of **2d** and **3e** by **2e**. Again, the reaction of triisopropyl phosphite with **1b** gave **3f** and **2f** in a ratio of 3:1. In this series the methanesulfonyl group may also be a proton source. On base hydrolysis **2c-f** and **3a-f** each gave the corresponding *de*phosphorylated compound (**4g**, **4h**; **4a-f**).

In conclusion, it is clear that despite the factors mentioned in the introduction, alkyl phosphites bond preferentially to the imide nitrogens of **1a** and **1b**, rather than to the ring carbons. The possibility remains, however, that appropriate substitution either on the imide nitrogen or on the ring may change the reaction locus. We are currently investigating this point. The results may also shed light on the mechanism of the reaction. With respect to the latter, we note that none of the reactions reported herein were accompanied by color formation.

Table[#]

2a: mp 172-173°; ir 3091cm^{-1} (N-H);pmr δ3.87 [d,6H,J_{PH}=12Hz,$P(OC\underline{H}_3)_2$], 6.77 [s*,4H,N-$C_6\underline{H}_4$-N], 7.25-7.80 [m,10H,$C_6\underline{H}_5SO_2$], 8.40 [broad s, N$\underline{H}$].

2b: mp 145-147°; ir 3143cm^{-1} (N-H);pmr δ1.33 [t,6H,J_{HH}=7Hz,$C\underline{H}_3$-C], 4.23 [m,4H,$C\underline{H}_2$], 6.76 [s*,4H,N-$C\underline{H}_4$-N], 7.24-7.76 [m,10H,$C_6\underline{H}_5SO_2$], 8.19 [broad s, N$\underline{H}$].

2c: mp 194-195°; ir 3100cm^{-1} (N-H);pmr δ1.31 [d,6H,J_{HH}=6Hz,$C\underline{H}_3$], 1.37 [d,6H,J_{HH}=6Hz, $C\underline{H}_3$], 4.81 [m,2H,J_{HH}=6Hz, J_{PH}=7Hz,C$\underline{H}$], 6.76 [s*,4H,N-$C\underline{H}_4$-N], 7.2-7.8 [m,10H,$C_6\underline{H}_5SO_2$], 8.20 [N$\underline{H}$].

2d: mp 200-201°; ir 3090cm^{-1} (N-H); pmr (DMSO-d_6) δ3.15 [s, 3H,$C\underline{H}_3SO_2$], 3.50 [s,3H,$C\underline{H}_3SO_2$],3.82 [d,6H,J_{PH}=12Hz,$P(OC\underline{H}_3)_2$], 7.27-7.51 [m,4H, aromatic].

2e: mp 138-140°; ir 3090cm^{-1} (N-H);pmr δ3.14 [t,6H,J_{HH}=7Hz,$C\underline{H}_3C$], 2.95 [s,3H,$C\underline{H}_3SO_2$], 3.23 [s,3H,$C\underline{H}_3SO_2$], 4.24 [m,4H,$C\underline{H}_2$], 7.10-7.35 [m,4H, aromatic], 8.10 [broad s, N$\underline{H}$].

2f: mp 129-130°; ir 3263cm^{-1} (N-H);pmr δ1.36 [d,12H,J_{HH}=6Hz,$(C\underline{H}_3)_2C$], 2.95 [s,3H,$C\underline{H}_3SO_2$], 3.21 [s,3H,$C\underline{H}_3SO_2$], 4.81 [m,2H,C$\underline{H}$], 7.08-7.39 [m,4H,aromatic], 7.95 [broad, N$\underline{H}$].

3a: mp 108-110°; no N-H bands in ir;pmr δ3.14 [s,3H,$NC\underline{H}_3$], 3.80 [d,6H,J_{PH}=12Hz,$P(OC\underline{H}_3)_2$], 7.03 [s*,4H,N-$C_6\underline{H}_4$-N], 7.30-7.90 [m,10H,$C_6\underline{H}_5SO_2$].

3b: mp 107°; no N-H bands in ir;pmr δ1.06 [t,3H,J_{HH}=7Hz, $NCH_2C\underline{H}_3$], 1.28 [double t,6H,J_{HH}=7Hz, J_{PH}=1.5Hz, $P(OCH_2C\underline{H}_3)_2$],3.58[q,2H,$J_{HH}$=7Hz,$NC\underline{H}_2$], 4.17 [m,4H,$J_{HH}$=7Hz,$J_{PH}$=8Hz,$P(OC\underline{H}_2CH_3)_2$], 6.99 [s*,4H,N-$C_6\underline{H}_4$-N], 7.28-7.92 [m,10H,$C_6\underline{H}_5SO_2$].

3c: mp 138-140°; no N-H bands in ir;pmr δ1.02 [d,6H,J_{HH}=6.7Hz,$NCH(C\underline{H}_3)_2$],1.26 [d,6H,J_{HH}=6.2Hz, $OCHC\underline{H}_3$],1.32 [d,6H,J_{HH}=6.2Hz,$OCHC\underline{H}_3$], 4.5 [1H,J_{HH}=6.7Hz, NC$\underline{H}$], 4.76 [m,2H,OC$\underline{H}$], 6.97 [m,4H,N-$C_6\underline{H}_4$-N], 7.30-7.90 [m,10H,$C_6\underline{H}_5SO_2$].

3e: mp 138-140°; no N-H bands in ir;pmr δ1.17 [t,3H,J_{HH}=7Hz,$NCH_2C\underline{H}_3$], 1.30 [double t,6H,J_{HH}=7Hz, J_{PH}=1.5Hz,$P(OCH_2C\underline{H}_3)_2$], 2.87 [s,3H,$C\underline{H}_3SO_2$], 3.28 [s,3H,$C\underline{H}_3SO_2$], 3.75 [q,2H,$J_{HH}$=7Hz, $NC\underline{H}_2$], 4.20 [m,4H,$P(OC\underline{H}_2CH_3)_2$], 7.38 [$s^*$,4H, aromatic].

3f: mp 129-130°; no N-H bands in ir;pmr δ1.18 [d,6H,J_{HH}=7Hz,$NCH(C\underline{H}_3)_2$], 1.29 [d,12H,J_{HH}=6Hz, $PO(OCH(C\underline{H}_3)_2)_2$], 2.93 [s,3H,$C\underline{H}_3SO_2$], 3.28 [s,3H,$C\underline{H}_3SO_2$], 4.52 [sept,1H,$J_{HH}$=7Hz, $NC\underline{H}$], 4.78 [m,2H,$OC\underline{H}$], 7.22-7.48 [m,4H, aromatic].

4a: mp 123-124°; ir 3220cm^{-1} (N-H);pmr δ3.11 [s,3H,$NC\underline{H}_3$], 6.86-7.12 [m,4H,$N-C_6\underline{H}_4-N$], 7.10-7.90 [m,10H,$C_6\underline{H}_5SO_2$].

4b: mp 170°; ir 3205cm^{-1}(N-H);pmr δ1.00 [t,3H,J_{HH}=7Hz,$C\underline{H}_3$], 1.82 [broad,s,1H,NH], 3.52 [q,2H, J_{HH}=7,$C\underline{H}_2$], 6.80-7.10 [m,4H,$N-C_6\underline{H}_4-N$], 7.30-7.88 [m,10H,$C_6\underline{H}_5SO_2$].

4c: mp 194°; ir 3230cm^{-1}(N-H);pmr (DMSO-d_6) δ0.94 [d,6H,J_{HH}=7Hz,$CH(C\underline{H}_3)_2$], 4,43 [sept,1H,J_{HH} =7Hz, $C\underline{H}$], 6.86-7.26 [m,4H,$N-C_6\underline{H}_4-N$], 7.36-7.98 [m,10H,$C_6\underline{H}_5SO_2$].

4d: mp 177-178°; ir 3222cm^{-1}(N-H);pmr (acetone-d_6) δ2.85 [s,3H,$C\underline{H}_3SO_2$], 2.97 [s,3H,$C\underline{H}_3SO_2$], 3.28 [s,3H,$NC\underline{H}_3$], 7.25-7.50 [m,4H,aromatic].

4e: mp 146-148°; ir 3240cm^{-1}(N-H);pmr (acetone-d_6) δ1.10 [t,3H,J_{HH}=7Hz, $C\underline{H}_3CH_2$], 2.90 [s,3H, $C\underline{H}_3SO_2$], 3.00 [s,3H,$C\underline{H}_3SO_2$], 3.73 [q,2H,J_{HH}=7Hz,$C\underline{H}_2$], 7.40 [s(degenerate m),4H,aromatic].

4f: mp 169-171°; ir 3249cm^{-1}(N-H);pmr δ1.16[d,6H,J_{HH}=7Hz,$CH(C\underline{H}_3)_2$], 1.72 [broad s,1H,NH], 2.95 [s,3H,$C\underline{H}_3SO_2$], 3.02 [s,3H,$C\underline{H}_3SO_2$], 4.50 [sept,1H,J_{HH}=7Hz,$C\underline{H}$], 7.22 [s^*, 4H,aromatic].

5a: mp 80°; ir 3239, 3124cm^{-1}(N-H);pmr δ3.46 [d,6H,J_{PH}=11.5Hz,$OC\underline{H}_3$], 7.06-7.88 [m,13H,aromatic].

5b: mp 168-169°; ir 3230, 3097cm^{-1}(N-H); pmr δ1.16 [t,6H,J_{HH}=7Hz,$C\underline{H}_3$], 3.80 [m,4H,$C\underline{H}_2$], 7.05-7.95 [m,13H aromatic].

[#] All compounds gave satisfactory elemental analyses and mass-spectra. IR on KBr pellets. Pmr on Varian HA-100 spectrometer in $CDCl_3$sol. [*] Degenerate AA'BB' multiplet. Tlc on silica, solvent systems:benzene-acetone, 4/1 and 3/1;benzene-ethyl acetate, 2/1; pentane-acetone, 2/1; cyclohexane-ethyl acetate 1/1(v/v). Mixtures separated by column chromatography on silica.

Footnotes and References

1. (a) From Ph.D. thesis of D.L., to be submitted to Senate of Tel-Aviv University. (b) On leave from Bar-Ilan University, Ramat-Gan, Israel.

2. M. Sprecher and D. Levy, Tetrahedron Letters, 4563 (1969); ibid. 4957 (1969).
3. R. Adams and A.S. Nagarkatti, J.Am.Chem.Soc.**72**, 4601 (1950), and subsequent papers.
4. A.J. Kirby and S.G. Warren, "The Organic Chemistry of Phosphorous", Elsevier, Amsterdam, 1967, pp.76-81, and references therein.
5. S.B. Hartley, W.S. Holmes, J.K. Jacques, M.F. Mole, J.C.McCobrey,Quat.Rev.(Lon.),**17**,204 (1963).
6. A.Mustafa, M.M.Sidky, S.M.A.D. Zayed and M.F. Zayed, Justus Liebigs Ann.Chem. **716**, 198(1968).
7. M.M. Sidky and M.F. Zayed, Bull. Chem. Soc. Jap. **43**, 3312 (1970).

8. (a) Contrast Ref. 6. (b) Contrast Ref. 7.
9. However, triethyl phosphite induces the reaction of diethyl phosphite, presumably by formation of "I" which acts as a base.
10. cf. K.J.M. Andrews and F.R. Atherton, J. Chem. Soc. 4682 (1960).
11. In alkali the anions of the sulfonamide groups are formed and base hydrolysis is impeded.