# Application of Diethyl Azodicarboxylate in the Synthesis of Spirophosphoranes

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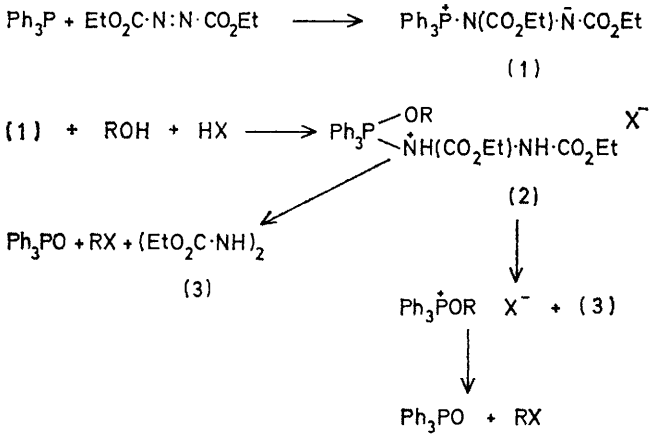
Diethyl azodicarboxylate is a convenient condensing agent in the synthesis of spirophosphoranes from cyclic $P^{III}$ compounds and 1,2- or 1,3-glycols. The variable-temperature $^1H$ n.m.r. spectra of some of the new spirophosphoranes are described.

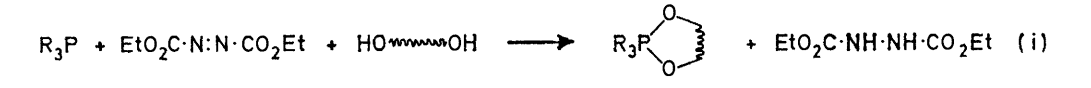
TRIPHENYLPHOSPHINE and diethyl azodicarboxylate form [1] a 1,3-dipolar species (1) which has been used as a



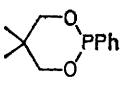
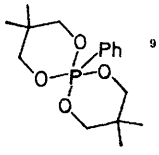

condensing agent in the coupling of alcohols and active-hydrogen compounds, HX, where X = phthalimido,[2] $(RO)_2PO_2$,[3,4] $RCO_2$,[4,5] CHYZ (Y = CN or MeCO, Z = CN or $CO_2Et$),[6] or ArO.[7] Inversion of configuration occurs at the alcohol carbon atom and reasonable intermediates are the phosphoranes (2), which could either undergo nucleophilic attack on carbon with simultaneous expulsion of the hydrazine (3) or fragment to give alkoxyphosphonium salts before nucleophilic attack.

We have used adducts analogous to (1) in a ready synthesis of spirophosphoranes which can be represented by the overall equation (i). Thus equimolar quantities of the cyclic phosphite (4; R = OPh), diethyl azodicarboxylate, and catechol in ether at room temperature gave the hydrazine (3) and the spirophosphorane (5; R = OPh) in 79% yield. The hydrazine (3) crystallises from the reaction mixture leaving the spirophosphorane in solution. Other spirophosphoranes obtained in a similar way include those listed in the Table. The method works well for 1,2- and 1,3-glycols but fails with 2-hydroxyethanethiol and 2-methylaminoethanol. A range of exocyclic *P*-substituents is permissible. The final cyclisation may involve either substitution at quinquecovalent phosphorus, *e.g.* (6), or prior fragmentation to an intramolecular phosphonium alkoxide, *e.g.* (7), followed by ring closure.

Besides providing a more convenient route to many spirophosphoranes the method allows the synthesis of others not hitherto accessible, *e.g.* the spirophosphoranes (8; R = H or Me). The $^1H$ n.m.r. spectrum of (8; R = Me) in 1-bromonaphthalene at room temperature consists of two signals of equal intensity in the methyl




Spirophosphoranes prepared according to equation (i)

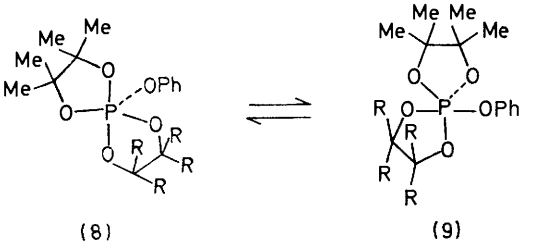
| $R_3P$ | HO~~OH | $R_5P$ | M.p. (°C) | % |
|---|---|---|---|---|
| (4; R = OPh) | Catechol | (5; R = OPh) [8] | 80—81 | 79 |
| (4; R = OPh) | Pinacol | (7; R = Me) | <25 | 74 |
| (4; R = OPh) | $(HO{\cdot}CH_2)_2$ | (7; R = H) | (B.p. 120° at 0.2 mmHg) | 47 |
| (4; R = OMe) | Catechol | (5; R = OMe) | 80—81.5 | 77 |
| (4; R = $NMe_2$) | Catechol | (5; R = $NMe_2$) | 104.5—106.5 | 73 |
| (4; R = $NMe_2$) | $(HO{\cdot}CH_2)_2$ | (10; $R^1$ = $NMe_2$, $R^2$ = H) | 37—39 | 56 |
| (4; R = SPh) | Catechol | (5; R = SPh) [8] | 136—137 | 70 |
|  | $(HO{\cdot}CH_2)_2CMe_2$ |  [9] | 61.5—63 | 87 |



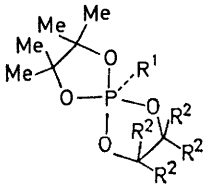


[1] E. Brunn and R. Huisgen, *Angew. Chem. Internat. Edn.*, 1969, **8**, 513.
[2] O. Mitsunobu, M. Wada, and T. Sano, *J. Amer. Chem. Soc.*, 1972, **94**, 679.
[3] O. Mitsunobu and M. Eguchi, *Bull. Chem. Soc. Japan*, 1971, **44**, 3427.
[4] O. Mitsunobu and M. Yamada, *Bull. Chem. Soc. Japan*, 1967, **40**, 2380.
[5] A. K. Bose, B. Lal, W. A. Hoffman, and M. N. Manhas, *Tetrahedron Letters*, 1973, 1619.
[6] M. Wada and O. Mitsunobu, *Tetrahedron Letters*, 1972, 1279.
[7] M. S. Manhas, W. H. Hoffman, B. Lal, and A. K. Bose, *J.C.S. Perkin I*, 1975, 461.
[8] S. Bone, S. Trippett, and P. J. Whittle, *J.C.S. Perkin I*, 1974, 2125.
[9] B. C. Chang, W. E. Conrad, D. B. Denney, D. Z. Denney. R. Edelmann, R. L. Powell, and D. W. White, *J. Amer. Chem, Soc.*, 1971, **93**, 4004.

region. These coalesce reversibly at 120 °C, a process associated with speeding up on the n.m.r. time-scale of the pseudorotation (8) ⇌ (9), involving placing the five-membered ring diequatorial and the phenoxy-group apical.[8] The free energy of activation of 20.5 kcal mol$^{-1}$ [*cf.*[10] 18.4 kcal mol$^{-1}$ for the same process in the tetraoxyphosphorane (10; $R^1$ = H, $R^2$ = Me)] supports the view[8] that hydrogen is a highly apicophilic atom.



(8) (9)



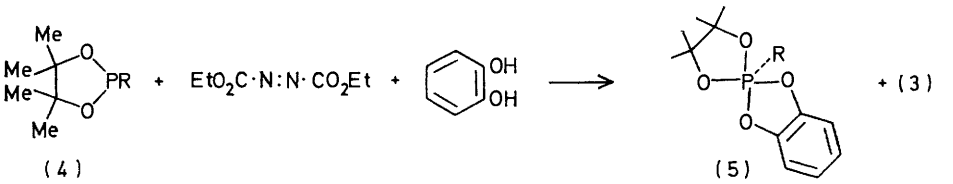
(10)

The variable-temperature n.m.r. spectra of compounds (8; R = H) and (10; $R^1$ = $NMe_2$, $R^2$ = H) in 1-bromonaphthalene show reversible coalescence of the two methyl signals at 41 and 157 °C, respectively, corresponding to free energies of activation for placing the unsubstituted rings diequatorial and the exocyclic substituents apical of 17.3 and 22.7 kcal mol$^{-1}$. The difference is a measure of the difference in apicophilicity between a phenoxy- and a dimethylamino-group in this system.

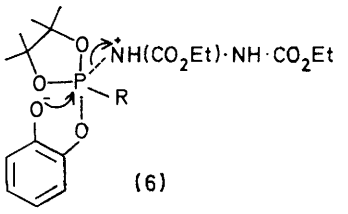
[10] D. Houalla, R. Wolf, D. Gagnaire, and K. B. Robert, *Chem. Comm.*, 1969, 443.

## EXPERIMENTAL

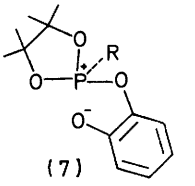
$^{31}$P N.m.r. spectra were obtained at 24.3 MHz for solutions in tetrahydrofuran; chemical shifts upfield from external 85% $H_3PO_4$ are quoted as positive. $^1$H N.m.r. spectra are for solutions in $CDCl_3$.



(4) (5) (3)



(6)



(7)

P-*Dimethylamino*-4′,4′,5′,5′-*tetramethyl*-1,3,2-*benzodioxaphosphole*-2-*spiro*-2′-1′,3′,2′-*dioxaphospholan* (5; R = $NMe_2$).—A solution of freshly distilled diethyl azodicarboxylate (0.87 g) in ether (5 ml) was added over 5 min to 2-dimethylamino-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan (0.95 g) in ether (10 ml) at 0 °C followed by a solution of catechol (0.55 g) in ether (5 ml), and the mixture was set aside at room temperature for 1 h. The crystalline hydrazine was then filtered off and the filtrate evaporated under reduced pressure. Extraction of the residue with light petroleum (b.p. 60—80°) and crystallisation of the product from the same solvent gave the *spirophosphorane* (5; R = $NMe_2$), m.p. 104.5—106.5°, $^{31}$P δ +31.6 p.p.m., τ 2.9—3.3 (4 H, m), 7.2 (6 H, d, *J* 10.5 Hz), and 8.7 (12 H, s) (Found: C, 56.0; H, 7.5; N, 4.6. $C_{14}H_{22}NO_4P$ requires C, 56.2; H, 7.4; N, 4.7%).

In a similar way were obtained 2,2,3,3,7,7,8,8-*octamethyl*-5-*phenoxy*-1,4,6,9-*tetraoxa*-5-*phosphaspiro*[4.4]*nonane*, m.p. below room temperature, $^{31}$P δ +44.2 p.p.m., τ 2.6—2.85 (5 H, m), 8.75 (6 H, s), and 8.9 (6 H, s); 2,2,3,3-*tetramethyl*-5-*phenoxy*-1,4,6,9-*tetraoxa*-5-*phosphaspiro*[4.4]*nonane*, b.p. 120° at 0.2 mmHg, $^{31}$P δ +37.2 p.p.m., τ 2.6—2.8 (5 H, m), 6.3—6.55 (4 H, m), and 8.85 (12 H, s); 5-*dimethylamino*-2,2,3,3-*tetramethyl*-1,4,6,9-*tetraoxa*-5-*phosphaspiro*[4.4]-*nonane*, m.p. 37—39°, $^{31}$P δ +33.7 p.p.m., τ 5.8—6.5 (4 H, m), 7.3 (6 H, d, *J* 10 Hz), 8.78 (6 H, s), and 8.82 (6H, s) (Found: C, 47.05; H, 8.7; N, 5.05. $C_{10}H_{22}NO_4P$ requires C, 47.8; H, 8.8; N, 5.6%); and P-*methoxy*-4′,4′,5′,5′-*tetramethyl*-1,3,2-*benzodioxaphosphole*-2-*spiro*-2′-1′,3′,2′-*dioxaphospholan*, m.p. 80—81.5°, $^{31}$P δ +32.9 p.p.m., τ 3.2 (4 H, m), 6.4 (3 H, d, *J* 12 Hz), and 8.7 (12 H, s) (Found: C, 54.4; H, 6.8. $C_{13}H_{19}O_5P$ requires C, 54.5; H, 6.6%).

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