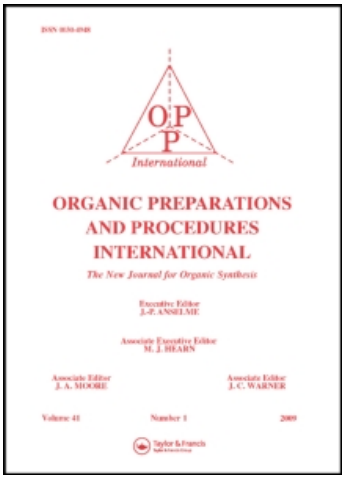

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

A FACILE SYNTHESIS OF NEW 2-PHOSPHONOBENZYLOXY-1,3,2-BENZOXAZA(DIOXA OR DIAZA)PHOSPHOLES

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To cite this Article Zhou, Jia and Chen, Ruyu(1998) 'A FACILE SYNTHESIS OF NEW 2-PHOSPHONOBENZYLOXY-1,3,2-BENZOXAZA(DIOXA OR DIAZA)PHOSPHOLES', Organic Preparations and Procedures International, 30: 6, 716 — 719
To link to this Article: DOI: 10.1080/00304949809355332
URL: http://dx.doi.org/10.1080/00304949809355332

5. a) A. Mckillop, J. D. Hunt, R. D. Naylor and E. C. Taylor, *J. Am. Chem. Soc.*, **93**, 4918 (1971); b) S. B. Shim, K. Kim and Y. H. Kim, *Tetrahedron Lett.*, **28**, 645 (1987).

6. G. A. Olah, T. L. Ho, *Synthesis*, 610 (**1976**).

7. Y. Yukawa, M. Sakai, S. Suzuki, *Bull. Chem. Soc. Jpn*, **39**, 2266 (1966).

8. P. Vankar, R. Rathore and S. Chandrasekaran, *J. Org. Chem.*, **51**, 3063 (1986).

9. J. G. Lee, K. H. Kwak and J. P. Hwang, *Synth. Commun.*, **22**, 2435 (1992).

10. H. Firouzabadi, N. Iranpoor, F. Kiaeezadeh and J. Toofan, *Tetrahedron*, **42**, 719 (1986).

11. A. Wall, P. A. Ganeshpure and S. Satish, *Bull. Chem. Soc. Jpn*, **66**, 1847 (1993).

12. B. Tamami and N. Goudarzian, *Eur. Polym. J.*, **28**, 1035 (1992).

13. H. Firouzabadi, E. Mottaghinejad and M. Seddighi, *Synth. Commun.*, **19**, 3469 (1989).

14. L. Singh and R. N. Kam, *ibid.*, **23**, 3139 (1993).

15. H. Firouzabadi and I. Mohammadpoor-Baltork, *ibid.*, **24**, 489 (1994).

16. J. Buckingham and S. M. Donaghy, Heilbron's "*Dictionary of Organic Compounds*", 5th ed., Chapman and Hall, New York, NY (**1982**).

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A FACILE SYNTHESIS OF NEW 2-PHOSPHONOBENZYLOXY-1,3,2-BENZOXAZA(DIOXA OR DIAZA)PHOSPHOLES

Submitted by
(04/06/98)

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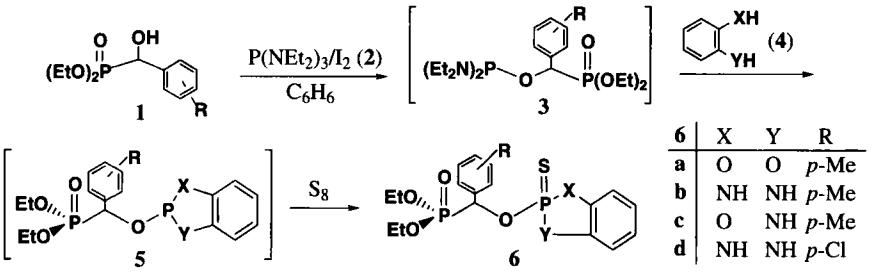
Phosphorus-containing heterocyclic compounds have received much attention due to their biological importance.[1-3] Previously, we reported the synthesis of some thio (seleno) phosphate-phosphonate derivatives and their significant herbicidal, antiviral and fungicidal activities.[4] In continuation of our work of elaborating phosphate-phosphonates into a variety of heterocyclic systems of biological

interest, we herein describe an efficient, one-pot synthesis of 2-phosphonobenzyloxy-1,3,2-benzoxaza(dioxa or diaza)phosphole 2-sulfides starting from the readily available synthon **1** (*Scheme*).



6	X	Y	R
a	O	O	*p*-Me
b	NH	NH	*p*-Me
c	O	NH	*p*-Me
d	NH	NH	*p*-Cl

Scheme

The phosphorylation of α-hydroxyalkylphosphonates **1** was carried out with *tris*(diethylamino)phosphine activated by iodine[5] to give the resultant phosphite-phosphonates **3** in nearly quantitative yields under mild conditions. Intermediates **3** underwent a cyclization with pyrocatechol, *o*-phenylenediamine or *o*-aminophenol to produce the cyclic phosphite-phosphonates **5**, which were then treated with sulfur to afford the expected title compounds **6a-d** in overall yields of 79.1-87.3%.

In summary, a convenient and efficient one-pot procedure has been developed for the synthesis of benzophospholes containing thio phosphate-phosphonate linkages in good yields under mild conditions. This method has considerable utility and can be extended to the syntheses of some new heterocyclic systems with potential biological interest.

EXPERIMENTAL SECTION

NMR spectra were taken on a Bruker AC-P200 spectrometer. Tetramethylsilane (TMS) was used as an internal standard for ^{1}H NMR, and 85% H_3PO_4 was used as an external standard for ^{31}P NMR spectroscopy. The nuclei that are deshielded relative to their respective standards are assigned a positive chemical shift. IR spectra were recorded on a Shimadzu-435 spectrometer. Mass spectra were recorded on a Hewlett-Packard 5988 instrument. Elemental analyses were carried out on a Yana MT-3 instrument. α-Hydroxyalkylphosphonates **1**[6] and tris(diethylamino)phosphine[7] were prepared according to published methods.

Representative Experimental Procedure. 2-[(P,P-Diethoxy)phosphono(*p*-methyl)benzyloxy]-1,3,2-benzodioxaphosphole 2-Sulfide (6a).- A mixture of *tris*(diethylamino)phosphine (0.78 g, 3.15 mmol) and iodine (0.038 g, 0.15 mmol) in 50 mL of anhydrous benzene was heated at 70° in a stream of nitrogen for approximately 20 min until the precipitate dissolved. The solution was cooled to ambient temperature, and diethyl 1-hydroxy-1-(*p*-methyl)benzyl phosphonate (0.77 g, 3.0 mmol) was added. After having been maintained at 75° for 1.5 h, the reaction mixture was cooled to room temperature, and pyrocatechol (0.33 g, 3.0 mmol) was added. Then the reaction mixture was heated at 75° for 3 h. Transformation to the desired compound **6a** was accomplished by adding sulfur (0.15 g, 4.69 mmol) and keeping the mixture at 70° for 2.5 h. The solvent was removed *in vacuo*, and the compound was extracted from the residue with 10 mL of acetone. After filtration, the solvent was

distilled off, and purification of the product was achieved with silica gel flash column chromatography using ethyl acetate/petroleum ether (bp. 60-90°) (1:4, v/v) as the eluent. This afforded **6a** as a colorless syrup (1.02 g, 79%). IR (film): 3190, 3031, 2909, 1602, 1499,1465, 1253 (s, P=O), 1053, 1016, 944, 881 (s, P-O-C), 830 (m), 754 (s), 714 (m, P=S) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.23 (t, 6 H, 2 CH_3), 2.28 (ds, 3 H, CH_3), 4.07 (m, 4 H, 2 CH_2), 5.67 (dd, 1 H, CH, J = 14.0 Hz), 6.71-7.33 (m, 8 H, 2 C_6H_4); ^{31}P NMR ($CDCl_3$); δ 15.77, 16.17, 69.69, 69.29 (two signals overlapped), 68.89, $^3J_{P1P2}$ = 32.34 Hz; MS (EI) *m/z*: 428 (M^+, 4.96%), 213 (15.1), 171 (13.09), 139 (12.82), 119 (24.49), 111 (17.24), 105 (100), 93 (22.26), 91 (35.67), 77 (14.9), 65(26.16).

Anal. Calcd for $C_{18}H_{22}O_6P_2S$: C, 50.46; H, 5.19. Found: C, 50.61; H, 5.42

2-[(P,P-Diethoxy)phosphono(*p*-methyl)benzyloxy]-1,3,2-benzodiazaphosphole 2-Sulfide (6b).- A colorless syrup; yield 87%. IR (film): 3388, 3127, 2971, 1607, 1511, 1490 (s), 1251 (s, P=O), 1091, 1049, 1015, 918 (s, P-O-C, P-N, C-N), 831 (s), 734 (s), 698 (s, P=S) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.22 (m, 6 H, 2 CH_3), 2.34 (ds, 3 H, CH_3), 3.92-4.18 (m, 4 H, 2 CH_2), 5.76 (dd, 1 H, CH, J = 12.6 Hz), 5.78 (d, 1 H, NH, J = 18 Hz), 6.14 (d, 1 H, NH, J = 18 Hz), 6.68-7.36 (m, 8 H, 2 C_6H_4). ^{31}P NMR ($CDCl_3$): δ 17.36, 16.69, 70.94, 70.27, $^3J_{P1P2}$ = 24.25 Hz; MS (EI) *m/z*: 426 (M^+, 19.12%), 290 (4.79), 242 (10.93), 213 (11.99), 185 (16.07), 169 (10.37), 154 (21.10), 137 (34.3), 119 (11.77), 109 (5.09), 105 (100), 93 (16.75), 91 (22.07), 65 (21.55).

Anal. Calcd for $C_{18}H_{24}N_2O_4P_2S$: C, 50.70; H, 5.68; N, 6.57. Found: C, 50.98; H, 5.61; N, 6.86

2-[(P,P-Diethoxy)phosphono(*p*-methyl)benzyloxy]-1,3,2-benzoxazaphosphole 2-Sulfide (6c).- A colorless syrup; yield 82%. IR (film): 3407 (m, N-H), 2969, 1617, 1588, 1502, 1458 (s), 1252 (s, P=O), 1182, 1054, 1021, 953, 923 (s, P-O-C, P-N, C-N), 848 (s), 745 (s), 710 (s, P=S) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.16 (m, 6 H, 2 CH_3), 2.32 (ds, 3 H, CH_3), 2.83-4.52 (m, 4 H, 2 CH_2), 5.58-5.92 (dq, 1 H, CH, J = 14.0 Hz), 6.54-6.83 (dd, 1 H, NH, J = 18.3 Hz), 6.63-7.42 (m, 8 H, 2 C_6H_4); ^{31}P NMR ($CDCl_3$): δ 17.54 (d), 17.47 (d), 74.02 (d), 73.34 (d), $^3J_{P1P2}$ = 42.22 Hz; MS (EI) *m/z:* 427 (M^+, 8.42%), 392 (25.87), 364 (39.42), 272 (14.49), 241 (11.69), 213 (42.16), 180 (26.78), 138 (13.0), 121 (30.97), 108 (56.04), 105 (100), 93 (29.78), 91 (21.71), 80 (41.97), 74 (24.40), 65 (29.24).

Anal. Calcd for $C_{18}H_{23}NO_5P_2S$: C, 50.58; H, 5.44; N, 3.28. Found: C, 50.39; H, 5.52; N, 3.41

2-[(P,P-Diethoxy)phosphono(*p*-chloro)benzyloxy]-1,3,2-benzodiazaphosphole 2-Sulfide (6d).- A colorless syrup; yield 87%. IR (film): 3380 (s, NH), 3123, 2964, 1628, 1602, 1488 (s), 1247 (s, P=O), 1083, 1011, 971, 918 (s, P-O-C, P-N, C-N), 827 (s), 733 (s), 709 (s, P=S) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.17-1.34 (m, 6 H, 2 CH_3), 3.96-4.17 (m, 4 H, 2 CH_2), 5.79 (dd, 1 H, CH, J = 12.52 Hz), 5.82 (d, 1 H, NH, J = 20.84 Hz), 6.21 (d, 1 H, NH, J = 18.78 Hz), 6.68-7.42 (m, 8 H, 2 C_6H_4); ^{31}P NMR ($CDCl_3$): δ 16.90, 16.61, 71.10, 70.81, $^3J_{P1P2}$ = 23.50 Hz; MS (EI) *m/z*: 446 (M^+, 29.24%), 290 (5.84), 262 (24.11), 233 (10.85), 206 (16.09), 185 (13.34), 169 (23.05), 154 (90.20), 137 (54.73), 127 (31.86), 125 (100), 121 (10.50), 105 (18.89), 93 (13.45), 77 (16.47), 65 (24.00).

Anal. Calcd for $C_{17}H_{21}ClN_2O_4P_2S$: C, 45.69; H, 4.75; N, 6.27. Found: C, 45.53; H, 4.62; N, 6.53

Acknowledgement.- The authors thank the National Natural Science Foundation of China for financial support.

REFERENCES

1. S. Y. Wu and J. E. Casida, *Phosphorus, Sulfur and Silicon,* **102**, 177 (1995); C. D. Reddy, M. S. Reddy and K. D. Berlin, *ibid.*, **102**, 103 (1995); A. Hirashima, *Agric. Bio. Chem.,* **53**, 175 (1989).

2. H. L. Wang, J. Zhou, Y. G. Qiu, K. S. Feng and R. Y. Chen, *Phosphorus, Sulfur and Silicon,* **104**, 135 (1995); R. Y. Chen and R. Bao, *Synthesis,* 618 (**1989**); R. Y. Chen and J. S. Tang, *Phosphorus, Sulfur and Silicon,* **48**, 259 (1990); R. Y. Chen and L. F. Cheng, *ibid.,* **44**, 193 (1989); R. Y. Chen and M. Zhang, *Science in China (Series B),* **38**, 152 (1995); *Chem. Abstr.,* **123**, 144000f (1995).

3. Y. Nishizuka, *Nature,* **308**, 693 (1984); V. L. Boyd, M. F. Summers, S. M. Ludeman, W. Egan, G. Zon and J. B. Regan, *J. Med. Chem.,* **30**, 366 (1987).

4. J. Zhou, R. Y. Chen and X. F. Yang, *Heteroatom Chem.,* **9**, 369 (1998).

5. H. Nöth and H. J. Vetter, *Chem. Ber.,* **94**, 1505 (1961).

6. F. Texier-Boullet and A. Foucaud, *Synthesis*, 916 (**1982**).

7. C. Stuebe and H. P. Lankelma, *J. Am. Chem. Soc.*, **78**, 976 (1956).

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