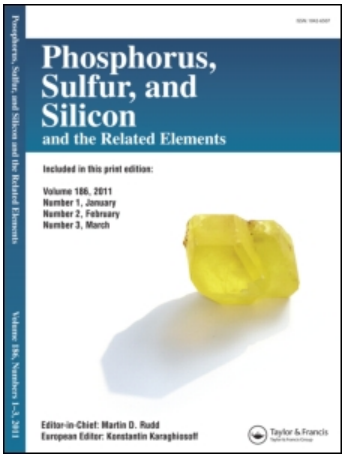
This article was downloaded by:
On: *29 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS OF (*R*)-1,1,2-TRIPHENYL-1,2-ETHANEDIOL DERIVED PHOSPHONATES

Bernhard Brodesser[a]; Manfred Braun[a]
[a] Institut für Organische Chemie und Makromolekulare Chemie der Universität Düsseldorf, Düsseldorf, FRG

To cite this Article Brodesser, Bernhard and Braun, Manfred(1989) 'SYNTHESIS OF (*R*)-1,1,2-TRIPHENYL-1,2-ETHANEDIOL DERIVED PHOSPHONATES', Phosphorus, Sulfur, and Silicon and the Related Elements, 44: 3, 217 — 221
To link to this Article: DOI: 10.1080/10426508908040612
URL: http://dx.doi.org/10.1080/10426508908040612

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

Phosphorus, Sulfur, and Silicon, 1989, Vol. 44, pp. 217–221
Reprints available directly from the publisher
Photocopying permitted by license only
© 1989 Gordon and Breach Science Publishers, Inc.
Printed in the United Kingdom

SYNTHESIS OF (*R*)-1,1,2-TRIPHENYL-1,2-ETHANEDIOL DERIVED PHOSPHONATES

BERNHARD BRODESSER and MANFRED BRAUN*
Institut für Organische Chemie und Makromolekulare Chemie der Universität Düsseldorf, Universitätsstraße 1, D-4000 Düsseldorf, FRG

(Received October 25, 1988)

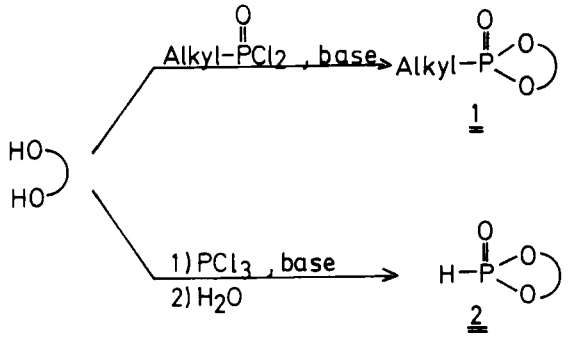
Methanephosphonic acid monoester **4** is synthesized by the reaction of (*R*)-1,1,2-triphenyl-1,2-ethanediol (**3**) with methanephoshonyl dichloride, followed by hydrolysis. In a similar way, phosphonic acid monoester **8** is obtained from triphenyl glycol **3** and phosphorus trichloride. When acid or alkaline hydrolyses are avoided, the cyclic phosphonate **5** is available from glycol **3** and methanephosphonyl dichloride in a diastereoselective manner.

Key words: C–P chirality transfer; nuclear Overhauser effect in cyclic phosphonate; condensation of methanephosphonyl dichloride with triphenylglycol; condensation of phosphorus trichloride with triphenylglycol; diazomethane esterification of methanephosphonic acid monoester.

Downloaded At: 18:44 29 January 2011

INTRODUCTION

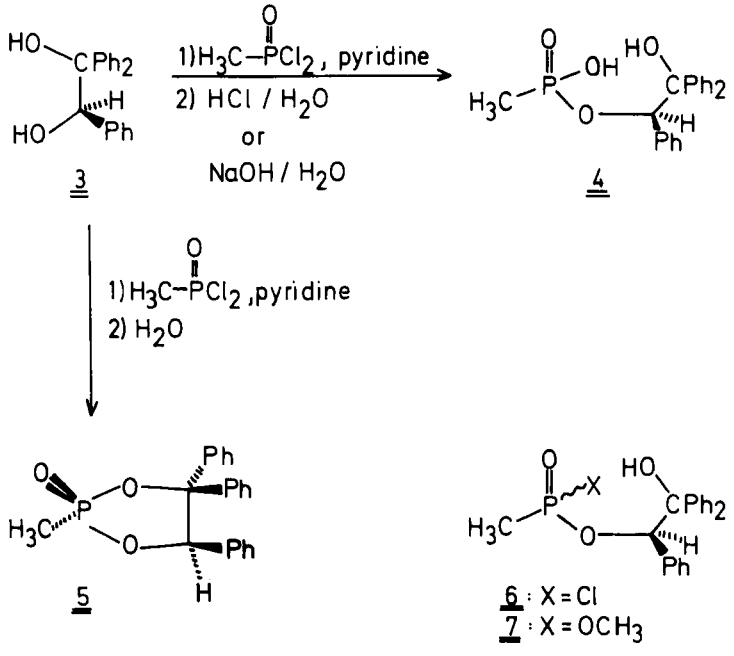
Cyclic esters **1** of alkanephosphonic acid are known to be available from the reaction of alkanephosphonyl dichlorides with diols.[1–3] On the other hand, phosphonic esters **2** are formed, when phosphorus trichloride is treated with diols, followed by hydrolysis.[4,5] Despite of numerous applications of these reactions, there are obviously some limitations. Thus, ethylene glycol and *meso*-2,3-butanediol were found to give not the expected dioxaphospholane but to deliver acyclic products.[1]



In this paper, we would like to report on the reaction of methanephosphonyl dichloride and of phosphorus trichloride with (*R*)-1,1,2-triphenyl-1,2-ethanediol (**3**), a derivative of (*R*)-mandelic acid,[6,7] which was recently used as chiral auxiliary group in stereoselective aldol reactions.[8]

RESULTS AND DISCUSSION

When a dichloromethane solution of methanephosphonyl dichloride and (*R*)-1,2,2-triphenyl-1,2-ethanediol (**3**) is heated in the presence of pyridine and treated, thereafter with dilute hydrochloric acid or with aqueous sodium hydroxide solution, a colourless solid product with extremely low solubility in less polar organic solvents as for example chloroform or diethyl ether is obtained. The decision, whether the structure of methanephosphonic acid monoester **4** or that of the dioxaphospholane **5** should be assigned, had to be made in favour of the former, not only according to the spectroscopic data, but also as a result of the elemental analysis. The coupling constant of the benzyl proton with the phosphorus atom, $^3J_{PH} = 8.7$ Hz, observed both in the ^{1}H- and in the ^{31}P-NMR spectra, indicates, that the esterification had occured with the secondary hydroxyl group of the diol **3**. The ^{13}C–^{31}P coupling constants of phosphorus to the secondary and to the tertiary carbon atoms $^2J_{PC}$ and $^3J_{PC}$ are within the same range (6.8 and 8.5 Hz), which is in accordance with corresponding data in the literature.[9]



The chloride **6** can be assumed to be an intermediate, which hydrolyzes to give the monoester **4**. With respect to the fact, that 2-oxo-1,3,2-dioxaphospholanes readily undergo a ring opening, which is induced by nucleophilic attack to the phosphorus atom,[10] the cyclic ester **5** could be anticipated as an intermediate, too: The cleavage of the heterocyclic ring of **5** during acid or alkaline hydrolysis should lead to the formation of the monoester **4**.

It was indeed possible, to obtain the cyclic phosphonate **5** as the major product, formed from diol **3** and methanephosphonyl dichloride, provided that strong

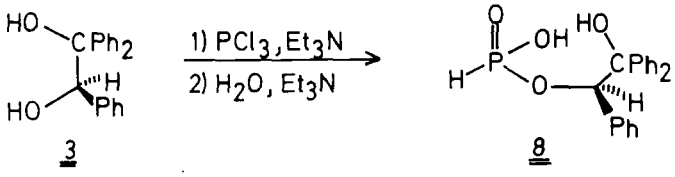
Downloaded At: 18:44 29 January 2011

bases and acids were excluded. To this purpose, the time, left to shake the mixture with water after completion of the reaction, was limited to a maximum of 45 seconds. Although the spectroscopic yield of crude methylphosphonate **5** amounts 75%, the purification by column chromatography leads to a considerable loss of material.

The synthesis of the cyclic phosphonate **5** occurs in a *diastereoselective* manner, which seems to be remarkable with respect to the fact, that ephedrine derived 2-oxo-1,3,2-oxaazaphospholidines are formed either without any[11] or only marginal[12] stereoselectivity. Contrarily, the phosphonate **5** is produced in a ratio of diastereomers of at least 9:1. By column chromatography, the main product is obtained in a diastereomerically pure form. The R_P, R_C configuration, outlined in formula **5**, is elucidated by a nuclear Overhauser experiment: The irradiation of the methyl protons causes a small but—as shown in the difference spectrum—unambiguous enhancement of the intensity of the benzyl proton (1.5%[13]) and of two (and just two) aromatic ortho protons, which are located in one of the phenyl substituents. Thus, the configuration of methyl group and benzyl proton has turned out to be *syn*.

When methanephosphonate **4** is treated with diazomethane, the methyl ester **7** is formed as 1:1 mixture of diastereomers. This transformation might be considered as a further proof for the structure of the mono-ester **4**.

Phosphorus trichloride was allowed to react with diol **3** in the presence of triethylamine, and the subsequent hydrolysis was also mediated by triethylamine. In this case, too, the acyclic monoester **8** is formed, whereas no cyclic product of type **2** can be detected. The structure of **8** is assigned, again, by spectroscopic data and elemental analysis.



3 8

Obviously, the bulky substituents in triphenylglycol (**3**) do not favour a ring closure to give type **1** or type **2** products. Although the synthesis of the cyclic phosphonate **5** could be accomplished, the ring strain of this compound diminishes significantly its stability: The monoester **4** is formed instantaneously, when **5** is treated with dilute acid or alkali.

EXPERIMENTAL

General: Melting points (uncorrected) were determined with a Büchi/Tottoli melting point apparatus. IR spectra; Perkin–Elmer spectrophotometer 710 B. NMR spectra: Varian VXR 300 and Bruker AM 200; ^{1}H- and ^{13}C-NMR spectra were recorded with tetrametylsilane as internal standard, whereas in the ^{31}P-NMR spectra, 85% phosphorus acid was used as external standard. Mass spectra: Varian MAT CH-5. Specific rotations were determined with a Perkin–Elmer 141 polarimeter. Elemental analyses were performed by Mikroanalytisches Laboratorium Beller, Göttingen. TLC: Polygram-Sil-G/UV$_{254}$-Fertigfolien (Macherey-Nagel). Preparative thin-layer chromatography: Kieselgel–Fertigplatten Sil G-200/UV$_{254}$ (Merck). Column chromatography: Kieselgel 60, mesh size 0.2–0.5 mm (Merck).

Downloaded At: 18:44 29 January 2011

(R)-1,1,2-Triphenyl-1,2-ethanediol (R)-**3**: is prepared according to the procedure given in Reference 14.

(1'R)-Methanephosphonic Acid 2'-Hydroxy-1',2',2'-triphenylethyl Ester (**4**). A solution of 4.6 g (34.5 mmol) methanephosphonyl dichloride in 50 ml dry dichloromethane is stirred at room temperature under nitrogen in a 250-ml three-necked flask, which is equipped with a dropping funnel, a magnetic stirrer, and a reflux condenser. Under vigorous strirring, a mixture of 10.0 g (34.5 mmol) **3**, 5.5 g (69 mmol) pyridine and 50 ml dry dichloromethane is added drop by drop. Thereafter, the solution is refluxed for 48 h.

Hydrolysis: Procedure A: When the reaction mixture has cooled down, 200 ml of 2M hydrochloric acid are added, and stirring is continued for 48 h at room temperature. At the borderline of the organic and the aqueous layer, a colourless, amorphous precipitate forms gradually. The solid material is filtered off, washed with chloroform and with water, dried in vacuo, and finally recrystallized several times from tetrahydrofuran to give 5.2 g (41%) of analytically pure **4**.

Hydrolysis: Procedure B: The reaction mixture, cooled down to room temperature, is transferred into a separatory funnel and washed three times with a total amount of 200 ml water. The organic layer is concentrated in vacuo, dissolved in a mixture of dioxane and 2M aqueous sodium hydroxyde solution, and refluxed for 8 h. When the cooled solution is acidified with dilute hydrochloric acid to $p_H = 2$, a colourless precipitate forms, which is filtered off, washed with chloroform and with water, and recrystallized from tetrahydrofuran. Thus, **4** is obtained in 35% yield.

m.p. 171°C; $[\alpha]_D^{25} = 108.3$ ($c = 0.4$ in pyridine). Anal. calc. for $C_{21}H_{21}O_4P$: C 68.47, H 5.75, P 8.41. Found: C 68.67, H 5.79, P 8.39. ^{1}H-NMR ([D$_6$]-DMSO; 300 MHz): $\delta = 0.82$ (d, $J = 17.4$ Hz, 3H, CH_3), 6.18 (d, $J = 8.7$ Hz, 1H, 1'-H), 7.05–7.65 (m, 17H, OH and aromatic H). ^{13}C-NMR ([D$_6$]-DMSO; 75 MHz): $\delta = 13.16$ (d, $J_{CP} = 153.1$ Hz, CH_3), 79.30 (d, $J_{CP} = 8.5$ Hz, C-2'), 80.19 (d, $J_{CP} = 6.8$ Hz, C-1'), 137.54, 144.60, 145.24 (aromatic ipso C), 126.21–129.0 (other aromatic C). ^{31}P-NMR ([D$_6$]-DMSO; 81 MHz): $\delta = 28.0$ (quartet of doublets, $^2J_{PH} = 17.4$ Hz; $^3J_{PH} = 8.8$ Hz).—IR (KBr): 3050–3200, 3060, 3020, 1490, 1445, 1390, 1310, 1210, 1180, 1000, 910, 850, 760, 750, 720, 700, 670, 640, 620 cm^{-1}. MS (70 eV): $m/e = 273$ (1%, $M^+ - CH_3PO_3H$), 255 (9%, 273-H_2O), 183 (69%, $[C_6H_5]_2COH^+$), 165 (fluorenyl kation[14]), 105 (100%, $C_7H_5O^+$), 77 (43%, $C_6H_5^+$).

(2R,5R)-2-Methyl-4,4,5-triphenyl-2-oxo-1,3,2-dioxaphospholan (**5**). As described in the procedure above, a mixture of 10 g (34.5 mol) **3**, 5.5 g (69 mmol) pyridine, and 50 ml dry dichloromethane is added dropwise under nitrogen to a solution of 4.6 g (34.5 mmol) methanephosphonyl dichloride in 50 ml dichloromethane. The mixture is refluxed for 48 h, cooled down to room temperature, transferred into a separatory funnel, and washed as quickly as possible twice with a total amount of 400 ml ice cold water. The organic layer is dried immediately with sodium sulfate and concentrated in vacuo at 25°C to give 11.2 g of a colorless solid material, which contains according to the ^{1}H-NMR spectrum the desired product **5** in at least 75% yield. The purification of a 2 g sample of the crude product by column chromatography (silical gel; chloroform/ethyl acetate 9:1) affords 0.292 g pure **5**; m.p. 160°C; $[\alpha]_D^{25} = 160.2$ (c = 0.1 in chloroform). Anal. Calc. for $C_{21}H_{19}O_3P$: C 71.99, H 5.47. Found: C 71.89, H 5.58. ^{1}H-NMR ($CDCl_3$; 300 MHz): $\delta = 1.49$ (d, $J = 17.6$ Hz, 3H, CH_3), 6.62 (d, $J = 13.3$ Hz, 1H, 5-H), 7.02–7.64 (m, 15H, aromatic H). IR (KBr): 3030, 3060, 2920, 1480, 1440, 1310, 1250, 970, 900, 810, 740, 680 cm^{-1}. MS (70 eV): $m/e = 350$ (1%, M^+), 273 (4%, $M - C_6H_5$). 272 (4%, $M - CH_3PO_2$), 254 (91%, $M - CH_3PO_3H_2$), 243 (10%, 272-CHO), 228 (29%, 254-C_2H_2), 183 (56%, $[C_6H_5]_2COH^+$), 165 (48%, fluorenyl kation), 104 (100%, $C_6H_5CHCH_2$), 77 (42%, $C_6H_5^+$).

(R_P,1'R)- and (S_P,1'R)-Methanephosphonic Acid [(2'-Hydroxy-1',2',2'-triphenylethyl)(methyl)]ester (**7**). To a mixture of 1.0 g (2.7 mmol) **4**, 250 ml tetrahydrofuran, and 10 ml water is added under stirring at room temperature as much of a freshly prepared etheral diazomethane solution, that the yellow colour of the reaction mixture just persists and the evolution of nitrogen ceases. Stirring is continued overnight at room temperature. The solvent is removed in a rotary evaporator, and the oily residue is dissolved in chloroform and dried with sodium sulfate. Evaporation of the solvent in vacuo affords a colourless, amorphous residue, which is recrystallized from chloroform/hexane to give 0.89 g (85%) **7** as a 1:1 mixture of diastereomers; m.p. 165°C; $[\alpha]_D^{25} = 104.4$ (c = 0.5 in chloroform). Anal. calc. for $C_{22}H_{23}O_4P$: C 69.10, H 6.06, P 8.10. Found: C 69.15, H 6.09, P 8.06. ^{1}H-NMR ($CDCl_3$; 300 MHz): $\delta = 1.01$ and 1.10 (2 d, J = 17.84 Hz, 3H, CH_3), 3.04 and 3.22 (2d, $J = 8.37$ Hz, 3H, OCH_3), 3.20 (m_c, 1H, OH), 6.27 and 6.37 (2d, $J = 9.03$ Hz, 1H, 1'-H), 7.03–7.85 (m, 15H, aromatic H). IR (KBr): 3500–3200, 3060, 3030, 2950, 1480, 1440, 1300, 1220, 1160, 1040, 1000, 950, 905, 805, 740, 700, 680 cm^{-1}. MS (70 eV): $m/e = 382$ (1%, M^+), 272 (2%, M-CH_3P[O][OH][OCH_3]), 254 (6%, 272-H_2O), 200 (100%, $M - [C_6H_5]_2CO$), 183 (30%, $[C_6H_5]_2COH^+$), 165 (14%, fluorenyl kation), 105 (63%, $C_6H_5CO^+$), 94 (90%, $M - [C_6H_5]_2C$[OH]C[O][C_6H_5]), 77 (36%, $C_6H_5^+$).

Downloaded At: 18:44 29 January 2011

(1'R)-Phosphonic Acid 2'-Hydroxy-1',2',2'-triphenylethyl Ester (**8**). A solution of 1.65 ml (2.35 g; 34.5 mmol) phosphorus trichloride in 50 ml dry benzene is added drop by drop at room temperature to a mixture of 5 g (17.25 mmol) triphenylglycol **3**, 4.8 ml (3.5 g; 34.5 mmol) triethylamine, and 150 ml dry benzene, which is vigorously stirred under nitrogen in a 500 ml three-necked flask, equipped with a reflux condenser, a dropping funnel, and a septum. The mixture is refluxed for 8 h and thereafter stirred at room temperature for another 12 h. Through the septum, 2.4 ml (1.17 g; 17.25 mmol) triethylamine and about 20 ml water are injected subsequently. The addition of the first few drops of water causes the precipitation of a white gelatinous material. Stirring is continued for 1 h. The precipitate is filtered off, washed several times with water, and dried in oil pump vacuum to give 4.3 g (74%) **8**; m.p. 127°C; $[\alpha]_D^{25} = 112.9$ (c = 0.5 in pyridine). Anal. calc. for $C_{20}H_{19}O_4P$: C 67.79, H 5.40, P 8.74. Found: C 67.68, H 5.54, P 8.73. ^{1}H-NMR ([D$_6$]-DMSO; 300 MHz): $\delta = 6.15$ (d, $J = 8.6$ Hz, 1H), 6.37 (d, $J = 668.1$ Hz, 1H, H-P), 7.07–7.62 (m, 17H, OH and aromatic H). ^{13}C-NMR ([D$_6$]-DMSO; 75 MHz): $\delta = 79.19$ (d, $J_{CP} = 8$ Hz, C-1'), 80.49 (d, $J_{CP} = 6$ Hz, C-2'), 137.00, 144.41, 145.02 (aromatic ipso C), 126.29–128.89 (other aromatic C). ^{31}P-NMR ([D$_6$]-DMSO; 81 MHz): $\delta = 4.0$ (doublets of doublets, $^1J_{PH} = 667.4$ Hz, $^3J_{PH} = 8.4$ Hz). IR (KBr): 3500–3200, 3060, 3020, 2450, 1490, 1440, 1390, 1310, 1200, 1000, 850, 800, 750, 730, 700, 620 cm^{-1}. MS (70 eV): $m/e = 337$ (3%, M − OH), 272 (11%, M − H_3PO_3), 254 (94%, 272-H_2O), 165 (100%, fluorenyl kation), 105 (64%, C_7H_5O), 77 (31%, C_6H_5).

ACKNOWLEDGEMENTS

This work was supported by the *Fonds der Chemischen Industrie* and by the *Karl-Winnacker Foundation*. We would like to thank *Prof. Dr. G. Hägele* and *Mr. M. Batz* (Institut für Anorganische Chemie, Univ. Düsseldorf) for recording the ^{31}P-NMR spectra. *Dr. A. Steigel* and *Mr. J. Keul* provided NMR and mass spectra.

REFERENCES AND NOTES

1. A. F. McKay, R. O. Braun and G. R. Vavasour, *J. Am. Chem. Soc.* **74,** 5540 (1952).
2. A. F. McKay, R. A. B. Bannard, R. O. Braun and R. L. Benness, *J. Am. Chem. Soc.* **76,** 3546 (1954).
3. C. Yuan, S. Li and Z. Cheng, *Synthesis* **1988,** 186.
4. H. J. Lucas, F. W. Mitchell, Jr. and C. N. Scully, *J. Am. Chem. Soc.* **72,** 5491 (1950).
5. A. Zwierzak, *Can. J. Chem.* **45,** 2501 (1967).
6. A. McKenzie and H. Wren, *J. Chem. Soc.* **97,** 473 (1910).
7. R. Roger, W. B. McKay, *J. Chem. Soc.* **1931,** 2229.
8. M. Braun, *Angew. Chemie* **99,** 24 (1987); *Angew. Chem. Int. Ed. Engl.* **26,** 24 (1987).
9. H. O. Kalinowski, S. Berger and S. Braun, *^{13}C-NMR-Spektroskopie*, Thieme Verlag, Stuttgart 1984, Chap. 4, pp. 530–538; *Carbon-13 NMR Spectral Data*, W. Bremser, Ed., VCH Verlag, Weinheim 1987, CNM 51988.
10. D. G. Gorenstein, A. Chang and J.-C. Yang, *Tetrahedron* **43,** 469 (1987); J.-C. Yang, D. G. Gorenstein, *Tetrahedron* **43,** 479 (1987).
11. D. H. Hua, R. Chan-Yu-King, J. A. McKie and L. Myer, *J. Am. Chem. Soc.* **109,** 5026 (1987).
12. D. B. Cooper, C. R. Hall, J. M. Harrison and T. D. Inch, *J. Chem. Soc., Perkin I* **1977,** 1969.
13. For a comparison, see the NOE effect of 1,3 diaxial protons in a cyclohexane ring, which amounts a maximum value of 3%: J. M. Sanders, B. Hunter, *Modern NMR Spectroscopy*, Oxford University Press 1987, p. 178.
14. R. Devant, U. Mahler and M. Braun, *Chem. Ber.* **121,** 397 (1988).

Downloaded At: 18:44 29 January 2011