Reaction between phosphines and itaconic anhydride in the presence of water: an efficient one-pot synthesis of 5-oxo-1,2λ5-oxaphospholanes

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5-Oxo-1,2λ5-oxaphospholane derivatives were obtained in excellent yields from the reaction between alkyl or aryl phosphines, and itaconic anhydride in presence of water in dichloromethane.

Keywords: itaconic anhydride, one-pot synthesis, 1,2λ5-oxaphospholane, phosphine, water

In recent years, heterocyclic compounds that contain phosphorus atoms have drawn the attention of synthetic chemists. This interest has resulted from the recognition of the value of such compounds in a variety of biological, industrial and chemical synthetic uses.[1,2] Heterocycles that include a phosphorus atom linked to an oxygen atom are common to a diverse array of important biological and industrial molecules, e.g. oxaphospholanes. Recently, 2-alkoxy-1,2λ5-oxaphospholan-2-one derivatives **1** attracted much attention as sugar surrogates since analogues with phosphorus atoms replacing the anomeric carbons could potentially serve as carbohydrate mimics.[3] Furthermore, 2-methyl-1,2λ5-oxaphospholane-2,5-dione **2** a cyclic anhydride of (2-carboxyethyl)methylphosphinic acid, is a commercial product of Fa Clariant (Germany), which is used to produce a flame retardant poly(butylene terephthalate)[4] and poly(ethylene terephthalate)[5] sold under the trade name Trevira® CS.

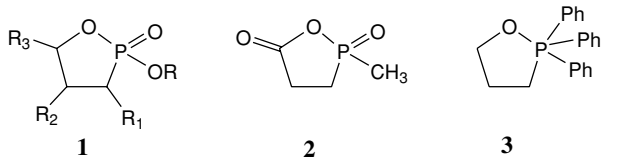
In 1967, Hands and Mercer reported the first isolation of a 2,2,2-triphenyl-1,2λ5-oxaphospholane **3**.[6] In continuation of this report, several synthetic methods, have been developed to prepare a variety of oxaphospholanes during recent decades.[7]

In connection with our previous works on a one-pot phosphine-based multi-component synthesis of target molecules,[8] the reaction of alkyl or aryl phosphines **4** with itaconic anhydride in the presence of water was examined and gave the corresponding 1,2-oxaphospholanes **5** in high yields (Scheme 2).

The structures of compounds **5a–c** were deduced from their elemental analyses and their IR, ^{1}H, ^{13}C and ^{31}P NMR spectra. The nature of these compounds as 1:1:1 adducts was apparent from the mass spectra which displayed molecular ion peaks at *m/z* 392, 332, and 248 for **5a**, **5b** and **5c**, respectively.

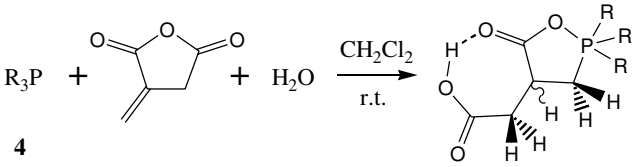
The methylene groups of compounds of **5a–c** are attached to an asymmetric carbon atom bearing a hydrogen atom and appear as AB systems. Although the presence of the ^{31}P nucleus complicates both the ^{1}H and ^{13}C NMR spectra of **5a–c**, it helps in assignment of the signals by long-range couplings with ^{1}H and ^{13}C nuclei.

The ^{1}H NMR spectrum of **5a** exhibited five distinct multiplets arising from methylenes and methine protons at δ 2.45 (1 H, dd, $^2J_{HH}$=12.6 Hz, $^3J_{HH}$=3.0 Hz, CH_AH$_B$CO$_2$H), 2.72 (1 H, dd, $^2J_{HH}$=12.6 Hz, $^3J_{HH}$=7.1 Hz, CH$_A$$H_BCO_2$H), 3.03 (1 H, m, CH), 3.30 (1 H, ddd, $^2J_{HP}$=12.0 Hz, $^2J_{HH}$=13.5 Hz, $^3J_{HH}$= 2.1 Hz, PCH_AH$_B$), 3.90 (1 H, ddd, $^2J_{HP}$=9.0 Hz, $^2J_{HH}$=13.5 Hz, $^3J_{HH}$= 9.0 Hz, PCH$_A$$H_B$), respectively. The phenyls protons appear as a multiplet signal in the aromatic region of the spectrum (δ 7.60–7.73). A fairly broad singlet was seen for the CO$_2$H group at δ 10.50. The vicinal proton-proton coupling constant ($^3J_{HH}$) as a function of torsion angle can be obtained from the Karplus equation.[12] Observation of $^3J_{HH}$=3.0 and 2.1 Hz for two vicinal H$_A$/H$_4$ in compound **5a** indicates a *trans* arrangement for these centres. Furthermore,



1 **2** **3**

Scheme 1



4,5	R	Yield of **5** (%)
a	Phenyl	94
b	*n*-Butyl	91
c	Ethyl	95

Scheme 2

the coupling constants of 7.1 and 9.0 Hz for two H$_B$/H$_4$ are only consistent with these protons being approximately *cis* periplanar.

The ^{1}H-decoupled ^{13}C NMR spectrum of **5a** showed eight characteristic doublets at δ 25.53 (d, $^1J_{PC}$= 53.7 Hz, PCH$_2$), 37.84 (d, $^3J_{PC}$= 1.0 Hz, *C*H$_2$CO$_2$H), 39.40 (d, $^2J_{PC}$= 12.2 Hz, CH), 119.40 (d, $^1J_{PC}$= 87.1 Hz, C$_{ipso}$), 130.16 (d, $^3J_{PC}$= 11.0 Hz, C$_{meta}$), 133.67 (d, $^2J_{PC}$= 10.0 Hz, C$_{ortho}$), 134.71 (d, $^4J_{PC}$= 2.0 Hz, C$_{para}$), 175.37 (d, $^2J_{PC}$= 3.7 Hz, P-O-C=O), respectively. The characteristic signal due to the CO$_2$H carbon was discernible at δ 174.43 as a singlet. The ^{13}C NMR spectra are in agreement with the structure of 5-oxo-1,2λ5-oxaphospholane **5a**. The ^{1}H-decoupled ^{31}P NMR spectrum of **5a** exhibited a sharp signal at δ 19.04 (downfield from 85% H$_3$PO$_4$).

The ^{1}H and ^{13}C NMR spectra of **5b** and **5c** are similar to those of **5a**, except for the *R* moieties, which exhibited characteristic resonances with appropriate chemical shifts. Also, to check whether the resulting conclusions regarding the nature of compound **5b** and **5c** are reasonable, the ^{31}P NMR spectra of these compounds were measured and a single ^{31}P signal was observed at δ 33.22 and 38.32 (downfield from 85% H$_3$PO$_4$), respectively. These shifts are similar to those observed for cyclic oxaphospholanes.[7]

The structural assignments made on the basis of the ^{1}H and ^{13}C NMR spectra of compounds **5a–c** were supported by measurement of their IR spectra. The carbonyl region of the spectrum exhibited two distinct absorption bands at 1643–1702 cm^{-1} for each compound.

Although the mechanism for the formation of 2-(2,2,2-triaryl or alkyl-5-oxo-1,2λ5-oxaphospholan-4-yl)acetic acids

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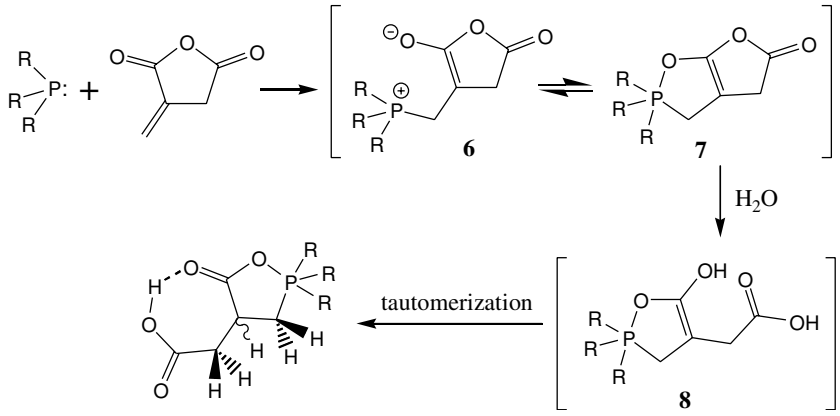

Scheme 3

5 has not been established in an experimental manner, but a mechanistic rationalisation is provided in Scheme 3. On the basis of the well established chemistry of trivalent phosphorus nucleophiles,[2,9] the successful nucleophilic attack by trivalent phosphines on a carbon atom is facilitated when the latter is conjugated with a carbonyl group, or when it is part of an unsaturated bond otherwise activated.[10,11] Therefore, the first step may involve addition of the phosphine to the itaconic anhydride and formation of the 1:1 adduct **6** in equilibrium with its bicyclic isomer **7**. Subsequent nucleophilic attack of water to carbonyl group of the adduct **7** would yield enol-acid intermediate **8**, that can be tautomerised to product **5**.

In conclusion, the present method may be considered as a practical route for the synthesis of 1,2λ^5-oxaphospholane derivatives using one-pot three-component reaction of phosphines and itaconic anhydride in presence of water under neutral conditions. This procedure has the advantages of high yields, mild reaction conditions, and simple experimental and work-up conditions. Subsequently, the flame retardancy of these products will be investigated in the near future.

Experimental

Elemental analyses were performed using a Heraeus CHN-O-Rapid analyser. Mass spectra were recorded on a Finnigan-Mat 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Bruker DRX-400 Avance spectrometer at 400.13, 100.77 and 161.97 MHz, respectively. All reagents and solvents used in this work are commercial materials and were purchased from Fluka (Buchs, Switzerland) or Merck chemical company and used without further purification.

Typical procedure for the preparation of 2-(2,2,2-triphenyl-5-oxo-1,2λ^5-oxaphospholan-4-yl)acetic acid **(5a)**: To a magnetically stirred solution of itaconic anhydride (0.112 g, 1.0 mmol) in water (5 ml) and dichloromethane (5 ml) was added dropwise a solution of triphenylphosphine (0.262 g, 1.0 mmol) in dichloromethane (2 ml) at 0 °C over 10 min. The reaction mixture was allowed to warm up to room temperature (25 °C) and stirred for 24 h. The solvent was removed under reduced pressure and the residue was separated by column chromatography using methanol as eluent. The solvent was evaporated at reduced pressure and the product was obtained as colourless oil, (0.369 g, 94 %). IR (KBr) ($\nu_{max,}$ cm^{-1}): 3405 (COO–H), 1692 (POC=O), 1645 (O=COH), 1582 (C=C), 1429, 1102 and 1000 (P–Ph), 915 (P–O). ^{1}H NMR ($CDCl_3$, Me_4Si): δ_H 2.45 (1 H, dd, $^2J_{HH}$=12.6 Hz, $^3J_{HH}$=3.0 Hz, CH_AH$_B$CO$_2$H), 2.72 (1 H, dd, $^2J_{HH}$=12.6 Hz, $^3J_{HH}$=7.1 Hz, CH$_A$$H_BCO_2$H), 3.03 (1 H, m, CH), 3.30 (1 H, ddd, $^2J_{HP}$=12.0 Hz, $^2J_{HH}$=13.5 Hz, $^3J_{HH}$= 2.1 Hz, PCH_AH$_B$), 3.90 (1 H, ddd, $^2J_{HP}$=9.0 Hz, $^2J_{HH}$=13.5 Hz, $^3J_{HH}$= 9.0 Hz, PCH$_A$$H_B$), 7.60–7.73 (15 H, m, 3 C_6H_5), 10.50 (1 H, br s, CO_2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ_C 25.53 (d, $^1J_{PC}$= 53.7 Hz, PCH_2), 37.84 (d, $^3J_{PC}$= 1.0 Hz, CH_2CO_2H), 39.40 (d, $^2J_{PC}$= 12.2 Hz, CH), 119.40 (d, $^1J_{PC}$= 87.1 Hz, C_{ipso}), 130.16 (d, $^3J_{PC}$= 11.0 Hz, C_{meta}), 133.67 (d, $^2J_{PC}$= 10.0 Hz, C_{ortho}), 134.71 (d, $^4J_{PC}$= 2.0 Hz, C_{para}), 174.43 (CO_2H), 175.37 (d, $^2J_{PC}$= 3.7 Hz, P-O-C=O). ^{31}P NMR ($CDCl_3$, Me_4Si): δ_P 19.04 [$Ph_3PO(CH_2)$]. MS (*m/z*, %) 392 (M$^+$, 2), 369 (5), 301 (8), 262 (100), 183 (76), 152 (11), 108 (47), 68 (23), 39 (45). Anal. Calcd. for $C_{23}H_{21}O_4P$ (392.38): C, 70.40; H, 5.39%. Found: C, 70.47; H, 5.44%.

2-(2,2,2-Tributyl-5-oxo-1,2λ^5-oxaphospholan-4-yl)acetic acid **(5b)**: Colourless oil (0.303 g, 91 %). IR (KBr) ($\nu_{max,}$ cm^{-1}): 3405 (COO–H), 2935 (C–H), 1702 (POC=O), 1643 (O=COH), 1453, 1090 and 964 (P–CH_2), 909 (P–O). ^{1}H NMR ($CDCl_3$, Me_4Si): δ_H 0.95 (9 H, m, 3 CH_3), 1.49 (12 H, m, 6 CH_2 of butyls), 2.25–2.30 (6 H, m, 3 CH_2 of butyls), 2.43 (1 H, dd, $^2J_{HH}$=13.4 Hz, $^3J_{HH}$=3.0 Hz, CH_AH$_B$CO$_2$H), 2.48 (1 H, dd, $^2J_{HH}$=13.4 Hz, $^3J_{HH}$=6.2 Hz, CH$_A$$H_BCO_2$H), 2.55 (1 H, ddd, $^2J_{HP}$=10.9 Hz, $^2J_{HH}$=16.0 Hz, $^3J_{HH}$=2.0 Hz, PCH_AH$_B$), 2.81 (1 H, ddd, $^2J_{HP}$=8.3 Hz, $^2J_{HH}$=16.0 Hz, $^3J_{HH}$= 9.1 Hz, PCH$_A$$H_B$), 3.02 (1 H, m, CH), 13.18 (1 H, br s, CO_2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ_C 13.41 (3 CH_3), 19.94 (d, $^1J_{PC}$= 48.5 Hz, PCH_2 of butyls), 22.60 (d, $^1J_{PC}$= 52.4 Hz, PCH_2), 23.72 (d, $^2J_{PC}$= 4.4 Hz, CH_2CH_2P), 23.94 (d, $^3J_{PC}$= 15.5 Hz, CH_3CH_2), 37.96 (d, $^3J_{PC}$= 4.2 Hz, CH_2CO_2H), 40.08 (d, $^2J_{PC}$= 14.2 Hz, CH), 174.55 (CO_2H), 176.64 (d, $^2J_{PC}$= 4.0 Hz, P–O–C=O). ^{31}P NMR ($CDCl_3$, Me_4Si): δ_P 33.22 [*n*-$Bu_3PO(CH_2)$]. MS (*m/z*, %) 332 (M$^+$, 1), 315 (5), 202 (25), 262 (100), 173 (32), 160 (14), 146 (34), 131 (20), 118 (33), 104 (40), 76 (100), 57 (60). Anal. Calcd. for $C_{17}H_{33}O_4P$ (332.41): C, 61.42; H, 10.01%. Found: C, 61.36; H, 9.96%.

2-(2,2,2-Triethyl-5-oxo-1,2λ^5-oxaphospholan-4-yl)acetic acid **(5c)**: Colourless oil (0.236 g, 95 %). IR (KBr) ($\nu_{max,}$ cm^{-1}): 3392 (COO–H), 2944 (C–H), 1698 (POC=O), 1649 (O=COH), 1445, 1103 and 944 (P–CH_2), 906 (P–O). ^{1}H NMR ($CDCl_3$, Me_4Si): δ_H 1.28 (9 H, dt, $^3J_{HP}$=18.1 Hz, $^3J_{HH}$=7.7 Hz, 3 CH_3), 2.22-2.41 (6 H, m, 3 PCH_2), 2.44 (2 H, m, CH_AH$_B$CO$_2$H), 2.63 (1 H, ddd, $^2J_{HP}$=3.8 Hz, $^2J_{HH}$=15.3 Hz, $^3J_{HH}$=1.0 Hz, PCH_AH$_B$), 2.75 (1 H, ddd, $^2J_{HP}$=9.2 Hz, $^2J_{HH}$=15.3 Hz, $^3J_{HH}$= 9.0 Hz, PCH$_A$$H_B$), 3.04 (1 H, m, CH), 11.33 (1 H, br s, CO_2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ_C 5.87 (d, $^2J_{PC}$= 5.5 Hz, 3 CH_3), 12.30 (d, $^1J_{PC}$= 50.3 Hz, PCH_2 of ethyls), 22.14 (d, $^1J_{PC}$= 56.3 Hz, PCH_2), 37.23 (d, $^3J_{PC}$= 4.0 Hz, CH_2CO_2H), 40.17 (d, $^2J_{PC}$= 13.9 Hz, CH), 173.55 (CO_2H), 176.24 (d, $^2J_{PC}$= 3.9 Hz, P–O–C=O). ^{31}P NMR ($CDCl_3$, Me_4Si): δ_P 38.32 [$Et_3PO(CH_2)$]. MS (*m/z*, %) 248 (M$^+$, 5), 231 (9), 219 (15), 189 (32), 161 (55), 117 (100), 91 (66), 57 (53). Anal. Calcd. for $C_{11}H_{21}O_4P$ (248.25): C, 53.22; H, 8.53%. Found: C, 53.30; H, 8.46%.

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References

1 F. Mathey, *Phosphorous-Carbon Heterocyclic Chemistry: The Rise of a New Domain;* Pergamon, Amsterdam, 2001.
2 R. Engel, *Synthesis of Carbon-Phosphorus Bonds*; CRC Press, Boca Raton, FL, 1998.
3 (a) S. Hanessian and O. Rogel, *J. Org. Chem.*, 2000, **65**, 2667; (b) S. Hanessian and O. Rogel, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 2441; (c) T.C. Harvey, C. Simiand, L. Weiler and S.G. Withers, *J. Org. Chem.*, 1997, **62**, 6722.
4 A.I. Balabanovich, A.M. Balabanovich and J. Engelmann, *Polym. Int.,* 2003, **52**, 1309.
5 A.I. Balabanovich, *Thermochimica Acta,* 2004, **409**, 33.
6 A.R. Hands and A.J.H. Mercer, *J. Chem. Soc.,* C 1967, 1099.

7 (a) F. Ramirez, J.F. Pilot, P. Madan and C.P. Smith, *J. Am. Chem. Soc*., 1968, **90**, 1275; (b) E.J. Enholm, H. Satici and G. Prasad, *J. Org. Chem.,* 1990, **55**, 324; (c) K. Okuma, Y.-I. Tanaka, S.-I. Hirabayashi, K. Shioji and H. Matsuyama, *Heterocycles,* 1997, **45**, 1385; (d) K. Okuma, S.-I. Himbayashi, M. Ono, K. Shioji, H. Matsuyama and H.J. Bestmann, *Tetrahedron,* 1998, **54**, 4243; (e) M. Bujard, V. Gouverneur and C. Mioskowski, *J. Org. Chem.,* 1999**, 64***,* 2119; (f) M.S.M. Timmer, H. Ovaa, D.V. Filippov, G.A. van der Marel and J.H. van Boom, *Tetrahedron Lett.,* 2001, **42**, 8231; (g) D.S. Stoianova and P.R. Hanson, *Org. Lett.,* 2001, **3**, 3285; (h) L. Hetherington, B. Greedy and V. Gouverneur *Tetrahedron,* 2000, **56**, 2053; (i) I. Yavari, A. Alizadeh and M. Anary-Abbasinejad, *Tetrahedron Lett.,* 2003, **44**, 2877; (j) J.H. Hah, B.S. Lee, S.Y. Lee and H.-Y. Lee, *Tetrahedron Lett.,* 2003, **44**, 5811; (k) M.D. McReynolds, J.M. Dougherty and P.R. Hanson, *Chem. Rev*., 2004, **104**, 2239 and references cited therein.

8 (a) A. Shaabani, M.B. Teimouri, I. Yavari, H. Norouzi Arasi and H.R Bijanzadeh, *J. Fluorine Chem.,* 2000, **103**, 155; (b) A. Shaabani, A. Bazgir and M.B. Teimouri, *Phosphorus Sulfur Silicon,* 2002, **177**, 833.

9 O.I. Kolodiazhynyi, *Russ. Chem. Rev*., 1997, **66**, 225.

10 H.J. Bestmann and O. Vostrowsky, *Top. Curr. Chem*., 1983, **109**, 85.

11 K.M. Pietrusiewiz and M. Zabloka, *Chem. Rev*., 1994, **94**, 1375.

12 M. Karplus, *J. Am. Chem. Soc.,* 1963, **85**, 2870.