Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2005, 15(4), 154–155
Mendeleev Communications

Synthesis of dimethyl (3-benzoyl-2,2,2-trimethoxy-5-phenyl-2,3-dihydro-1,2λ^5-oxaphosphol-4-yl)phosphonate

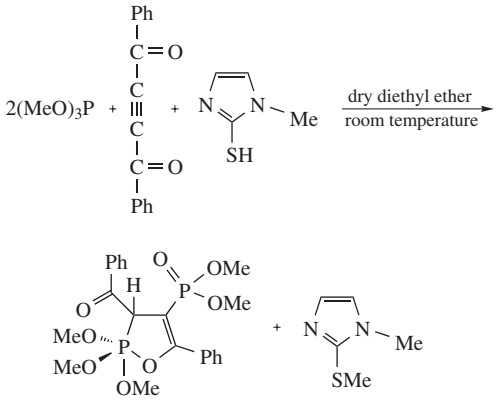
Abdolali Alizadeh and Issa Yavari*

Department of Chemistry, Tarbiat Modarres University, 14115-175 Tehran, Iran.
Fax: +98 21 800 6544; e-mail: yavarisa@modares.ac.ir

DOI: 10.1070/MC2005v015n04ABEH002018

Stable dimethyl (3-benzoyl-2,2,2-trimethoxy-5-phenyl-2,3-dihydro-1,2λ^5-oxaphosphol-4-yl)phosphonate was obtained in 98% yield from the reaction between dibenzoylacetylene and 1-methylimidazole-2-thiol in the presence of trimethyl phosphite in dry diethyl ether.

In recent years, phosphoryl transfer has resulted in the synthesis of phosphonates as analogues of biologically active substances.[1] Therefore, the straight synthesis of compounds with C–P bonds *via* trimethyl phosphite is of importance. The successful attack of nucleophilic 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.[1–7] The reactions between trivalent phosphorus nucleophiles and α,β-unsaturated carbonyl compounds in the presence of a proton source such as an alcohol or a CH acid have been studied.[3,7]



1

Scheme 1

When dibenzoylacetylene[8,9] and 1-methylimidazole-2-thiol in dry diethyl ether were allowed to react with trimethyl phosphite at room temperature, a crystalline compound was formed in nearly quantitative yield.† This product was identified as dimethyl (3-benzoyl-2,2,2-trimethoxy-5-phenyl-2,3-dihydro-1,2λ^5-oxaphosphole-4-yl)phosphonate **1** (Scheme 1).

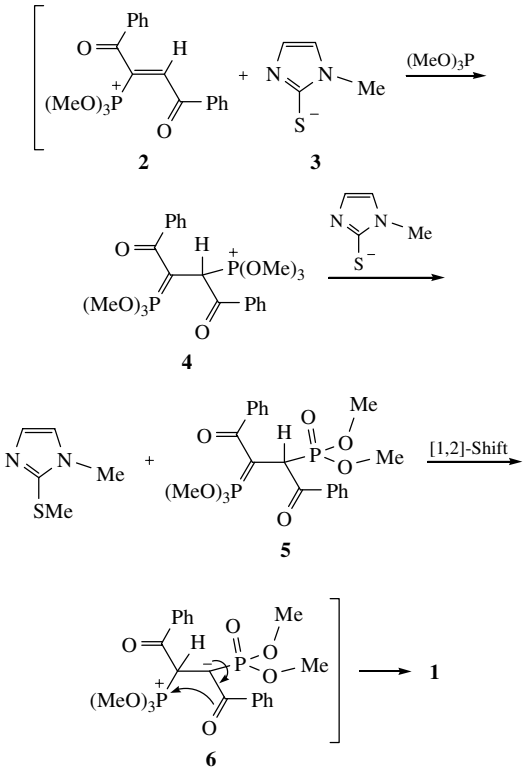
When the reaction was carried out in the presence of triethyl or triphenyl phosphite, a fairly complex mixture of products was obtained. Using CH_2Cl_2 as a solvent leads to a complex reaction mixture. We were not able to isolate pure products from these reaction mixtures.

The ^{1}H NMR spectrum of **1** in $CDCl_3$ at room temperature exhibited two characteristic doublets at δ 3.27 and 3.32 ppm for the diastereotopic methoxy groups of the $(MeO)_2PO$ moiety and another doublet at δ 3.54 ppm for the methoxy protons of the $(MeO)_3P$ group. The methine proton exhibited a double doublet ($^2J_{HP}$ 20 Hz, $^3J_{HP}$ 3 Hz) at δ 5.21 ppm. The phenyl residues gave rise to characteristic signals in the aromatic region of the spectrum. The {^{1}H} ^{13}C NMR spectrum of **1** showed three characteristic double doublets at δ 52.2 ($^1J_{CP}$ 151 Hz, $^2J_{CP}$ 10 Hz), 93.8 ($^1J_{CP}$ 217 Hz, $^2J_{CP}$ 5 Hz) and 165.2 ppm ($^2J_{CP}$ 23 Hz, $^2J_{CP}$ 15 Hz) for the P–CH, O–C=*C*, and O–*C*=C moieties, respectively. The {^{1}H} ^{31}P NMR spectrum of **1** exhibited two doublets at δ –29.2 [$^3J_{PP}$ 77 Hz, $(MeO)_3P$] and 21.4 ppm ($^3J_{HH}$ 77 Hz, P=O).†

A plausible mechanism for the formation of **1** is shown in Scheme 2. On the basis of the well-established chemistry of phosphorus nucleophiles,[2,3] it is reasonable to assume that intermediate **4** results from the initial addition of trimethyl phosphite to dibenzoylacetylene and the subsequent protonation of the adduct by 1-methylimidazole-2-thiol followed by an attack of trimethyl phosphite. This ion is converted to phosphorane **5** by transferring a methyl group to the anion of the SH acid. Ylide **5** apparently isomerises, under the reaction conditions employed, to produce 2,3-dihydro-1,2-oxaphosphole derivative **1**.

The above method carries the advantage that, not only is the reaction performed under neutral conditions, but the substances can be mixed without any activation or modification. The simplicity of the present procedure makes it an interesting alternative to complex multistep approaches.

† *Synthesis of dimethyl (3-benzoyl-2,2,2-trimethoxy-5-phenyl-2,3-dihydro-1,2λ^5-oxaphosphol-4-yl)phosphonate* **1**. To a stirred solution of dibenzoylacetylene (0.47 g, 2 mmol) and 1-methylimidazole-2-thiol (0.23 g, 2 mmol) in dry Et_2O (5 ml) was added dropwise a solution of trimethyl phosphite (0.50 g, 4 mmol) in dry Et_2O (3 ml) at room temperature for 10 min. The reaction mixture was stirred for 30 min. The resulting solid was filtered off, washed with dry Et_2O and dried in a vacuum. White powder; yield 0.46 g (98%), mp 120–122 °C. ^{1}H NMR (500.1 MHz, $CDCl_3$) δ: 3.27 (d, 3H, O=POMe, $^3J_{HP}$ 12 Hz), 3.32 (d, 3H, O=POMe, $^3J_{HP}$ 12 Hz), 3.54 [d, 9H, $P(OMe)_3$, $^3J_{HP}$ 13 Hz], 5.21 (dd, 1H, P–CH, $^2J_{HP}$ 20 Hz, $^3J_{HP}$ 3 Hz), 7.36–7.43 (m, 5H, 2Ph), 7.49 (dd, 1H, CH_{para} of Ph, $^3J_{HH}$ 7 Hz), 7.84 (d, 2H, $2CH_{ortho}$ of Ph, $^3J_{HH}$ 6 Hz), 8.02 (d, 2H, $2CH_{orhto}$ of Ph, $^3J_{HH}$ 8 Hz). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ: 51.4 (d, O=POMe, $^2J_{CP}$ 6 Hz), 52.1 (d, O=POMe, $^2J_{CP}$ 6 Hz), 52.2 (dd, P–CH, $^1J_{CP}$ 151 Hz, $^2J_{CP}$ 10 Hz), 55.3 [d, $P(OMe)_3$, $^2J_{CP}$ 11 Hz], 93.8 (dd, O–C=*C*, $^1J_{CP}$ 217 Hz, $^2J_{CP}$ 5 Hz), 127.8 (s, C_{ipso} of Ph), 127.8 (s, 2CH of 2Ph), 128.1 (s, 2CH of 2Ph), 128.6 (s, 2CH of 2Ph), 128.8 (s, 2CH of 2Ph), 130.1 (s, $2CH_{para}$ of 2Ph) and 132.3 (s, $2CH_{para}$ of 2Ph), 138.1 (d, C_{ipso} of Ph, $^3J_{CP}$ 4 Hz), 165.2 (dd, O–*C*=C, $^2J_{CP}$ 23 Hz, $^2J_{CP}$ 15 Hz), 197.4 (d, C=O, $^2J_{CP}$ 6 Hz). ^{31}P NMR (202.4 MHz, $CDCl_3$) δ: –29.2 [d, $P(OMe)_3$, $^3J_{PP}$ 77 Hz], 21.4 (d, P=O, $^3J_{PP}$ 77 Hz). IR (KBr, ν/cm^{-1}): 1661 (C=O), 1579 and 1555 (Ph), 1269 (P=O), 1235 and 1200 (O=P–O), 1062, 1039 and 1018 (P–O). MS, *m*/*z* (%): 469 (M^+ + 1, 6), 443 (53), 381 (100), 349 (89), 321 (65), 209 (18), 181 (49), 105 (90), 62 (46), 54 (40), 38 (22). Found (%): C, 53.90; H, 5.50. Calc. for $C_{21}H_{26}O_8P_2$ (468.4) (%): C, 53.85; H, 5.59.



Scheme 2

References

1 R. R. Holmes, *Acc. Chem. Res*., 2004, **37**, 746.
2 B. E. Maryanoff and A. B. Reitz, *Chem. Rev*., 1989, **89**, 863.
3 (*a*) I. Yavari, M. Adib and L. Hojabri, *Tetrahedron*, 2001, **57**, 7537; (*b*) I. Yavari and M. Adib, *Tetrahedron*, 200l, **57**, 5873; (*c*) I. Yavari, M. Adib and M. H. Sayahi, *Tetrahedron Lett*., 2002, **43**, 2927; (*d*) I. Yavari, M. Adib and M. H. Sayahi, *J. Chem. Soc., Perkin Trans. 1*, 2002, l517; (*e*) I. Yavari and A. Alizadeh, *Tetrahedron*, 2001, **57**, 9873; (*f*) I. Yavari, M. Anari-Abbasinejad and Z. Hossaini, *Org. Biomol. Chem*., 2003, **1**, 560; (*g*) I. Yavari and A. Alizadeh, *Synthesis*, 2004, 237; (*h*) M. H. Mosslemin, I. Yavari, M. Anary-Abbasinejad and M. R. Nateghi, *Synthesis*, 2004, 1029.
4 A. J. Arduago and C. A. Stewart, *Chem. Rev*., 1994, **94**, 1215.
5 K. M. Pietrusiewiz and M. Zabloka, *Chem. Rev*., 1994, **94**, 1375.
6 H. J. Bestmann and O. Vostrowsky, *Top. Curr. Chem*., 1983, **109**, 85.
7 R. Burgada, Y. Leroux and Y. O. El Khoshnieh, *Tetrahedron Lett*., 1981, **22**, 3533.
8 L. Skattebol, E. R. H. Jones and M. C. Whiting, *Org. Synth. Coll. Vol*., 1963, **4**, 792.
9 K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. Weedon, *J. Chem. Soc*., 1946, 39.

Received: 25th August 2004; Com. 04/2343