Tetrahedron Letters,Vol.25,No.23,pp 2489-2492,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

SYNTHESIS OF MONO- AND 1,4-DICARBONYL COMPOUNDS BASED ON THE OXYGENATION OF PHOSPHONATE CARBANIONS. SYNTHESIS OF DIHYDROJASMONE, ALLETHRONE AND METHYLENOMYCIN B[†]

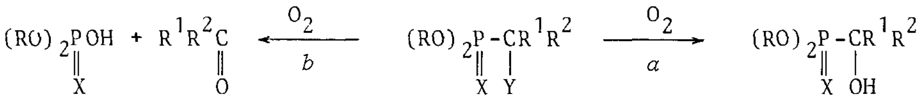
Marian Mikołajczyk*, Wanda Midura and Sławomir Grzejszczak

Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences,
Department of Organic Sulphur Compounds, 90-362 Łodz, Boczna 5, Poland

Summary: *Oxidation of the α-alkylthio-substituted phosphonate carbanions was found to give the corresponding carbonyl compounds. A new synthesis of 1,4-dicarbonyl systems involving the oxygenation of phosphonate carbanions as a key step is described. Total synthesis of dihydrojasmone and allethrone and formal synthesis of methylenomycin B is reported.*

The oxidation of phosphorus ylides and phosphinoxide carbanions is a well-known reaction which has been found to occur with a cleavage of the phosphorus-carbon bond and to result in the formation of symmetrical olefins[1,2]. In some cases ketones formed as primary reaction products in the oxidation of phosphinoxide carbanions were also obtained[2,3].

In the course of our studies on the chemistry of phosphonate and thiophosphonate carbanions we have shown[4] that their oxidation is bidirectional and gives the corresponding α-hydroxyphosphonates (direction *a*) and/or the products derived from the C-P bond fission (direction *b*).



$$\underset{X}{\overset{\|}{(RO)_2POH}} + \underset{O}{\overset{\|}{R^1R^2C}} \xleftarrow[b]{O_2} \underset{X\ \ Y}{\overset{\|\ \ |}{(RO)_2P-CR^1R^2}} \xrightarrow[a]{O_2} \underset{X\ \ OH}{\overset{\|\ \ |}{(RO)_2P-CR^1R^2}}$$

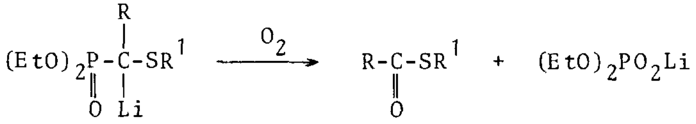
X = O,S; Y = Li,MgBr; R^1,R^2 = H,alkyl,aryl

The latter direction is of interest for organic synthesis and recently aroyl anilides[5] and thiol esters[6] have been prepared by the oxygenation of the anions derived from phosphonates and phosphinoxides, respectively. This prompted us to publish our results on the oxygenation of α-carbanions derived from the easily available α-phosphoryl sulfides and related compounds[7] as well as to report a new and short synthesis of 1,4-diketones in which the generation of the second carbonyl group is based on the phosphonate oxygenation.

[†] Presented by one of us (M.M.) as part of the lecture given at the International Conference on Phosphorus Chemistry, Nice, France, September 1983.

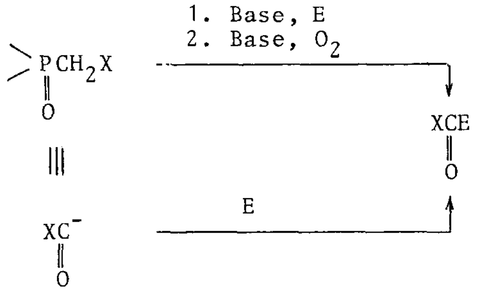
It was found that oxygenation of the lithio derivatives of α-phosphoryl sulfides, 1, α-phosphoryl dithioacetals, 2, and α-phosphoryl-α-methylthio-acetic acid, 3, affords the corresponding carboxylic acid thiol esters, 4, dithiocarbonates, 5, and monothiooxalic acid S-ester 6 in a moderate to good yield. (See Scheme I) In all cases the following experimental procedure was applied. To a solution of phosphonate (0.001 mol) in THF *n*-BuLi (0.001 mol) was added at -78°C under an argon atmosphere. The reaction mixture was stirred at this temperature for 10 min and dry oxygen was bubbled slowly trough the mixture for the next 15 min. Then, the reaction mixture was quenched with water. The products 4, 5 and 6 formed were isolated in a usual way and identified spectroscopically (^{1}H-NMR, IR) and by comparison of their physical properties with those of authentic samples.

Scheme I

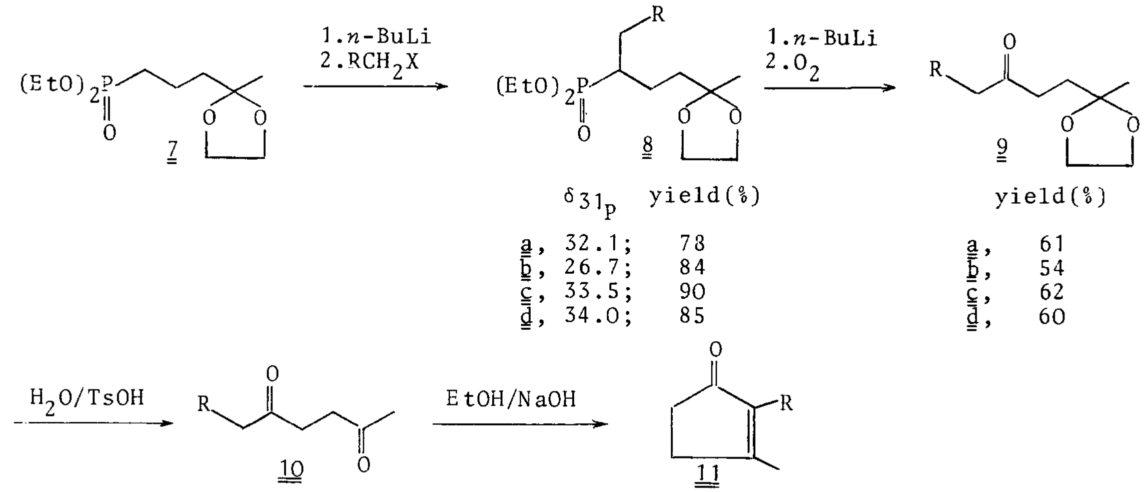


				yield(%)
1a,	R=Me	R^1=Me	4a,	30
1b,	R=Ph	R_1=Me	4b,	73
1c,	R=$PhCH_2$	R_1=Et	4c,	70
2a,	R=MeS	R_1=Me	5a,	72
2b,	R=EtS	R_1=Me	5b,	71
3,	R=CO_2Li	R^1=Me	6,	60

Our results in combination with those reported in the literature indicate that the oxidative cleavage of the C-P bond is a general reaction and the phosphonate grouping represents a synthetic equivalent of a carbonyl anion which may be used for synthesis of other carbonyl compounds according to the Umpolung concept[8].



Utilizing this property of the phosphonate moiety we developed a new method for the synthesis of 1,4-diketones which are most important precursors to many natural products of the cyclopentenoid structure[9]. In our synthesis of 1,4-diketones and functionalized cyclopentenones, which is outlined in Scheme II, the protected ketophosphonate, 7, was taken as a convenient and readily accessible starting material[7]. Treatment of the lithium salt of 7 with various halides (a, benzyl bromide; b, *n*-hexyl iodide; c, homoallyl bromide and d, Scheme II



8

	$\delta^{31}P$	yield(%)
a,	32.1;	78
b,	26.7;	84
c,	33.5;	90
d,	34.0;	85

9

	yield(%)
a,	61
b,	54
c,	62
d,	60

10

	yield(%)
a,	85
b,	83
c,	78
d,	93

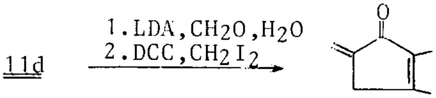
11

	yield(%)
a,	84
b,	83
c,	79
d,	76

a, R=C_6H_5
b, R=C_5H_{11}
c, R=CH_2=$CHCH_2$
d, R=CH_3

ethyl iodide) afforded the corresponding α-substituted phosphonates 8. The reaction of the lithium salts of 8 with oxygen - a key step in our synthesis - carried out under the conditions described above resulted in the formation of the half-protected 1,4-diketones 9[10]. After acidic hydrolysis they were converted to the desired 1,4-diketones 10. Base catalyzed cyclization of 10, gave 2,3-disubstituted cyclopentenones: 2-phenyl-3-methyl-cyclopent-2-en-1-one (11a), dihydrojasmone (11b), allethrone (11c) and 2,3-dimethyl-cyclopent-2-en-1-one (11d) having the spectral properties (^{1}H-NMR, MS) identical with those reported in the literature[11,12].

The synthesis of the cyclopentenone 11d is of interest in connection with the total synthesis of methylenomycin B. Since 11d has been converted by Jernow et al.[13] and later by us[7] to methylenomycin B, our new access to 11d constitutes a formal total synthesis of this antibiotic.



In conclusion, we have described a new synthesis of 1,4-diketones and functionalized cyclopentenones which compares favourably in terms of brevity, use of simple reagents and overall yield with the methods described in the literature[14].

References

1. H.J.Bestmann, *Angew.Chem.*, 72, 34 (1960); H.J.Bestmann and O.Kratzer, *Chem.Ber.*, 96, 1899 (1963); H.J.Bestmann, H.Haberlein and O.Kratzer, *Angew. Chem.*, Int.Ed., 3, 226 (1964); H.J.Bestmann, *Angew.Chem.*, Int.Ed., 4, 830 (1965).
2. L.Horner, H.Hoffmann, G.Klahre, V.G.Toscano and H.Ertel, *Chem.Ber.*, 94, 1987 (1961).
3. A.H.Davidson and S.Warren, *J.C.S.Chem.Commun.*, 1975, 148.
4. M.Mikolajczyk, S.Grzejszczak, W.Midura, M.Popielarczyk and J.Omelanczuk, *Phosphorus Chemistry*, ACS Symposium Series, Vol.171, p,55 (1981)
5. H.Zimmer, R.E.Koenigkramer, R.L.Cepulis and D.M.Nene, *J.Org.Chem.*, 45, 201§ (1980)
6. E.Vedejs, H.Mastalerz, G.P.Meier and D.W.Powell, *J.Org.Chem.*, 46, 5233 (1981).
7. M.Mikolajczyk, *Current Trends in Organic Synthesis*, Ed. H.Nozaki, Pergamon Press, Oxford and New York, p. 347 (1983).
8. B.T.Gröbel and D.Seebach, *Synthesis*, 1977, 357.
9. R.A.Ellison, *Synthesis*, 1973, 397.
10. Satisfactory elemental analyses for C and H have been obtained for all 9. Their spectroscopic properties are as follows:
    9a: ^{1}H-NMR($CDCl_3$): δ=1.27(s,3H,CH_3-C(OCH_2)$_2$)1,85(t,2H,CH_2-C(OCH_2)$_2$),2.62 (t,2H,CH_2C(O)), 3.72(s,2H,PhCH_2), 3.88(s,4H,O(CH_2)$_2$O), 7.3(m,5H,aromatic); MS(70 eV): m/e(%)=234(<1),219(5.9),87(100).
    9b: ^{1}H-NMR($CDCl_3$): δ=0.9(t,3H,J_{H-H}=5.5 Hz, CH_3CH_2),1.1-1.85(m,10H),1.2(s,3H, CH_3C(OCH_2)$_2$),2.4(m,4H,CH_2C(O)CH_2), 3.90(s,4H,O(CH_2)$_2$O); M.S.(70 eV): m/e (%)=228(<1),213(6.2),87(100).
    9c: ^{1}H-NMR($CDCl_3$): δ=1.22(s,3H,CH_3C(OCH_2)$_2$), 1,7-2,6(m,8H), 3.82(s,4H,O(CH_2)$_2$O) 4,73-5.13(m,2H,CH_2=C), 5.63(m,1H,CH_2=CH-); M.S. (70 eV): m/e (%) = 198(<1), 183(9.7), 87(100).
    9d: ^{1}H-NMR($CDCl_3$): δ=1.02(t,3H,J_{H-H}=7.5 Hz,CH_3CH_2), 1.28(s,3H,CH_3C(OCH_2)$_2$), 1,91(t,2H,J_{H-H}=7Hz,CH_2-C(OCH_2)$_2$), 2.40(q,2H,CH_3CH_2), 2.47(t,2H,C(O)CH_2CH_2) 3.90(s,4H,O(CH_2)$_2$O); M.S. (70 eV): m/e(%)=172(<1),157(8.8),87(100).
11. M.Mikolajczyk, S.Grzejszczak and K.Korbacz, *Tetrahedron Lett.*, 22, 3097 (1972)
12. T.Kumamoto, S.Kabayashi, T.Mukaiyama, *Bull.Chem.Soc.Jap.*, 45, 866 (1972)
13. J.Jernow, W.Tautz, P.Rosen and T.H.Williams, *J.Org.Chem.*, 44, 4212 (1979)
14. Y.Ito, T.Konoike, T.Harada, T.Saegusa, *J.Am.Chem.Soc.*, 99, 1487 (1977); M.C.Musatto, D.Savoia, C.Trombini, A.Umani-Ronchi, *J.Org.Chem.*, 45, 4002 (1980); G.Rosini, R.Ballini and P.Sorrenti, *Tetrahedron*, 39, 4127 (1983); J.H.Clark, D.G.Cork, H.W.Gibbs, *JCS Perkin I*, 1983, 2253; and references cited therein.

(Received in UK 26 March 1984)