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PHOSPHORUS HETEROCYCLE SYNTHESIS BY $RPX_2 \cdot AlX_3$ ADDITION TO [1,n]DIENES VII.

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Abstract. The $RPX_2 \cdot AlX_3$ complex (1) reacts with unsaturated ketones and imines to give novel 7-oxa and 7-aza-2-phosphabicyclo[2.2.1]heptanes (compounds 3 and 6 respectively).

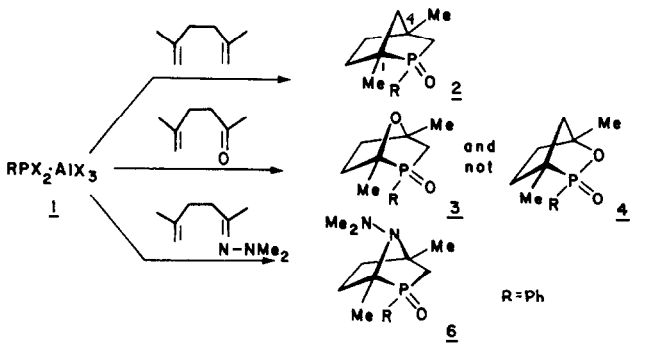
A new 1,3-dipolar addition of $(CH_3)_2\overset{+}{C}CH_2\ddot{P}XR$ to Ar-N=C=S was disclosed resulting in the formation of the 2-imino-1,3-thiaphospholanes (7).

The use of the $RPX_2 \cdot AlX_3$ complex (1) for the synthesis of new phosphaheterocycle systems starting from 1,n-dienes, has already been described by us[1]. Here we wish to represent the use of the above complex for the synthesis of other novel heterocycles which contain, apart from the P-atom, an oxygen, sulfur or a nitrogen atom in a mono or bicyclic skeleton.

The synthesis of phosphaheterocycles by the reaction of complex 1 with 1,n-dienes, led us to the examination of the reaction of 1 with βγ and higher unsaturated ketones.

In contrast to oxo compounds which are reported to give with RPX_2 (without AlX_3) interesting phosphaheterocycles[2], βγ and γδ unsaturated ketones, tested by us (vide infra), failed to give any identifiable compounds.

2-Methylhex-1-en-5-one[3], however, gave with 1 an addition product 3. In analogy to the reaction of 1 with 2,5-dimethylhexa-1,5-diene (compound 2, Scheme 1)[1a], an oxaphosphabicyclo[2.2.1]heptane was expected to be produced. Furthermore, the obtained product should possess the relatively strong P-O bond[4].

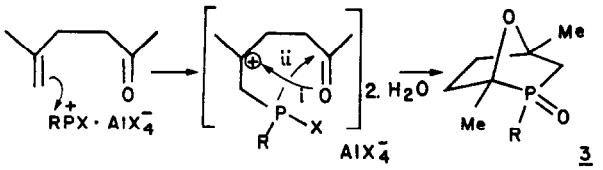


Scheme 1

The structure of 3 ($C_{13}H_{17}O_2P$)[5], obtained in ca. 25%, was determined mainly on the basis of its ^{13}C and ^1H-NMR spectra (see Table 1) as 2-oxo-2-phenyl-2phospha-7-oxabicyclo[2.2.1]heptane. Most significant for this assignment were the ^{13}C resonance lines of the -C-O-C-P(O)Ph-CH_2- moiety. Furthermore, the δ_H and J_{PC} values of the two methyl groups suggest the phosphorus atom in 3, to have the same stereochemistry as in 2a.

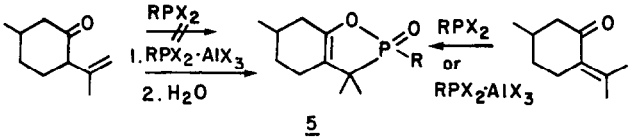
Obtaining 3 rather than a compound containing the P-O-C linkage (as e.g. 4, Scheme 1) was

quite surprising, suggesting that the olefin rather than the carbonyl group is first attacked by the complex to give a tertiary carbonium ion, which then reacts further with the carbonyl group to give compound 3 (see Scheme 2).



Scheme 2

Reacting 1 with 1-methyl-4-isopropenylcyclohexan-3-one, a βγ-unsaturated ketone, gave in high yields a crystalline compound (5, $C_{16}H_{12}O_2P$) as outlined in Scheme 3. The spectral data of 5[6] are in full agreement with the proposed oxaphospholane structure. On the first step the isomerisation of the βγ double bond produces an α,β-unsaturated ketone which is subsequently cyclised to give 5. Such a cyclisation is known in the synthesis of 1,2-oxaphospholanes by the reaction of dihalophosphanes with αβ-unsaturated ketones[7]. Indeed, reacting the corresponding αβ-unsaturated ketone, pulegone, with RPX_2 also gave compound 5 (Scheme 3)[8].

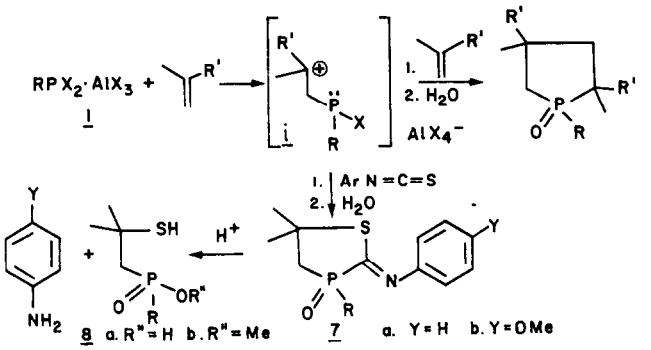


Scheme 3

In order to investigate the scope of the reaction, complex 1 was also reacted with γδ-unsaturated imines. For example the reaction of the dimethylhydrazone of 2-methylhex-1-en-5-one[9] with 1 gave compound 6[10] which was obtained in low yield (see Scheme 1). Compound 6 is suggested to possess the 7-aza-2-phosphabicyclo[2.2.1]heptane skeleton, its structure being deduced mainly from the ^1H and ^{13}C-NMR spectra (Table 1). According to the resonance lines of the two methyl groups, the stereochemistry of the P-atom in 6 appears to be identical to that of 2b (epimeric to 2a and 3).

The reaction of 1 with isobutylene produces a 2,2,4,4-tetrasubstituted phospholane in a 2:1 addition via the suggested intermediate i (Scheme 4)[1b]. In an attempt to capture this carbonium-phosphiranium ion (i) whose exact structure is as yet unknown[11], it was reacted with several dienophiles. Phenylisothiocyanate led to the isolation of compound 7a following the isothiocyanate addition to a solution of isobutylene and complex 1, immediately after completing the addition of the olefin at -78° to the CH_2Cl_2 solution. Compound 7a was obtained in ca. 15% yield ($C_{17}H_{18}NOPS$)[12]. The spectral data suggested that 7a possess the 2-imino-1,3-thiaphospholane skeleton. However, a 2-thio-1,3-azaphospholane could not be excluded[13]. The differentiation between the two possible structures was achieved from the structure of the hydrolysis product[14] of 7a (8a[15], Scheme 4). Methylation of 8a with CH_2N_2 gave the methylated compound 8b[16] which possessed the characteristic $\geq$P(O)OMe absorption in the ^1H-NMR spectrum proving the presence of the $\geq$P(O)OH moiety in 8a. Compound 7a is unstable and decomposes quite rapidly under acidic conditions, to compound 8a and aniline[17]. Reacting p-methoxy phenylisothiocyanate[18]

with i gave compound 7b[19] which was more stable than 7a, explained by the electron donating OMe group. The synthesis of 7 represents the first example for a new 1,3-dipolar addition of the $R_2\overset{+}{C}-CH_2-\ddot{P}XR'$ species, a reaction which may find its application in the preparation of other new heterocycles.



Scheme 4

Table 1 ^{13}C chemical shifts and $^{13}C-^{31}P$ coupling constants[a].

C-	1	3	4	5,6		C_1-Me	C_4-Me	^{1}H-NMR data.[b] C_1-Me	C_4-Me
2a[c]	43.4 (68)	40.0 (59)	43.8 (0)	37.5 (0)	31.5 (7)	14.9 (0)	24.1 (12)	1.00s (14)	1.30s (3)
3	82.6 (77)	41.2 (67)	84.7 (0)	38.2 (0)	31.8 (7)	16.1 (7)	24.4 (6)	1.20s (12)	1.60s (3)
2b[c]	45.2 (68)	41.5 (59)	43.2 (0)	36.9 (0)	31.1 (0)	13.9 (0)	23.5 (12)	1.30s (12)	1.30s (3)
6	66.9 (63)	42.8 (65)	68.2 (0)	38.2 (0)	31.8 (0)	13.7 (0)	22.6 (11)	1.53s (13.5)	1.53s (2)

a. Chemical shifts, in parts per million, relative to TMS, determined on a Bruker WH-90 instrument (in $CDCl_3$). Numbers in parentheses stand for the coupling constants in Hz.

b. The δ_H values of the methyl groups of the pair 2a and 3 and the pair 2b and 6 indicate their similarity. In the case of 2b and 6 the chemical shifts are identical whereas in 2a and 3 they appear separately.

c. The stereochemistry of the P-atom in the two P-epimers, 2a and 2b, is still unidentified.

References and Notes

1. a. Y. Kashman and A. Rudi, Tetrahedron Letters, 2819 (1976), b. ibid, 2209 (1978), c.ibid, 1077 (1979), d. Tetrahedron, in press.
2. S. Kh. Nurtdinov, V.S. Tsivunin, R.S. Khairullin, V.G. Khashtanova and G. Kh. Kamai, Zhur. Obshchei. Khim. 40, 36 (1970).
3. W. Kimel and A.C. Cope, J. Am. Chem. Soc. 65, 1992 (1943).
4. The strength of the P-O bond is 86 kcal/mole whereas the strength of the P-C bond is 65 kcal/mole only; R.F. Hudson, "Structure and Mechanism in Organo-Phosphorus Chemistry", Academic Press 1965, N.Y., p.11.
5. An oil, m/e 236 (M^+,100), 221 (M^+-Me,20), 180(30), 139(98) and 140(95); ν_{max}^{neat}2900, 1440, 1380, 1320, 1230, 1220, 1180 and 1100 cm^{-1}; ^{1}H-NMR ($CDCl_3$,60MHz, δ; the multiplicity is given after P-decoupling): 1.20s(3H,J_{PH}=12Hz), 1.60s(3H,J_{PH}=3Hz), 1.80m(3H), 2,10brs(2H, J_{PH}=12Hz) and 2.80m(1H).
6. A crystalline compound m.p. 175°, m/e 276(M^+,30) and 281(M^+-Me,100), ν_{max}^{neat}2900, 1690,1430, 1350, 1220, 1100, 1010, 940, 860, 810, 780, 720 and 690 cm^{-1}; ^{1}H-NMR: 0.84d (3H,J_{PH}=21,

J=7Hz), 1.05d(3H,J=6Hz), 1.38s(3H,J_{PH}=16Hz) and 3.0m(1H); ^{13}C-NMR(22.63MHz, δ): 19.3dq(J_{PC}=9Hz), 20.1q, 21.2q, 23.3dt(J_{PC}=4Hz), 29.0dd(J_{PC}=6Hz), 31.2t, 32.5dt(J_{PC}=7Hz), 39.7d(J_{PC}=81Hz), 118.2d(J_{PC}=5Hz) and 146.8s.

7. L. Anschutz, E. Klein and G. Cermak, Chem. Ber. 77b, 726 (1944).
8. 1,4-Dimethyl-4-isopropenylcyclohexan-3-one, which cannot isomerize to the αβ-unsaturated ketone, yields upon phosphorylation an adduct the structure of which is under investigation.
9. Azeotropic reflux of equimolar amounts of 2-methylhex-1-en-5-one and 1,1-dimethyl hydrazine yielded the corresponding hydrazone; ^{1}H-NMR: 1.70s(Me),1.80s(Me), 2.30s(NMe_2) and 4.85 brs(2H)
10. An oil, $C_{15}H_{23}N_2OP$, m/e 278(M^+,20) and 234(M^+-NMe_2,100); ν_{max} 2950, 1440, 1370, 1180, 1110, 850 and 690 cm^{-1}; ^{1}H-NMR: 1.53s(3H,J_{PH}=13.5Hz), 1.53s(3H,J_{PH}=2Hz), 1.60m(4H), 2.12s(2H, J_{PH}=6Hz), and 2.72s(6H,NMe_2).
11. The three-membered phosphiran ring is believed to be highly strained and very unstable; G. Markl, Angew. Chem. Int. Ed. 4, 1023 (1965).
12. A. crystalline compound; m.p. 110°; $C_{17}H_{18}NOPS$, m/e 315(M^+,30), 260(15), 213(15), 180(30), 160(30), 133(100) and 124(90); ν_{max} 2900, 1580, 1570, 1490, 1440, 1380, 1210, 1180, 1130, 1120, 1080, 970, 940 and 850 cm^{-1}; $\lambda_{max}^{CH_3CN}$ 320nm(26,000), 274(41,500) and 213(130,000); ^{1}H-NMR: 1.60s(3H,J_{PH}=1.5Hz), 1.82s(3H), 2.46 AB quartet (2H), 6.90-7.20m(5H), 7.80-8.10 (3H) and 8.00-8.40 (2H) ^{13}C-NMR: 32.4dq(J_{PC}=8Hz), 33.6q, 43.4dt(J_{PC}=77Hz), 51.9s and 151.0d(J_{PC}=20Hz).
13. For a review of additions to ArC=N=S see S.St.C. Black and K.G. Watson, Aust. J. Chem. 26, 2473 (1973).
14. The hydrolysis of the thiaphospholanes is expected to occur via a similar mechanism as the one suggested for the hydrolysis of ortho-esters.
15. An oil, $C_{10}H_{15}O_2PS$, m/e 230(M^+,80), 196(M^+-H_2S,100), 170(15) and 140(90); ν_{max}^{neat} 2900, 1560, 1490, 1110, 1080 and 970 cm^{-1}, ^{1}H-NMR: 1.45s(6H). 1.70s(2H,J_{PH}=13.5Hz) and 7.50-8.00m(5H); ^{13}C-NMR: 33.8dq(J_{PC}=5Hz), 43.5dt(J_{PC}=78Hz) and 49.5s.
16. An oil $C_{11}H_{17}O_2PS$, m/e 244(M^+,5), 211(M^+-SH,50) and 156(PhP(OH)OMe,100); ^{1}H-NMR: 1.55s (6H), 2.29AB quart.(2H) and 3.5s(3H,J_{PH}=12Hz).
17. 3-Phenyl-2-phenylimino-1,3-thiaphospholane, synthesized in another way, was found to be unstable to acid; K. Issleib and Kl.D. Franze, J. für Prakt. Chem. 315, 471 (1973).
18. F.B. Dains, R.Q. Brewster and C.P. Olander, Org. Syn I, p. 447.
19. A. crystalline compound, m.p. 150°; $C_{18}H_{20}NO_2PS$, m/e 345(M^+,15), 235(3), 215(15), 165(100), 150(80) and 149(80); ν_{max}^{KBr} 2900, 1600, 1550, 1500, 1430, 1290, 1250, 1180, 1100, 1020, 930, 920, 820 and 730 cm^{-1}: $\lambda_{max}^{CH_3CN}$ 335(8300), 283(9200), 274(8800) and 254(9200); ^{1}H-NMR: 1.55s(3H,J_{PH}=3Hz), 1.82s(3H) 2.45AB quart.(2H), 3.75s(OCH_3), 6.75-8.00m (9H) ^{13}C-NMR: 32.3dq(J_{PC}=9Hz), 33.6q, 43.0dt(J_{PC}=77Hz), 51.9s, 55.4q and 143.4d(J_{PC}=22Hz).

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