COMMUNICATION

A new reaction of 1-(2,4,6-trialkylphenyl)phospholes with heteroaromatic character; aromatic electrophilic substitution under the conditions of Friedel–Crafts acylation

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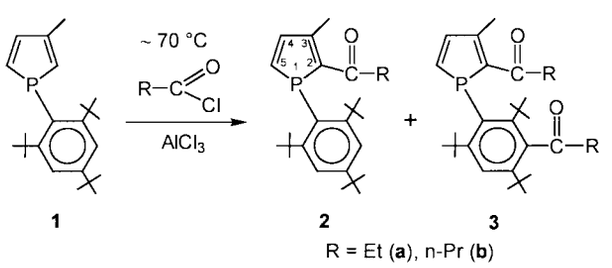
Received (in Cambridge, UK) 13th June 2000, Accepted 31st July 2000
Published on the Web 9th August 2000

Two (trialkylphenyl)phospholes (1 and 4) with significant heteroaromatic character due to the flattened P-pyramid underwent Friedel–Crafts acylation with acyl halides to afford 2-acylphosphole derivatives (*e.g.* 2 and 6, respectively); the 2-acyl-5-arylphosphole by-product 7 may have been formed by sigmatropic rearrangement through 2*H*-phosphole 9 or dibromophosphorane 12.

Phospholes, the representative class of five-membered P-heterocycles, have attracted much attention recently.[1] Of special interest is the problem of aromaticity in phospholes. Due to the pyramidal geometry around the phosphorus atom, common phenyl- and alkylphospholes display only a small degree of aromaticity.[2] The 1-(2,4,6-trialkylphenyl)phospholes with a flattened phosphorus pyramid due to the presence of the sterically demanding P-substituent, possess, however, significant aromaticity.[3–5] For the (triisopropylphenyl)phosphole, a Bird index (BI) of 40.4 was calculated,[3] while the value of 56.5 obtained for the tri-*tert*-butylphenyl derivative[5] suggested an aromaticity that is comparable with that of pyrrole (BI = 59). In the light of the extent of aromaticity in the (trialkylphenyl)-phospholes and on the basis of the preliminary results,[5] it seemed to be interesting to evaluate their reactivity in aromatic electrophilic substitutions, such as in Friedel–Crafts acylations. In this paper, we disclose our results on the scope and limitation of this new type of reaction of phospholes.

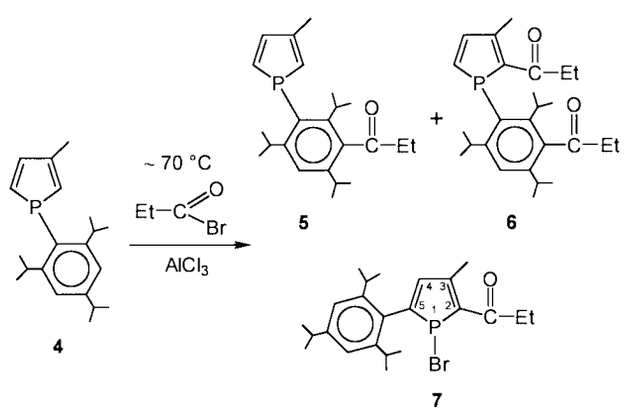
(Tri-*tert*-butylphenyl)phosphole **1** underwent a substitution reaction with propionyl chloride and with butyryl chloride in the presence of aluminium chloride in boiling *n*-hexane to afford the corresponding mixture of monoacylated product **2** and diacylated derivative **3** (Scheme 1). It is worthy of mention



Scheme 1

that for product **2** only the most crowded 2-acylphospholes **2a**,**b** were found to have been formed. As an analogy, a similar outcome was observed for the electrophilic substitution of 3-methylpyrrole.[6] The monoacylphospholes (**2a**,**b**) were separated from the reaction mixtures by repeated column chromatography in moderate yields (33–36%). The structure of the products (**2a**,**b**) was supported by ^{31}P, ^{1}H and ^{13}C NMR, as well as by mass spectroscopic methods. The ^{1}H NMR spectra revealed the coupling between the two hydrogen atoms of the phosphole ring ($^{3}J_{HH} \sim 7$ Hz) suggesting their vicinal disposition, and hence a 2-substitution. The diacyl products (**3a**,**b**) were characterised by ^{31}P NMR and mass spectral data.

The above electrophilic substitutions serve as evidence for the heteroaromatic character of (tri-*tert*-butylphenyl)phosphole **1** (BI = 56.5[5]). We noted, however, that other acid chlorides, such as benzoyl chloride and diphenylphosphinoyl chloride failed to participate in aromatic electrophilic substitutions with phosphole **1**. This was probably due to steric hindrance. The question then emerged of whether the triisopropylphenyl derivative **4** with lower electron delocalisation (BI = 40.4[3]) also enters into aromatic electrophilic substitution with aliphatic carboxylic halogenides. We found that in reaction with propionyl bromide using aluminium chloride as the catalyst, monoacylphosphole **5** and diacyl derivative **6** were formed in poor yields (Scheme 2). Product **5** was formed by acylation



Scheme 2

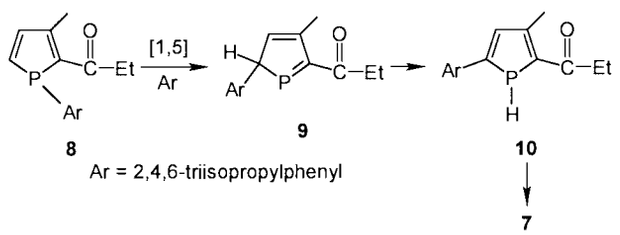
of the trialkylphenyl ring, as was suggested by the absence of a J_{PC} coupling constant for the carbonyl carbon atom in the ^{13}C NMR spectrum. A new type of product, 2-acyl-5-aryl-1-bromophosphole **7** was isolated from the reaction mixture as the main component (35%) (Scheme 2). The use of propionyl

DOI: 10.1039/b004695g

chloride with aluminium bromide led to similar results. Bromophosphole **7** was characterised by ^{31}P, ^{13}C and ^{1}H NMR, as well as by mass spectroscopic methods. The ^{13}C NMR assignments were confirmed by two dimensional correlation diagrams, such as HMQC and HMBC spectra.

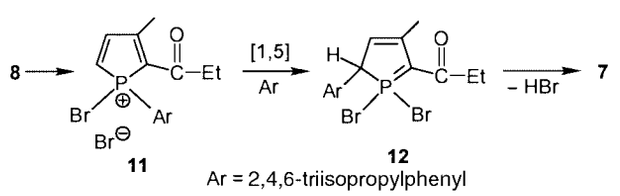
The electrophilic substitution that results in acylphosphole **6** indicates the aromatic character of the hetero ring in **4**; the poor conversion reflects, however, the lower electron delocalisation represented by the BI of 40.4.[3]

According to our explanation, based on speculation, 2*H*-phosphole **9**, formed by a sigmatropic rearrangement from monoacylphosphole **8** (also present in the reaction mixture), might be the key intermediate of the unexpected by-product **7** (Scheme 3). On the basis of Mathey's extensive work, a number



Scheme 3

of rearrangements of 1-arylphospholes to their 2*H*-isomers are known.[1,7] It is not clear, however, how intermediate **9** is converted to bromophosphole **7**. One possibility is that the reaction sequence leading to product **7** involves a prototropic rearrangement of 2*H*-phosphole **9** to 1*H*-phosphole **10** driven by the energy gain of aromatization. The fate of intermediate **10** is, however, unknown at the present stage of the work. The intermediacy of α-aryl-1*H*-phospholes, which are analogous to species **10**, has been described in some transformations of phospholes.[8] One of the referees raised the point that if the conversion of phosphole **10** to bromo derivative **7** requires bromination, the halogenation of acylphosphole **8** may also be assumed to result in formation of the phospholium bromide **11**. Intermediate **11** may then afford dibromophosphorane **12** (resonating with an ylide that is stabilised by the electron-withdrawing effect of the keto group) to give product **7** by the loss of hydrogen bromide (Scheme 4). It is not clear, however,



Scheme 4

how the bromine may be formed under the conditions of the reaction. Further investigation to get better insight into the mechanism will be carried out soon.

To summarise our results, we found that the (trialkylphenyl)-phospholes with aromatic character due to the flattened P-pyramid underwent Friedel–Crafts acylations. The efficiency greatly depended on the extent of the electron delocalisation. An interesting side-reaction resulting in the formation of a bromophosphole was also observed.

Experimental

The acylation of (tri-*tert*-butylphenyl)phosphole 1 with propionyl chloride

A mixture of 0.50 g (1.46 mmol) phosphole **1**, 0.23 g (1.75 mmol) aluminium chloride, and 0.18 cm^3 (2.05 mmol) propionyl chloride in 30 cm^3 *n*-hexane was refluxed with stirring for 60 h. The volatile components were evaporated, and the residue was taken up in 40 cm^3 chloroform. The mixture was treated with 6 cm^3 water and the organic phase was dried (Na_2SO_4). Evaporation of the solvent left an oil containing 61% of acylphosphole **2a** and 39% of diacylphosphole **3a**. Repeated column chromatography (silica gel, 2% methanol in chloroform) afforded 0.22 g (36%) acylphosphole **2a** in a purity of *ca*. 96% and 0.12 g (17%) diacylphosphole **3a** in a purity *of ca*. 92%.

Compound 2a. ^{31}P NMR ($CDCl_3$) δ 7.0; ^{1}H NMR ($CDCl_3$) δ 0.75 (t, J = 7.3, 3H, CH_2CH_3), 1.32 (s, 9H, *p*-$C(CH_3)_3$), 1.36 (s, 18H, *o*-$C(CH_3)_3$), 1.40 (s, 3H, C_3–CH_3), 2.95–3.02 (m, 2H, CH_2CH_3), 6.79 (dd, J_1 = 7.0, J_2 = 17.8, 1H, C_4–H), 7.24 (dd, J_1 = 7.0, J_2 = 30.5, 1H, C_5–H); ^{13}C NMR ($CDCl_3$) δ 8.6 (CH_2CH_3), 19.1 (C_3–CH_3), 39.2 (CH_2CH_3), 132.9 (J = 14.9, C_4*), 134.3 (J = 11.7, C_5*), 200.7 (J = 27.8, C=O), *may be reversed; MS *m*/z (rel. int.) 398 (M^+, 73%), 383 (M − 15, 87), 341 (M − 57, 88), 57 (100); HRMS, M^+_{found} = 398.2721, $C_{26}H_{39}OP$ requires 398.2739.

Compound 3a. ^{31}P NMR ($CDCl_3$) δ 9.7; MS *m*/*z* (rel. int.) 454 (M^+, 9%), 439 (M − 15, 8), 397 (M − 57, 20), 57 (100); HRMS M^+_{found} = 454.3013, $C_{29}H_{43}O_2P$ requires 454.3001.

The acylation of (tri-*tert*-butylphenyl)phosphole 1 with butyryl chloride

The reaction was performed as above using 0.21 cm^3 (2.05 mmol) butyryl chloride. Yield: 0.21 g (33%) acylphosphole **2b** in a purity of *ca*. 95% and 0.11 g (14%) diacyl derivative **3b** in a purity of *ca*. 92%.

Compound 2b. ^{31}P NMR ($CDCl_3$) δ 7.1; ^{1}H NMR ($CDCl_3$) δ 0.58 (t, J = 7.3, 3H, $(CH_2)_2CH_3$), 1.32 (s, 9H, *p*-$C(CH_3)_3$), 1.36 (s, 18H, *o*-$C(CH_3)_3$), 1.40 (s, 3H, C_3–CH_3), 2.87–2.94 (m, 2H, $CH_2CH_2CH_3$), 6.79 (dd, J_1 = 6.9, J_2 = 17.7, 1H, C_4–H), 7.25 (dd, J_1 = 6.9, J_2 = 30.5, 1H, C_5–H); ^{13}C NMR ($CDCl_3$) δ 14.0 ($(CH_2)_2CH_3$), 20.1 (C_3–CH_3), 132.9 (J = 15.7, C_4*), 134.3 (J = 11.8, C_5*), 198.2 (J = 24.6, C=O), *may be reversed; MS *m*/*z* (rel. int.) 412 (M^+, 76%), 397 (M − 15, 46), 355 (M − 57, 23), 341 (M − 71, 66), 71 (49), 57 (100); HRMS M^+_{found} = 412.2900, $C_{27}H_{41}OP$ requires 412.2895.

Compound 3b. ^{31}P NMR ($CDCl_3$) δ 9.4; MS *m*/*z* (rel. int.) 482 (M^+, 24%), 467 (M − 15, 10), 425 (M − 57, 7), 411 (M − 71, 36), 71 (92), 57 (100); HRMS M^+_{found} = 482.3310, $C_{31}H_{47}O_2P$ requires 482.3314.

The reaction of (triisopropylphenyl)phosphole 4 with propionyl bromide

The reaction was performed as above using 0.28 g (2.05 mmol) of propionyl bromide. Repeated column chromatography led to two fractions. The first one contained the 3 : 1 mixture of acylphosphole **5** and diacyl derivative **6** (total yield: 10%), while the second fraction was compound **7** (yield: 35%).

Compound 5. ^{31}P NMR ($CDCl_3$) δ 2.0; ^{13}C NMR ($CDCl_3$) δ 8.2 (CH_2CH_3), 18.8 (C_3–CH_3), 211.9 (C=O); MS *m*/*z* 356 (M^+), 341 (M − 15), 299 (M − 57); HRMS M^+_{found} = 356.2275, $C_{23}H_{33}OP$ requires 356.2269.

Compound 6. ^{31}P NMR ($CDCl_3$) δ 4.1; MS *m*/*z* 412; HRMS M^+_{found} = 412.2543, $C_{26}H_{37}O_2P$ requires 412.2531.

Compound 7. ^{31}P NMR ($CDCl_3$) δ 8.5; ^{1}H NMR ($CDCl_3$) δ 0.97 (t, J = 7.3, 3H, CH_2CH_3), 1.13 (broad signal, 6H, *o*-$CH(CH_3)_2$), 1.18 (d, J ~ 6, 6H, *o*-$CH(CH_3)_2$), 1.26 (d, J = 7.0, 6H, *p*-$CH(CH_3)_2$), 2.44 (q, J = 7.0, 2H, CH_2CH_3), 2.52 (d, J = 8.5, 3H, C_3–CH_3), 2.58–2.66 (m, 1H, *o*-$CHMe_2$), 2.68–2.74

(m, 1H, *o*-$CHMe_2$), 2.88 (septet, J = 7.0, 1H, *p*-$CHMe_2$), 6.99 (d, J = 8.8, 1H, C_4–H), 7.01 (2H, Ar); ^{13}C NMR ($CDCl_3$) δ 8.6 (J = 2.4, 3H, CH_2CH_3), 19.1 (C_3–CH_3), 23.8 (*p*-$CH(CH_3)_2$), 24.4 (J = 1.1, *o*-$CH(CH_3)_2$), 25.4 (J = 1.2, *o*-$CH(CH_3)_2$), 32.3 (broad signal, *o*-$CHMe_2$), 34.4 (*p*-$CHMe_2$), 37.1 (J = 4.2, CH_2CH_3), 118.5 (J = 3.0, C_2), 122.8 (J = 6.7, $C_{3'}$), 134.3 (J = 8.5, $C_{1'}$), 139.8 (J = 16.3, C_4), 143.0 (J = 7.9, C_5), 151.5 (J = 18.8, C_3), 153.3 ($C_{4'}$), 157.5 (J = 15.1, $C_{2'}$), 197.4 (J = 22.7, C=O); MS *m*/*z* (rel. int.) 434 (M^+, 38%), 377 (M − 57, 100), 355 (M − 79, 49), 297 (M − 57 − 79 − H, 28); HRFAB $[M + H]_{found}$ = 435.1452, $C_{23}H_{33}BrOP$ requires 435.1452 for the ^{79}Br isotope.

Acknowledgements

The authors are grateful for support of the research by OTKA (Hungarian Scientific Research Fund) (Grant No. T 029039).

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