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SOME PECULIAR CASES OF 7-TELESUBSTITUTION BY ANIONIC PHOSPHORUS NUCLEOPHILES ON 2-HALOTROPONES

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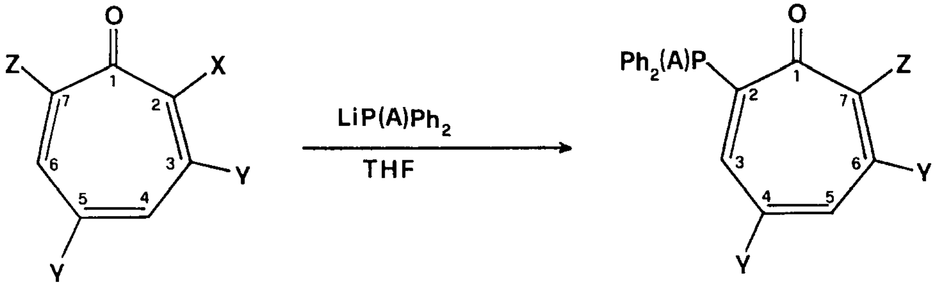
Summary: Both 2-chloro- and 2-fluoro[3,5,7-$^2H_3$]tropone were found to react with lithium diphenylphosphide in tetrahydrofuran to give 2-diphenylphosphino[4,6-$^2H_2$]tropone in what constitutes the first example of telesubstitution by an anionic nucleophile in a non-protic solvent on tropones carrying nucleofugal groups; lithium diphenylphosphide oxide showed the same behaviour.

In the course of our search for novel covalent adducts between bases and troponoids,[1] we needed a tropone carrying a dialkyl- or a diarylphosphino group at C-2.[2]

We report here on the synthesis of such an intermediate from 2-halotropones and lithium diphenylphosphide which reveals peculiar cases of nucleophilic 7-telesubstitution with troponoids.



1a,X = Cl; Y = H; Z = H
1b,X = Cl; Y = D; Z = D
1c,X = F ; Y = H; Z = H
1d,X = F ; Y = D; Z = D

2a, Y=Z=H; A=nil
2b, Y=D (and partial deuteriation at C-7);A=nil
2c, Y=Z=H; A=O
2d, Y=D (and partial deuteriation at C-7); A=O

Thus, to 2-chlorotropone[§] (1a) (0.504 g, 3.6 mmol) in tetrahydrofuran[⌖] (10 ml) was added,dropwise, at room temperature under nitrogen, slightly less than one molar equivalent of lithium diphenylphosphide (LiP Ph_2).◇ The mixture, which immediately turned to yellow-brown, was evaporated *in vacuo* to leave a tarry residue which was chromatographed on a Merck Kieselgel 60 P_{254} silica gel plate, 2 mm thick, eluant ethyl ether. The R_F 0.7 band gave 2a (0.45 g; yield 43%, based on the starting 1a)‡ yellow crystals; mp 139-140°C;† uv, $\lambda_{max}^{CH_3OH}$ 224, 306 nm, logε= 3.5, 2.8; ^1H nmr,‡ δ (C_6D_6) = 7.4 (4H,m), 7.0 (6H,m), 7-6 (5H,m); ^{13}C nmr, δ‡186.73, 187.44, $\Delta\delta$=-0.71 (d, ^{2}*J*(PCC) = 16.5, 16.8, C-1), 139.54, 139.76, $\Delta\delta$=-0.22(d, ^{2}*J*(PCC)= 4.8, 5.2, C-3), 138.33, 139.66, $\Delta\delta$=- 1.33 (d, ^{3}*J*(PCCC)= 2.7, 2.7, C-7), 135.42, 137.68, $\Delta\delta$= - 2.26 (d, ^{1}*J*(PC) = 13.3, 12.8, C-2), 135.21, 135.06, $\Delta\delta$=0.15 (poorly resolved d, C-4), 133.32, 133.36, $\Delta\delta$=- 0.04 (d, ^{4}*J*(PCCCC) = 2.6, 2.9, C-5), (the signal for C-6 in $(CD_3)_2CO$-$CDCl_3$ was obscured by a phenyl resonance at 132.82), 133.10, $\Delta\delta$= -0.3 (s,C-6), and four phenyl resonances; ms (EI, 70 eV), m/e(%) = 292 (3.1), 291 (21.2),290 (100). These ^{13}C nmr data are in accordance with structure 2a. In particular, the two largest differential shifts ($\Delta\delta$) allow us to assign the two carbons in the α-position to the carbonyl group.[3] Moreover, all other assignments are compatible with known trends for carbon to phosphorus coupling.[3] The data below for the deuteriated analogue 2b confirm this assignment.

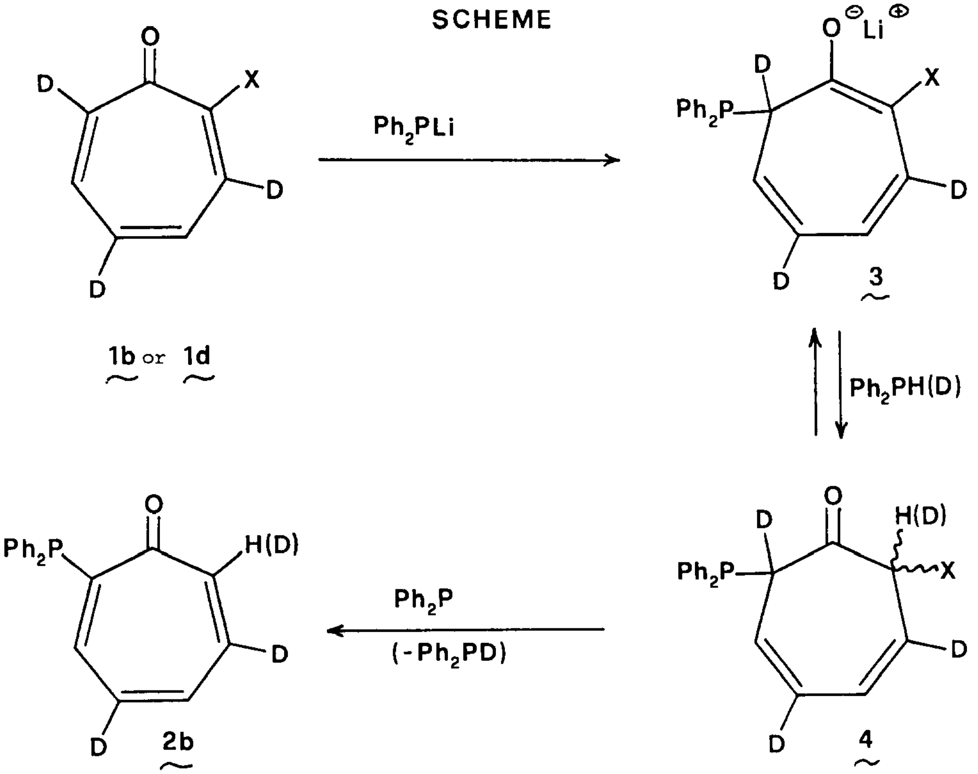
Starting from 2-fluorotropone§ (1c), under the same conditions used for 1a, we obtained 2a in a lower, ca. 10%, yield (based on the starting 1c).‡ Both in this and in the above case no other troponoidal compound could be detected besides 2a.

The reaction of 2-chloro[3,5,7- $^2H_3$]tropone[4,§] (1b) with lithium diphenylphosphide,under identical conditions to those used for 1a and 1c, gave 2-diphenylphosphino[4,6-$^2H_2$]tropone (2b), partially (ca.20%) deuteriated at C-7,¤ yellow crystals, mp 140°C,† in a ca.10% yield; ms(EI, 70 eV) m/e (%) = 294(8.2), 293(44.7), 292(100); uv spectrum identical to that of 2a. Starting from 2-fluoro-[3,5,7-$^2H_3$]tropone[4,§] (1d), under the same conditions used for 1c, the yield of 2b was low, as in the case of 2a from 1c, while the extent of deuteriation at C-7 was high (ca.60%); ms(EI, 70 eV), m/e(%)= 294(19), 293(80), 292(100). In the reaction mixtures obtained from either 1b or 1d we could not detect any other troponoidal compound besides 2b.

In accordance with complete deuteriation at both C-4 and C-6, the ^{13}C nmr spectra of 2b in either 1:2 $(CD_3)_2CO$-$CDCl_3$ or C_6D_6 revealed only extremely weak, broad resonances at the values attributed to C-4 and C-6 for 2a. Structure 2b is also fully supported by the results in the accompanying paper.[2]

Similar results were obtained with 1a or 1b and lithium diphenylphosphide oxide (LiP(A)Ph_2= Li P(O)Ph_2) to give, respectively, 2-diphenylphosphinyltropone (2c), mp 173°C,† and 2-diphenylphosphinyl[4,6- $^2H_2$] tropone (2d), mp 172°C, in 21% and 13% yields, based on starting 1. Structures 2c and 2d are fully supported by the ^{13}C nmr spectra in 1:2 $(CD_3)_2CO$-$CDCl_3$. In particular, for 2c, δ=184.8 (d, ^{2}*J*(PCC) = 22.0, C = O), 145.1 (d, ^{2}*J*(PCC) = 6.7, C-3), 142.5 (d, ^{3}*J*(PCCC) = 5.8, C-7), 137.3 (d, ^{4}*J*(PCCCC) = 1.1, C-5), 135.5 (s,C-6), 133.1(d, ^{3}*J*(PCCC)= 16.7, C-4). For 2d, in accordance with complete deuteriation at both C-4 and C-6, and partial deuteriation at C-7, no signals were detectable for either C-4 or C-6, while the doublet for C-7 (δ=142.5, $^3\underline{J}$(PCCC) = 5.7) was much weaker, and broadened, than with 2c.

The whole body of the above results can be rationalized by the mechanism in the Scheme which, for simplicity, is drawn for the case of lithium diphenylphosphide only. According to this mechanism, the halogen X activates attack at C-7 by $Ph_2P^\ominus$, to give the intermediate 3.[5] That this


SCHEME

step cannot be reversible is in accordance with the extremely low nucleofugic aptitude of $Ph_2P^\ominus$. Therefore, 3 can only await for protonation at C-2 to give 4. We propose that the actual protonating agent is, at the beginning, Ph_2PH, generated by the reaction of $Ph_2P^\ominus$ with traces of moisture. Elimination of DX from intermediate 4 by the available base ($Ph_2P^\ominus$ and/or $OH^\ominus$) generates bideuteriated 2b. Now, as Ph_2PD has become available, deuteriation can occur in the step 3 → 4, leading to trideuteriated 2b. The overall result is 2b partially deuteriated at the carbon vacated by the halogen. According to this view, it is the irreversibility of the 1→ 3 step that determines the C-7 regiospecifity for these reactions.[5]

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FOOTNOTES

[§] Freshly sublimed. Stored material, even in the cold, gave poorer yields.

⸸ Freshly distilled from lithium aluminum hydride.

◊ Prepared by the addition of one molar equivalent of n-butyl lithium to Ph_2PH.

† Satisfactory elemental analyses were obtained.

‡ Yields of **2** varied somewhat from run to run, under identical experimental conditions. The yields reported here represent the mean values from several runs and have actually to be compared with the maximum theoretical yield for **2** which, according to the mechanism at the Scheme, is 50%. A lower yield for the reaction of 2-fluoro- vs. 2-chlorotropone has no precedent.[5] Actually, the reverse order of yields was always found for ipso-nucleofilic substitutions of fluorine.[5] We believe that the present reaction of 2-fluorotropone is disfavoured with respect to that of the chloro-analogue, because the rate is limited by the elimination of HX from C-7 — C-2.[5] In fact,elimination of HF is expected to be more difficult than elimination of HCl.

ǂ δ is given in ppm with respect to internal $SiMe_4$ as reference while J is given in Hz. The ^{13}C nmr spectra are fully proton decoupled. In the case of **2a** the ^{13}C chemical shifts are reported first in a 1:2 $(CD_3)_2CO-CDCl_3$ solvent mixture and then in C_6D_6, followed by the differential shift (Δδ) and, within parenthesis, by the multiplicity and the coupling constants of ^{13}C to ^{31}P in the two solvent media, is the order given above.

¤ The extent of deuteriation at C-7 varied from run to run, under the same experimental conditions. A higher deuteriation extent at C-7 when starting from **1d** than **1b** may well reflect other, contingent causes than the presence of fluorine in the place of chlorine,as will be apparent from the ensuing discussion in the text.

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