

A facile one-pot synthesis and temperature dependence of NMR spectra of stable heterocyclic phosphorus ylids[†]

Robabeh Baharf^a, Akbar Heydari^b and Narges Saffarian^a

^aChemistry Department, Mazandaran University, P. O. Box 453, Babolsar, Iran

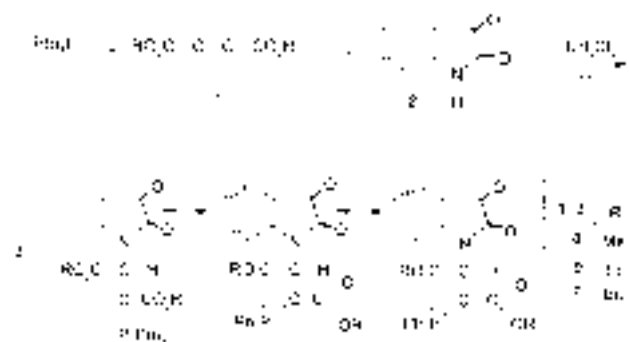
^bChemistry Department, Tarbiat Modarres University, Tehran, Iran

The addition of dialkyl acetylenedicarboxylates to isatin, a strong N–H acid, in the presence of triphenylphosphine leads to stable crystalline phosphorus ylids in excellent yields. Some of these ylid derivatives exist as a mixture of two rotational isomers. Interconversion between these two forms was investigated by variable temperature NMR spectroscopy.

Keywords: acetylenic esters, triphenylphosphine, NH-acids, organophosphorus compounds

In recent years there has been increasing interest in the synthesis of organophosphorus compounds, *i.e.* those bearing a carbon atom bound directly to a phosphorus atom. This interest has resulted from the recognition of the value of such compounds for a variety of industrial and chemical synthetic uses. Phosphorus ylids are reactive systems, which take part in many reactions of value in the synthesis of organic products.^{1–8}

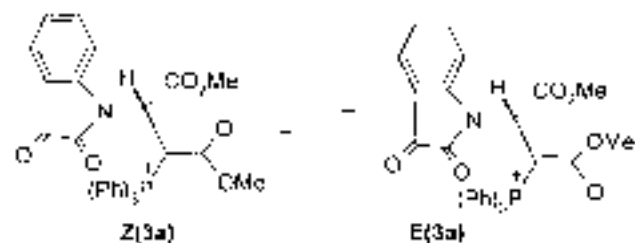
We have already described the synthesis of a group of these systems using triphenylphosphine, dialkyl acetylenedicarboxylates and a carbon acid.⁵ With the purpose of preparation of phosphorus ylids using N–H acids, we performed the reaction of isatin (**2**) with triphenylphosphine and dialkyl acetylenedicarboxylates (**1**).



On the basis of the well established chemistry of trivalent phosphorus nucleophiles it is reasonable to assume that phosphorus ylid **3** resulted from the initial addition of triphenylphosphine to the acetylenic ester and a subsequent protonation of the 1:1 adduct by N–H acid, isatin. Then the positively charged ion is attacked by the anion of the amide to form phosphorane **3**.

The structures of compounds **3a–c** were deduced from their elemental analysis and their ¹H, ¹³C and ³¹P NMR and IR spectral data. Of special interest are the strong carbonyl absorption bands at 1609–1734 cm⁻¹ for all compounds. We have examined the proton NMR spectrum of **3a** in CDCl₃ at various temperatures. The 500 MHz ¹H NMR spectrum of **3a** at room temperature (25°C) exhibited a pair of sharp doublets at δ 3.09, 3.78 ppm and δ 3.67, 3.76 ppm with an intensity ratio of 4:1. As the temperature was increased, two doublets

collapsed to one doublet at δ 3.09 and 3.78 ppm. This observation is attributed to the temperature dependent equilibrium between the geometric (rotational) isomers, *E* and *Z* (**3a**), *i.e.* the result of restricted rotation. The coalescence temperature was about 65°C. At 75°C only one doublet was observed for methoxy groups and no further dynamic NMR effect was observed up to 90°C. From the spectrum it is clear that the dominant (major) isomer, in fact, does have the most shielded methoxy group, because of anisotropic effects of phenyl groups. The methine proton appeared as a pair of symmetrical doublets of unequal intensity centered at δ 5.30 and 5.23 ppm (³J_{PH} 16.2 and 17.9 Hz, respectively), at 25°C. Raising the temperature also led to the gradual collapse of this quartet to a doublet. This collapse is attributed to the same temperature dependent equilibrium between *E* and *Z* (**3a**) isomers. The ³¹P NMR spectrum of **3a** also exhibited two single peaks at δ 22.62 and 19.92 ppm in agreement with the presence of two isomers, *E* and *Z*.



The aromatic protons appear as a multiplet at δ 7.08–7.84 ppm. The ¹³C NMR spectrum of **3a** displayed two sets of 32 distinct resonance, in agreement with two rotational isomers. Although the presence of the ³¹P nucleus complicates both the ¹H and ¹³C NMR spectra of **3a**, it helps in assignment of the signals by long-range coupling with ¹H and ¹³C nuclei.

The ¹H and ¹³C NMR spectra of **3b** and **3c** show that only one isomer (*E*) exists, probably, because of steric hindrance between bulky ester groups and triphenylphosphine group, rotation about C=C bond is hindered, and only *E* isomer exists. The ¹H and ¹³C NMR spectra of these isomers are similar to those of **3a**, except for the ester groups, which exhibited characteristic resonance with appropriate chemical shifts.

In conclusion, the procedure that we have described here, may be an acceptable method for the preparation of phosphoranes with variable functionalities. Functionalized heterocyclic phosphorus ylids **3a–c** may be considered as potentially useful synthetic intermediates.

* To receive any correspondence. E-mail: baharf@umcc.ac.ir

[†] This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

Experimental

Dialkyl acetylenedicarboxylates, triphenylphosphine and isatin were obtained from Fluka (Buchs, Switzerland) and were used without further purification. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyser. ^1H , ^{13}C and ^{31}P NMR spectra were measured with a Bruker DRX-500 Avance spectrometer at 500, 125.8 and 202.5 MHz, respectively. IR spectra were recorded on a Shimadzu IR-470 spectrometer.

General procedure for synthesis of dialkyl 2-(N-isatin)-3-(triphenylphosphoranylidene)butanedioate (3): To a magnetically stirred solution of triphenylphosphine (0.524 g, 2 mmol) and isatin (0.294 g, 2 mmol) in CH_2Cl_2 (6 ml) was added, dropwise, a mixture of dialkyl acetylenedicarboxylate (2 mmol) in CH_2Cl_2 (4 ml) at -10°C over 10 min. The reaction mixture was then allowed to stand at room temperature and stirred for 24 h. The solvent was removed under reduced pressure and the viscous residue was purified by silica gel (Merck silica gel 60, 230–400 mesh) column chromatography using ethyl acetate-hexane. The solvent was removed under reduced pressure and the product was obtained from recrystallization from ether-pentane.

(3a): Yellow solid, m.p. 110°C , yield 75%; IR (KBr) (ν_{max} , cm^{-1}): 1733, 1635 and 1609 (C=O); ^1H NMR (500 MHz, CDCl_3) (**3a-Z**): δ_{H} 3.09 and 3.78 (6 H, 2 s, 2 OCH_3), 5.30 (1 H, d, $^3J_{\text{PH}}$ 16.21 Hz, CH), 7.08–7.84 (19 H, m, arom); (**3a-E**): δ_{H} 3.67 and 3.76 (6 H, 2 s, 2 OCH_3), 5.23 (1 H, d, $^3J_{\text{PH}}$ 17.95 Hz, CH), 7.08–7.84 (19 H, m, arom); ^{13}C NMR (125.77 MHz, CDCl_3) (**3a-Z**): δ_{C} 38.02 (d, $^1J_{\text{PC}}$ 122.66 Hz, P=C), 49.43 and 52.80 (2 OMe), 54.79 (d, $^2J_{\text{PC}}$ 15.48 Hz, P=C-CH), 115.51, 123.21, 124.34 and 138.48 (4 CH, isatin), 118.03 (N-C=C), 125.67 (d, $^1J_{\text{PC}}$ 91.69 Hz, C_{ipso}), 129.07 (d, $^3J_{\text{PC}}$ 12.20 Hz, C_{meta}), 132.52 (d, $^4J_{\text{PC}}$ 2.39 Hz, C_{para}), 133.38 (d, $^2J_{\text{PC}}$ 9.81 Hz, C_{ortho}), 150.45 (N-C=C), 156.77 (C=O, amide), 169.65 (d, $^2J_{\text{PC}}$ 12.20 Hz, C=O ester), 170.73 (d, $^3J_{\text{PC}}$ 14.97, C=O ester), 184.46 (C=O, ketone); (**3a-E**): δ_{C} 38.72 (d, $^1J_{\text{PC}}$ 132.06 Hz, P=C), 50.62 and 52.59 (2 OMe), 54.97 (d, $^2J_{\text{PC}}$ 15.58 Hz, P=C-CH), 115.4, 123.12, 124.63 and 138.1 (4 CH, isatin), 118.31 (N-C=C), 125.04 (d, $^1J_{\text{PC}}$ 91.81 Hz, C_{ipso}), 128.54 (d, $^3J_{\text{PC}}$ 12.07 Hz, C_{meta}), 132.14 (d, $^4J_{\text{PC}}$ 2.5 Hz, C_{para}), 133.46 (d, $^2J_{\text{PC}}$ 11.70 Hz, C_{ortho}), 150.77 (N-C=C), 157.05 (C=O, amide), 169.85 (d, $^2J_{\text{PC}}$ 12.6 Hz, C=O ester), 170.73 (d, $^3J_{\text{PC}}$ 14.96, C=O ester), 184.14 (C=O, ketone). ^{31}P NMR (202.46 MHz) (**3a-Z**): δ_{P} 22.62 [(Ph) $_3$ P=C]; (**3a-E**): δ_{P} 19.92 [(Ph) $_3$ P=C]; (Found: C, 69.7; H, 4.8; N, 2.5. $\text{C}_{32}\text{H}_{26}\text{NPO}_6$ requires C, 69.2; H, 4.74; N, 2.45 %).

(3b): Orange powder, m.p. 106°C , yield 83%; IR (KBr) (ν_{max} , cm^{-1}): 1733, 1626 and 1609 (C=O); ^1H NMR (500 MHz, CDCl_3): δ_{H} 0.5 and 1.3 (6 H, 2 t, $^3J_{\text{HH}}$ 9 Hz, 2 CH_3), 3.75 and 4.3 (4 H, 2 q, $^3J_{\text{HH}}$ 9 Hz, 2 OCH_2), 5.3 (d, $^2J_{\text{PC}}$ 18 Hz, CH), 7–8 (19 H, m, arom); ^{13}C NMR (125.77 MHz, CDCl_3): δ_{C} 13.8 and 14.1 (2 CH_3), 37.3 (d, $^1J_{\text{PC}}$ 122.2 Hz, P=C), 57.98 (d, $^2J_{\text{PC}}$ 15 Hz, P=C-CH), 61.42 and 62.0 (2

OCH_2), 115.44, 122.97, 124.0 and 138.32 (4 CH, isatin), 117.88 (N-C=C), 125.78 (d, $^1J_{\text{PC}}$ 91.21 Hz, C_{ipso}), 128.86 (d, $^3J_{\text{PC}}$ 11.85 Hz, C_{meta}), 132.38 (d, $^4J_{\text{PC}}$ 2.3 Hz, C_{para}), 133.34 (d, $^2J_{\text{PC}}$ 10.04 Hz, C_{ortho}), 150.3 (N-C=C), 156.77 (C=O, amide), 169.3 (d, $^2J_{\text{PC}}$ 12.51 Hz, C=O ester), 170.37 (d, $^3J_{\text{PC}}$ 14.95 Hz, C=O ester), 184.5 (C=O, ketone); (Found: C, 70.4; H, 5.2; N, 2.4. $\text{C}_{34}\text{H}_{30}\text{NPO}_6$ requires C, 68.04; H, 5.01, N, 2.3 %).

(3c): Yellow powder, m.p. 135 – 137°C , yield 95%; IR (KBr) (ν_{max} , cm^{-1}): 1734, 1630 and 1610 (C=O); ^1H NMR (500 MHz, CDCl_3): δ_{H} 1 and 1.6 (18 H, 2 s, 2 CMe_3), 5.1 (1 H, d, $^3J_{\text{PH}}$ 18 Hz, CH), 7–8.2 (19 H, m, arom); ^{13}C NMR (125.77 MHz): δ_{C} 28.18 and 28.36 (s, 2 CMe_3), 37.10 (d, $^1J_{\text{PC}}$ 121.92 Hz, P=C), 55.44 (d, $^2J_{\text{PC}}$ 16.02 Hz, P=C-CH), 77.73 and 81.35 (2 CMe_3), 115.65, 122.97, 124.16 and 138.46 (4 CH, isatin), 117.95 (N-C=C), 126.24 (d, $^1J_{\text{PC}}$ 91.18 Hz, C_{ipso}), 128.83 (d, $^3J_{\text{PC}}$ 12.07 Hz, C_{meta}), 132.36 (d, $^4J_{\text{PC}}$ 2.52 Hz, C_{para}), 133.53 (d, $^2J_{\text{PC}}$ 9.68 Hz, C_{ortho}), 150.75 (N-C=C), 156.86 (C=O, amide), 168.78 (d, $^2J_{\text{PC}}$ 11.57 Hz, C=O ester), 169.03 (d, $^3J_{\text{PC}}$ 14.34 Hz, C=O ester), 184.93 (C=O, ketone); (Found: C, 71.79; H, 6.02; N, 2.2. $\text{C}_{38}\text{H}_{38}\text{NPO}_6$ requires C, 71.77; H, 5.95; N, 2.08 %).

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