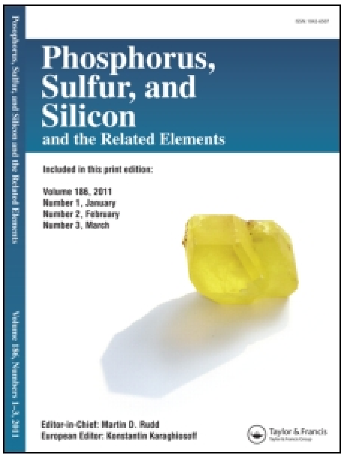

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A Facile Synthesis of Stable Phosphorus Ylides Derived from Harmin, Harman, and Carbazole

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A Facile Synthesis of Stable Phosphorus Ylides Derived from Harmin, Harman, and Carbazole

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Stable crystalline phosphorus ylides were obtained in excellent yields from the 1:1:1 addition reaction between triphenylphosphine and dialkyl acetylenedicarboxylates in the presence of strong NH-acids, such as harman, harmin, and carbazole. These stable ylides exist in solution as a mixture of two geometrical isomers as a result of the restricted rotation around the carbon–carbon partial double bond resulting from the conjugation of the ylide moiety with the adjacent carbonyl group.

Keywords Acetylenic ester; NH— acids; stable phosphorus ylides; triphenylphosphine

INTRODUCTION

The development of simple synthetic routes for widely used organic compounds from readily available reagents is one of the major tasks in organic chemistry.[1] Phosphorus ylides are reactive systems, which take part in many valuable reactions of the organic synthesis.[2–12] These are most often prepared by the treatment of a phosphonium salt with a base. Most of the phosphonium salts are usually made from the phosphine and an alkyl halide,[3–7] and they are also obtained by the Michael addition of phosphorus nucleophiles to activated olefins.[2,3] Here, we wish to describe an efficient synthetic route of stable phosphorus ylides using triphenylphosphine, dialkyl acetylenedicarboxylates, and strong NH— acids, such as harman, harmin, and carbazole. As noted earlier,

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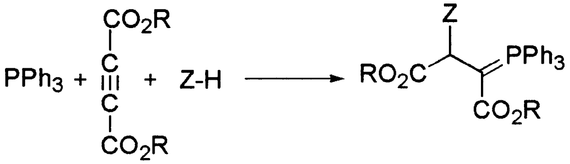
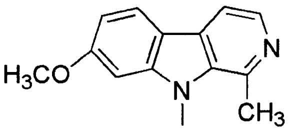
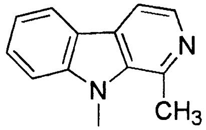
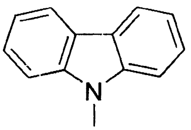
the carbazole moiety and its derivatives are widely used in making medicines.[13] With respect to the importance of the mentioned purpose, this work was undertaken for the generation of stable phosphoranes and the reaction of triphenylphosphine with dialkyl acetylenedicarboxylates **1** in the presence of strong NH— acids **2**, which led to the corresponding stable heterocyclic phosphorus ylides **3** in excellent yields (see Scheme 1).



1 2 3

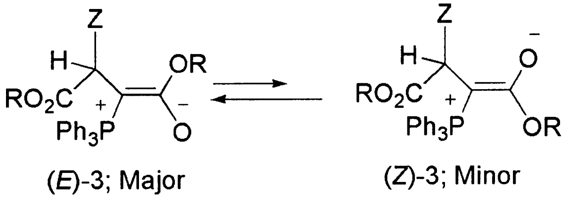
3	Z	R	% Yield
a		Bu^t	96
b		Et	93
c		Bu^t	95
d		Me	95
e		Et	93
f		Bu^t	96

SCHEME 1

RESULTS AND DISCUSSION

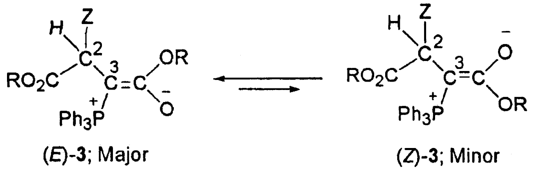
The reactions of harman, harmin, and carbazole with dialkyl acetylenedicarboxylates **1** in the presence of triphenylphosphine were carried out in acetone solvent at r.t. and were finished within a few hours. The ^{1}H and ^{13}C NMR spectrum of the crude product clearly indicated the formation of stable phosphorus ylides **3**. Any product other than **3** could not be detected by NMR spectroscopy. The structures of compounds **3a–f** were deduced from their IR, ^{1}H, ^{13}C, and ^{31}P NMR spectra. The mass spectra of them displayed molecular ion peaks at appropriate *m*/*z* values. Any initial fragmentations involve the missing parts or complete loss of the side chains and scission of the heterocyclic ring system. The ^{1}H, ^{13}C, and ^{31}P NMR spectrum of ylides **3a–f** are consistent with the presence of two isomers. The ylides moiety of these compounds are strongly conjugated with the adjacent carbonyl group, and rotation around the partial double bond in (*E*)-**3** and (*Z*)-**3** geometrical isomers is slow on the NMR timescale at ambient temperature (see Scheme 2). Selected ^{1}H, ^{13}C, and ^{31}P NMR chemical shifts and coupling constants in the major (M) and minor (m) geometrical isomers of compounds **3a–f** are shown in Table I.

As can be seen, only one geometrical isomer was observed for the di-tert-butyl derivatives of **3**, presumably because of the bulky tert-butyl groups.



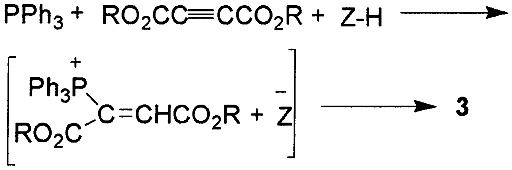
SCHEME 2

TABLE I Selected ^{1}H, ^{13}C, and ^{31}P NMR Chemical Shifts (δ in ppm) and Coupling Constants (*J* in Hz) for H-2, OR, CO$_2$R, C-2, and C-3, in the Major (M) and Minor (m) Diastereoisomers of Compounds 3a–f



Compound	Isomer (%)	^{1}H NMR spectroscopy data H-2 ($^3J_{PH}$)	OR	CO$_2$R	^{13}C NMR data C-2 ($^2J_{PC}$)	C-3 ($^1J_{PC}$)	^{31}P NMR
3a	M	5.68 (18.9)	0.99	1.65	61.18 (16.4)	42.07 (121.5)	23.47
3b	M (58)	5.80 (16.8)	4.26	4.34	61.56 (15.4)	43.31 (123.0)	23.26
3b	m (42)	5.83 (19.0)	3.70	3.88	61.58 (15.6)	43.84 (131.5)	25.02
3c	M	5.64 (18.1)	1.02	1.50	60.02 (15.2)	42.78 (122.5)	23.30
3d	M (67)	5.43 (16.2)	3.27	3.76	58.32 (15.2)	41.70 (123.1)	23.78
3d	m (33)	5.35 (18.7)	3.73	3.80	58.37 (15.6)	42.43 (131.9)	24.52
3e	M (57)	5.40 (16.8)	4.25	4.29	58.39 (15.3)	41.42 (123.0)	23.76
3e	m (43)	5.30 (19.3)	3.82	3.94	58.74 (15.5)	42.14 (131.9)	24.87
3f	M	5.23 (8.3)	0.98	1.52	57.92 (15.5)	40.58 (124.9)	24.46

On the basis of the wellestablished chemistry of trivalent phosphorus nucleophiles,[2–6] it is reasonable to assume that phosphorus ylide **3** results from the initial addition of triphenylphosphine to the acetylenic ester and subsequent protonation of the 1:1 adduct by the NH— acid to form phosphoranes **3** (see Scheme 3).



SCHEME 3

Briefly, we have prepared novel phosphorus ylides using a one-pot reaction between triphenylphosphine and dialkyl acetylenedicarboxylates in the presence of strong NH—acids, such as harman, harmin, and carbazole. The present method carries the advantage that not only the reaction is performed under neutral conditions, but also the substances can be mixed without any activation or modifications. Harman-harmin- and carbazole-containing phosphorus ylides **3a–f** may be considered potentially useful synthetic intermediates. It seems that the procedure described here may be employed as an acceptable method for the preparation of phosphoranes with variable functionalities.

EXPERIMENTAL

Melting points and IR spectra of all compounds were measured on an Electrothermal 9100 apparatus and a Shimadzu IR-460 spectrometer, respectively. Also, the ^1H, ^{13}C, and ^{31}P NMR spectra were obtained from a BRUKER DRX-500 AVANCE instrument with $CDCl_3$ as a solvent at 500.1, 125.8, and 202.4 MHz, respectively. In addition, the mass spectra were recorded on a Shimadzu QP 1100 EX mass spectrometer operating at an ionization potential of 70 eV. Dialkyl acetylenedicarboxylates, triphenlphosphine, harman, harmin, and carbazole were purchased from Fluka, (Buchs, Switzerland) and used without further purifications.

Preparation of Di-tert-buthyl 2-(harmin-1-yl)-3-(triphenylphosphoranylidene)butanedioate (3a)

General Procedure

To a magnetically stirred solution of triphenylphosphine (0.26 g or 1 mmol) and harmin (0.17 g or 1 mmol) in 10 mL of dry ethyl acetate, a mixture of di-tert-buthyl acetylenedicarboxylate (0.23 g or 1 mmol) was added dropwise in 4 mL of dry ethyl acetate at −5°C over 10 min. after approximately 12 h stirring at r.t., the product was filtered and recrystallized from ethyl acetate.

Colorless crystals. m.p. 129–131°C, yield 0.67 g, 96%. IR (KBr) ($\nu_{\max}$, cm^{-1}) 1736 and 1629 (C=O). MS (*m*/*z*, %): 489 (M-heterocycle, 10), 388 (M-heterocycle and CO_2 CMe_3, 21), 262 (PPh_2, 3), 211 (heterocycle, 4), 183 (PPh_2, 18), 108 (PPh, 3), 77 (Ph, 54), 67 (heterocyclic, 3), 57 (CMe_3, 2).

Diethyl 2-(harman-1-yl)-3-(triphenylphosphoranylidene)-butanedioate (3b)

Colorless crystals. m.p. 126–127°C, yield 0.57 g, 93%. IR (KBr) ($\nu_{\max}$, cm^{-1}): 1731 and 1623 (C=O). MS (*m*/*z*, %): 463 (M-PPh and OEt, 24), 262 (PPh_3, 1), 183 (PPh_2, 31), 108 (PPh, 2), 77 (Ph, 33), 73 (CO_2Et, 2).

Di-tert-buthyl 2-(harman-1-yl)-3-(triphenylphosphoranylidene)-butanedioate (3c)

Colorless crystals. m.p. 150–152°C, yield 0.53 g, 95%. IR (KBr) ($\nu_{\max}$, cm^{-1}) 1736 and 1629 (C=O). MS (*m*/*z*, %): 556 (M^+, 17), 489 (M-heterocycle, 10), 455 ($M\text{-}CO_2CMe_3$, 38), 262 (PPh_2, 21), 183 (PPh_2, 14), 108 (PPh, 13), 77 (Ph, 6), 67 (heterocyclic, 3), 57 (CMe_3, 47).

Dimethyl 2-(carbazole-1-yl)-3-(triphenylphosphoranylidene)-butanedioate (3d)

Yellow powder, m.p. 172–74°C, yield 0.62 g, 95%. IR (KBr) ($\nu_{\max}$, cm^{-1}): 1741, 1629 (C=O), MS (*m*/*z*, %): 571 (M^+, 2), 512 ($M - CO_2Me$, 17), 405 (M-heterocycle, 13), 262 (PPh_3, 87), 183 (PPh_2, 41), 108 (PPh, 23), 81 (heterocycle, 19), 77 (Ph, 39), 59 (CO_2Me, 14).

Diethyl 2-(carbazole-1-yl)-3-(triphenylphosphosphoranylidene)-butanedioate (3e)

White powder, m.p. 143–145°C, yield 0.56 g, 93%. IR (KBr) ($\nu_{\max}$, cm^{-1}): 1725, 1620 (C=O). MS (*m*/*z*, %).

Di-tert-butyl 2-(carbazole-1-yl)-3-(triphenylphosphoranylidene)-butanedioate (3f)

White powder, m.p. 208–210°C, yield 0.63 g, 96%. IR (KBr) ($\nu_{\max}$, cm^{-1}): 1729, 1621 (C=O). MS (*m*/*z*, %): 655 (M^+, 62), 554 ($M\text{-}CO_2CMe_3$, 3), 489

(M-heterocycle, 12), 262 (PPh_3, 100), 183 (PPh_2, 70), 108 (PPh, 22), 101 (CO_2CMe_3, 13), 77 (Ph, 14).

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