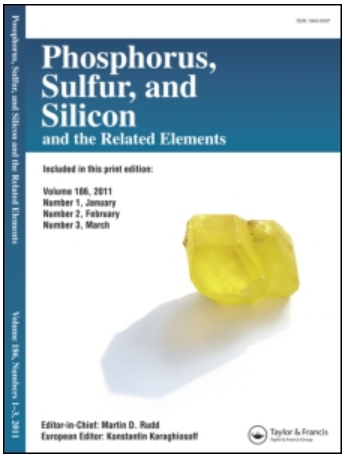


Phosphorus, Sulfur, and Silicon and the Related Elements

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

An Efficient Synthesis of Stable Phosphorus Ylides Derived from Pyrazole and Indazole

Malek Taher Maghsoodlou[a]; Nourollah Hazeri[a]; Sayyed Mostafa Habibi Khorasani[a]; Reza Kakaei[a]; Mahmoud Nassiri[a]

[a] Department of Chemistry, The University of Sistan and Baluchestan, Zahedan, Iran

To cite this Article Maghsoodlou, Malek Taher , Hazeri, Nourollah , Khorasani, Sayyed Mostafa Habibi , Kakaei, Reza and Nassiri, Mahmoud(2006) 'An Efficient Synthesis of Stable Phosphorus Ylides Derived from Pyrazole and Indazole', Phosphorus, Sulfur, and Silicon and the Related Elements, 181: 1, 25 — 30

To link to this Article: DOI: 10.1080/104265090968479

URL: http://dx.doi.org/10.1080/104265090968479

Phosphorus, Sulfur, and Silicon, 181:25–30, 2006

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/104265090968479

Taylor & Francis
Taylor & Francis Group

An Efficient Synthesis of Stable Phosphorus Ylides Derived from Pyrazole and Indazole

Malek Taher Maghsoodlou
Nourollah Hazeri
Sayyed Mostafa Habibi Khorasani
Reza Kakaei
Mahmoud Nassiri
Department of Chemistry, The University of Sistan and Baluchestan, Zahedan, Iran

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 pyrazole, indazole and 5-nitro Indazole. These stable ylides exist in solution as a mixture of two geometrical isomers as a result of restricted rotation around the carbon–carbon partial double bond resulting from conjugation of the ylide moiety with the adjacent carbonyl group.

Keywords Acetylenic ester; NH-acid; stable phosphorus ylides; triphenylphosphine

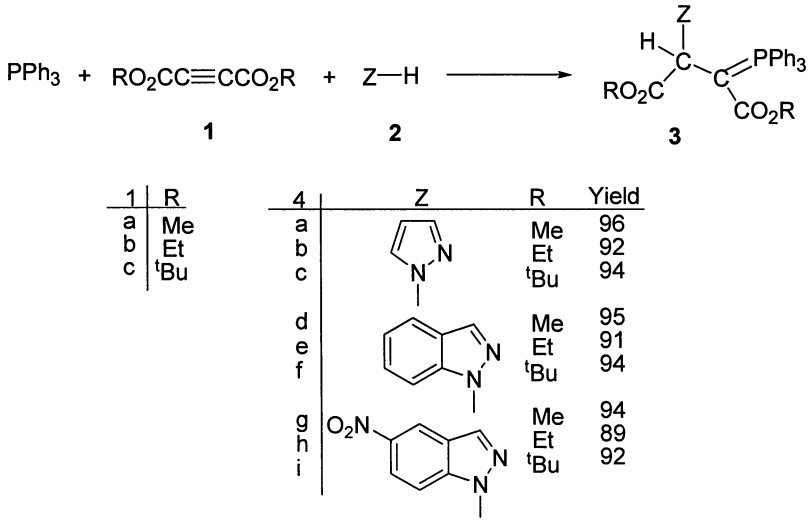
INTRODUCTION

Phosphorus ylides are reactive systems, which take part in many valuable reactions of organic synthesis.[1–11] These ylides most often are prepared by treatment of a phosphonium salt with a base, and phosphonium salts usually are made from the phosphine and an alkyl halide.[1–5] Phosphonium salts also are obtained by the Michael addition of phosphorus nucleophiles to activated olefins, among other methods.[1,2] We wish to describe here an efficient synthetic route to pyrazole or indazole-containing stable phosphorus ylides. The pyrazole moiety and its derivatives have been used commercially as pharmaceuticals, pesticides, and dyestuffs.[12] Thus, the reaction of triphenylphosphine with dialkyl acetylenedicarboxylates **1** in the presence of strong

Received January 13, 2005; in final form March 17, 2005.

Address corresponding to Malek Taher Maghsoodlou, The University of Sistan and Baluchestan, Department of Chemistry, P.O. Box 98135-674, Zahedan, Iran. E-mail: MT_ maghsoodlou @yahoo.com

NH-acids **2** leads to the corresponding stable heterocyclic phosphorus ylides **3** in excellent yields (see Scheme 1).



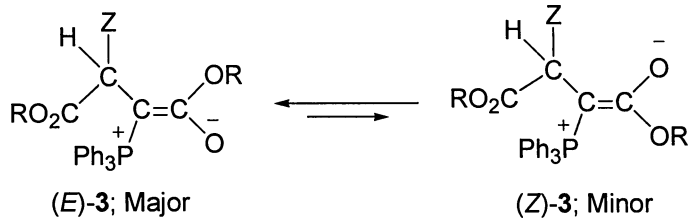
SCHEME 1

RESULTS AND DISCUSSION

The reaction of pyrazole, indazole, and 5-nitro indazole with dialkyl acetylene- dicarboxylates **1** in the presence of triphenylphosphine proceeded at room temperature in ethyl acetate, and was finished within a few hours. ^{1}H and ^{13}C NMR spectrum of the crude product clearly indicated the formation of stable phosphorus ylide **3**. Any product other than **3** could not be detected by NMR spectroscopy. The structures of compounds **3a–i** were deduced from their IR, ^{1}H, ^{13}C, and ^{31}P NMR spectra. The mass spectra of these stable ylides displayed molecular ion peaks appropriate *m/z* values. Any initial fragmentation involved, the loss of the side chains and the scission of the heterocyclic ring system.

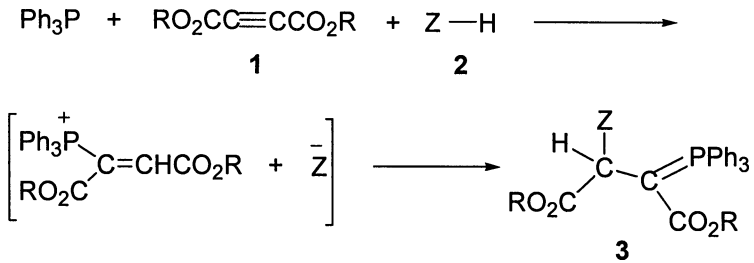
The ^{1}H, ^{13}C, and ^{31}P NMR spectra of ylides **3a–i** are consistent with the presence of two isomers. The ylide moiety of these compounds is strongly conjugated with the adjacent carbonyl group and rotation about the partial double bond in (*E*)-**3** and (*Z*)-**3** geometrical isomers (see Scheme 2) is slow on the NMR time scale at ambient temperature. 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–i**

are shown in Table I. Only one geometrical isomer was observed for di-*tert*-butyl derivatives of **3**, presumably, because of the bulky *tert*-butyl groups.



SCHEME 2

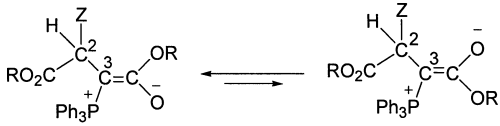
On the basis of the well-established chemistry of trivalent phosphorus nucleophiles,[1–5] it is reasonable to assume that phosphorus ylide **3** results from the initial addition of triphenylphosphine to the acetylenic ester and subsequent protonation of the 1:1 adduct by the N—H acid to form phosphoranes **3** (see Scheme 3).



SCHEME 3

In summary, we have prepared novel pyrazole or indazole-containing phosphorus ylides using a one-pot reaction between triphenylphosphine and dialkylacetylenedicarboxy-lates in the presence of strong N—H acids such as pyrazole, indazole, and 5-nitro indazole. The present method carries the advantage that not only is the reaction performed under neutral conditions, but the substances also can be mixed without any activation or modification. Pyrazole or indazole-containing phosphorus ylides **3a–i** may be considered potentially useful synthetic intermediates. The procedure described here may be an acceptable method for the preparation of phosphoranes with variable functionalities.

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_2R, C-2, and C-3 in the Major (M) and Minor (m) Diastereoisomers of Compounds 3a–i



(*E*)-**3**; Major (*Z*)-**3**; Minor

		^{1}H NMR spectroscopy data			^{13}C NMR data		
Compound	Isomer (%)	H-2 ($^{3}J_{PH}$)	OR	CO_2R	C-2 ($^{2}J_{PC}$)	C-3 ($^{1}J_{PC}$)	^{31}P NMR
3a	M(57)	5.01 (16.8)	3.18	3.70	65.03 (15.8)	43.93 (129.6)	24.12
3a	m(43)	5.05 (21.2)	3.60	3.72	64.38 (15.4)	44.19 (133.9)	24.93
3b	M(58)	4.98 (16.5)	4.11	4.20	64.98 (16.7)	43.67 (128.0)	24.08
3b	m(42)	5.01 (16.0)	3.72	3.78	64.33 (16.0)	44.13 (136.4)	25.02
3c	M	4.83 (17.2)	0.98	1.51	65.45 (16.9)	43.37 (128.3)	23.81
3d	M(62)	5.49 (16.4)	3.19	3.65	63.47 (15.0)	41.83 (127.7)	23.64
3d	m(38)	5.43 (18.0)	3.65	3.68	62.27 (15.3)	42.47 (136.0)	23.82
3e	M(60)	5.50 (17.1)	4.07	4.14	63.71 (15.3)	41.60 (127.1)	23.65
3e	m(40)	5.37 (18.7)	3.73	3.85	63.03 (15.7)	42.29 (135.7)	24.27
3f	M	5.31 (17.9)	1.01	1.51	65.24 (16.1)	41.20 (125.8)	23.83
3g	M(61)	5.52 (16.4)	3.19	3.69	64.78 (14.7)	42.00 (126.5)	23.78
3g	m(39)	5.44 (17.5)	3.67	3.69	63.80 (15.7)	42.26 (134.6)	24.00
3h	M(59)	5.53 (17.0)	4.11	4.18	65.02 (15.8)	41.90 (126.4)	23.83
3h	m(41)	5.39 (18.6)	3.72	3.81	64.19 (16.3)	42.20 (134.7)	24.48
3i	M	5.34 (17.5)	1.01	1.53	66.25 (16.7)	41.65 (125.2)	23.83

EXPERIMENTAL

Melting points and IR spectra were measured on an Electrothermal 9100 apparatus and a Shimadzu IR 460 spectrometer, respectively. ^{1}H, ^{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. The mass spectra were recorded on a Shimadzu QP 1100 EX mass spectrometer operating at an ionization potential of 70 eV. Triphenylphosphine, dialkyl acetylenedicarboxylates **1a–c**, pyrazole, indazole, and 5-nitroindazole were obtained from Fluka (Buchs, Switzerland) and were used without further purification.

Dimethyl 2-(pyrazole-1-yl)-3-(triphenylphosphoranylidene)-butanedioate (3a): General Procedure

To a magnetically stirred solution of triphenylphosphine (0.26 g or 1 mmol) and pyrazole (0.68 g or 1 mmol) in 10 mL of ethyl acetate a

mixture of dimethyl acetylenedicarboxylate (0.14 or 1 mmol) in 3 mL of ethyl acetate was added dropwise at −5°C over 10 min. After 12 h upstirring at room temperature, the product was filtered and recrystallized from ethyl acetate. Colorless crystals, m.p. 168–170°C, yield 0.45 g, 96%; IR (KBr) (ν_{max}, cm^{-1}): 1754 and 1635(C=O). MS (*m/z*, %): 472 (M^+, 8), 413 (M^+-CO_2Me, 100), 405 (M^+-heterocycle, 30), 262 (PPh_3, 49), 183 (PPh_2, 38), 108 (PPh, 31), 77 (Ph, 29), 67 (heterocycle, 3), 59 (CO_2Me, 22),

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

Colorless crystals, m.p. 185–187°C, yield 0.46 g, 92%; IR (KBr) (ν_{max}, cm^{-1}): 1730 and 1613 (C=O).

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

Colorless crystals, m.p. 130–133°C; yield 0.52 g, 94%; IR (KBr) (ν_{max}, cm^{-1}) 1736 and 1629 (C=O).

Dimethyl 2-(indazole-1-yl)-3-(triphenylphosphoranylidene) –butanedioate (3d)

Colorless crystals, m.p. 145.147°C; yield 0.50 g, 95%; IR (KBr) (ν_{max}, cm^{-1}) 1724 and 1637 (C=O). MS (*m/z*, %): 522 (M^+, 5), 405 (M^+-hetrocycle, 61), 262 (PPh_3, 100), 183 (PPh, 38), 117 (heterocycle, 4), 108 (PPh, 36), 77(Ph, 9), 59 (CO_2Me,3).

Diethyl 2-(indazole-1-yl)-3-(triphenylphosphoranylidene)–butanedioate (3e)

Colorless crystals, m.p. 138–140°C; yield 0.50 g, 91%. IR (KBr) (ν_{max}, cm^{-1}) 1735 and 1629 (C=O).

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

Colorless crystals, m.p. 165–167°C; yield 0.56 g, 94%. IR (KBr) (ν_{max}, cm^{-1}) 1729 and 1629 (C=O).

Dimethyl 2-(5-nitro-indazole-1-yl)-3-(triphenylphosphoranylidene)-butanedioate (3g)

Colorless crystals, m.p. 137–139°C; yield 0.51 g, 94%; IR (KBr) (ν_{max}, cm^{-1}) 1745 and 1636 (C=O). MS (*m/z*, %): 567 (M^+, 1), 508 (M^+−CO2Me,

1), 305 (M^+-PPh_3, 74), 262 (δ PPh_3, 95), 183 (PPh_2, 100), 108 (PPh, 72), 77(Ph, 11), 69 (CO_2Me, 4).

Diethyl 2-(5-nitro-indazole-1-yl)-3-(triphenylphosphoranylidene)-butanedioate (3h)

Colorless crystals, m.p. 147–149°C; yield 0.53 g, 89%; IR (KBr) (ν_{max}, cm^{-1}) 1723 and 1623 (C=O).

Di- tert- butyl 2-(5-nitro-indazole 1-yl)-3-(triphenylphosphoranylidene)-butandioate (3i)

Colorless crystals, m.p. 127–129°C; yield 0.59 g, 92%; IR (KBr) (ν_{max}, cm^{-1}) 1728 and 1624 (C=O).

REFERENCES

[1] A. W. Johnson, *Ylied Chemistry* (Academic Press, London, 1966).
[2] J. I. G. Cadogan, *Organophosphorus Reagents in Organic Synthesis* (Academic Press, New York, 1979).
[3] R. Engel, *Synthesis of Carbon-Phosphors Bonds* (CRC Press, Boca Raton, FL, 1988).
[4] H. R. Hudson, *The Chemistry of Organophosphorus Compounds*, *Vol. 1. Primary, Secondary*, *and Tertiary Phosphates and Heterocyclic Organophosphorus (3) Compounds*, Ed., F. R. Hartley (Wiley, New York, 1990), pp. 382–472.
[5] D. E. C. Corbridge, *Phosphorus: An Outline of Chemistry, Biochemistry and Uses* (Elsevier, Amsterdam, 1995), 5th ed, ch. 3.
[6] O. I. Kolodiazhnyi, *Russ. Chem. Rev*., **66,** 225 (1994).
[7] R. A. Cherkasov and M. A. Pudovic, *Russ. Chem. Rev*., **63,** 1019 (1994).
[8] K. M. Pietrusiewiz and M. Zablocka, *Chem. Rev*., **94,** 1375 (1994).
[9] B. E. Maryanoff and A. B. Rietz, *Chem. Rev*., **89,** 863 (1989).
[10] K. C. Nicolaou, M. W. Harter, J. L. Gunzner, and A. Nadin, *Liebigs Ann*., **7,** 1283 (1997).
[11] Y. Shen, Acc. *Chem. Res*., **31,** 584 (1998).
[12] T. L. Gilchrist, *Heterocyclic Chemistry* (Wiley, NewYork, 1985).