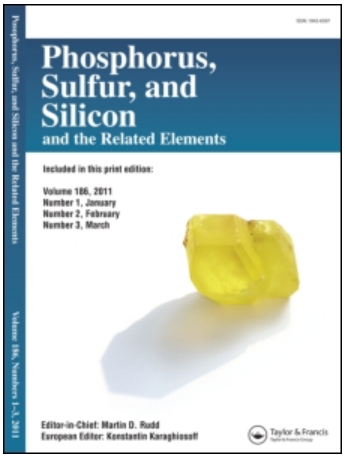

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SYNTHESIS OF NEW COMPLEX YLIDENETRIPHENYLPHOSPHORANES FROM THE REACTION OF ARYLIDENEMALONONITRILES WITH WITTIG-REAGENTS

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SYNTHESIS OF NEW COMPLEX YLIDENETRIPHENYLPHOSPHORANES FROM THE REACTION OF ARYLIDENEMALONONITRILES WITH WITTIG-REAGENTS

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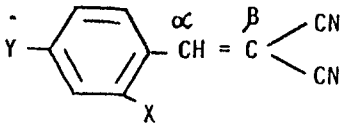
The resonance-stabilized Wittig reagent **2** adds to the exocyclic ethylenic linkage of the arylidenemalononitriles **1a–g** to yield the new complex ylidenetriphenylphosphoranes **4a–g**. The reaction is regiospecific which yields the **E** conformers of structure "**4c**." Possible reaction mechanisms are considered and structures of the new products were confirmed on the basis of elemental analyses and spectral studies.

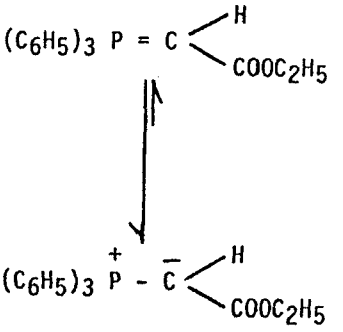
Key words: Arylidenemalononitriles; Wittig reagents; regiospecific addition.

INTRODUCTION

α,β-Unsaturated nitriles are versatile compounds which attract much interest by virtue of their broad synthetic utilities.[1] Many candidates which belong to this class of compounds possess diverse biological activities[2] and receive many biomedical



1a, X = Y = H
b, X = Cl ; Y = H
c, X = F ; Y = H
d, X = H ; Y = Cl
e, X = H ; Y = F
f, X = H ; Y = CN
g, X = H ; Y = NO_2



2

applications.[3] In response to our growing interest in the chemistry of arylidenemalononitriles,[4,5] we have recently reported on their reactivity towards nucleophilic phosphorus compounds, namely alkyl phosphites.[5] In a contribution to this work, we have now studied the reaction of arylidenemalononitriles **1a–g** with a resonance stabilized ylidene phosphorane, ethoxymethylenetriphenylphosphorane (**2**) which encorporates a nucleophilic centre in its molecule.[6,7]

RESULTS AND DISCUSSION

Benzylidenemalononitriles **1a–g** were found to react with carbethoxymethylenetriphenylphosphorane (**2**) in dry toluene at reflux temperature to give colourless crystalline materials as sole reaction products. They were assigned structures **4a–g** since their ^{31}P-NMR spectra (in $CDCl_3$) showed positive chemical shifts (vs. 85% H_3PO_4) around δ 25 ppm, which match an ylid-phosphorane structure[8] and exclude other alternative betain structures such as **3** and **4A**. Moreover, the ^{1}H-NMR spectrum of **4a**, taken as an example (in $CDCl_3$) showed two signals due to the exocyclic methine protons at δ 3.20 (d of d, $H_{(a)}$, $^3J_{HP}$ = 10.5 Hz) and δ 6.30 (d, $H_{(b)}$, $^4J_{HP}$ = 6.2 Hz). This large coupling constant clearly shows that $H_{(a)}$ and $H_{(b)}$ are **E** with respect to each other.[9] The spectrum also showed signals at 0.40 (3H, carbethoxy-$\underline{CH_3}$, t) and 3.65 (2H, carbethoxy-$\underline{CH_2}$, q). The aromatic protons (20 H) appeared as a multiplet centered at 7.60 ppm. The main features of the IR spectrum of **4a** (in KBr, expressed in cm^{-1}) were the presence of absorption bands at 2250 (C≡N) and 1730 (C=O, ester). It also revealed the presence of strong bands around 1680 and 1510 characteristic of the C=P group absorption,[10,11] as well as around 1430 and 990 for the P—C (phenyl) absorption.[10,11] Structures of adducts **4b–g** were also based on compatible spectral measurements (cf. Tables I and II).

TABLE I

Chemical shifts of the exocyclic methine (H_a, H_b), methylene and methyl group protons in adducts **4a–g**

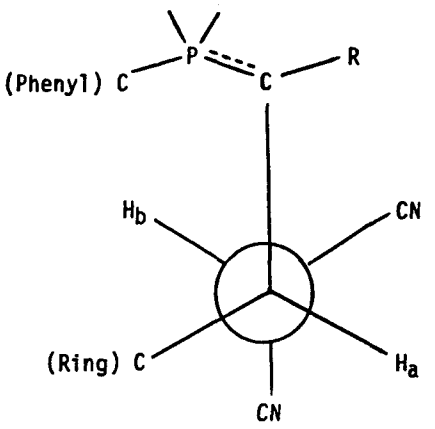
Adduct	δ ppm			
	$\underline{H_a}$*	$\underline{H_b}$**	$\underline{CH_2}$	$\underline{CH_3}$
4a	3.20	6.30	3.65	0.40
b	4.32	6.72	3.76	0.48
c	3.80	6.25	3.65	0.40
d	3.30	6.40	3.72	0.45
e	3.25	6.50	3.75	0.48
f	3.40	6.45	3.60	0.88
g	3.30	6.30	3.70	0.40

* $^3J_{HP}$ is 10-12 Hz; ** $^4J_{HP}$ is 6-8 Hz

TABLE II
The IR spectral data of adducts **4a–g**

Adduct	cm^{-1}				
	C=O ester	C≡N	C=P	C-P (phenyl)	C=C aromatic
4a	1730	2250	1680,1510	1430,990	1490
b	1810	2260	1620,1530	1440,995	1490
c	1790	2255	1615,1485	1450,1000	1500
d	1740	2250	1660,1510	1445,990	1490
e	1720	2250	1610,1485	1435,995	1500
f	1780	2250	1655,1510	1420,990	1510
g	1780	2255	1610,1525	1420,995	1500

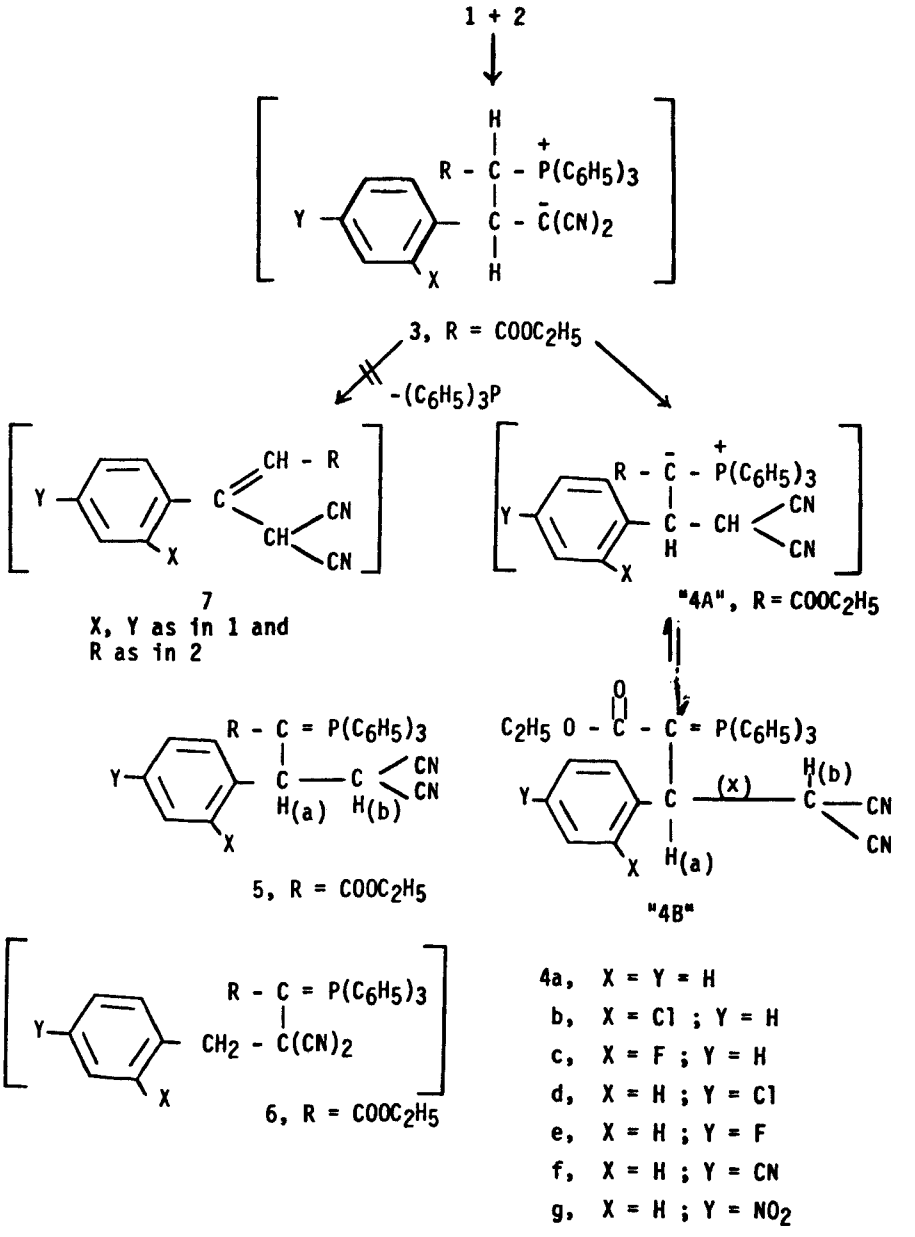
The unique structure of compounds **4a–g** was also verified by careful inspection of the ^{1}H-NMR spectra with respect to chemical shifts of the exocyclic methine (H_a and H_b), methylene and methyl group protons as depicted in Table I. Apparently, the exocyclic methine proton H_b in compounds **4** is highly deshielded. This may be attributed to the ring current effect[9] as result of its proximity to the $[(C_6H_5)_3P{=}\underset{|}{C}{-}]$ grouping. Inspection of a Newman projection[12] shows that adducts **4** should be in the staggered anti-conformer (cf. **4C**) which seems plausible for steric considerations.



4C Staggered

(anti)

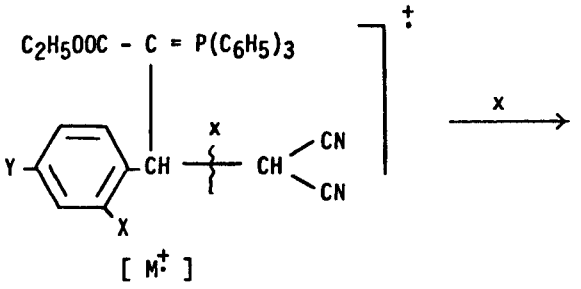
Based upon the aforementioned spectral arguments other alternative structures like **5** and **6** for the reaction products of **1a–g** with **2**, can be excluded from further considerations. The non-formation of adducts possessing the **Z**-configuration (cf. **5**) favors the conclusion that the **E**-configuration **4** is the thermodynamically more stable structure.[13]



Scheme 1

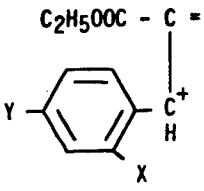
It is worthy to mention that the molecular ion peaks do not appear in the mass spectra of compounds **4** unless the fast atomic bombardment (FAB) technique is adopted. However, the spectra show the appropriate ions with highest masses at $[M—CH(CN)_2]$ due to cleavage at axis x (cf. Scheme 2). This behavior clearly indicates that adducts **4** are relatively stable toward electron bombardment.

The mechanism for the formation of adducts **4a–g** is depicted in Scheme 1. It comprises a nucleophilic attack by the carbanionic centre in **2** on the α-carbon atom of the exocyclic $—\overset{|}{C}=\overset{|}{C}—$ linkage which is the more electrophilic site par-



4c, MS (FAB) , m/z 521.2

4g, MS (FAB) , m/z 548.2



X	Y	m/z	%
H	H	437	70
Cl	H	471	65
F	H	455	80
H	Cl	471	50
H	F	455	56
H	CN	462	60
H	NO_2	482	44

Scheme 2

TABLE III

The physical constants and analytical data for new compounds **4a–g**

Adduct	Reaction time (min.)	Crystal's colour*	m.p. °C	Yield %	Molecular formula (mol.wt.)	Analysis Calcd. / Found					
						C	H	Cl	F	N	P
4a	280	buff	184-186	80	$C_{32}H_{27}N_2O_2P$	76.48	5.42	-	-	5.57	6.16
					(502.5)	76.30	5.25	-	-	5.40	6.02
4b	200	colourless	182-184	85	$C_{32}H_{26}ClN_2O_2P$	71.57	4.88	6.60	-	5.22	5.77
					(536.9)	71.45	4.70	6.48	-	5.10	5.67
4c	180	orange	175-177	85	$C_{32}H_{26}FN_2O_2P$	73.84	5.04	-	3.65	5.38	5.95
					(520.5)	73.75	4.95	-	3.52	5.27	5.80
4d	230	colourless	305-307	90	$C_{32}H_{26}ClN_2O_2P$	71.57	4.88	6.60	-	5.22	5.77
					(536.9)	71.42	4.66	6.45	-	5.08	5.62
4e	210	pink	161-163	85	$C_{32}H_{26}FN_2O_2P$	73.84	5.04	-	3.65	5.38	5.95
					(520.5)	73.72	5.00	-	3.52	5.25	5.89
4f	180	colourless	178-180	90	$C_{33}H_{26}N_3O_2P$	75.13	4.97	-	-	7.97	5.87
					(527.6)	75.01	4.88	-	-	7.81	5.70
4g	150	yellow	176-178	90	$C_{32}H_{26}N_3O_4P$	70.19	4.79	-	-	7.68	5.66
					(547.5)	69.99	4.60	-	-	7.65	5.62

* Ethanol was used as a solvent for crystallization.

ticularly due to the —I effect of the —C≡N groups and/or substituents X (or Y) of the aryl nucleus. The resulting betain structure undergoes then intramolecular rearrangement *via* hydrogen proton migration to afford the dipolar form "**4A**" which exists probably in an equilibrium with the ylid-phosphorane structure "**4B**." The decomposition of the initial dipolar intermediate **3** *via* elimination of $(C_6H_5)_3P$ to give non-phosphorylated products like **7** (not formed) is thus overlooked.

Table III compiles the physical constants and analytical data of the new adducts **4a–g**.

CONCLUSION

The reaction of arylidenemalononitriles **1a–g** with stabilized ylid-phosphorane **2** to give adducts of type **4** represents a novel process for the preparation of complex ylidene phosphoranes in high percentage yields. This reaction seems to be a regiospecific process which proceeds to yield the staggered anticonformers (vicinal **E**, **4C**) which are thermodynamically more stable than the alternative **Z**-conformers (**5**, not formed). Reduction of the exocyclic ethylenic linkage in compounds **1** by reagent **2** is also of particular biological significance since this approach is expected to reduce the toxicity of **1** (especially **1b**)[14–16] to humans.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were run on a Perkin Elmer Infracord Spectrometer Model 197 (Grating) in KBr. The ^{1}H-NMR spectra were recorded with a Bruker Spectrometer Model WH-90 and the chemical shifts are recorded in δ ppm scale relative to TMS. The ^{31}P-NMR spectra were taken on a Varian CFT 20 (vs. external 85% H_3PO_4). The mass spectra were done at 70 eV with MS-50 Kratos (A.E.I) spectrometer provided with data system. Elemental analyses were carried out at the "Microanalysis Laboratory, Faculty of Science, Cairo University, Cairo."

Arylidene malononitriles **1a–g** were freshly prepared,[17–19] and twice crystallized before used. Carbethoxymethylenetriphenyl-phosphorane (**2**) was prepared according to a known procedure.[20]

The reaction of arylidenemalononitriles **1a–g** *with carbethoxy-methylenetriphenylphosphorane* **2**.

General procedure: To a suspension of 0.005 mol of arylidene malononitrile (**1a–g**) in dry toluene (30 ml) was added a solution of 0.005 mol reagent **2** in the same solvent (20 ml) and the reaction mixture was refluxed for 2–5 h (TLC). The reaction mixture was then evaporated at 60°C under reduced pressure. The residual substance was triturated with ethanol, collected and recrystallized from ethanol to give adducts **4a–g**.

For physical and analytical data of adducts **4a–g**, cf. Table III.

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