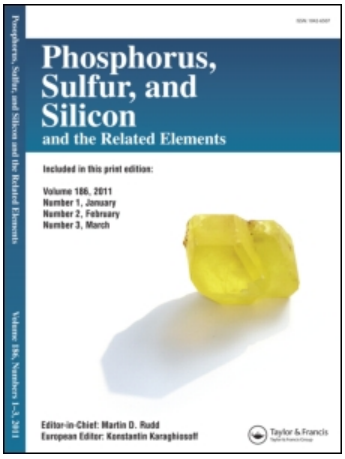


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

REACTION OF N-ALKYLPYRIDINIUM SALTS WITH PHOSPHORUS TRICHLORIDE

Raj K. Bansal[a]; Neelima Gupta[a]; Rakhi Gupta[a]; Garima Pandey[a]; Mamta Agarwal[a]
[a] Department of Chemistry, University of Rajasthan, Jaipur, India

To cite this Article Bansal, Raj K. , Gupta, Neelima , Gupta, Rakhi , Pandey, Garima and Agarwal, Mamta(1996) 'REACTION OF N-ALKYLPYRIDINIUM SALTS WITH PHOSPHORUS TRICHLORIDE', Phosphorus, Sulfur, and Silicon and the Related Elements, 112: 1, 121 — 130
To link to this Article: DOI: 10.1080/10426509608046355
URL: http://dx.doi.org/10.1080/10426509608046355

Phosphorus, Sulfur, and Silicon, 1996, Vol. 112, pp. 121–130
Reprints available directly from the publisher
Photocopying permitted by license only

REACTION OF N-ALKYLPYRIDINIUM SALTS WITH PHOSPHORUS TRICHLORIDE

RAJ K. BANSAL,* NEELIMA GUPTA, RAKHI GUPTA, GARIMA PANDEY and MAMTA AGARWAL

Department of Chemistry, University of Rajasthan, Jaipur 302 004, India

Dedicated to Prof. A. Schmidpeter on his 65th Birth Anniversary

(Received August 10, 1995; in final form October 18, 1995)

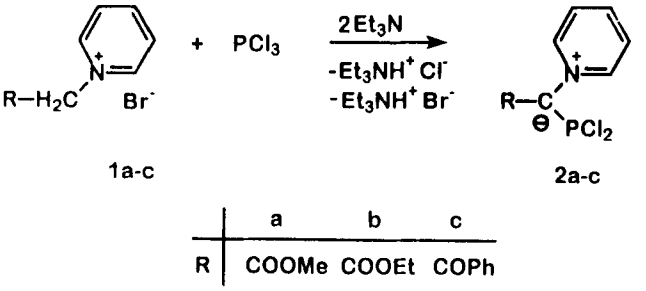
1-Alkylpyridinium bromides **1** having activated N-methylene group react with phosphorus trichloride to give N-(dichlorophosphinomethylene)pyridinium ylides **2**. The site of the reaction in 1,2-dialkylpyridinium halides **3** under these conditions is determined by the relative activation of 1- and 2-methylene groups; in the absence of sufficient activation of N-methylene group, reaction occurs at the 2-methylene group to give dichlorophosphinylated anhydrobases **5** and **11**. 1,4-Dialkylpyridinium bromide **13** behaves analogously to give the corresponding dichlorophosphinylated anhydrobase **14**.

Key words: N-Alkylpyridinium halides, N-(dichlorophosphinomethylene)pyridinium ylides, 1-alkyl-2-(dichlorophosphinomethylene)pyridinium anhydrobases, 1-alkyl-2(or 4)-{bis(dichlorophosphino)methylene}pyridinium anhydrobases, ^{1}H-, ^{13}C- and ^{31}P-NMR spectra.

INTRODUCTION

We have recently developed a facile synthesis of anullated azaphospholes from [4+1]cyclocondensation of 2-substituted cycloiminium salts with phosphorus trichloride in the presence of triethylamine.[1–3] In connection with the synthesis of 2-phosphaindolizines through this synthetic route,[4,5] two observations were made which were not completely understood at that time. Firstly, if the N-methylene group was not sufficiently activated, either the reaction stopped at the intermediate stage or only 1-dichlorophosphino substituted 2-phosphaindolizine could be generated. For example, 1-benzyl-2-methylpyridinium bromide formed an intermediate ($\delta^{31}P = 145$) which did not cyclize to give the corresponding 2-phosphaindolizine under the given reaction conditions,[5] whereas 2-methyl-1-(4-nitrobenzyl)pyridinium bromide under these conditions gave a very poor yield (~5%) of 1-unsubstituted 2-phosphaindolizine,[4] though the corresponding 1-dichlorophosphino-2-phosphaindolizine could be generated quantitatively.[6] At that time, it was further suggested that 1-dichlorophosphino-2-phosphaindolizine was formed from the substitution of the initially formed 2-phosphaindolizines.[4] Characterization of the isolated reaction intermediate as 1-(dichlorophosphinomethylene)pyridinium ylide in one case[4] gave the impression that the reaction always initiated at the N-methylene group.

In view of the analogy of our 2-phosphaindolizine synthesis with Kröhnke's synthesis of indolizines,[7] we have now investigated the reactions of differently substituted N-pyridinium salts with phosphorus trichloride in the presence of triethylamine to understand the role of the N-methylene group in determining the site of the initial attack of phosphorus trichloride. The results obtained clearly show that while cycli-



SCHEME 1

zation to 2-phosphaindolizine occurs only if the N-methylene group is sufficiently activated, the reaction may be initiated at either of the two terminal methylene groups depending on their relative activation.

RESULTS AND DISCUSSION

Reaction of 2-Unsubstituted 1-Alkylpyridinium Bromides

1-Alkylpyridinium bromides **1** (R = COOMe, COOEt, COPh) react with phosphorus trichloride (1 equiv.) in the presence of triethylamine (2 equiv.) at room temperature to give 1-(dichlorophosphinomethylene)pyridinium ylides **2** (Scheme 1).

1-Benzyl- and 1-(4-nitrobenzyl)pyridinium bromides do not show any reactivity under these conditions which indicates that in the above reaction, the pyridinium salt with an activated N-methylene group undergoes deprotonation in the presence of triethylamine to generate the N-pyridinium ylide which reacts with phosphorus trichloride to form **2**. This is analogous to the alkylation of N-pyridinium ylides.[8] Compounds **2a,b** are isolated in a pure state as yellow crystalline solids. The **2c**, however, could not be separated from the ammonium salt due to its insolubility in diethyl ether. A sample of **2c** obtained directly from the filtrate of the reaction mixture (benzene) contains traces of the ammonium salt.

The structure of **2** has been confirmed on the basis of ^{31}P- and ^{1}H-NMR spectroscopy (Table I). The ^{31}P-NMR chemical shift at $\delta \sim 146$ agrees well with those reported for dichlorophosphino derivatives.[4,9] The ylidic nature of **2** is supported by the absence of any ^{1}H-NMR signal in the range $\delta 6-7$ characteristic for the proton on the ylidic carbon of N-pyridinium ylides.[10]

1-(Dichlorophosphino, methoxycarbonylmethylene)pyridinium ylide **2a** on refluxing in methylene chloride forms a dark orange solution (δ^{31}P = 182.8) from which a highly insoluble solid separates out, the structure of which could not be determined.

Reaction of 1,2-Dialkylpyridinium Halides

1-Alkyl-2-methylpyridinium halides **3** (R = H, C_6H_5, $C_6H_4NO_2$-*p*) react with phosphorus trichloride (2 equiv.) in presence of triethylamine (3 equiv.) in benzene at

TABLE I

Physical and spectral data of **2**, **5**, **11** and **14**

Cpd.	R	mp. °C	Yield (%)	Mol. Form.	^{1}H-NMR : δ ppm (J Hz)[a]
2a	COOMe	75-77	62	$C_8H_8NO_2PCl_2$	3.44(s, 3H; OCH_3), 6.16 (t, $^3J_{HH}$ = 7.5, 2H; 3-H, 5-H), 6.47 (t, $^3J_{HH}$ = 8.0, 1H; 4-H), 7.99 (d, $^3J_{HH}$ = 7.4, 2H; 2-H, 6-H).
2b	COOEt	81-82	65	$C_9H_{10}NO_2PCl_2$	0.88 (t, $^3J_{HH}$ = 7.1, 3H; CH_3), 3.97 (q, $^3J_{HH}$ = 7.1, 2H; OCH_2), 5.97 (t, $^3J_{HH}$ = 6.4, 2H; 3-H, 5-H), 6.19 (t, $^3J_{HH}$ = 7.6, 1H; 4-H), 7.84 (d, $^3J_{HH}$ = 5.9, 2H; 2-H, 6-H).
2c	COPh	84-90[b]	—	$C_{13}H_{10}NOPCl_2$	7.63-7.39 (m, 3H; *m*-H, *p*-H), 7.94 (t, $^3J_{HH}$ = 7.5, 2H; 3-H, 5-H), 8.02 (t, $^3J_{HH}$ = 7.5, 2H; *o*-H), 8.39 (t, $^3J_{HH}$ = 8.0, 1H; 4-H), 9.38 (dd, $^3J_{HH}$ = 5.1, $^4J_{HH}$ = 1.5, 2H; 2-H, 6-H)[b].
5a	H	116-19	58	$C_7H_7NP_2Cl_4$	4.48 (s, 3H; CH_3), 7.80 (t, $^3J_{HH}$ = 6.1, 1H; 5-H), 7.95 (d, $^3J_{HH}$ = 8.0, 1H; 3-H), 8.89 (t, $^3J_{HH}$ = 7.0, 1H; 4-H), 8.73 (d, $^3J_{HH}$ = 6.4, 1H; 6-H).
5b	C_6H_5	115-17	66	$C_{13}H_{11}NP_2Cl_4$	5.74 (s, 2H; CH_2), 6.23 (t, $^3J_{HH}$ = 7.4, 1H; 5-H), 6.95 (dd, $^3J_{HH}$ = 7.3, $^4J_{HH}$ = 2.0, 2H; *o*-H), 7.01-7.12 (m, 3H; *m*-H, *p*-H), 7.16 (t, $^3J_{HH}$ = 7.8, 1H; 4-H), 7.21 (d, $^3J_{HH}$ = 6.5, 1H; 3-H), 7.80 (d, $^3J_{HH}$ = 7.8, 1H; 6-H)
11a	H	104-10[b]	—	$C_{13}H_{12}NPCl_2$	4.60 (s, 3H; CH_3), 7.41 (bs, 5H; C_6H_5), 7.68 (t, $^3J_{HH}$ = 7.0, 1H; 5-H), 7.99 (d, $^3J_{HH}$ = 7.5, 1H; 3-H), 8.35 (t, $^3J_{HH}$ = 7.5, 1H; 4-H), 9.64 (d, $^3J_{HH}$ = 7.0, 1H; 6-H)[b].
14a	C_6H_5	107-10	53	$C_{13}H_{11}NP_2Cl_4$	3.79 (s, 2H; CH_2), 6.30 (d, $^3J_{HH}$ = 7.6, 2H; 3-H, 5-H), 6.34 (t, $^3J_{HH}$ = 8.0, 1H; *p*-H), 6.89 (t, $^3J_{HH}$ = 6.6, 2H; *m*-H), 6.90 (d, $^3J_{HH}$ = 7.0, 2H; *o*-H), 7.85 (d, $^3J_{HH}$ = 7.6, 2H; 2-H, 6-H).

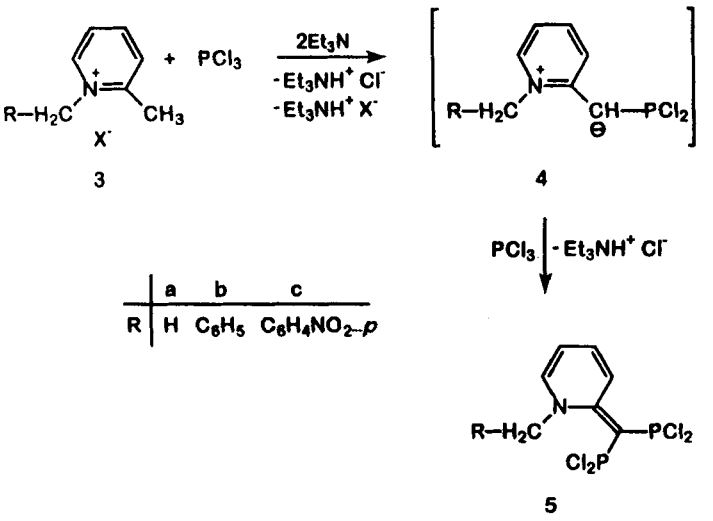
a 2a-c, 11a and 14a in C_6D_6; 5a in CD_2Cl_2; 5b in C_6D_6 + CD_2Cl_2.

b of impure sample containing traces of the ammonium salt.

room temperature to give 1-alkyl-2-{bis(dichlorophosphino)methylene}-1,2-dihydropyridines **5** (Scheme 2).

Compounds **5a,b** are orange amorphous solids, highly sensitive to moisture and are soluble in common organic solvents. Its characterization as the bis dichlorophosphino derivative is supported by elemental analysis and NMR-spectroscopy (Table I). The ^{31}P-NMR signal at $\delta \sim 145$ does not split under the proton coupled mode showing the absence of any proton on 2-methylene carbon. In the ^{13}C-NMR spectrum (Table II) of **5b**, the signal of 2-methylene carbon appears as a triplet at δ88.4 ($^1J_{PC}$ = 77.8 Hz) indicating the presence of two dichlorophosphino moieties on this carbon. The C-2 also gives a triplet at δ157.5 ($^2J_{PC}$ = 14.2 Hz).

These results indicate that if the N-methylene group is not activated, deprotonation of the 2-methylene group is preferred as the resulting anhydrobase is stabilized by



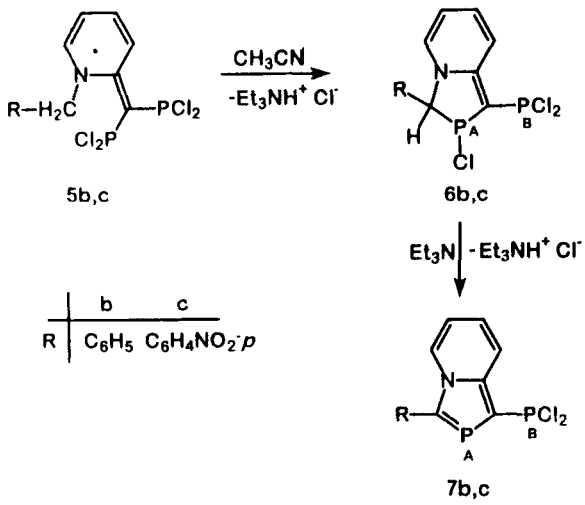
3 4 5

SCHEME 2

TABLE II

^{13}C-NMR data of **5b** (C_6D_6 + CD_2Cl_2) δ(ppm), *J*(Hz)

C-2	157.5	C-*i*	134.1
$^2J_{PC}$	14.2	$^2J_{CH}$	4.7
$^2J_{CH}$	5.7	C-*o*	130.0
C-3	142.4	$^1J_{CH}$	152.6
$^3J_{PC}$	5.7	$^2J_{CH}$	8.1
$^1J_{CH}$	169.7	C-*m*	130.6
$^2J_{CH}$	7.1	$^1J_{CH}$	158.7
C-4	135.6	$^2J_{CH}$	10.4;4.7
$^4J_{PC}$	2.9	C-*p*	130.1
$^1J_{CH}$	176.8	$^1J_{CH}$	161.1
$^2J_{CH}$	7.1	$^2J_{CH}$	7.9
C-5	123.9	2-C(P)(P)	88.4
$^1J_{CH}$	173.4	$^1J_{PC}$	77.8
$^2J_{CH}$	7.5;2.9	N-CH_2	61.3
C-6	139.2	$^1J_{CH}$	150.5
$^1J_{CH}$	170.0		



SCHEME 3

resonance.[8] The initially formed monodichlorophosphino derivative **4** could not be isolated even on using one equivalent of phosphorus trichloride under controlled conditions. This shows that the methine proton of **4** is highly activated and undergoes instantaneous substitution by phosphorus trichloride. In the case of **3a**, a ^{31}P-NMR signal at δ173.1 of very low intensity which splits into a doublet ($^2J_{PH}$ = 7.0 Hz)[11] under ^{1}H-coupled ^{31}P-NMR mode indicates the initial formation of the monodichlorophosphino derivative **4a**.

The polarity of the solvent influences the progress of the above reactions. While in benzene, the reaction stops at stage **5**, in acetonitrile the initially formed bis(dichlorophosphino)methylene derivative **5** undergoes intramolecular cyclocondensation if R = C_6H_5 or $C_6H_4NO_2$-*p* to form species **6** and finally 1-dichlorophosphino-2-phosphaindolizine **7** (Scheme 3). The formation of species **6** is revealed by ^{31}P-NMR spectrum of the reaction mixture in which two doublets (R = C_6H_5, δP_A = 39.5, δP_B = 170.0, $^2J_{PP}$ = 166.7 Hz; R = $C_6H_4NO_2$-*p*, δP_A = 29.4, δP_B = 142.0, $^2J_{PP}$ = 88.9 Hz) corresponding to a characteristic AB spin system are observed. The reason for a large difference in $^2J_{PP}$ coupling constants in the above two cases is not understandable, although we have made a similar observation in the case of 1-dichlorophosphino-2-phosphaindolizines.[6] Furthermore, several cases of such large differences in $^2J_{PP}$ coupling constants in differently substituted β-phosphino-1-phosphaethenes have been reported earlier.[12,13] This type of cyclization is not observed if R = H (**5a**).

Furthermore, in the case where R = C_6H_5, the initially formed **7b** undergoes disproportionation to form **9b** (Scheme 4) as revealed by A_2B spin system in the ^{31}P-NMR spectrum. A highly downfield chemical shift of P_A in **9b** (δ^{31}P = 310.5, $^2J_{PP}$ = 30.6 Hz) indicates the presence of cationic charge on the ring system.[14] The ionic nature of **9b** is also supported by its insolubility in diethyl ether due to which it could not be separated from the ammonium salt.

A reinvestigation of the synthesis of 1,3-diphenyl-2-phosphaindolizine from the

TABLE III

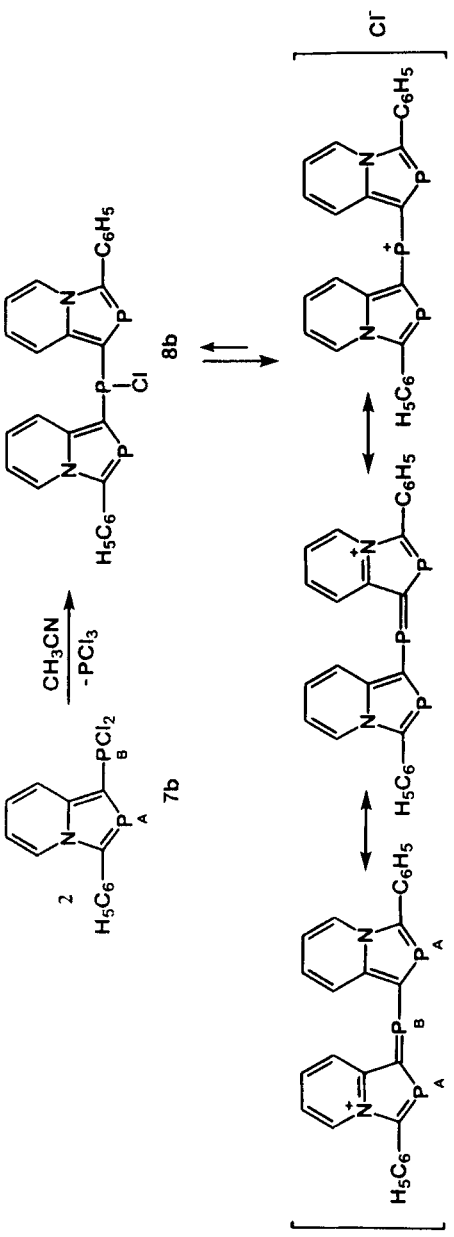
^{31}P-NMR data of **2**, **4–7**, **9**, **11**, **12** and **14**

Cpd.	δP_A	δP_B	$^2J_{PP}$(Hz)	Solvent
2a	145.4			C_6D_6
2b	145.9			C_6D_6
2c	146.2			C_6D_6
4a	173.1			C_6H_6
5a	144.7			CD_2Cl_2
5b	145.5			C_6D_6+CD_2Cl_2
5c	146.3			CH_3CN
6b	39.5	170.0	166.7	CH_3CN
6c	29.4	142.0	88.9	CH_3CN
7b	136.0	165.0	133.9	CH_3CN
7c	142.4	164.3	130.0	CH_3CN
9b	310.5	293.0	30.6	CH_3CN
11a	169.3			C_6D_6
11b	168.3			C_6H_6
12b	120.9			CH_3CN
14a	152.1			C_6D_6
14b	153.7			C_6H_6
14b'	145.4			C_6H_6

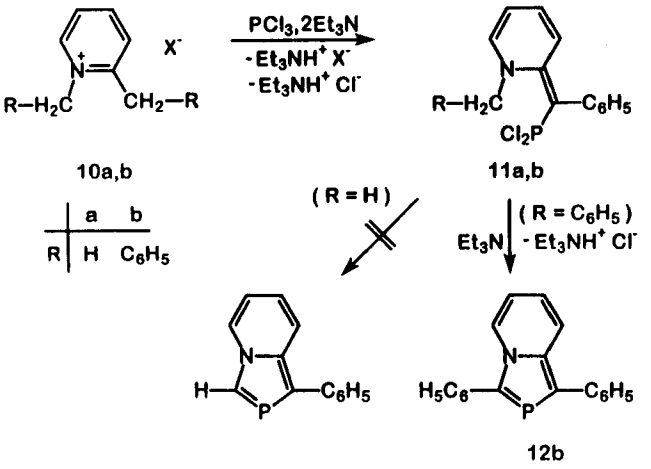
cyclocondensation of 1,2-dibenzylpyridinium bromide with phosphorus trichloride[5] indicates that in this case also the reaction is initiated at the 2-methylene group. The reaction of 2-benzyl-1-methylpyridinium iodide **10a** with phosphorus trichloride in the presence of triethylamine in benzene, gives **11a** which does not cyclize on heating or carrying out the reaction in acetonitrile (Scheme 5). The structure of **11a** has been confirmed on the basis of ^{31}P- and ^{1}H-NMR spectra (Table I). Likewise, 1,2-dibenzylpyridinium bromide forms **11b** in benzene ($\delta^{31}P$ = 168.3) which does not cyclize to 2-phosphaindolizine under these conditions. However, if the reaction is carried out in acetonitrile the initially formed **11b** finally changes into 2-phosphaindolizine **12b** ($\delta^{31}P$ = 120.9).[5]

Reaction of 1,4-Dialkyl- and 1,2,4-Trialkylpyridinium Halides

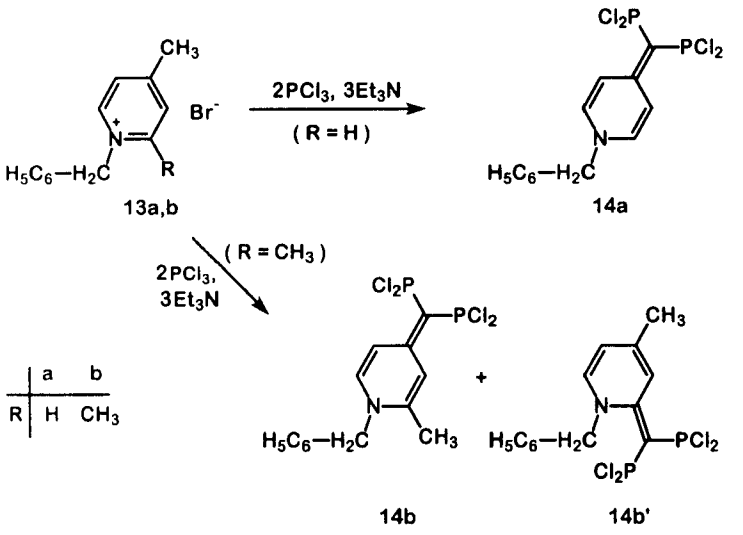
1-Benzyl-4-methylpyridinium bromide **13a** reacts with phosphorus trichloride (2 equiv.) in presence of triethylamine (3 equiv.) to give 1-benzyl-4-{bis(dichloro-



SCHEME 4



SCHEME 5



SCHEME 6

phosphino)methylene}-1,4-dihydropyridine **14a** (Scheme 6). As in the case of **3**, the reaction does not stop at the stage of monodichlorophosphinylation. In the case of 1-benzyl-2,4-dimethylpyridinium bromide **13b**, dichlorophosphinylation occurs at either of the two methyl groups forming a mixture of two products **14b** and **14b'** (Scheme 6) as indicated by ^{31}P-NMR signals at δ153.7 and δ145.4. Although **14a** has been obtained as a yellow crystalline solid (Table I), **14b** and **14b'** could not be separated in the pure form. It may be mentioned that formation of 2- and 4-{bis(dichlorophosphino)methylene} derivatives **5** and **14** parallels bisbenzoylation in the reaction of 1,2- and 1,4-dialkylpyridinium halides with benzoic anhydride.[7]

EXPERIMENTAL

All manipulations involving phosphorus compounds were carried out under dry nitrogen. Solvents and commercial reagents were distilled and dried by standard procedures before use. Melting points were determined by capillary method and are uncorrected. NMR spectra were recorded on a Jeol FX-90Q (^{1}H and ^{31}P) and Jeol EX-400 (^{13}C) spectrometer. Chemical shifts are given with respect to 85% H_3PO_4 (^{31}P) as external and TMS (^{1}H and ^{13}C) as internal standards.

N-Alkylpyridinium halides (**1, 3, 10, 13**). *General Procedure*[10]: To a solution of alkyl halide (0.1 mol) in tetrahydrofuran or diethyl ether (50 ml) an equimolar amount of pyridine or alkylpyridine was added and reaction mixture was stirred for 24–48 hrs at r.t. (~25°C). The precipitated solid was filtered, washed with diethyl ether (30 ml) and dried *in vacuo*. The salts obtained in 70–90% yield were used without further purification.

1-(Dichlorophosphinomethylene)pyridinium ylides (**2**). *General Procedure*: To a well stirred suspension of 1-alkylpyridinium bromide **1** (10 mmol) in benzene (40 ml) at r.t. was added triethylamine (2.02 g, 20 mmol) followed by the addition of a solution of phosphorus trichloride (1.37 g, 10 mmol) in benzene (10 ml). The reaction was completed in 4–6 hrs as revealed by ^{31}P-NMR. The solvent was thereafter removed *in vacuo* and the residue was extracted with diethyl ether (2 × 50 ml). The combined extracts were concentrated to about 25 ml and left in the refrigerator overnight when yellow to red crystals deposited which were filtered and dried *in vacuo*. The **2c** however could not be obtained in pure form due to its poor solubility in diethyl ether. A sample directly obtained from the benzene filtrate by removal of the solvent was found to contain traces of the ammonium salt.

2a (% Found C 38.52; H 3.45; N 5.32. Calc. for $C_8H_8NO_2PCl_2$: C 38.12; H 3.20; N 5.56%).
2b (% Found C 40.98; H 3.99; N 5.03. Calc. for $C_9H_{10}NO_2PCl_2$: C 40.63; H 3.79; N 5.26%).

1-Alkyl-2-{bis(dichlorophosphino)methylene}-1,2-dihydropyridines (**5**) *and 1-Alkyl-4-{bis-(dichlorophosphino)methylene}-1,4-dihydropyridine* (**14**). *General Procedure*: The above procedure was followed using 1,2- or 1,4-dialkylpyridinium halide (10 mmol), triethylamine (3.03 g, 30 mmol) and phosphorus trichloride (2.74 g, 20 mmol). The reaction mixture was directly filtered and on removing the solvent from the filtrate under vacuum an amorphous orange solid was obtained.

5b (% Found: C 41.08; H 2.93; N 3.59. Calc. for $C_{13}H_{11}NO_2PCl_4$: C 40.55; H 2.88; N 3.64%).

1-Alkyl-2-(dichlorophosphino, phenylmethylene)-1,2-dihydropyridine (**11**). *General Procedure*: The above procedure was followed using 1-alkyl-2-benzylpyridinium halide (10 mmol), triethylamine (2.02 g, 20 mmol) and phosphorus trichloride (1.37 g, 10 mmol). The sample (**11a**) obtained from removing the solvent from benzene filtrate contained traces of the ammonium salt.

ACKNOWLEDGEMENT

We are grateful to the Department of Science and Technology, New Delhi for financial support. Our thanks are due to Dr. K. Karaghiosoff, Munich for many helpful suggestions.

REFERENCES

1. R. K. Bansal, K. Karaghiosoff and A. Schmidpeter, *Tetrahedron*, **50,** 7675 (1994).
2. R. K. Bansal, R. Mahnot, G. Pandey and R. Gupta, *J. Indian Chem. Soc.*, **71,** 415 (1994).
3. R. K. Bansal, K. Karaghiosoff, N. Gandhi and A. Schmidpeter, *Synthesis*, 361 (1995).
4. R. K. Bansal, K. Karaghiosoff, N. Gupta, A. Schmidpeter and C. Spindler, *Chem. Ber.*, **124,** 475 (1991).
5. R. K. Bansal, V. Kabra, N. Gupta and K. Karaghiosoff, *Indian J. Chem.*, **31B,** 254 (1992).
6. R. K. Bansal, N. Gupta, V. Kabra, C. Spindler, K. Karaghiosoff and A. Schmidpeter, *Heteroatom Chem.*, **3,** 359 (1992).
7. F. W. Kröck and F. Kröhnke, *Chem. Ber.*, **102,** 669 (1969).
8. O. R. Rodig in "Quaternary Pyridinium Compounds" in the series "The Chemistry of Heterocyclic Compounds," Vol. 14, Part II, R. A. Abramovitch, ed., Interscience, New York, 1974, p. 309.
9. J. C. Tebby in "Phosphorus-31 NMR Spectroscopy in Stereochemical Analysis," Vol. 8, J. G. Verkade and L. D. Quin, eds., VCH, USA, 1987, p. 18.
10. W. G. Phillips and K. W. Ratts, *J. Org. Chem.*, **35,** 3144 (1970).

11. D. G. Gorenstein in "Non-biological Aspects of Phosphorus-31 NMR Spectroscopy" in the series "Progress in NMR Spectroscopy," Vol. 16, Pergamon Press, Oxford, 1983, p. 36.
12. R. Appel, F. Knoll and I. Ruppert, *Angew. Chem.*, **93,** 771 (1981); *Angew. Chem. Int. Ed. Engl.*, **20,** 731 (1981).
13. R. Appel, F. Knoch, B. Laubach and R. Sievers, *Chem. Ber.*, **116,** 1873 (1983).
14. G. Jochem, Ph.D. Thesis, University of Munich, Germany, 1994.