α-Thiocarbonyl-stabilized Triphenylphosphonium Ylides: Preparation, Structure, and Alkylation Reactions

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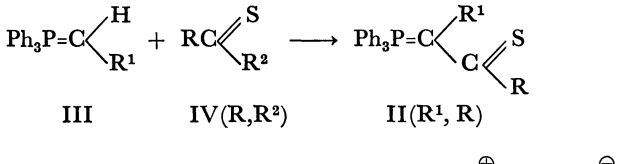
A number of α-thiocarbonyl-stabilized ylides II were prepared in moderate yields, and their alkylation reactions were studied. II(H, MeO), II(H, EtO), II(H, i-PrO), and II(H,H) were mixtures of *cis* and *trans* isomers, and the II_{cis}/II_{trans} ratios were solvent-dependent. II(H, Ph), II(H, Me_2N), II(H, MeS), and II(H, EtS) were composed of only *cis* isomers. All these ylides II with alkyl iodide gave S-alkylation products in good yields.

The physical and chemical properties of carbonyl-stabilized phosphonium ylides (I) have been widely studied in recent years.[1] In this report we will discuss the structure and alkylation reactions of thiocarbonyl-stabilized triphenylphosphonium ylides (II).

Results and Discussion

Preparation of II(R^1,R). The reaction of triphenylphosphonium alkylide (III) with *S*-alkyl thiolcarboxylates yields phosphonium acylalkylides in good yields.[2]

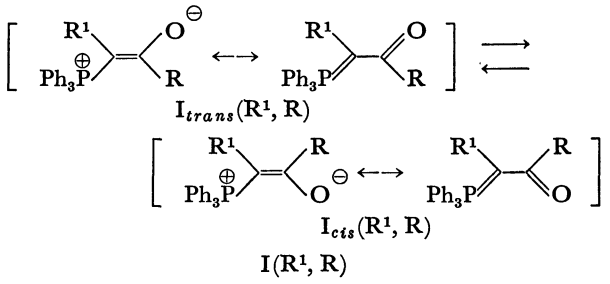
The treatment of III with a two-fold excess of thionocarboxylate (IV) was performed in benzene under a nitrogen atmosphere at room temperature or under ice-water cooling. The product was then purified by crystallization. The results are collected in Table 1.



III IV(R,R^2) II(R^1, R)

Structure of II(R^1,R) and Alkylation Reaction. The NMR spectra of carbonyl-stabilized phosphonium ylides (I) have been widely studied in recent years. The NMR spectra of ester-stabilized ylides I(H, Alkyl-O) have been shown to be a mixture of *cis* and *trans* isomers;[3] however, keto-stabilized ylides I(R^1, Alkyl or Aryl) are only *cis* isomers[4] unless R is large and R^1 is strongly electron-withdrawing.[5] Keto-stabilized ylides I(Cl, Ph) and I(I, Ph) have been shown to be *cis* by X-ray studies.[6,7]

It is known that ester-stabilized ylides I(R^1, Alkyl-O) undergo alkylation with alkyl halides to give normal C-alkylation products,[8] whereas alkylation with triethyloxonium fluoroborate yields a mixture of C- and



$I_{trans}(R^1, R)$

$I_{cis}(R^1, R)$

$I(R^1, R)$

Table 1. Preparation of II(R^1, R) and their physical properties

II(R^1, R)	IV	Yield (%)	Mp (°C)	II(R^1, R) in $CDCl_3$	
				Conf. (%)	NMR(δ)[a], *J* are in Hz.
II(H, MeO)	$MeOCS_2Me$	38	164—165	*cis*(45)	3.83(s, MeO), 4.32(d, J=26.0, methine)
				trans(55)	3.53(s, MeO), 4.64(d, J=26.0, methine)
II(H, EtO)	$EtOCS_2Me$	41	133—134	*cis*(40)	1.30(t, J=7.9, Me), 4.35(J=26.0, methine), 4.42(q, CH_2)
				trans(60)	0.67(t, J=7.9, Me), 4.23(q, CH_2), 4.68(d, J=25.5, methine)
II(H, *i*-PrO)	*i*-$PrOCS_2Me$	56	156—158	*cis*(21)	1.27(d, J=6.5, Me), 4.33(d, J=26.0, methine)
				trans(79)	0.72(d, J=6.5, Me), 4.68(d, J=25.9, methine), 5.52(sept, methine)
II(Me, MeO)	$MeOCS_2Me$	43	251—253	*cis*(16)	1.66(d, J=14.8, Me), 3.95(s, MeO)
				trans(84)	1.97(d, J=14.9, Me), 3.37(s, MeO)
II(H, Ph)	$PhCS_2Me$	45	179—181	*cis*(100)	5.66(d, J=30.0, methine)
II(H, MeS)	$MeSCS_2Me$	40	183—184	*cis*(100)	2.53(s, MeS), 5.10(d, J=28.1, methine)
II(H, EtS)	$EtSCS_2Et$	47	125—127	*cis*(100)	1.30(t, J=8.0, Me), 3.13(q, CH_2), 5.11(d, J=28.2, methine)
II(H, Me_2N)	Me_2NCS_2Me	28	142—144	*cis*(100)	3.28(s, Me_2N), 3.61(d, J=27.9, methine)
II(H, H)	HCSOMe	54	213—215	*cis*(19) *trans*(81)	see Table 4
II(Me, H)	HCSOMe	48	267—269	*trans*(100)	see Table 4

a) Phenyl protons were observed at about 7.2—7.8(m).

Table 2. Alkylation of II with alkyl iodide (R'I) in $CDCl_3$

II	R'I	V (R^1, R, R') Conf.	Mp (°C)	NMR (δ in $CDCl_3$)[a], J are in Hz
II(H, MeO)	MeI	*cis*	Resinous	2.27(s, MeS), 4.33(s, MeO), 5.36(d, J=10.8, methine)
		trans		2.83(s, MeS), 3.60(s, MeO), 5.11(d, J=13.6, methine)
II(H, EtO)	MeI	*cis*	Resinous	1.51(t, J=7.9, Me), 2.29(s, MeS), 4.62(q, CH_2), 5.30 (d, J=10.9, methine)
		trans		0.73(t, J=7.8, Me), 2.83(s, MeS), 4.05(q, CH_2), 5.04 (d, J=13.9, methine)
II(H, *i*-PrO)	MeI	*cis*	Resinous	1.52(d, J=6.5, Me), 2.25(s, MeS), 5.28(d, J=10.5, methine), 5.41(sept, methine)
		trans		0.87(d, J=6.5, Me), 2.88(s, MeS), 4.78(sept, methine), 4.98(d, J=15.0, meshine)
II(H, Ph)	MeI	*cis*	198—200	1.91(s, MeS), 6.41(d, J=21.8, methine)
II(H, MeS)	MeI	*cis*	195—197	2.39(s, MeS), 2.92(s, MeS), 6.02(d, J=16.2, methine)
II(H, EtS)	MeI	*cis*	125—127	1.47(t, J=7.3, Me), 2.38(s, MeS), 3.39(q, CH_2), 5.95 (d, J=16.1, methine)
II(H, MeS)	EtI	*cis*	167—169	1.03(t, J=7.2, Me), 2.94(q, CH_2), 2.85(s, MeS), 6.04 (d, J=17.1, methine)
II(H, Me_2N)	MeI	*cis*	191—192	1.69(s, MeS), 3.39(s, Me_2N), 4.39(d, J=19.2, methine)

a) Phenyl protons were appered at about 7.2—7.8(m).

Table 3. *cis*/*trans* ratios for I[a] and II[b] in various solvents

Solvent(ε)	I(H, MeO)	II(H, MeO)	I(H, EtO)	II(H, EtO)	I(H, *i*-PrO)	II(H, *i*-PrO)
PhH(2.27)	*cis*	3.5	5.9	2.1	2.9	1.8
CD_3CN(37.5)	5	1.9	2.3	1.2	1.3	0.82
CD_3NO_2(38.6)	4.0	2.1	2.4	1.2	1.4	0.56
$CDCl_3$(4.7)	4.6	0.82	1.8	0.67	1.0	0.36

a) Taken from Ref. 3. Recorded at −10—0 °C. b) Recorded at 34.5 °C.

O-alkylation products (O-rich).[9] Keto-stabilized ylides I(R^1, Alkyl or Aryl) react with alkyl halides to give O-alkylation products.[10] Contrary to these results, the alkylation of II with alkyl iodides takes place exclusively at sulfur and easily at room temperature to give salts V in quantitative yields (Table 2).

The stereochemistry of the products was assigned on the assumptions that the protons of the R group *cis* to the phosphorus are shielded by the phenyl rings and that they appear at a higher field than the R *trans* to the phosphorus.

The variable-temperature NMR study of I(H, MeO) shows the methyl protons as a singlet above the coalescence temperature (T_c=35±3 °C for I(H, MeO)) and an unsymmetrical doublet at a lower temperature.[4] The NMR spectra of II(H, Alkyl-O) at 34.5 °C gave clean peaks of two groups corresponding to the *cis* and *trans* isomers (Table 1). These results indicate that the T_c for II (H, Alkyl-O) may be higher than the T_c for I(H, Alkyl-O). However, the rotation for II is not restricted, since II (H, Alkyl-O) reached equilibrium fairly rapidly in any solvent and the II_{cis}/II_{trans} ratio was nearly constant during the reaction with alkyl halides.

In a previous communication[11] we have reported on the effect of solvents on the II_{cis} (H, Alkyl-O)/II_{trans} (H, Alkyl-O) isomer ratios and on the effect of alkylating reagents on the V_{cis}(H, Alkyl-O, R')/V_{trans} (H, Alkyl-O, R') products ratios. Here, only representative data are collected in Table 3.

It is clear that $P^{\oplus}/O^{\ominus}$ or $P^{\oplus}/S^{\ominus}$ attraction is maximized in I_{cis} or II_{cis}. For ester-stabilized ylides I, it has been reported that a large R and an increasing solvent aggregation about the ester carbonyl favor a relatively high population of the *trans* form.[3] The regular variation in I_{cis}/I_{trans} found for ylides I is interpreted as a result of steric inhibition of solvation.[3] As is shown in Table 3, both I(H, Alkyl-O) and II(H, Alkyl-O) show similar properties. The smaller *cis*/*trans* value for II than for I seems to show a higher solvent aggregation around thiocarbonyl than that around carbonyl. This result clearly reflects the higher mesomeric character of the thiocarbonyl than the carbonyl group. This trend is especially marked in the chloroform solvent, with which negative oxygen or sulfur associates by hydrogen-bonding interaction.[3]

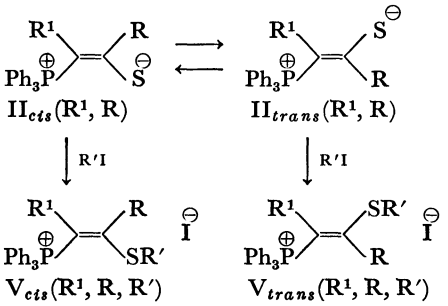
The ylides II(H, Ph), II(H, Me_2N), II(H, MeS), and II(H, EtS) gave only a single *cis* isomer. The structure was confirmed as follows.

The methylation of II(H, MeS) with methyl iodide gave needles whose NMR spectrum showed two *S*-methyl peaks, at δ 2.39 and 2.92 in $CDCl_3$. The ethylation of II(H, MeS) with ethyl iodide gave needles with a mp of 167—169 °C, which showed only one *S*-methyl signal, at δ 2.85. II(H, EtS) reacted with methyl iodide to give needles (mp 125—127 °C) which showed one *S*-methyl signal, at 2.38. Thus, these alkylation products were confirmed to be V_{cis}(H, MeS, Me), V_{cis}(H, MeS, Et), and V_{cis}(H, EtS, Me). These products were stable for more than 20 hr at 80—90 °C

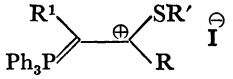
Table 4. NMR data for II(H, H), II(Me, H) and their methylation products in $CDCl_3$.

Compound	δ_{R^1}	δ_R	J_{R^1R}	$J_{PCR'}$(Hz)	J_{PCCR}(Hz)	δ_{SMe}
II_{cis}(H, H)	5.17	9.34	8.1	30.2	45.0	
II_{trans}(H, H)	5.94	8.69	14.8	26.0	15.3	
V_{cis}(H, H, Me)	6.80	8.73	12.0	15.9	44.0	2.54
V_{trans}(H, H, Me)	a)	a)				2.81
II_{trans}(Me, H)	2.21	8.66		13.7	18.6	
V_{trans}(Me, H, Me)	2.11	7.19		13.7	21.1	2.55

a) Signals were appered in the phenyl proton region.



in $CDCl_3$, and they showed no isomerization. However, on irradiation with a high-pressure mercury lamp for 6 hr in $CDCl_3$, V_{cis}(H, MeS, Et) and V_{cis}(H, EtS, Me) gave the same 1 : 1 mixture of V_{cis}(H, MeS, Et) and V_{cis}(H, EtS, Me). These results indicate that the structure of the ylides II(H, MeS) and II (H, EtS) was *cis* and that alkylation products have a structure of a vinylphosphonium salt like V, not that of a carbonium ion like VI.



VI

The NMR spectrum of the methylation product V(H, Ph, Me) of II (H, Ph) with methyl iodide showed signals at δ 1.91 (s, MeS) and 6.41 (d, J=21.8 Hz, methine). The compound gave new peaks at 2.87 (s, MeS) and 6.38 (d, J=14.1, methine) on ultraviolet irradiation. The results show that the ylide II(H, Ph) is *cis* and that the methylation product is V_{cis}(H, Ph, Me), which gives V_{trans}(H, Ph, Me) on ultraviolet irradiation. The equilibrium ratio, V_{cis}(H, Ph, Me): V_{trans}(H, Ph, Me), was 6 : 4 after 6 hr.

The ylide II (H, Me_2N) gave an isomer on methylation, but the product showed no change on ultraviolet irradiation for 10 hr. Although we have no direct evidence, the structure of II(H, Me_2N) was assumed to be *cis* judging from the kinetic studies of methylation reaction (see the next section).

Formylmethylenetriphenylphosphorane I(H, H) exists as a mixture of *cis* and *trans* isomers, whose ratio (about 1 : 1) is constant in any solvent,[1,12,13] but I(Me, H) gives only the *trans* isomer.[1]

The NMR spectrum of II(H, H) was shown to be a mixture of *cis* and *trans* isomers, while II(Me, H) gave only *trans* (Table 4). Interestingly, II(H, H) showed a solvent dependence like that of ester-stabilized ylides I(H, Alkyl-O) and II(H, Alkyl-O); however the small solubility of II(H, H) inhibited precise studies. A sample crystallized from benzene gave a *cis*-rich product of *cis*/*trans*=7, one of *cis*/*trans*=1.1 from nitrobenzene, and one of *cis*/*trans*=0.23 from chloroform. These data were obtained by the analysis of the NMR spectra of samples in the $CDCl_3$–Et_3N (5%) solvent. A sample from benzene attained equilibrium quickly (*cis*/*trans*=0.23) without the addition of any dry sodium carbonate (in 3—5 min); with the addition of dry sodium carbonate, attaining equilibrium took rather longer (about 60 min). However, the sample attained equilibrium slowly (about 25 hr) in the $CDCl_3$–Et_2N solvent. These results indicate that the acid-catalyzed *cis-trans* isomerization is a lower energy process than the thermally induced one, as has been reported in connection with the ester-stabilized ylides I (H, Alkyl-O).[1,3]

Table 5. Second-order rate constants for the methylation of II with methyl benzenesulfonate in $CDCl_3$ at 34.5 °C

II	$k_2 \times 10^3$ l/mol·s	
	cis	*trans*
II(H MeO)	1.60	3.59
II(H, EtO)	1.77	4.13
II(H, *i*-PrO)	2.12	4.36
II(H, Ph)	11.2	
II(H, Me_2N)	24.1	
II(H, MeS)	3.45	

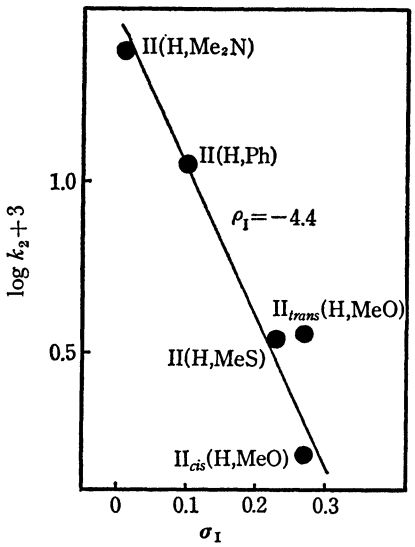


Fig. 1. The relation between σ_I and $\log k_2$.

Kenetic Studies of the Methylation of II with Methyl Benzenesulfonate. Since the reaction of II with methyl iodide was too fast to follow by means of the NMR spectra (within one min), methyl benzenesulfonate was used as the methylating reagent. The reaction gave good second-order rate constants (k_2), first-order with II and benzenesulfonate respectively. The results are shown in Table 5 and Fig. 1. The large negative ρ_I value seems to indicate that, in the transition state of the reaction, the negative charge is highly localized on the thiocarbonyl sulfur (*i.e.*, the betaine form).

As was observed on II(H, Alkyl-O), the *trans* isomer showed nearly twice as much reactivity with methyl benzenesulfonate as the *cis* isomer. The ylide II(H, Me_2N) was supposed to be *cis*, since there was a much deviation of II_{trans}(H, MeO) from the line (Fig. 1).

Experimental

Preparation of II. A suspension of triphenylmethylphosphonium bromide (5.0 g, 14 mmol) and sodium amide (1.5 g) in 50 ml of dry benzene was stirred for 12 hr in a stoppered flask at room temperature. After the separation of the precipitate, the ammonia was removed *in vacuo* to give a yellow solution of triphenylphosphonium methylide. After the solution had then been cooled in an ice-water bath, methyl methylxanthate (1.7 g, 14 mmol) in 10 ml of benzene was added in one portion, and the resulting mixture was allowed to stand for 1 hr at room temperature. The mixture was then treated with charcoal and condensed *in vacuo* to give an oil. The oil was washed several times with petroleum ether, II(H, MeO) was then obtained in a 38% yield from benzene–petroleum ether.

Similarly several other II were prepared in moderate yields; the results are collected in Table 1.

Alkylation of II. A solution of II(H,Ph) in chloroform was treated with twice as much methyl iodide at room temperature. The subsequent evaporation of the solvent *in vacuo* afforded needles (mp 198—200 °C) in a quantitative yield.

The similar treatment of II(R^1,R) with alkyl iodide (R'I) gave V(R^1,R,R') in a good yield (Table 2).

The photo-isomerization of V(H,Ph,Me), V(H,MeS,Et), and V(H,EtS,Me) in $CDCl_3$ was performed in NMR tubes (Pyrex), following at suitable time intervals by observing NMR spectral change.

Kinetic Studies. A solution of II and methyl benzenesulfonate in $CDCl_3$ was sealed in an NMR sample tube. The rate was followed at suitable time intervals by analyzing the NMR spectra of the *O*-methyl and *S*-methyl groups. The results are collected in Table 5.

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