Dialkyl *p*-Toluenesulfonylcarbamoylphosphonates

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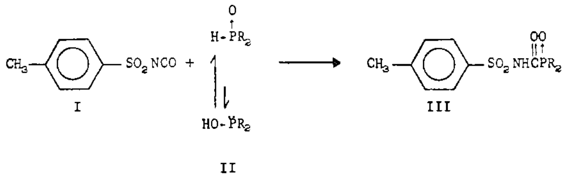
Treatment of *p*-toluenesulfonyl isocyanate with dialkyl hydrogenphosphonates has provided an excellent synthesis of several new dialkyl *p*-toluenesulfonylcarbamoylphosphonates, of the general formula *p*-$CH_3C_6H_4SO_2NHC(O)P(O)(OR)_2$. The proton on nitrogen is acidic to sodium bicarbonate and readily exchanges with D_2O. Infrared, NMR, and elemental analyses support the structures. In the example with R = $(CH_3)_2CH$—, magnetic nonequivalence of the two sets of geminal methyl groups is observed in its NMR spectrum.

SEVERAL new carbamoylphosphonates have been synthesized from readily available starting materials. Insecticidal and rodenticidal activities of a few simple carbamoylphosphonates were recently discovered (*9, 17*). This general class of compounds has also been used in the manufacture of flameproofings, plastics, extreme-pressure additives, and plasticizers (*17*).

Carbamoylphosphonates were prepared by the Arbuzov reaction (*2, 7*), the Michaelis reaction (*11*), amidation of methyl dialkoxyphosphinylformate, or the reactions of dialkyl hydrogenphosphonates with isocyanates (*8–11*).

Base-catalyzed reactions of dialkyl hydrogenphosphonates with isocyanates (*1, 4, 6*) gave several arylcarbamoylphosphonates. With the exception of ethylcarbamoylphosphonates, the liquid products were undistillable, even at 1 mm., without decomposition to the original reactants at temperatures on the order of 160° C.

In the present work, a series of new disubstituted carbamoylphosphonates has been prepared. The general procedure for the synthesis is given in Equation 1.



(1)

R. a, CH_3O—; b, C_2H_5O; c, *n*-C_3H_7O—; d, i-C_3H_7O; e, *n*-C_4H_9O; f, *n*-$C_8H_{17}O$; g, $CH_2{=}CHCH_2O$—; h, C_6H_5O—; i, C_6H_5.

Members of this group of compounds, *p*-toluenesulfonylcarbamoylphosphonates (III) (Table I), were synthesized (72 to 92%) by the addition of *p*-toluenesulfonyl isocyanate (I) to dialkyl (or aryl) hydrogenphosphonates (II). A derivative, diphenyl-*p*-toluenesulfonylcarbamoylphosphine oxide (IIIi), was obtained in 36% yield. NMR, infrared (Table II), and elemental analyses support the structures. All the compounds investigated were acidic to sodium bicarbonate and the labile amide hydrogen was easily removed by deuterium oxide. $^{31}P—^{1}H$ splitting (6.0 to 11.0 c.p.s.) was observed (Figures 1 and 2) in the NMR spectra of some of the dialkyl compounds. Long-range phosphorus splitting ($J_{P—O—C—C—H}$), as reported by Hellwege (*5*) for some related systems, was not observed for the compounds studied. However, a case of magnetic nonequivalence of methyl substituents of isopropyl groups was observed in IIId; a similar case was reported by Siddall and Prohaska (*14, 16*). An explanation has been given regarding the magnetic nonequivalence of several phosphorus esters and organonitrogen compounds in terms of symmetry properties (*15*). Slow rotation around the C—N bond in amides reduced the probability of a symmetrical system, and the attached groups are therefore nonequivalent at room temperature. A difference in the environments of methyl groups in IIId due to restricted rotation around the C—N bond (and in turn around the C—P bond) is believed to be responsible for the nonequivalence of the methyl groups at room temperature. In IIId, rotation of the large isopropoxy groups around the P—O bond is probably slow, causing a nonequivalence of the two sets of geminal methyl groups (Figure 2).

Unlike the methods used by previous authors (*4, 7–9, 11*), the reaction uncovered in this work involved no catalyst. Pudovik (*9*) indicated that $(CH_3O)_2PSH$ adds to C_6H_5NCO in the absence of catalyst. The increase in reactivity of I compared to isocyanates may be attributed to the influence of the polar sulfonyl group. It is expected that the SO_2 group would greatly enhance the electro-

Table I. Physical Properties of Products

			Analysis, %					
			N		P		S	
Compound	M.P., ° C.	Yield, %	Calcd.	Found	Calcd.	Found	Calcd.	Found
IIIa	126-27	72	4.56	4.79	10.08	10.22	10.44	10.52
IIIb	78.5-80	95.6	...	...	9.24	9.36	9.56	9.64
IIIc	73-74	90	...	...	8.52	8.43	8.82	8.78
IIId	92.5-93.5	87.5	3.86	3.72	8.52	8.50	8.82	8.92
IIIe[a]	...	77.5	3.58	3.63	...	...	...	...
IIIf[a]	...	97.7	2.78	2.80	6.15	6.09	...	...
IIIg	87.5-88.5	97.0	...	...	8.62	8.51	8.89	8.72
IIIh	139.5-41.5	83.5	3.25	3.36	7.18	7.52	7.43	7.83
IIIi	133.5-34.5 (dec.)	36.1	3.51	3.39	7.76	7.80	8.02	8.15

[a] Refractive indices of compounds IIIe and IIIf were n_D^{27} 1.5060 and 1.4806, respectively. These compounds were undistillable oils, purified by petroleum ether extraction. Analyses performed by Galbraith Laboratories, Knoxville, Tenn.

Table II. Spectral Data on III

	Infrared, Cm.$^{-1}$			NMR Chemical Shift (δ), P.P.M.[a]					
Compd.	NH	C=O	P → O	NH	*p*-$CH_3C_6H_4SO_2$ J = 8 c.p.s.	*p*-$CH_3C_6H_4$	OCH	JPOCH, c.p.s.	Others
IIIa	3300	1686	1274, 1256	11.18m	7.38d, 7.88d	2.44s	3.86d	11.0	. . .
IIIb	3311	1692	1267	ca. 9.57m	7.39d, 7.91d	2.42s	4.23dq (J = 7.2 c.p.s.)	9.2	1.30t(J = 6.8 c.p.s.)
IIIc	3333	1686	1264	ca. 11.37m	7.45d, 7.84d	2.46s	4.10, 4.23dt (J = 6.4 c.p.s.)	7.9	0.89t(J = 6.8 c.p.s.) 1.69s (J = 6.4 c.p.s.)
IIId	3322	1692	1261 (sh at 1239)	ca. 11.27m	7.38d, 7.90d	2.43s	4.82m (J = 6.2 c.p.s.)	6.0	1.27, 1.32dd (J = 6.0 c.p.s.)
IIIe	3333	1695 (sh at 1751)	1250	ca. 11.06m	7.34d, 7.87d	2.38s	4.08, 4.20dt (J = 6.0 c.p.s.)	7.5	0.86t (J = 6.0 c.p.s.) 1.49m
IIIf	3333	1692 (sh at 1748)	1252	ca. 10.61m	7.39d, 7.81d	2.43s	4.08, 4.22dt (J = 6.2 c.p.s.)	7.9	0.88t (J = 5.0 c.p.s.) 1.26m
IIIg	3311	1704	1248	ca. 11.41m	7.35d, 8.04d	2.43s	4.70m	8.2	5.47, 5.30, 5.17m 5.97 (J = 4.6 c.p.s.)
IIIh	3322	1704	1276	ca. 16.14m	7.12m 8.30d	2.21s	. . .	. . .	. . .
IIIi	3289	1686	1188	ca. 10.61m	7.57m	2.39s	. . .	. . .	. . .

[a] s (singlet), d (doublet), m (multiplet), q (quartet), t (triplet), s′ (sextet), dd (doublet of doublets), dt (doublet of triplets), dq (doublet of quartets). Solvents for NMR spectra: compounds IIIa-g, i ($CDCl_3$); IIIh (pyridine-d_5), same NH observed in IIIh at δ 10.85 in tetramethylurea.

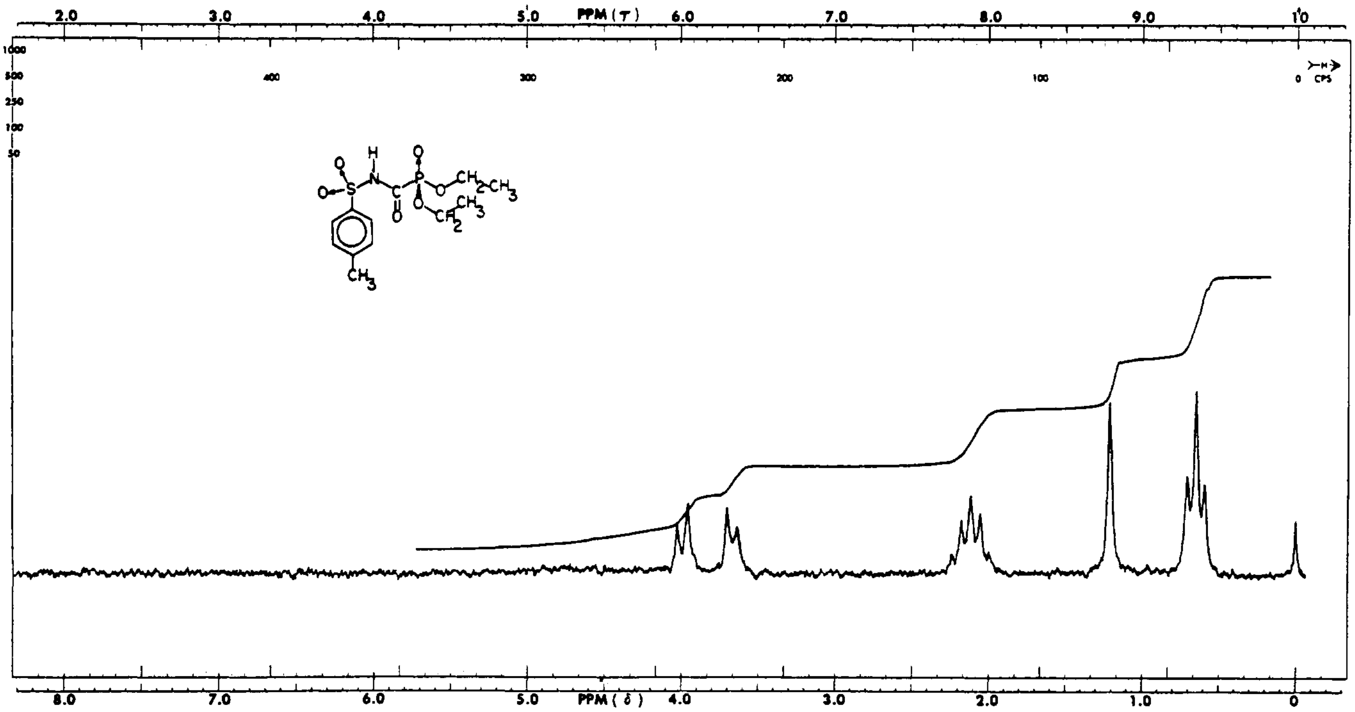
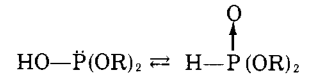


Figure 1. NMR spectrum of diethyl *p*-toluenesulfonylcarbamoylphosphonate (IIIb) in $DCCl_3$

1000-Hz. sweep width

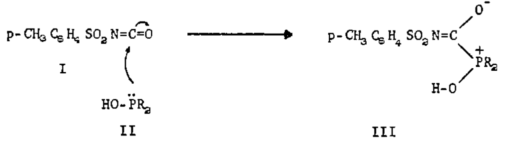
philicity of the isocyanato group and render it increasingly vulnerable toward nucleophilic attack.

A tautomeric equilibrium between certain phosphite-phosphonate forms has been substantiated by kinetic studies (*3, 12, 13*) as given in Equation 2.



$$\mathrm{HO{-}\ddot{P}(OR)_2 \rightleftharpoons H{-}\overset{\overset{O}{\uparrow}}{P}(OR)_2} \quad (2)$$

A tentative mechanism postulated involves nucleophilic attack of II (the trivalent phosphorus form) on the isocyanato group followed by rearrangement of a suspected intermediate to give III, as shown in Equation 3.



(3)

EXPERIMENTAL

Materials. The following chemical reagents were purchased or made by known procedures: *p*-toluenesulfonyl isocyanate, Aldrich Chemical Co., Inc.; dimethyl hydrogenphosphonate, diethyl hydrogenphosphonate, dibutyl hydrogenphosphonate, diisopropyl hydrogenphosphonate, di-*n*-octyl hydrogenphosphonate, diallyl hydrogenphosphonate, and diphenylphosphine.

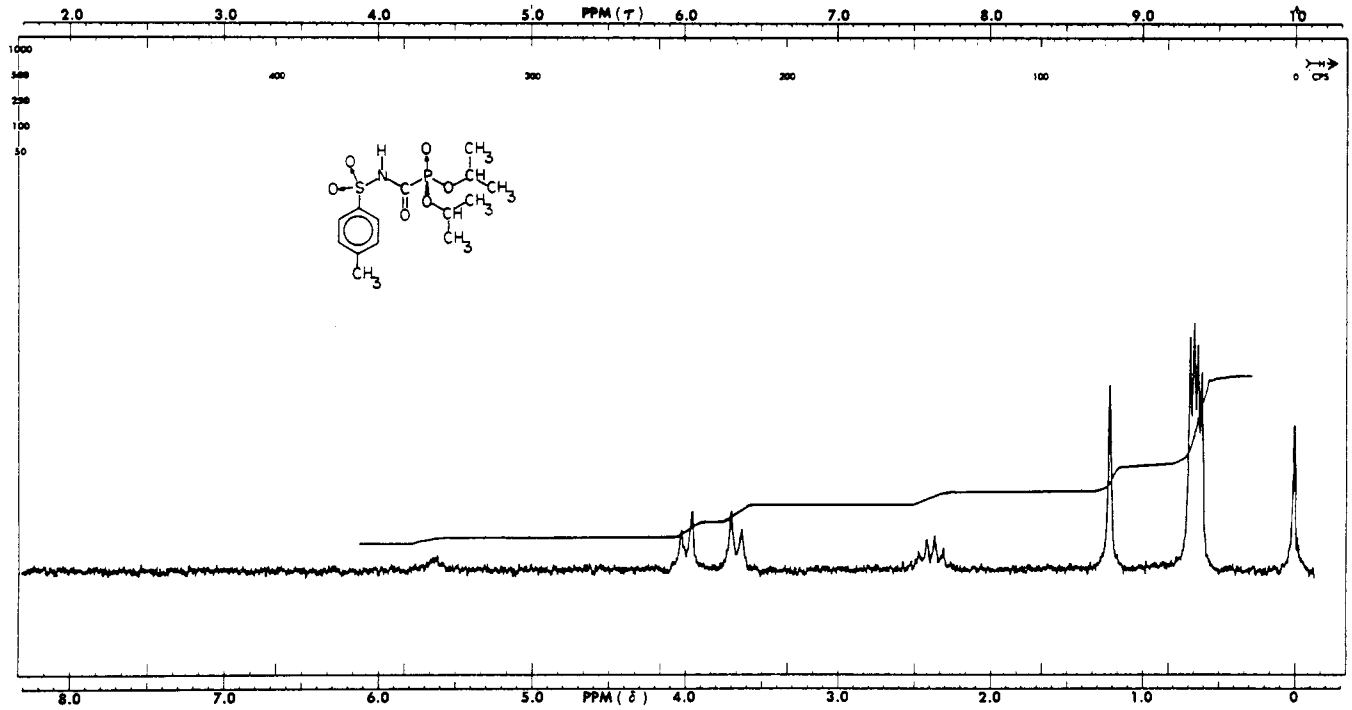


Figure 2. NMR spectrum of diisopropyl *p*-toluenesulfonylcarbamoylphosphonate (IIId) in $DCCl_3$
1000-Hz. sweep width

Dialkyl (or diaryl) *p*-Toluenesulfonylcarbamoylphosphonates. A typical preparation is that of dimethyl *p*-toluenesulfonylcarbamoylphosphonate (IIIa). A 50-ml., one-necked, round-bottomed flask fitted with a drying tube (3A molecular sieve), magnetic stirring bar, and nitrogen inlet was charged by dropwise addition of 3.32 grams (0.016 mole) of *p*-toluenesulfonyl isocyanate (I) to 1.80 grams (0.016 mole) of dimethyl hydrogenphosphonate (IIa) dissolved in 25 ml. of anhydrous diethyl ether at −5° C. The resulting mixture was allowed to warm to room temperature with stirring over an 11-hour period. A white crystalline precipitate formed as the ether was decanted (or evaporated under aspirator pressure). The product was washed with ether (10 ml.) ten times; weight was 3.74 grams (72%), m.p. 124.5–26° C. A sample recrystallized from aqueous methanol gave the properties indicated in Table I.

Amide absorption for III occurred in the infrared spectra at 3333 to 3289 $cm.^{-1}$. Carbonyl bands were observed in the range of 1686 to 1751 $cm.^{-1}$ and the phosphoryl absorption appeared at 1188 to 1276 $cm.^{-1}$.

The NMR spectra of III gave typical A_2B_2 (aromatic ring protons) patterns at 60 MHz. with peaks δ 7.34 to 7.45 and δ 7.81 to 8.04, $J \sim 8$ c.p.s. The A_2B_2 splitting pattern ($\nu_o = \nu_1 - \nu_2 = 29.5$ to 33 c.p.s.) was observed for III. A broad multiplet appeared at *ca.* δ 9.57 to 11.41 for the NH proton of the amide linkages.

Decoupling of the beta-methylene or beta-methyl protons from the alpha-methylene or methine protons of the alkoxyl group gave $J_{P-O-C-H}$ values 6.0 to 11.0 c.p.s. in the series. Upon decoupling the methine protons from the methyl protons in IIId, a field separation of 3 c.p.s. was confirmed for the magnetically nonequivalent methyl groups and $J_{P-O-C-H}$ values could be obtained (Table II).

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