as a result of the decomposition of part of the 1-benzyl-4-bromo-4-bromoacetylpiperidine.

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Ring-Opening Reactions of P-1-Aziridinyl-N,N,N′,N′-tetramethylphosphonic Diamides

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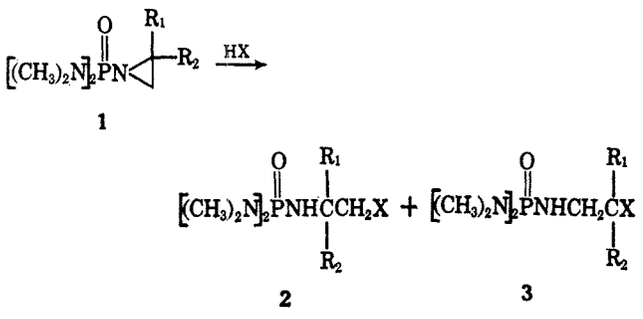
Ring-opening reactions of the aziridine rings of P-1-aziridinyl- (**1a**), P-(2-methyl-1-aziridinyl)- (**1b**), and P-(2,2-dimethyl-1-aziridinyl)-N,N,N′,N′-tetramethylphosphonic diamide (**1c**) are described. For those reactions in which mixtures of ring-opened isomers were produced, an estimate of the composition was made from the proton nmr spectra of the mixtures. Reactions of **1b** with acidic reagents gave mostly the products of direct attack upon the aziridine ring, whereas **1c** yielded mainly products formally derived from a tertiary carbonium ion. Three of the addition products prepared exhibited magnetically nonequivalent dimethylamino groups.

In our studies of the structure–activity relationships in insect chemosterilants, we observed that the sterilizing activity of aziridinylphosphine oxides was inversely related to the degree of substitution on the aziridine ring carbons.[1] Because the process of ring cleavage is considered to be a necessary step in the physiologically important reaction of aziridine-containing sterilants, and because the direction of cleavage of such ring-substituted aziridines had not been studied chemically to any great extent,[2] we investigated ring-opening reactions of P-1-aziridinyl- (**1a**), P-(2-methyl-1-aziridinyl)- (**1b**), and P-(2,2-dimethyl-1-aziridinyl)-N,N,N′,N′-tetramethylphosphonic diamide (**1c**). The structures of the products were confirmed by chemical analyses, and proton nmr and infrared spectra. For reactions in which a mixture of two possible open-chain isomers was produced, an estimate of the product composition was made from the nmr data. The generalized equation for the additions is shown in Scheme I; the physical properties and chemical analyses of the products are summarized in Table I.

SCHEME I



1–3a, $R_1 = R_2 = H$
b, $R_1 = H$; $R_2 = CH_3$
c, $R_1 = R_2 = CH_3$

The C-unsubstituted aziridine (**1a**) reacted with pyridine hydrochloride in chloroform to give, in high yield, **2a** (X = Cl) which polymerized on attempted distillation; the resulting viscous liquid cooled to a glass. Reactions of 1a with thiophenol in carbon tetrachloride, with pyrrolidine, and with methanol containing sodium methoxide also produced high yields of the corresponding adducts. Compounds **2a** (X = 1-pyrrolidinyl) and **2a** (X = OCH_3) were distillable liquids but **2a** (X = phenylthio) decomposed on attempted distillation. Correct chemical analyses were obtained for each of these products and their infrared spectra in carbon tetrachloride solution exhibited absorptions at 3150–3300 cm^{-1} ascribed to NH stretching.

Reaction of **1a** with *p*-nitrobenzoic acid in chloroform produced a complex of *p*-nitrobenzoic acid with the adduct **2a** (X = *p*-nitrobenzoyloxy). Compound **2a** itself was obtained by treatment of the complex with aqueous sodium carbonate. Acidification of the carbonate solution produced an equivalent of *p*-nitrobenzoic acid. The proton nmr spectra of these adducts are listed in Table II. The NH nmr absorption for these compounds would be expected to be concentration dependent because of hydrogen bonding with the oxygen atom bound to phosphorus. Conceivably there might also be hydrogen bonding with the substituent X. The NH absorption for **2b** (X = *p*-nitrobenzoyloxy) was obscured by the N-methyl absorptions when the concentration was 20%. At a 40% concentration the NH appeared as a multiplet centered at τ 6.8 clear of the N-methyl absorptions and to the low-field side of them; at a 5% concentration the NH absorption had moved clear and to the high-field side of the N-methyl absorptions at τ 7.8. Upon addition of D_2O the absorption ascribed to NH disappeared. In the nmr spectra of the various adducts the amidic proton absorption is expected to be in the region of τ 6.8–7.8. The two methylene absorptions of **2a** (X = *p*-nitrobenzoyloxy) can therefore be identified. The methylene group adjacent to oxygen appeared as the expected triplet centered at τ 5.61, whereas the other was a complex multiplet at 5.8–6.9 containing the amidic proton absorption.

The reaction of P-(2-methyl-1-aziridinyl)-N,N,N′,N′-tetramethylphosphonic diamide (**1b**) with pyridine

(1) (a) Advances in Chemistry Series, 41, American Chemical Society, Washington, D. C., 1963, p 475; (b) A. B. Bořkovec, C. W. Woods, and R. T. Brown, *J. Med. Chem.*, **9**, 522 (1966).

(2) Principal references dealing with cleavage of aziridine rings activated toward nucleophilic attack by substitution on the aziridine ring nitrogen with electron-withdrawing substituents are: (a) Y. Iwakura and A. Nabeya, *J. Org. Chem.*, **25**, 1118 (1960); (b) N. P. Grechkin and I. A. Nuretdinov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 295 (1962); (c) H. W. Heine, *J. Am. Chem. Soc.*, **85**, 2743 (1963); (d) G. E. Ham, *J. Org. Chem.*, **29**, 3052 (1964); (e) H. Stamm, *Angew. Chem. Intern. Ed. Engl.*, **4**, 524, 714 (1965); (f) P. E. Fanta and E. N. Walsh, *J. Org. Chem.*, **30**, 3574 (1965).

TABLE I

P-(1-AZIRIDINYL)-N,N,N′,N′-TETRAMETHYLPHOSPHONIC DIAMIDES AND THEIR ADDITION PRODUCTS[a]

No.	R_1	R_2	X	Yield, %[b]	Bp (mm) or mp, °C[c]	Calcd, % C	H	Cl	N	P	S	Found, % C	H	Cl	N	P	S
1a[d]	H	H	...	88.7	42–46 (0.15)	40.67	9.10	...	23.71	...	...	40.41	8.99	...	23.51	...	...
1b[e]	H	CH_3	...	86.8	54–59 (0.05)	...	...	...	...	16.20	...	...	...	...	...	16.44	...
1c[e]	CH_3	CH_3	...	80.9	51–54 (0.04)	...	...	...	...	15.09	...	...	...	...	...	15.51	...
2a[f]	H	H	Cl	>95	...	33.73	8.02	16.60	19.67	14.50	...	33.85	7.99	16.80	19.43	14.33	...
	H	H	SC_6H_5	>95	...	50.15	7.72	...	14.62	10.78	11.16	50.00	7.58	...	14.33	10.60	11.14
	H	H	$O_2CC_6H_4NO_2$	>95	90–92	45.35	6.15	...	16.27	9.00	...	45.17	5.92	...	16.11	8.88	...
	H	H	$O_2CC_6H_4NO_2$. $HO_2CC_6H_4NO_2$	>95	128–129	46.97	5.12	...	13.69	6.05	...	47.34	5.19	...	13.33	6.03	...
	H	H	$NCH_2CH_2CH_2CH_2$	84.7[g]	150–154 (0.55)	48.37	10.15	...	22.56	12.48	...	48.42	10.20	...	22.77	12.70	...
	H	H	OCH_3	>95	107–117 (0.25)	40.18	9.64	...	20.08	14.81	...	40.10	9.72	...	20.10	14.85	...
2b, 3b[f]	H	CH_3	Cl	65.0[g]	115–119 (0.15)	36.92	8.41	15.58	18.45	13.61	...	36.78	8.32	15.47	18.28	13.53	...
	H	CH_3	SC_6H_5	>95	...	51.80	8.03	...	13.94	10.28	10.64	51.74	8.16	...	13.89	10.52	10.82
	H	CH_3	$O_2CC_6H_4NO_2$	80.6	126–127	46.92	6.47	...	15.64	8.65	...	47.02	6.39	...	15.62	8.75	...
2b (3b?)	H	CH_3	$O_2CC_6H_4NO_2$. $HO_2CC_6H_4NO_2$	61.8	81–85	48.00	5.37	...	13.33	5.90	...	48.03	5.41	...	13.16	5.90	...
	H	CH_3	$NCH_2CH_2CH_2CH_2$	40.1[g]	144–150 (0.45)	50.36	10.38	...	21.36	11.81	...	50.18	10.33	...	21.18	11.80	...
	H	CH_3	OCH_3	61.8[g]	91–102 (0.03)	43.04	9.93	...	18.82	13.88	...	42.84	9.81	...	18.72	14.13	...
3c[h]	CH_3	CH_3	Cl	>95	117–119	39.75	8.76	14.67	17.38	12.82	...	39.81	8.60	14.56	17.33	12.84	...
2c	CH_3	CH_3	$NCH_2CH_2CH_2CH_2$	84.0	48.5–50	52.15	10.58	...	20.27	11.21	...	51.83	10.43	...	19.96	11.48	...
2c	CH_3	CH_3	OCH_3	22.7[e]	58–60.5	45.55	10.19	...	17.71	13.06	...	45.87	10.04	...	17.73	13.25	...

[a] The infrared spectra of all compounds were measured with a Perkin-Elmer 21 infrared spectrophotometer. Each of the addition products showed NH absorption in the region 3150–3300 and a characteristic phosphonyl absorption at 1250–1300 cm^{-1} as well as the distinctive absorptions for the various groups X, if any. Ultraviolet spectra were obtained for **2a** and **b** (X = *p*-nitrobenzoyloxy) and their complexes with *p*-nitrobenzoic acid with a Beckman DB spectrophotometer. These are recorded in the Experimental Section. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. [b] Yields recorded are of crude product unless otherwise stipulated. [c] Melting points (corrected) were determined with a Fisher-Johns apparatus. [d] See ref 1b. [e] Satisfactory combustion analyses could not be obtained for **1b** and **c**. [f] The crude product was submitted for analysis. [g] Yield of distilled product. [h] Analysis was obtained on pure **3c** (X = Cl).

TABLE II

NMR SPECTRAL DATA[a]

Compd	CH_3N	CH_2N	CH_2X	CH_3CHN	CH_3CHX	$(CH_3)_2CN$	$(CH_3)_2CX$	Other
1a	d, 7.34 (9.4)	d, 8.07 (14.5)	...	...	...	...	...	
1b	d, 7.36 (9.5)	m, 7.8	...	d, 8.88 (5.0)	...	...	...	Methine H:m, 8.41
1c	d, 7.34 (9.4)	d, 8.04 (13.0)	...	...	...	s, 8.64	...	
2a (X = Cl)	d, 7.39 (9.8)	m, 6.3–7.1	m, 6.3–7.1	...	...	...	...	
2a (X = SC_6H_5)	d, 7.42 (10.0)	m, 6.4–7.2	m, 6.4–7.2	...	...	...	...	Aryl H:m, 2.8
2a (X = $O_2CC_6H_4NO_2$)	d, 7.28 (9.8)	m, 6.6	t, 5.61 (5.5)	...	...	...	...	Aryl H:s, 1.74
2a (X = $NCH_2CH_2CH_2CH_2$)	d, 7.40 (9.7)	m, 6.8–7.6	m, 6.8–7.6	...	...	...	...	Pyrrolidine β-CH_2:m, 8.1–8.4
2a (X = OCH_3)	d, 7.40 (10.0)	m, 6.5–7.2	m, 6.5–7.2	...	...	...	...	OCH_3:s, 6.69
2b (X = Cl)	d, 7.34 (9.9)	...	m, 6.4	d, 8.74 (6.5)	...	...	...	Methine H:m, 6.6–7.1
3b (X = Cl)	d, 7.34 (9.9)	m, 6.6–7.1	...	...	d, 8.50 (6.5)	...	...	
2b (X = SC_6H_5)	d, 7.46 (9.5)	...	m, 6–7	d, 8.81 (6.0)	...	...	...	Aryl H:m, 2.7; Methine H:m, 6–7
3b (X = SC_6H_5)	d, 7.46 (9.5)	m, 6–7	...	...	d, 8.57 (6.5)	...	...	Aryl H:m, 2.7; Methine H:m, 6–7
2b (X = $O_2CC_6H_4NO_2$)	d, 7.35 (9.8) d, 7.30 (9.8)	...	m, 5.6	d, 8.65 (6.5)	...	...	...	Aryl H:s, 1.70; Methine H:m, 6.0–6.5
2b (X = $NCH_2CH_2CH_2CH_2$)	d, 7.43 (9.7) d, 7.42 (9.7)	...	...	d, 8.90 (6.4)	...	...	...	Pyrrolidine β-CH_2:m, 8.1–8.4
2b (X = OCH_3)	d, 7.41 (9.8)	...	m, 6.0–6.9	d, 8.87 (6.0)	...	...	...	OCH_3:s, 6.70; Methine H:m, 6.0–6.9
2c (X = Cl)	d, 7.32 (9.8)	...	s, 6.37	...	...	s, 8.62	...	
3c (X = Cl)	d, 7.32 (9.8)	m, 6.9	...	...	...	...	s, 8.40	
2c (X = $NCH_2CH_2CH_2CH_2$)	d, 7.44 (9.7) d, 7.43 (9.7)	...	m, 6.7–7.2	...	...	s, 8.80	...	Pyrrolidine β-CH_2:m, 8.1–8.4
2c (X = OCH_3)	d, 7.44 (9.7)	...	s, 6.78	...	...	s, 8.81	...	OCH_3

[a] Spectra were determined with a Varian A-60 spectrometer with carbon tetrachloride as solvent (deuteriochloroform for **2a** and **b** wherein X = *p*-nitrobenzoyloxy) and with tetramethylsilane as internal standard. Values given are in τ and abbreviations are s for singlet, d for doublet, t for triplet, and m for multiplet. Coupling constants are given in parentheses following the chemical shifts. The amidic proton in **2b** (X = *p*-nitrobenzoyloxy) was shown by dilution experiments to be at τ 6.8 (40% concentration), *ca.* 7.4 (20%), and 7.8 (5%). Spectra of bracketed compounds were determined from a mixture of the pair in question. In addition, **3c** (X = Cl) was obtained pure by repeated crystallization of the mixture containing the isomeric **2c**. Therefore the spectrum of pure **3c** (X = Cl) was obtained.

hydrochloride produced a mixture of the two open-chain isomers, **2b** (X = Cl) and **3b** (X = Cl). Because considerable decomposition occurred during attempted distillation, the crude, partially solid product was analyzed. The nmr spectrum of the mixture exhibited C-methyl doublets at τ 8.74 and at 8.50. The low-field doublet was assigned to **3b** (X = Cl) because of the expected greater deshielding of the protons of a methyl group bound to carbon bearing chlorine rather than to carbon bearing an amidic nitrogen. The N-methyl absorptions appeared simply as one doublet owing to splitting by phosphorus (J = 9.9 cps). From the relative areas of the C-methyl doublets the ratio of **2b** (X = Cl):**3b** (X = Cl) was 75:25.

These assignments were supported by the results obtained from a study of the reaction of P-(2,2-dimethyl-1-aziridinyl)-N,N,N′,N′-tetramethylphosphonic diamide (**1c**) with pyridine hydrochloride. Again a mixture of isomers was produced. Repeated crystallization from cyclohexane produced a pure sample of **3c** (X = Cl) as white needles, melting at 117–119°. The nmr spectrum of this compound exhibited a C-dimethyl singlet at τ 8.40, whereas the isomeric product **2c** (X = Cl) had its analogous singlet at 8.62 as ascertained from the nmr spectrum of the mixture. Again the N-methyl absorptions appeared as a doublet (J = 9.8 cps) in the mixture. The ratio of the areas of the C-dimethyl singlets in the mixture was 76:24; this time the signal at lower field was the larger one of the two. Because **1c** would be expected to cleave to a tertiary carbonium ion more readily then **1b** would to a secondary carbonium ion, the isomers having the lower field C-methyl absorptions must correspond to the product derived formally from a carbonium ion; the C-methyl absorptions at higher field correspond to the isomers derived by direct attack of chloride ion either upon the aziridine ring itself, or its protonated counterpart.

The reaction product from **1b** and thiophenol was also a mixture. The low-field C-methyl doublet in the nmr spectrum of this mixture was assigned in analogous fashion to the methyl group attached to the carbon atom bound to the sulfur. The ratio of isomers was 82:18 with **2b** (X = phenylthio) predominating.

The addition of *p*-nitrobenzoic acid to **1b** yielded a complex from which **2b** and/or **3b** (X = *p*-nitrobenzoyloxy) was liberated by treatment with aqueous sodium carbonate. This solid had a rather broad melting range and may have been a mixture of isomers. Its nmr spectrum could not be interpreted.

After several crystallizations from benzene, a sharp-melting compound was obtained. The nmr spectrum of this compound (see Figure 1) showed a C-methyl doublet at τ 8.65 (J = 6.5 cps), a multiplet at 5.6 (2 H) ascribed to the methylene group, and a broad multiplet at 6.0–6.5 ascribed to the methine proton. The NH absorption, as previously discussed, was obscured by the N-methyl absorptions which appeared as two doublets centered at τ 7.30 and 7.35 (J_{PH} = 9.8 cps for each doublet). This compound was assigned structure **2b** (X = *p*-nitrobenzoyloxy) because of the position of the methylene protons relative to the methine proton; protons on the carbon atom bound to the oxygen atom would be expected to appear at lower field than the protons on the carbon bound to the nitrogen. Thus, the major product of ring opening of **1b** was again derived from direct attack of the nucleophile on the ring. The source of the magnetic nonequivalence of the dimethylamino groups of **2b** (X = *p*-nitrobenzoyl-

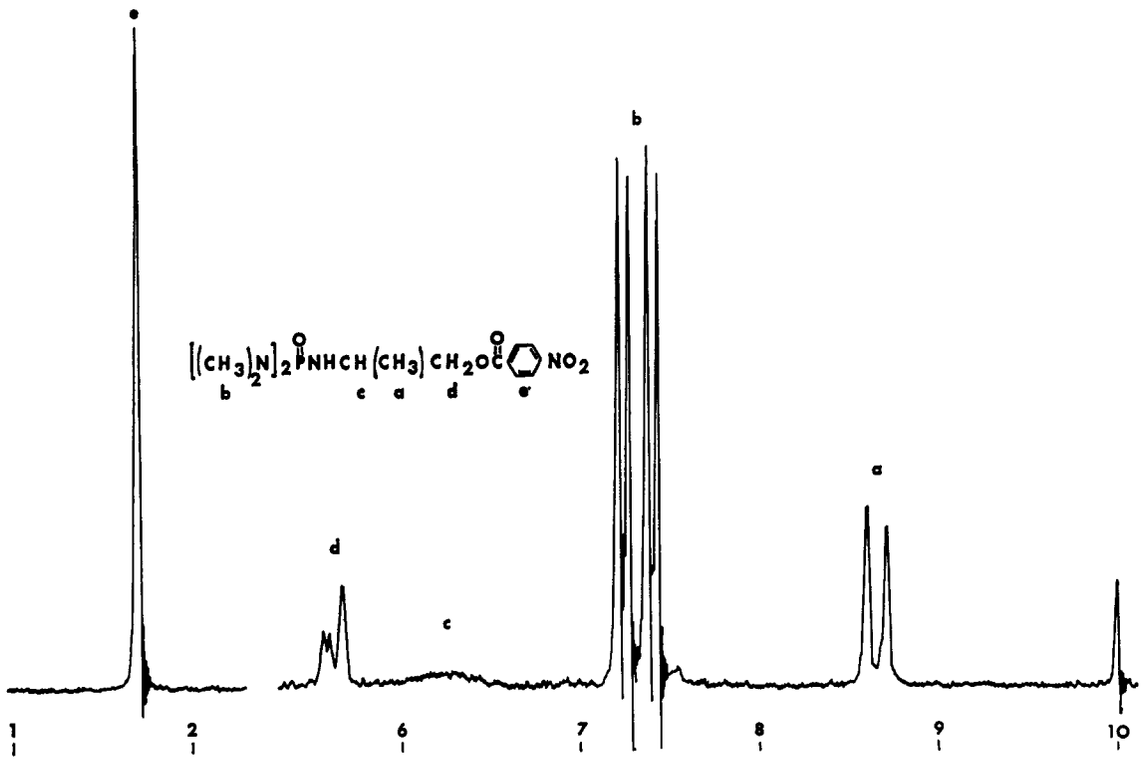


Figure 1. Nmr spectrum of 2b (X = *p*-nitrobenzoyloxy) taken with a Varian A-60 spectrometer. Concentration was 18% in $CDCl_3$ and TMS was employed as internal standard. Chemical shifts are given as τ.

oxy) might be the center of asymmetry present in the molecule. Although this center is five bonds removed from the protons involved, Bentrude has reported the occurrence of magnetic nonequivalence of the CH_3O groups in a dimethyl phosphate and he tentatively assigned the cause to a center of asymmetry five bonds removed from the nonequivalent protons.[3]

The reaction of **1b** with pyrrolidine produced a mobile liquid, the nmr spectrum of which had a sharp C-methyl doublet at τ 8.90. This compound, which is probably **2b** (X = 1-pyrrolidinyl), also exhibited magnetically nonequivalent dimethylamino groups. The assignment of structure was based on the conclusions of Clapp,[4] who found that C-substituted aziridines reacted in the presence of ammonium chloride with primary and secondary amines to form products resulting from rupture of the nitrogen–primary carbon bond. Treatment of **1b** with sodium methoxide in methanol gave a liquid product which was assigned on a similar basis structure **2b** (X = OCH_3).

Unexpectedly, compound **1c**, when treated with *p*-nitrobenzoic acid, produced N,N-dimethyl-*p*-nitrobenzamide as the only isolated product. Identification was made by means of mixture melting point and infrared comparison with an authentic sample. The reactions of **1c** with pyrrolidine, and with sodium methoxide in methanol produced crystalline adducts assigned the structures **2c** (X = 1-pyrrolidinyl) and **2c** (X = OCH_3), respectively. The nmr spectrum of **2c** (X = 1-pyrrolidinyl) again showed magnetically nonequivalent dimethylamino groups; because this compound has no asymmetric carbon atom, the source of the magnetic nonequivalence in this compound is hindrance to internal rotation.

(3) W. G. Bentrude, *J. Am. Chem. Soc.*, **87**, 4026 (1965).
(4) L. B. Clapp, *ibid.*, **70**, 184 (1948).

In conclusion, aziridine rings bound to phosphorus in phosphonic diamides add various reagents H–Y (Y = Cl, *p*-nitrobenzoyloxy, phenylthio, 1-pyrrolidinyl, and OCH_3) and yield the corresponding phosphoric triamides. When one of the aziridine carbons is substituted and the reaction medium is basic, the addition is slow and single products corresponding to an attack on the unsubstituted aziridine carbon are obtained. When the reaction medium is acidic, the addition is quite rapid and two isomeric products are isolated. The proportion of the product derived from an attack on the unsubstituted aziridine carbon decreases with increasing substitution on the other aziridine carbon. These observations are in good agreement with previously described additions to basic aziridines.[5] However, the C-substituted aziridines with a nitrogen activated toward nucleophilic attack, unlike the basic aziridines, yield a single adduct in the absence of acid catalysts.

Experimental Section

Preparation of the P-1-Aziridinyl-N,N,N′,N′-tetramethylphosphonic Diamides.—N,N,N′,N′-Tetramethylphosphorodiamidic chloride[6] (1 equiv) in ether solution was added to a stirred ethereal solution of 1.1 equiv each of the aziridine and triethylamine while cooling in an ice bath. The mixture was allowed to stand at room temperature overnight. After filtration, the mixture was concentrated and distilled under reduced pressure.

Reaction of the Aziridines 1a–c with Pyridine Hydrochloride.—Pyridine hydrochloride (1 equiv) in chloroform containing 1 equiv of the aziridine **1a**, **b**, or **c** was heated under reflux for 4 hr and concentrated to the crude product. Compound **2a** (X = Cl) could not be distilled, the mixture of **2b** (X = Cl) and **3b** (X = Cl) distilled with decomposition to produce a waxy solid, and the mixture of **2c** (X = Cl) and **3c** (X = Cl) was an oily solid from

(5) (a) D. S. Tarbell and P. Noble, Jr., *ibid.*, **72**, 2657 (1950); V. B. Schatz and L. B. Clapp, *ibid.*, **77**, 5113 (1955).
(6) H. G. Cook, J. D. Ilett, B. C. Saunders, G. J. Stacey, H. G. Watson, I. G. E. Wilding, and S. G. Woodcock, *J. Chem. Soc.*, 2921 (1949).

which white needles of pure **3c** (X = Cl) were obtained after three crystallizations from cyclohexane.

Reaction of the Aziridines 1a and b with Thiophenol.—Thiophenol (1 equiv) and 1 equiv of **1a** or **b** were heated under reflux in carbon tetrachloride for 24 hr. The reaction mixture was washed (aqueous Na_2CO_3), dried (Na_2SO_4), and concentrated. The products could not be distilled without decomposition.

Reaction of the Aziridines 1a–c with *p*-Nitrobenzoic Acid.—A solution of 2 equiv of *p*-nitrobenzoic acid and 1 equiv of the aziridine **1a** or **b** was heated under reflux in chloroform for 16 hr. The solvent was removed and the resulting solid was recrystallized from benzene. The products were complexes of *p*-nitrobenzoic acid with the adducts. Equimolar quantities of *p*-nitrobenzoic acid and aziridine would produce the complex and unreacted aziridine after 16 hr. The ultraviolet spectrum of the complex from **1a** in ethanol exhibited λ_{max} 262 mμ (ε 21,500); the complex from **1b**, λ_{max} 263 mμ (ε 22,100). Treatment of a methylene chloride solution of the complex with aqueous sodium carbonate produced the corresponding adduct **2a** (X = *p*-nitrobenzoyloxy) or **2b** (X = *p*-nitrobenzoyloxy), which was recrystallized from benzene. Compound **2a** (X = *p*-nitrobenzoyloxy) exhibited λ_{max} 258 mμ (ε 12,400); **2b** (X = *p*-nitrobenzoyloxy), λ_{max} 258 mμ (ε 13,600). Treatment of **1c** with *p*-nitrobenzoic acid (2 equiv) produced an oil which was washed (aqueous Na_2CO_3) to remove any unreacted or complexed *p*-nitrobenzoic acid. The organic phase was dried (Na_2SO_4) and evaporated. The residue was diluted with ether and N,N-dimethyl-*p*-nitrobenzamide was deposited (0.96 g from 2.05 g of **1c**). Identification was made by mixture melting point and infrared comparison with an authentic sample.

Reaction of the Aziridines 1a–c with Pyrrolidine.—The aziridine **1a**, **b**, or **c** was heated in pyrrolidine under reflux for 16 hr (**1a** and **b**), or for 96 hr (**1c**). The first two adducts could be distilled under reduced pressure, although considerable decomposition occurred with **2b** (X = 1-pyrrolydinyl). A small forerun of unreacted **1b** was obtained when the reaction time was 16 hr. Compound **2c** (X = 1-pyrrolidinyl) was obtained as a mushy solid when the crude product was kept at 0.2 mm for 24 hr; **2c** (X = 1-pyrrolidinyl) was further purified by dissolving it in pentane and chilling (ice–methanol bath). The process was repeated four times and white needles, mp 48.5–50°, were obtained.

Reaction of the Aziridines 1a–c with Methanol Containing Sodium Methoxide.—Sodium (1 equiv) in excess methanol and 1 equiv of the aziridine **1a**, **b**, or **c** was heated under reflux for 16 hr (**1a** and **b**), or 92 hr (**1c**). After cooling to room temperature, sufficient acetic acid was added to neutralize the sodium methoxide, and the methanol was evaporated *in vacuo*. The product was taken up in ether, filtered, and concentrated. Distillation under reduced pressure produced **2a** (X = OCH_3) and **2b** (X = OCH_3). A forerun of unreacted aziridine was obtained from the reactions of **1b** and **c**. In the latter case, once the unreacted aziridine had been removed, pure **2c** (X = OCH_3) was obtained from the residue by sublimation at 80–85° (0.025 mm).

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Ketenes. X. Heterocyclic Systems Derived from Dimethylmalonyl Chloride[1]

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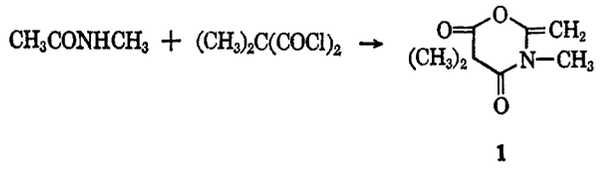
Dimethylmalonyl chloride was found to react with a number of N-monosubstituted amides to afford dihydro-2-methylene-4H-1,3-oxazine-4,6(5H)-diones and with N-monosubstituted thioamides and N,N′-disubstituted amidines to give the corresponding thiazine and pyrimidine analogs. Several reactions producing these heterocycles are described. The dihydro-2-methylene-4H-1,3-oxazine-4,6(5H)-diones were found to rearrange to 3-oxoglutarimides if the methylene group was substituted with one or two groups other than hydrogen. The reaction of dimethylmalonyl chloride with aromatic amides unsubstituted on the nitrogen gave 4H-1,3-oxazine-4,6(5H)-diones. A similar reaction with aliphatic amides unsubstituted on the nitrogen gave dihydro-2-methylene-4H-1,3-oxazine-4,6(5H)-diones; however, if triethylamine was used as an acid acceptor, dihydro-3-isobutyryl-2-methylene-4H-1,3-oxazine-4,6(5H)-diones resulted. Imines having at least one α-methylene group and dimethylmalonyl chloride gave substituted 2,4(1H,3H)-pyridinediones.

Ziegler and Meindl[2,3] have described the reactions of monosubstituted malonyl chlorides with aromatic amides and also with certain enamines. We have examined the reaction of dimethylmalonyl chloride[4] with a number of amides, thioamides, and enamines, and the present paper is a report of this work.

Dimethylmalonyl chloride was found to react with N-methylacetamide in the presence of triethylamine to produce a compound subsequently identified as dihydro-3,5,5-trimethyl-2-methylene-4H-1,3-oxazine-4,6(5H)-dione (**1**). The structural assignment of **1** was based on its elemental analysis, on its infrared and nmr spectra, and on some of its chemical reactions which are described later in the paper.



1

This ring closure was found to be a general reaction for a number of N-monosubstituted amides and thioamides with dimethylmalonyl chloride. Variations in the R groups from H to CH_3 to C_6H_5 did not affect the course of the reaction or greatly influence the ultimate yield. Table I affords a list of the amides which combined with dimethylmalonyl chloride to give cyclic compounds. N-Methylcrotonamide afforded a butadiene-type product (**2a**) in 84% yield, and 2-pyrrolidinone gave the bicyclic product (**2b**) in 65% yield. The alternate carbon–nitrogen closure leading to the 3-oxoglutarmides **3** was not observed in any case.

The use of a tertiary amine as a hydrogen chloride acceptor was unnecessary when R′ and R″ were not hydrogen. N-Methylisobutyramide and dimethylmalonyl chloride when refluxed in ethylene dichloride afforded a 90% yield of dihydro-2-isopropylidene-3,5,5-trimethyl-4H-1,3-oxazine-4,6(5H)-dione (**2c**). How-

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(2) E. Ziegler and H. Meindl, *Monatsh. Chem.*, **95**, 1318 (1964).

(3) E. Ziegler, F. Hradetzky, and K. Belegratis, *ibid.*, **96**, 1347 (1965).

(4) R. G. Nations and K. C. Brannock (to Eastman Kodak Co.), U. S. Patent 3,220,935 (1965).