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STUDIES OF ACYL ISOCYANATE—IV[1]

SYNTHESIS OF DIOYL DIISOCYANATES*

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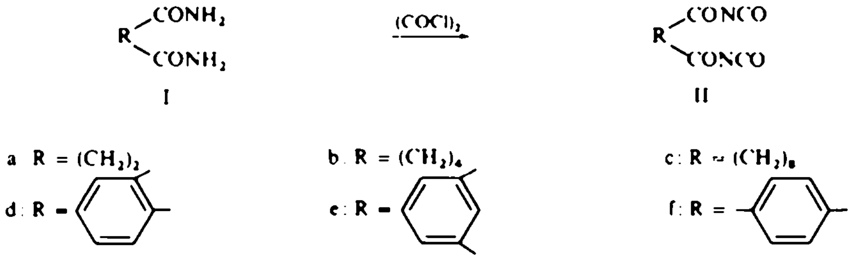
Abstract An attempt has been made to prepare aliphatic and aromatic dioyl diisocyanates according to Speziale's method. The reactions of sebac-, phthal-, isophthal- and terephthalamide with oxalyl chloride progressed smoothly, forming the corresponding isocyanate, which in turn gave quantitatively the corresponding bifunctional acylurea on treatment with aniline in all cases except phthaloyl isocyanate. In the reaction of succin- or adipamide, however, the amide required a large amount of oxalyl chloride, and in addition to the expected isocyanate, 1,2-bis[2-(1,3-oxazolidine-4,5-dione)] ethanediylidene or 1,3-adipoylimidazoline-2,4,5-trione was obtained. The hydrazinolysis and anilinolysis of the above by-products are also presented

ALTHOUGH an excellent method[2] for the preparation of acyl isocyanates has been reported, no information is available for the preparation of dioyl diisocyanates. In previous papers in which the di- or trimerization[3] and dipolar cycloaddition reaction[4] of benzoyl or thiobenzoyl isocyanates were investigated, it was shown that 1,2- and 1,4-dipolar cycloaddition products were formed.

The preparation of the dioyl diisocyanate from aliphatic or aromatic diamides was investigated by application of Speziale's method in order to provide starting material for the synthesis of new heterocyclic compounds and interesting poylmers.

The preparation of dioyl diisocyanates (II) was generally undertaken in the following manner: a mixture of the corresponding amide (I; 0·02 mole) and oxalyl chloride (0·06 mole) in dichloroethane (30 ml) was refluxed for 3 hr. In the case of sebac- (Ic), phthal- (Id), isophthal- (Ie) or terephthalamide (If), the reaction progressed smoothly with evolution of carbon monoxide and hydrogen chloride, and the corresponding diisocyanate was obtained in excellent yield.



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* A part of this work was presented at the 19*th Annual Meeting of the Chemical Society of Japan* Yokohama, March (1966).

The same reaction using succin- (Ia) or adipamide (Ib) formed the corresponding diisocyanate in poor yield, leaving a large amount of unreacted amide.

By varying the amount of succinyl isocyanate (IIa) and the reaction time, the results were as follows: for times for 2, 3, 5 and 12 hr, the yield of IIa was 17, 34, 33 and 33%, respectively. After the reaction of Ia by the above general procedure for 3 hr, an additional 0·06 mole of oxalyl chloride was added and the reaction mixture refluxed for 7 hr. It was found that IIa and yellow needles (III), m.p. 189° dec, were formed in 79 and 13% yield, respectively.

In the reaction of Ib with oxalyl chloride for 15 hr according to the general procedure, adipoyl isocyanate (IIb) was formed only in 12% yield and the unreacted Ib recovered. When three equal parts of oxalyl chloride (0·06 mole × 3) were added to the reaction mixture at intervals of 3 hr and the mixture heated under reflux for 15 hr, IIb and white crystals (IV), m.p. 312° dec, formed in 40 and 27% yield, respectively, and a small amount of Ib was recovered.

With the exception of isophthaloyl (IIe) and terephthaloyl isocyanate (IIf),* the above diisocyanates decomposed on vacuum distillation, yielding the corresponding nitrile. Consequently, except for IIe and IIf, the yields of II are those of the corresponding bifunctional acylureas (V) which were obtained by the reaction with aniline.† The yields and properties of II and V are summarized in Table 1.

The properties of ethyl- (VI) and phenylurethanes (VII) of II, which were obtained by the reaction with ethanol and phenol, respectively, are shown in Table 2.

However, the reaction of IId with ethanol or phenol did not give the corresponding urethanes, but phthalimide was obtained quantitatively. The formation of phthalimide is due to decomposition of the urethanes, as no phthalimide was obtained in the reaction of IId with aniline.

The yellow needles (III) which were obtained in the reaction of Ia, were in agreement with the formula $C_8H_4O_6N_2$. As is shown in Fig. 1, the IR spectrum of III shows very distinct bands at 1830, 1740 and 1680 cm^{-1}, besides the weak band at about 3200 cm^{-1}.

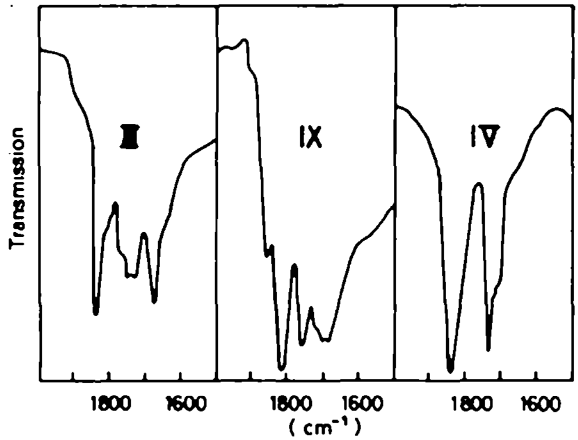

FIG. 1 IR spectra of II, IV and IX in KBr disk.

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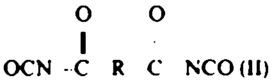
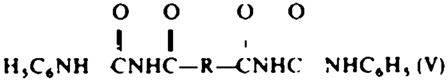
* Recently, we learned that the reaction of terephthalamide with oxalyl chloride in CCl_4 was independently carried out.[5]

† It was made clear that IIe or IIf gave the corresponding urea quantitatively in the reaction with aniline.

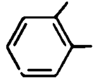
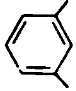
TABLE 1. DIOYL DIISOCYANATES AND ACYLUREAS



$OCN\text{-}\overset{O}{\overset{\|}{C}}\text{-}R\text{-}\overset{O}{\overset{\|}{C}}\text{-}NCO$ (II)



$H_5C_6NH\overset{O}{\overset{\|}{C}}NH\overset{O}{\overset{\|}{C}}\text{-}R\text{-}\overset{O}{\overset{\|}{C}}NH\overset{O}{\overset{\|}{C}}NHC_6H_5$ (V)

	R	b.p.	Yield[a]	ν_{NCO}[b]	m.p.	$\nu_{C=O}$[c]		Found (%)			Calc (%)		
		°C/mm Hg	%	cm⁻¹	°C	cm⁻¹		C	H	N	C	H	N
1	$(CH_2)_2$	—	(79)	2260	219	1715	1610	60·86	4·83	15·37	61·01	5·12	15·81
2	$(CH_2)_4$	—	(40)	2270	218	1697	1603	60·42	5·60	14·74	62·81	5·80	14·65
3	$(CH_2)_8$		(quant)	2270	198	1698	1608	65·39	7·13	12·72	65·73	6·90	12·78
4			(17)	2270	191	1695	1605	66·03	4·60	14·03	65·66	4·51	13·92
5		126/2[d]	83	2260	238	1695	1602	65·25	4·38	13·81	65·66	4·51	13·92
6		158/3[d]	79	2270	237	1698	1602	65·26	4·38	13·62	65·66	4·51	13·92

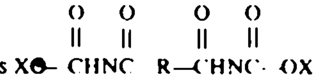
[a] Figures in parentheses represent the yield of V.

[b] Measured in dichloroethane soln.

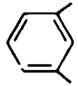
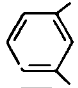
[c] Measured in KBr disk.

[d] The distillate solidified at room temperature respectively, but m.ps were not measured. IIe: m.p. 100–102° (Ref. 5).

TABLE 2. ACYLURETHANES



$XO\overset{O}{\overset{\|}{C}}NH\overset{O}{\overset{\|}{C}}—R—\overset{O}{\overset{\|}{C}}NH\overset{O}{\overset{\|}{C}}OX$

Urethane			m.p.	ν_{CO}*		Found (%)			Calc (%)		
	R	X	°C	cm⁻¹		C	H	N	C	H	N
VIa	$(CH_2)_2$	Et	157	1760	1690	46·23	6·12	11·04	46·15	6·20	10·77
VIb	$(CH_2)_4$	Et	180	1762	1692	50·00	7·24	9·92	49·99	6·99	9·97
VIc	$(CH_2)_8$	Et	153	1760	1690	55·33	7·88	7·98	55·80	8·20	8·13
VIe		Et	192	1763	1681	54·63	5·41	9·20	54·54	5·23	9·09
VIf		Et	236†	1765	1681	54·44	5·28	9·22	54·54	5·23	9·09
VIIa	$(CH_2)_2$	Ph	174	1778	1715	60·20	4·58	8·01	60·67	4·53	7·86
VIIb	$(CH_2)_4$	Ph	173	1780	1712	62·36	5·15	7·16	62·46	5·24	7·29
VIIc	$(CH_2)_8$	Ph	158	1776	1710	65·37	6·44	6·43	65·44	6·41	5·36
VIIe		Ph	166	1790	1717	65·03	3·86	6·84	65·34	3·99	6·93
VIIf		Ph	232†	1783	1690	65·04	3·78	7·07	65·34	3·99	6·93

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* IR spectra were measured in KBr disk.

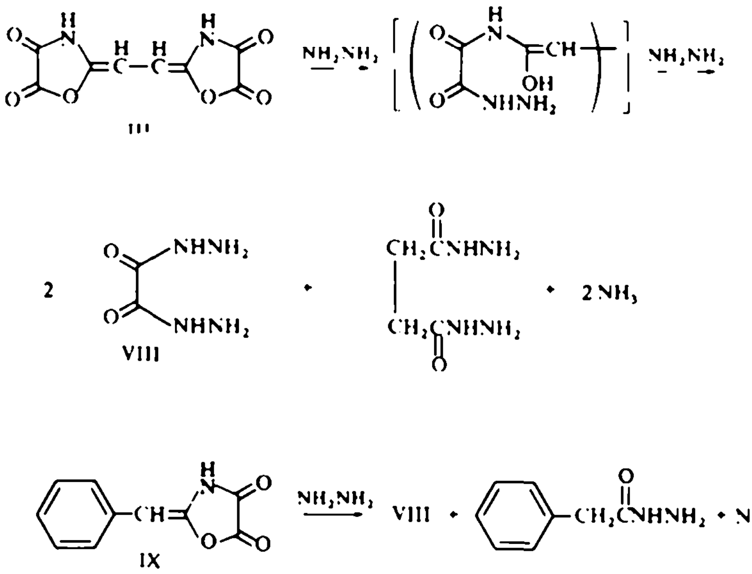
† The m.ps of VIf and VIIf, 227–228° and 178–179° dec, respectively, have been reported R. Neidlein *et al.*, *Chem. Ber.* **100**, 698 (1967).

In addition, the reaction of III with hydrazine hydrate gave oxalic dihydrazide (VIII) and succinhydrazide in 2:1 molar ratio.

A similar reaction of 2-benzylidene-1,3-oxazolidine-4,5-dione (IX),[2b] whose IR spectrum is similar to that of III as shown in Fig. 1, with hydrazine hydrate afforded VIII and phenylacetohydrazide.

On the basis of these observations, the compound III is 1,2-bis[2-(1,3-oxazolidine-4,5-dione)]ethanedilylidene. The reaction course of III with hydrazine is illustrated in Scheme 1.

Although the reaction course of amide with oxalyl chloride is not clear, Speziale *et al.*[2] postulated the possible path through the 1,3-oxazolidine-4,5-dione intermediate. In fact, the thermal decomposition of IX gives phenylacetyl isocyanate.



SCHEME 1

However, the isocyanate IIa was not formed on heating of III in dichloroethane or xylene. It has been known that 2-benzylidene-1,3-thiazolidine-4,5-dione does not give any phenylthioacetyl isocyanate.[6]

On the other hand, the white needles (IV) obtained in the reaction of Ib agree with the formula $C_9H_8O_5N_2$. The mass spectrum of IV shows the parent peak at *m/e* 224 and the IR spectrum exhibits characteristic bands in the region from 1840 to 1700 cm^{-1} as shown in Fig. 1.

When IV was treated with hydrazine hydrate, VIII and a new compound (X), m.p. 318° dec, were obtained. Also, the treatment with aniline gave oxanilide and X.

The compound X agrees with the formula $C_7H_8O_2N_2$, whose IR spectrum exhibits characteristic bands at 3200 and about 1700 cm^{-1} ascribed to the NH and CO groups, respectively. As illustrated in Fig. 2, the NMR spectrum in CF_3CO_2H exhibits multiplets at τ 7·7 (2H), τ 7·15 (5H) and a broad singlet at τ 10·27 (1H).

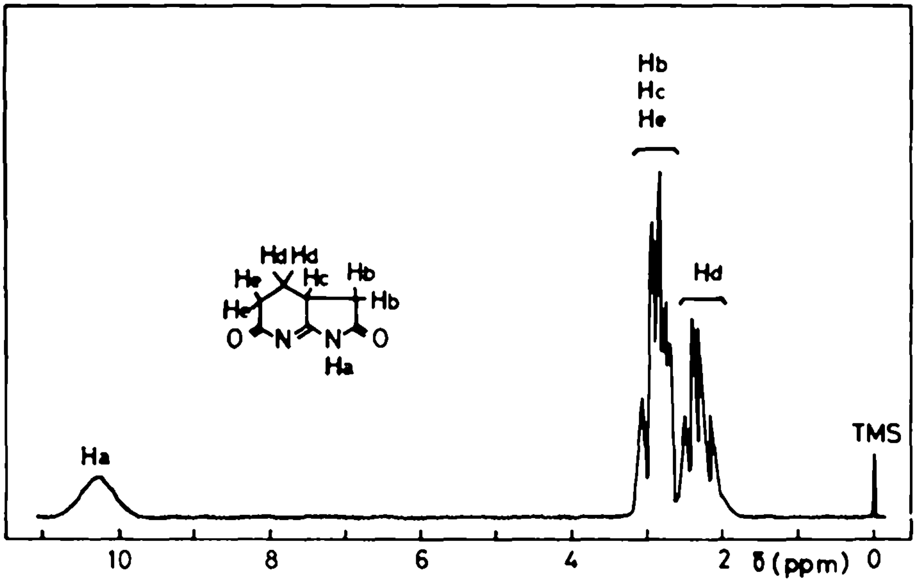


Fig. 2. NMR spectrum of X in CF_3CO_2H.

Also, the mass spectrum is shown in Fig. 3.

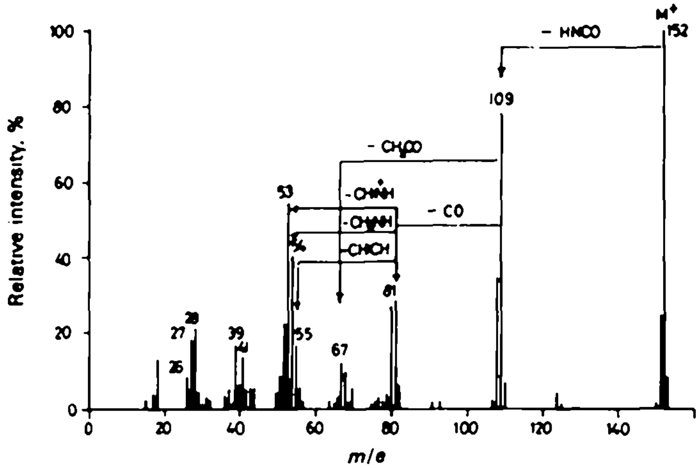
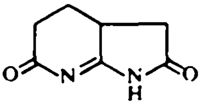
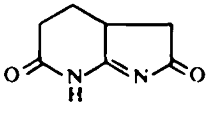


Fig. 3. Mass spectrum of X.

On the basis of the above observations, the structure of X is consistent with 3,3a,4,5-tetrahydro-7-azaindole-2,6-dione (Xa) or its isomer (Xb).

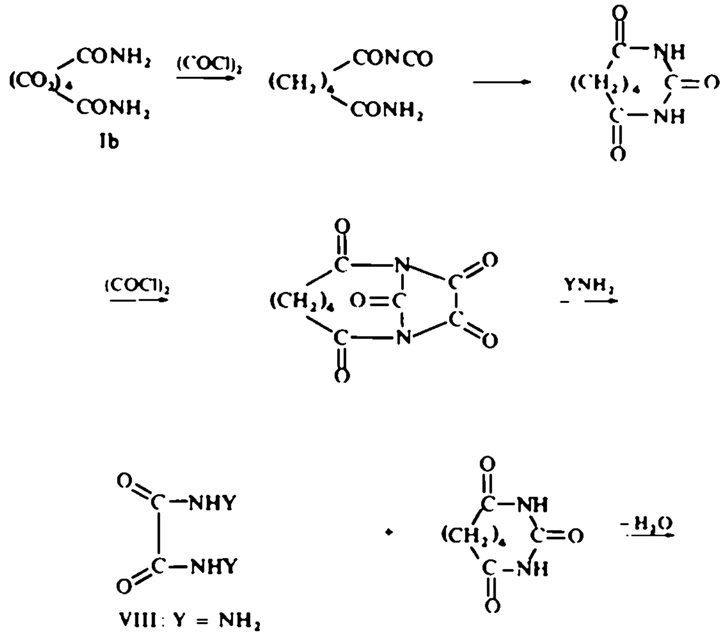


Xa



Xb

On the basis of the above facts, the structure of IV is 1,3-adipoylimidazoline-2,4,5-trione, and its formation and aminolysis course are shown in Scheme 2.



SCHEME 2

EXPERIMENTAL

M.ps and b.ps are uncorrected. IR spectra were recorded on a Nippon Bunko IR-S spectrophotometer. NMR spectra were determined at 60 Mc with a Japan Electron Optics JNM-3H-60 NMR spectrometer, using TMS as internal reference. Mass spectra were obtained on a Hitachi RMU-6D instrument using a heated inlet, an ionization energy of 70 eV, an inlet temp of 200–250°, and a source temp of 250°. Elemental analyses were done by Mr. Eiji Shiozaki.

Materials. Commerical grades of succin- (Ia), m.p. 260°, and phthalamide (Id), m.p. 228°, were used. Adip- (Ib), m.p. 221°, sebac- (Ic), m.p. 173°, isophthal- (Ie), m.p. 275°, and terephthalamide (If), m.p. > 300°, were prepared by the reaction of the corresponding dichloride with conc NH_4OH, and were purified by recrystallization. Oxalyl chloride was prepared by the reaction of oxalic acid with PCl_5 and was purified by fractional distillation: b.p. 58–64°.

General method for the preparation of isocyanate. After oxalyl chloride (0·06 mole) was added to a suspension of the corresponding amide (0·02 mole) in dichloroethane (30 ml), the mixture was refluxed for 3 hr. During this time a clear soln was obtained with evolution of CO and HCl. In order to estimate the yield of the isocyante, after the solvent and oxalyl chloride were removed *in vacuo* aniline was added to the residue, yielding the corresponding urea (V) which was purified by recrystallization from dioxan, except for the reactions of Ie and If.

In the case of Ie or If, vacuum distillation of the above-mentioned residue afforded the corresponding isocyanate IIe or IIf. The results are shown in Table 1.

When the residue or isocyanate was treated with ethanol or phenol in place of aniline, the corresponding urethane, VI or VII, was obtained. The results are summarized in Table 2.

Reaction of Ia *with oxalyl chloride.* After a suspension of Ia (2·32 g) and oxalyl chloride (7·6 g) in dichloroethane (30 ml) was refluxed for 3 hr, oxalyl chloride (7·6 g) was added and heating under reflux continued for another 7 hr. After cooling, a yellow ppt was collected by filtration. From the filtrate the solvent and oxalyl chloride were removed *in vacuo*, and then aniline was added to the residue, yielding the corresponding urea Va which was purified by recrystallization from dioxan; yield 5·6 g (79%).

Reprecipitation from the DMSO soln of the above yellow ppt by addition of ether gave III as yellow needles, m.p. 189° dec, yield, 0·57 g (13%). (Found: C, 43·03; H, 2·21; N, 12·67. Calc. for $C_8H_4O_6N_2$: C, 42·87; H, 1·80; N, 12·50%.)

Reaction of Ib *with oxalyl chloride*. After a suspension of Ib (2·88 g) and oxalyl chloride (7·6 g) in dichloroethane (30 ml) was refluxed for 3 hr, additional oxalyl chloride (7·6 g × 2) was added at intervals of 3 hr and it was refluxed for 12 hr. After it had cooled, a brown solid was collected by filtration. Treatment of the filtrate as above gave Vb; yield 3·0 g (40%).

Recrystallization of the brown solid from acetone using active charcoal afforded IV as white needles, m.p. 312° dec, yield, 1·2 g (27%). (Found: C, 48·29; H, 3·46; N, 12·42. Calc. for $C_9H_8O_5N_2$: C, 48·22; H, 3·60; N, 12·50%). IR (KBr) ν_{CO} cm^{-1}: 1840, 1810 (sh), 1740, 1720 (sh) and 1700. UV λ_{max}^{THF} mμ (log ε): 229 (3·96), 303 (1·95).

Reaction of III *with hydrazine*. A mixture of III (0·80 g; 3·6 mmole) and hydrazine hydrate (5 ml) in EtOH (40 ml) was refluxed for 10 min. After the mixture had cooled, filtration afforded colourless needles (0·42 g; 6·4 mmole), m.p. 232°, which were proved, by the admixed m.p. and IR spectrum, to be identical with oxalic dihydrazide (VIII).

After the filtrate had been concentrated *in vacuo*, colourless needles, m.p. 161°, identical with the authentic sample of succin hydrazide were obtained, yield, 0·46 g (3 mmole).

Reaction of 2-benzylidene-1,3-oxazolidine-4,5-dione (IX) *with hydrazine*. A mixture of IX (1·9 g; 10 mmole) and hydrazine hydrate (7 ml) in EtOH (50 ml) was refluxed for 20 min. Treatment as above gave 1·0 g (8 mmole) of VIII and 1·1 g (7 mmole) of phenylacetohydrazide as colourless needles, m.p. 117° (lit.[7] 114°), whose IR spectrum showed at 3300 and 1640 cm^{-1} ascribed to the NH and CO groups, respectively, and elemental analyses in agreement with the formula $C_8H_{10}ON_2$. (Found: C, 63·83; H, 6·71; N, 18·55%).

Reaction of IV *with hydrazine*. A mixture of IV (0·43 g; 1·9 mmole) and hydrazine hydrate (3 ml) in EtOH (30 ml) was refluxed for 10 min. Treatment as above afforded 0·18 g (1·5 mmole) of VIII and 0·24 g (1·6 mmole) which on recrystallization from acetone–water (1:1) gave colourless needles of X, m.p. 318° dec. (Found: C, 55·25; H, 5·33; N, 18·65. Calc. for $C_7H_8O_2N_2$: C, 55·25; H, 5·30; N, 18·41%).

Reaction of IV *with aniline*. A suspension of IV (0·43 g; 1·9 mmole) in aniline (5 ml) was refluxed for 5 min. After the mixture had cooled, benzene was added, yielding colourless crystals which were extracted with EtOH leaving 0·24 g (1·1 mmole) of colourless needles, m.p. 246°,* whose IR spectrum (3320 and 1670 cm^{-1} assigned to the NH and CO groups) and elemental analyses were in agreement with the formula $C_{14}H_{12}O_2N_2$. (Found: C, 69·81; H, 4·90; N, 11·88%).

The EtOH-extract was concentrated *in vacuo*, yielding 0·34 g (1·5 mmole) of X.

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* The m.p. given in the literature varies from 245 to 254°.

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