437. *Derivatives of Acetoacetic Acid. Part IX.* The Reaction of Diketen with Carbodi-imides.*

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Diketen reacts with carbodi-imides to give 2 : 3-dihydro-2-imino-4-oxo-1 : 3-oxazine derivatives such as have previously been prepared from diketen and *NN'*-disubstituted derivatives of *S*-alkylthiourea. Certain unsymmetrical carbodi-imides gave single products for which structural evidence was afforded by hydrolysis. Infrared and ultraviolet spectroscopic evidence in this field is reported.

CONDENSATION products of keten, substituted ketens, and keten dimers with carbodi-imides have been described in a recent German patent [1] assigned to Farbenfabriken Bayer Aktiengesellschaft of Leverkusen. As typical carbodi-imides falling within the scope of their claims, the Bayer workers listed, amongst others, *NN'*-di*iso*propyl-, *N-tert.*-butyl-*N'-cyclo*hexyl-, *NN'*-di*cyclo*hexyl-, and *N-cyclo*hexyl-*N'-tert.*-octyl-carbodi-imide, and examples of the reaction of these derivatives with diketen were given. Arylcarbodi-imides, *e.g.*, *N-tert.*-butyl-*N'*-phenylcarbodi-imide and *NN'*-diphenylcarbodi-imide were also quoted as possible starting materials but no experimental details of examples involving arylcarbodi-imides were given. In all the examples involving reaction of diketen with carbodi-imides, good yields of sharp-melting solid products were obtained. No analyses for these solid products were given and no suggestions as to their structure were made; they were described as hitherto unknown addition compounds.

We found the reaction of diketen with *NN'*-dialkylcarbodi-imides to proceed smoothly in boiling benzene, to give good yields of crystalline products in agreement with the findings of the German workers. Analytical values were consistent with the supposition that the products arose from the simple addition of one mole of diketen to one mole of the carbodi-imide. The reaction of *NN'*-diethylcarbodi-imide with diketen, not described in the above patent, gave direct structural evidence for this group of compounds since the product so obtained proved to be identical with that previously obtained [2] by one of us from the reaction of diketen with *NN'*-diethyl-*S*-methyl*iso*thiourea with the elimination of methanethiol. The reaction of carbodi-imides with diketen may therefore be formulated as below, the products being 2-imino-1 : 3-oxazine derivatives of general formula (II).
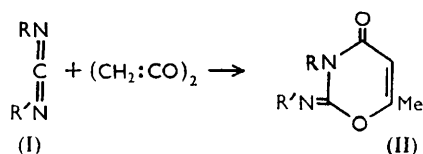
Comparison of the infrared spectrum of the product arising from *NN'*-diethylcarbodi-imide with that of authentic (II; R = R' = Et) afforded structural confirmation, and infrared spectroscopic evidence (see Table 4) showed that the products arising from [I; R = R' = Pr^{i}; R = R' = *cyclo*hexyl; R = *cyclo*hexyl, R' = Bu^{t}; and R = *cyclo*hexyl, R' = 1 : 1 : 3 : 3-tetramethylbutyl (" *tert.*-octyl ")] had the same general structure. The ultraviolet spectroscopic evidence, presented in Table 1, was in general agreement.

The oxazines (II, where R and R' are both alkyl) are weak bases and dissolve in dilute hydrochloric acid. Potentiometric titration with perchloric acid in acetic acid showed a sharp inflection denoting a monoacid base; pK values ($\pm$ 0·05) for certain of these

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* Part VIII, *J.*, 1954, 854.

[1] Hofmann, Schmidt, Wamsler, Reichle, and Moosmüller, G.P. 960,458 (21/3/57).

[2] Lacey, *J.*, 1954, 845.

derivatives were: R = R′ = Et 9·35, R = R′ = Pr^i 9·85, R = *cyclo*hexyl, R′ = Bu^t 10·70.

Acid-hydrolysis of the oxazines (II; R = R′ = *cyclo*hexyl; R = R′ = Pr^i) afforded not only the corresponding dioxo-oxazines (III) with a mole of aliphatic amine as found previously [2] for (II; R = R′ = Et), but also the ureas (IV) and the isomeric uracils (V). Formation of the last two types of product had previously been observed with only the aromatic substituted oxazines (II).
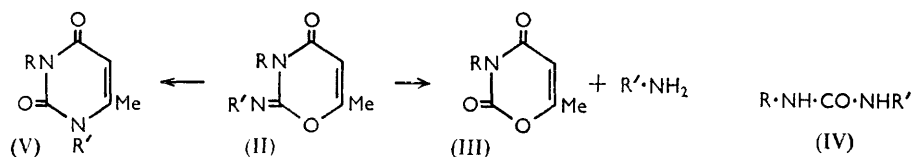
Hydrolysis of the compound (II; R = *cyclo*hexyl, R′ = Bu^t) with dilute hydrochloric acid (3%) gave the dione (III; R = *cyclo*hexyl) and, the urea (IV; R = *cyclo*hexyl, R′ = Bu^t) and some *cyclo*hexylurea. The use of stronger acid (15%) gave the dioxo-oxazine and *cyclo*hexylurea but none of the dialkylurea. It was established that the urea (IV; R = *cyclo*hexyl, R′ = Bu^t) is converted into *cyclo*hexylurea in high yield with removal of the elements of *iso*butene by heating in the presence of acid. This reaction is effectively the reverse of that disclosed by Harvey and Caplan,[3] who showed that urea can be converted into a *tert.*-alkylurea by treatment with a tertiary alcohol in the presence of sulphuric acid. Hydrolysis of the oxazine (II; R = *cyclo*hexyl, R′ = 1 : 1 : 3 : 3-tetramethylbutyl) with hydrochloric 15% acid similarly gave the dione (III; R = *cyclo*hexyl) and *cyclo*hexylurea; the urea (IV; R = *cyclo*hexyl, R′ = 1 : 1 : 3 : 3-tetramethylbutyl) afforded *cyclo*hexylurea in almost quantitative yield on treatment with boiling 15% hydrochloric acid.

The reaction of arylcarbodi-imides with diketen in boiling benzene was found to be slow but, in agreement with the claim of Hofmann *et al.*,[1] the condensation was catalysed by cuprous chloride. *NN*′-Diphenylcarbodi-imide gave the known [2] oxazine (II; R = R′ = Ph) and *N-cyclo*hexyl-*N*′-phenylcarbodi-imide gave (II; R = *cyclo*hexyl, R′ = Ph), both preparations giving low yields. The structure of the latter oxazine was established by hydrolysis to the dione (III; R = *cyclo*hexyl) and *N-cyclo*hexyl-*N*′-phenylurea. The reaction of diketen with *N*-benzyl-*N*′-phenylcarbodi-imide was catalysed by toluene-*p*-sulphonic acid, giving a small yield of the uracil (V; R = Ph·CH₂, R′ = Ph) formed, very possibly, by the known [2] acid-catalysed re-arrangement of the imino-oxazine (II; R = Ph·CH₂, R′ = Ph).

Diketen may be formally regarded as the inner anhydride of acetoacetic acid. Schulz and Fiedler [4] have suggested that acid anhydrides react with carbodi-imides to give *ON*-diacylureas (VI) (they did not isolate reaction products of this type but, after the addition of water, obtained *N*-acylureas), products analogous to the oxazines (II) derived from diketen.

$$(I) + (R''\cdot CO)_2O \longrightarrow \underset{\underset{\displaystyle R'N\!:\!C\cdot O\cdot COR''}{|}}{RN\cdot COR''} \quad (VI)$$
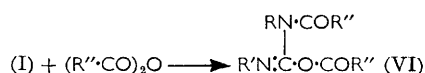
The orientation of the attack of the diketen molecule upon the unsymmetrical carbodi-imides deserves comment. Khorana [5] showed that in the reaction of carboxylic acids with *N-cyclo*hexyl-*N*′-phenylcarbodi-imide the acyl group was attached to the less basic nitrogen atom of the original carbodi-imide, *i.e.*, that adjacent to the phenyl group, and postulated that the reaction proceeded by a three-step mechanism in which the more

[3] Harvey and Caplan, U.S.P. 2,247,495 (15/4/38).
[4] Schulz and Fiedler, *Chem. Ber.*, 1956, **89**, 2681.
[5] Khorana, *J.*, 1952, 2083.

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basic nitrogen atom is first attacked by a proton, this being followed by nucleophilic attack of the acid anion and re-arrangement as shown:

$$R \cdot N = C = NR' + R'' CO_2^- \longrightarrow R \cdot \overset{\overset{\displaystyle H}{|}}{N} - \overset{|}{\underset{O-COR''}{C}} = NR' \longrightarrow R \cdot NH \cdot CO \cdot \underset{COR''}{NR'}$$
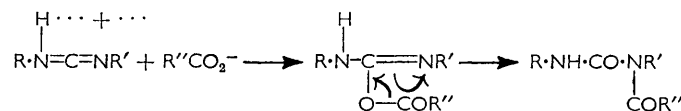
The orientation of the attack of diketen is clearly in the opposite sense. *N*-Alkyl-*N'*-phenylcarbodi-imides afford oxazines (II) in which attack has evidently occurred at the nitrogen atom adjacent to the alkyl substituent; this result is consistent with electrophilic attack of the diketen molecule on the point of maximum electron-density in the carbodi-imide molecule:

$$\longrightarrow \quad (II)$$
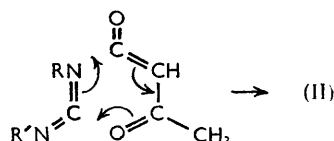
When R' is *tert.*-alkyl, the inductive effect of the substituent directs attack at the nitrogen atom remote from this substituent. It follows from the above that the attack of a carboxylic anhydride on an unsymmetrical carbodi-imide should take place at the

TABLE 1. *Oxazines* (II).

	$\lambda_{max.}$ (Å)	$\varepsilon_{max.}$
(II; R = R' = *cyclo*hexyl)	2620	1950
(II; R = R' = Pr^i)	2580	1950
(II; R = *cyclo*hexyl, R' = Bu^t) ...	2580	2000
(II; R = R' = Et)	2580	2050
(II; R = *cyclo*hexyl, R = C$_8$H$_{17}$ ^{a})	2590	1800
(II; R = Me, R' = Ph)	2485	12,300
(II; R = *cyclo*hexyl, R' = Ph) ...	2500	11,700
(II; R = Ph·CH$_2$, R' = Ph)	2510	12,800
(II; R = R' = Ph)	*ca.* 2490	12,400

TABLE 2. *Oxazines* (III).

	$\lambda_{max.}$ (Å)	$\varepsilon_{max.}$
(III; R = Me)	2270	7500
(III; R = Et)	2270	7900
(III; R = Pr^i)	2270	7900
(III; R = *cyclo*hexyl) ...	2275	8200
(III; R = Ph·CH$_2$)	2275	9000
(III; R = Ph)	2310	10,400

TABLE 3. *6-Methyluracils* (V).

	$\lambda_{max.}$ (Å)	$\varepsilon_{max.}$	$\lambda_{min.}$ (Å)	$\varepsilon_{min.}$
(V; R = Me, R' = H)	2590	9100	2320	2300
(V; R = Et, R' = H)	2610	9500	2320	2300
(V; R = Pr^i, R' = H)	2615	8600	2320	2300
(V; R = *cyclo*hexyl, R' = H)	2620	8300	2340	2600
(V; R = Ph·CH$_2$, R' = H)	2615	8800	2360	2800
(V; R = Ph, R' = H)	2620	9800	2320	3600
(V; R = R' = Me)	2660	10,600	2340	2100
(V; R = R' = Pr^i)	2685	10,900	2380	2400
(V; R = R' = *cyclo*hexyl)	2710	10,500	2380	2600
(V; R = Me, R' = Ph·CH$_2$)	2660	11,400	2350	2600
(V; R = Me, R' = Ph)	2635	11,200	2350	3700
(V; R = Ph·CH$_2$, R' = Me)	2680	9400	2380	2400
(V; R = Ph, R' = Me)	2680	10,600	2380	3400
(V; R = Ph·CH$_2$, R' = Ph)	2640	12,100	2380	4200

^{a} C$_8$H$_{17}$ = 1 : 1 : 3 : 3-tetramethylbutyl.

more basic nitrogen atom, *i.e.*, the opposite orientation to that observed with a carboxylic acid; this question merits further study.

The ultraviolet light absorption evidence shown in Tables 1 and 2 is in agreement with the formulations assigned. The strong absorption exhibited at about 2500 Å by the compounds (II) having R' = Ph is characteristic of the Ph·N:C system. Both compounds (III; R = Ph and Ph·CH$_2$) show general additional long-wavelength absorption, the

benzyl derivative exhibiting a shoulder at 2700 Å (ε *ca.* 400). The ultraviolet light absorption data for the 6-methyluracils (V) described in this and earlier work [2] are shown in Table 3; good general agreement with earlier data [6,7] on substituted uracils was found. The compounds (V) having R or R' = Ph show a pronounced increase in ε at the position of minimum absorption (2350—2380 Å) over those uracils bearing non-aromatic

TABLE 4. *Oxazines* (II).[a]

	C=O str.	C=C str.	C=N str.	5C–H def.		
(II; R = R' = *cyclo*hexyl)	1693 (1320)	1646 (800)	*ca.* 1590 (*ca.* 10)	823 (250)	731 (28)	690 (55)
(II; R = R' = Pr^i)	1692 (1060)	1649 (700)	*ca.* 1590 (*ca.* 10)	823 (190)	731 (27)	690 (55)
(II; R = *cyclo*hexyl, R' = Bu^t)	1693 (1230)	1649 (770)	*ca.* 1590 (*ca.* 10)	824 (220)	733 (24)	692 (50)
(II; R = R' = Et)	1692 (1320)	1649 (690)	Not detected	823 (180)	729 (20—25)[b]	689 (60)
(II; R = *cyclo*hexyl, R' = C₈H₁₇ [d])	1691 (1300)	1645 (800)	*ca.* 1580 (*ca.* 10)	823 (230)	731 (25)	691 (55)
(II; R = Me, R' = Ph)	1692 (2100)	1649 (990)	1595 (400)	824 (280)	732 (25)	[b]
(II; R = *cyclo*hexyl, R' = Ph)	1690 (1290)	1642 (870)	1594 (410)	825 (250)	730 (32)	[b]
(II; R = Ph·CH₂, R' = Ph)	1691 (1670)	1651 (740)	1594 (410)	825 (210)	[b]	[b]
(II; R = R' = Ph)	1689 (1650)	1650 (1070)	1594 (450)	822[c]	[b]	[b]

[a] Carbon tetrachloride and *cyclo*hexane used as solvents (see Experimental section). [b] Interference from underlying bands. [c] Saturated solution used, concentration undetermined. [d] C₈H₁₇ = 1 : 1 : 3 : 3-tetramethylbutyl.

TABLE 5. *Oxazines* (III).[a]

	2-oxo C=O str.	4-oxo C=O str.	C=C str.	5C–H def.	
(III; R = Me) [d]	1776 (650)	1711 (1320)	1670 (50—100)	830 (200)	755 (310)
(III; R = Et)	1779 (790)	1712 (1620)	1675 (50—100)	829 (190)	759 (230)
(III; R = Pr^i)	1779 (650)	1711 (1850)	1672 (50—100)	829 (190)	761 (230)
(III; R = *cyclo*hexyl) [d]	1773 (450)	1711 (1350)	1672 (50—100)	830 (160)	758 (250)
(III; R = Ph·CH₂)	1776 (430)	1711 (1150)	1670 (50—100)	831 (200)	754 (260)
(III; R = Ph) [b]	1776 (—)	1721 (—)	1672 (—)	827 (—)	—[c] (—)

[a] Carbon tetrachloride and carbon disulphide used as solvents (see Experimental section). [b] Material sparingly soluble in solvents employed; saturated solutions used. [c] Interference from aromatic bands. [d] A 0·5 mm. cell was used.

substituents. This evidence and that afforded by infrared measurements (Table 6) confirm the structures proposed earlier [2] for (V; R = Me and Ph·CH₂, R' = Ph).

The frequencies of infrared absorption maxima (see Tables 4—7) are measured in cm.⁻¹; the ε values are in parentheses and are approximate only. All three groups of compounds exhibit bands attributable to the C=O stretching frequency of the 4-oxo-grouping in 'conjugation with the C=C group (see Table 7); the dioxo-oxazines, however, show this band at about 1711 cm.⁻¹ rather than at the expected value of 1690—1695 cm.⁻¹ exhibited by the imino-oxazines (II), while the uracils show a band at about

[6] Evans, *J. Amer. Chem. Soc.*, 1952, **54**, 641.
[7] Austin, *ibid.*, 1934, **56**, 2141.

1670 cm.$^{-1}$.   Compounds (III) and (V) show bands characteristic of the C=O stretching of the 2-oxo-group; the uracils show this band at about 1700 cm.$^{-1}$, whereas in the dioxo-oxazines the frequency is raised to 1775 cm.$^{-1}$, the C=O group in these compounds being part of a vinyl ester-like system.   The imino-oxazines (II) show a C=N stretching band at 1590 cm.$^{-1}$ which is strong in intensity where R' = Ph but only just observable where R' is alkyl.

Table 7 shows the marked variations in both frequency and intensity exhibited by the stretching frequency of the C=C group conjugated with the 4-oxo-group.   All three

TABLE 6.   *6-Methyluracils.*[a]

		2-oxo C=O str.	4-oxo C=O str.	C=C str.	5C–H def.	
(V; R = R′ = Me)	(i)	1712	1675	1630	816	762
		(750)	(1500)	(250)	(240)	(230)
	(ii)	1700	1660	1621	847	766
		(750)	(1900)	(400)		
(V; R = R′ = Pr^i)	(i)	1706	1670	1627	817	771
		(600)	(1800)	(200)	(210)	(220)
	(ii)	1694	1660	1616	823, 823	776
		(500)	(1800)	(250)		
(V; R = R′ = *cyclo*hexyl)	(i)	1706	1670	1627	815	768
		(650)	(2000)	(250)	(220)	(230)
	(ii)	1694	1656	1619	811, 820	772
		(500)	(1800)	(350)		
(V; R = Me, R′ = Ph·CH$_2$)	(i)	1705	1672	1626	818	765[b]
		(650)	(1900)	(200)	(250)	(190)
	(ii)	1697	1661	1624	874	767, 739, 735,
		(600)	(1800)	(300)	—	728, 694
(V; R = Me, R′ = Ph)	(i)	—[c]	1675	—	—	—
	(ii)	1703	1667	1626	848	769, 763, 703
		(650)	(1800)	(250)		
(V; R = Ph, R′ = Me)	(i)	—	—	—	—	—
	(ii)	1705	1667	1630	847	767, 753, 704
		(650)	(2100)	(shoulder)		693
(V; R = Ph·CH$_2$, R′ = Ph)	(i)	1705	1675	—	—	—
	(ii)	1703	1664	1624	847	774, 766, 763
		(600)	(1500)	(250)		711, 705, 669

[a] Series (i): carbon tetrachloride and carbon disulphide as solvents (see Experimental section). Series (ii): chloroform (1800—1600 cm.$^{-1}$), liquid paraffin mull (900—670 cm.$^{-1}$).   The phenyl-substituted uracils were sparingly soluble in carbon tetrachloride.   [b] Other bands due to the benzyl group were observed at 720 and 693 cm.$^{-1}$.   [c] Where values for wave number are not quoted, bands were not of measurable intensity.

TABLE 7.   *Light absorption (infrared) data* (CCl$_4$ *solutions*).

	4-oxo C=O str.		C=C str.	
	cm.$^{-1}$	ε	cm.$^{-1}$	ε
(II) [a]	1691—1693	1100—1300	1645—1649	700—800
(III) [b]	1711—1712	1300—1800	1664—1672	*ca.* 100
(V) [a]	1670—1675	1500—2000	1627—1630	200—250

[a] R and R′ are both aliphatic substituents.   [b] R is aliphatic.

groups of compounds show bands of moderate intensity in the region 815—830 cm.$^{-1}$ which are attributed to the C–H deformation frequency of the grouping in the 5-position. Large variable frequency shifts were observed in the solid-phase spectra which were recorded for the uracils (Table 6, series ii) but the C–H deformation frequencies were clearly identifiable (underlined in the Table where two bands are quoted).   No assignment can yet be offered for the bands exhibited in the 690—770 cm.$^{-1}$ range.

EXPERIMENTAL

M. p.s were determined on a Kofler block and are corrected.

pK values were obtained by titration of a 0·02M-solution in 50% v/v aqueous ethanol with 0·2N-sulphuric acid. A glass–calomel electrode system was used and an average of values given at 40%, 50%, and 60% complete neutralisation was taken. No corrections were imposed.

Ultraviolet-light absorptions refer to EtOH solutions. Infrared spectra were recorded by means of a Hilger H 800 double-beam instrument with a sodium chloride prism; carbon tetra-chloride or chloroform (5000—850 cm.$^{-1}$), and *cyclo*hexane or carbon disulphide (850—670 cm.$^{-1}$), were used as solvents; the sample cell length was 0·1 mm.; frequencies are accurate to ± 3 cm.$^{-1}$ at 1700 cm.$^{-1}$ and ± 2 cm.$^{-1}$ at 820 cm.$^{-1}$.

3-cyclo*Hexyl*-2-cyclo*hexylimino*-2 : 3-*dihydro*-6-*methyl*-4-*oxo*-1 : 3-*oxazine* (II; R = R′ = *cyclo*hexyl).—Diketen (10·3 g.) was added during 0·5 hr. to a refluxing mixture of NN′-di*cyclo*-hexylcarbodi-imide [8] (24 g.) and benzene (85 ml.), and the whole refluxed for a further 6 hr. Removal of the solvent gave a partly crystalline solid which on being rubbed with light petroleum (b. p. 60—80°) gave a solid (14·4 g.), m. p. 82°. Crystallisation from light petroleum (b. p. 60—80°) afforded the *oxazine* (II; R = R′ = *cyclo*hexyl) as prisms, m. p. 82—83° (lit.,[1] m. p. 82—83°) (Found: C, 70·4; H, 8·95; N, 9·7. C$_{17}$H$_{26}$O$_2$N$_2$ requires C, 70·3; H, 9·05; N, 9·65%).

This oxazine (5·00 g.) was refluxed with a mixture of concentrated hydrochloric acid (5 ml.) and water (50 ml.) for 1 hr. The solid dissolved but, after a few min., precipitation ensued. The precipitate (3·95 g.) was collected and extracted (Soxhlet) with hot light petroleum (b. p. 60—80°), to give (*a*) a residue (0·975 g.) insoluble in light petroleum, m. p. 233°, identified by mixed m. p. as NN′-di*cyclo*hexylurea (lit.,[9] m. p. 229—230°), (*b*) material (1·40 g.) soluble in hot light petroleum (b. p. 60—80°) but crystallising from it as plates, m. p. 178°, shown to be 3-cyclo-*hexyl*-2 : 3-*dihydro*-6-*methyl*-2 : 4-*dioxo*-1 : 3-*oxazine* (III; R = *cyclo*hexyl) (Found: C, 62·85; H, 6·8; N, 6·8. C$_{11}$H$_{15}$O$_3$N requires C, 63·15; H, 7·25; N, 6·7%), and (*c*) material (1·20 g.) soluble in cold light petroleum, which was separated from traces of (III; R = *cyclo*hexyl) by chromatography on alumina whence chloroform eluted 1 : 3-*dicyclohexyl*-6-*methyluracil* (V; R = R′ = *cyclo*hexyl) which crystallised from aqueous methanol as plates, m. p. 137° (Found: C, 70·5; H, 8·85; N, 9·6. C$_{17}$H$_{26}$O$_2$N$_2$ requires C, 70·3; H, 9·05; N, 9·65%). The filtrate from the hydrolysis was shown, after the addition of alkali, to contain *cyclo*hexylamine by the reaction with *cyclo*hexyl *iso*thiocyanate to give NN′-di*cyclo*hexylthiourea, m. p. and mixed m. p. 188—189° (lit.,[9] m. p. 180—181°).

The oxazine (III; R = *cyclo*hexyl) (0·5 g.) was heated at 60—70° with ethanol (10 ml.) and aqueous ammonia (*d* 0·88; 10 ml.) for 2 hr. The mixture was evaporated to dryness; the residue, crystallised from ethyl acetate–light petroleum (b. p. 60—80°), gave 3-cyclo*hexyl*-6-*methyluracil*, needles, m. p. 238·5—239° (Found: C, 62·9; H, 7·25; N, 12·9. C$_{11}$H$_{16}$O$_2$N$_2$ requires C, 63·45; H, 7·75; N, 13·45%).

2 : 3-*Dihydro*-6-*methyl*-4-*oxo*-3-iso*propyl*-2-iso*propylimino*-1 : 3-*oxazine* (II; R = R′ = Pr^i).—Prepared according to the previous method from NN′-di*iso*propylcarbodi-imide [10] (22·7 g.) and diketen (16·8 g.) in benzene (60 ml.), the *oxazine* (II; R = R′ = Pr^i) (32·7 g.) had b. p. 89—92°/1·5 mm., m. p. 30° (prisms) (lit.,[1] b. p. 80—82°/0·5 mm., m. p. 32°) (Found: N, 13·5. C$_{11}$H$_{18}$O$_2$N$_2$ requires N, 13·3%).

This oxazine (12·0 g.) was refluxed with concentrated hydrochloric acid (12 ml.) and water (120 ml.), an oil being deposited. Isolation with ether gave an oil (8·4 g.) from which, after addition of light petroleum (b. p. 40—60°), a solid (0·2 g.), m. p. 200°, identified by mixed m. p. as NN′-di-*iso*propylurea (lit.,[11] m. p. 192°), was deposited. Evaporation of the filtrate gave a solid which crystallised as sharp-melting prisms, m. p. 44—45°, but nevertheless, was shown by infrared analysis to be a mixture of (III; R = Pr^i) (54%) and (V; R = R′ = Pr^i) (44%). The mixture was chromatographed on alumina; elution with light petroleum (b. p. 40—60°)– benzene and crystallisation from light petroleum (b. p. 60—80°) gave 2 : 3-*dihydro*-6-*methyl*-2 : 4-*dioxo*-3-iso*propyl*-1 : 3-*oxazine* (III; R = Pr^i), prisms, m. p. 62·5—63° (Found: C, 56·5;

[8] Schmidt, Hitzler, and Lahde, *Ber.*, 1938, **71**, 1933.
[9] Skita and Rolfes, *Ber.*, 1920, **53**, 1242.
[10] Schmidt and Striewsky, *Ber.*, 1941, **74**, 1285.
[11] Hofmann, *Ber.*, 1882, **15**, 752.

H, 6·3; N, 8·15. $C_8H_{11}O_3N$ requires C, 56·8; H, 6·55; N, 8·3%). Elution with benzene–chloroform and crystallisation from water gave 6-*methyl*-1 : 3-*diiso*propyluracil (V; R = R′ = Pr^i), needles, m. p. 93—94° (Found: C, 62·75; H, 8·2; N, 13·2. $C_{11}H_{18}O_2N_2$ requires C, 62·8; H, 8·65; N, 13·3%).

The aqueous layer from the hydrolysis was made alkaline and distilled; titration of the distillate showed it to contain 44% of the amine theoretically obtainable by conversion of (II; R = R′ = Pr^i) into (III; R = Pr^i).

The oxazine (III; R = Pr^i) (0·5 g.) was heated in a boiling-water bath with aqueous ammonia (*d* 0·880; 10 ml.) for 1 hr. Evaporation and crystallisation of the residue from ethyl acetate–light petroleum (b. p. 60—80°) gave 6-*methyl*-3-iso*propyluracil* (V; R = Pr^i, R′ = H) as needles, m. p. 193° (Found: C, 57·3; H, 7·2; N, 16·5. $C_8H_{12}O_2N_2$ requires C, 57·15; H, 7·2; N, 16·65%).

3-*Ethyl*-2-*ethylimino*-2 : 3-*dihydro*-6-*methyl*-4-*oxo*-1 : 3-*oxazine* (II; R = R′ = Et).—*NN′*-Diethylcarbodi-imide [8] (9·1 g.; b. p. 71—72°/100 mm.; lit.,[12] b. p. 24·5°/11 mm.) with diketen (8·5 g.) in benzene (30 ml.) gave the oxazine (II; R = R′ = Et) (15·1 g.), b. p. 82°/1 mm., n_D^{20} 1·4996. The identity of the product was established by comparison of the infrared spectrum with that of an authentic specimen and acid hydrolysis to compound (III; R = Et), m. p. and mixed m. p. 71° (lit.,[2] m. p. 69—70°).

2-tert.-*Butylimino*-3-cyclo*hexyl*-2 : 3-*dihydro*-6-*methyl*-4-*oxo*-1 : 3-*oxazine* (II; R = cyclo-hexyl, R′ = Bu^t). The *oxazine* was obtained by the standard procedure from *N*-*tert.*-butyl-*N′*-cyclohexylcarbodi-imide [13] (25 g.) and diketen (12·5 g.) in benzene (40 ml.) as an oil (29·8 g.), b. p. 134—137°/1·5 mm., needles, m. p. 69° (from aqueous methanol) (lit.,[1] m. p. 58—60°) (Found: C, 67·9; H, 9·0; N, 10·9. $C_{15}H_{24}O_2N_2$ requires C, 68·15; H, 9·15; N, 10·6%).

This oxazine (2·0 g.) was refluxed with concentrated hydrochloric acid (2 ml.) and water (20 ml.) for 1 hr. After cooling, the product (0·87 g.; m. p. 167°) was collected and crystallised from light petroleum (b. p. 80—100°), giving compound (III; R = cyclohexyl), m. p. and mixed m. p. 178°. The filtrate was concentrated to small bulk and made alkaline; the precipitate (0·39 g.; m. p. 197°), recrystallised from ethyl acetate, gave cyclohexylurea as plates, m. p. and mixed m. p. 199° (lit.,[14] m. p. 195—196°). Experiments with more concentrated acid gave lower yields of (III; R = cyclohexyl) and higher yields of cyclohexylurea. Hydrolysis of the oxazine (2·0 g.) with concentrated hydrochloric acid (4 ml.) gave only a trace of (III; R = cyclo-hexyl), and 0·76 g. of cyclohexylurea. When concentrated hydrochloric acid (0·5 ml.) and water (4·5 ml.) were used, cyclohexylurea (0·08 g.) and a mixture of non-basic solids (1·29 g.) were obtained; the latter was resolved by Soxhlet extraction with light petroleum (b. p. 60—80°) into (III; R = cyclohexyl) (0·47 g.) and a residue (0·49 g.) which, on crystallisation from aqueous ethanol, gave N-tert.-*butyl*-N′-cyclo*hexylurea* as needles, m. p. and mixed m. p. 227° (Found: C, 66·9; H, 11·15; N, 13·7. $C_{11}H_{22}ON_2$ requires C, 66·6; H, 11·15; N, 14·15%).

An authentic specimen of *N*-*tert.*-butyl-*N′*-cyclohexylurea was prepared by refluxing *N*-*tert.*-butyl-*N′*-cyclohexylcarbodi-imide (4 g.) with concentrated hydrochloric acid (0·5 ml.) and water (10 ml.) for 10 min., to give a solid (3·9 g.) which crystallised from aqueous ethanol as needles, m. p. 227°. Hydrolysis of the urea (1·0 g.) in boiling concentrated hydrochloric acid (2 ml.) and water (2 ml.) for 1 hr. gave, after concentration and addition of alkali, cyclohexylurea (0·60 g., 85%), m. p. and mixed m. p. 197°.

N-cyclo*Hexyl*-N′-1 : 1 : 3 : 3-*tetramethylbutylthiourea*.—cyclo*Hexyl* iso*thiocyanate* (28 g.) was added during 0·5 hr. to 2-amino-2 : 4 : 4-trimethylpentane (26 g.; redistilled; b. p. 140—140·5°) in boiling light petroleum (b. p. 40—60°; 100 ml.), and the mixture was refluxed for 2 hr. The *thiourea* (45·6 g.; m. p. 123—125°) was collected; it formed needles, m. p. 125°, from light petroleum (b. p. 80—100°) (Found: N, 10·05. $C_{15}H_{30}N_2S$ requires N, 10·35%).

N-cyclo-*Hexyl*-N′-1 : 1 : 3 : 3-*tetramethylbutylcarbodi-imide*.—Prepared by the standard method of Schmidt *et al.*, the *carbodi-imide* was obtained in 81% yield as an oil 110—112°/1·5 mm., n_D^{20} 1·4835 (Found: C, 76·4; H, 12·0; N, 11·8. $C_{15}H_{28}N_2$ requires C, 76·2; H, 11·95; N, 11·85%).

3-cyclo*Hexyl*-2 : 3-*dihydro*-6-*methyl*-4-*oxo*-2-(1 : 1 : 3 : 3-*tetramethylbutyl*)*imino*-1 : 3-*oxazine* (II; R = cyclohexyl, R′ = 1 : 1 : 3 : 3-tetramethylbutyl).—*N*-cyclo*Hexyl*-*N′*-1 : 1 : 3 : 3-tetra-methylbutylcarbodi-imide (15 g.), diketen (6 g.), and benzene (20 ml.) were refluxed for 6 hr. Isolation gave a semi-solid fraction (15 g.), b. p. 140—158°/1·5 mm., a portion (3·4 g.) of which

[12] Staudinger and Hauser, *Helv. Chim. Acta*, 1922, **4**, 861.
[13] Schmidt, Striewsky, and Hitzler, *Annalen*, 1948, **560**, 222.
[14] Wallach, *Annalen*, 1905, **343**, 46.

was separated by chromatography on alumina to give, (*a*) by elution with benzene–light petroleum (b. p. 40—60°) the *oxazine* (II; R = *cyclo*hexyl, R' = 1 : 1 : 3 : 3-tetramethylbutyl) (2·4 g.) which crystallised as needles, m. p. 59·5—60° (lit.,[1] m. p. 59—60°), from aqueous methanol (Found: C, 71·5; H, 10·15; N, 8·65. $C_{19}H_{32}O_2N_2$ requires C, 71·2; H, 10·05; N, 8·75%), and (*b*) by elution with ether *N*-*cyclo*hexyl-*N'*-1 : 1 : 3 : 3-tetramethylbutylurea (0·6 g.), m. p. and mixed m. p. 158—159°. An authentic sample was prepared by the action of hot dilute hydrochloric acid on the di-imide (I; R = *cyclo*hexyl, R' = 1 : 1 : 3 : 3-tetramethylbutyl); the *urea* crystallised from aqueous ethanol as needles, m. p. 160·5° (Found: N, 10·7. $C_{15}H_{30}ON_2$ requires N, 11·0%).

The oxazine (II; R = *cyclo*hexyl, R' = 1 : 1 : 3 : 3-tetramethylbutyl) (0·5 g.) was refluxed with concentrated hydrochloric acid (1 ml.) and water (1 ml.) for 1 hr. Filtration of the cooled product afforded compound (III; R = *cyclo*hexyl), m. p. and mixed m. p. 177—178°, and concentration and basification of the filtrate gave a solid (0·30 g.), m. p. 187—188°, which, on crystallisation from ethyl acetate gave *cyclo*hexylurea, m. p. and mixed m. p. 198°. Hydrolysis of compound (IV; R = *cyclo*hexyl, R' = 1 : 1 : 3 : 3-tetramethylbutyl) under similar conditions gave *cyclo*hexylurea in high yield.

3-cycloHexyl-2 : 3-dihydro-6-methyl-4-oxo-2-phenylimino-1 : 3-oxazine (II; R = *cyclo*hexyl, R' = Ph).—A mixture of *N*-*cyclo*hexyl-*N'*-phenylcarbodi-imide[5] (11·0 g.), diketen (5 g.), benzene (30 ml.), and cuprous chloride (0·1 g.) was refluxed for 6 hr. Isolation and distillation afforded a viscous oil (8·0 g.), b. p. 165—195°/2 mm., which crystallised; crystallisation from aqueous methanol afforded the *oxazine* as prisms, m. p. 109·5° (Found: C, 72·1; H, 7·15; N, 9·8. $C_{17}H_{20}O_2N_2$ requires C, 71·8; H, 7·1; N, 9·85%). From a similar preparation without the cuprous chloride, the carbodi-imide was recovered with 80% efficiency.

The oxazine was refluxed with concentrated hydrochloric acid (1 ml.) and water (10 ml.) for 1·5 hr. and the product was crystallised from aqueous methanol, to give compound (III; R = *cyclo*hexyl) (0·19 g.), m. p. and mixed m. p. 176—177°. Addition of water to the mother-liquors gave a precipitate which recrystallised from benzene–light petroleum (b. p. 60—80°) as prisms, m. p. 192°, undepressed on admixture with authentic *N*-*cyclo*hexyl-*N'*-phenylurea (lit.,[9] m. p. 182°).

2 : 3-Dihydro-6-methyl-4-oxo-3-phenyl-2-phenylimino-1 : 3-oxazine (II; R = R' = Ph).—A mixture of *NN'*-diphenylcarbodi-imide (19·4 g.), diketen (9 g.), benzene (50 ml.), and cuprous chloride (0·1 g.) was refluxed for 8 hr. Filtration and removal of solvents gave a dark glass from which, by rubbing with methanol, a brown solid (8·0 g.), m. p. 155—165°, was isolated. Crystallisation from ethyl acetate–light petroleum (b. p. 60—80°) gave the oxazine (II; R = R' = Ph) as prisms, m. p. and mixed m. p. 182—183° (lit.,[2] m. p. 184—185°).

Reaction of N-*Benzyl*-N'-*phenylcarbodi-imide with Diketen.*—This *carbodi-imide* was prepared by the standard method of Schmidt and Striewsky[10] in 54% yield as an oil, b. p. 148—152°/2·5 mm., n_D^{20} 1·6118 (Found: N, 13·6. $C_{14}H_{12}N_2$ requires N, 13·45%). The preparation was remarkably difficult to reproduce. A mixture of the carbodi-imide (15·6 g.), diketen (6·5 g.), benzene (20 ml.), and toluene-*p*-sulphonic acid (0·1 g.) was refluxed for 6 hr. Distillation afforded a semi-solid fraction, b. p. 200—225°/2 mm., from which, by rubbing with methanol, 1-benzyl-6-methyl-3-phenyluracil (3·0 g.), m. p. and mixed m. p. 223—224° (lit.,[2] m. p. 226—227°), was isolated.

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