Tetrahedron Vol. 27, pp 5481 to 5494. Pergamon Press 1971. Printed in Great Britain

VINYLAMINES—XI[1]

STRUCTURE AND REACTIVITY OF 2-CARBALKOXY,2-ACYL- AND 2-PHENYLCARBAMYL-CYCLOHEXANONE ENAMINES WITH ETHYL AZODICARBOXYLATE AND PHENYLISOCYANATE

F. P. COLONNA, G. PITACCO and E. VALENTIN
Istituto di Chimica, Università, 34127 Trieste, Italy

(*Received in the UK* 24 *March* 1971; *Accepted for publication* 17 *June* 1971)

Abstract—The title enamines were prepared and their structures, as regards the C=C isomerism, were established by NMR and IR spectroscopy. Morpholino- and piperidino-derivatives exist more or less as substituted isomer mixtures, whereas pyrrolidino-enamines are almost exclusively in the more substituted form. As expected, the less substituted isomers of all these enamines reacted with both ethyl azodicarboxylate and phenylisocyanate. However, contrary to what occurs with 2-alkyl-cyclohexanone enamines, the reaction yields were much higher than those expected on the basis of the percentages of the reactive isomers found by NMR analysis. These results are discussed and an interpretation of this unusual chemical behaviour is given.

AS PREVIOUSLY reported,[1] the determination of the mixture composition of 2-methyl-cyclohexanone enamines can be accomplished by chemical methods, that is by reaction in the cold with ethyl azodicarboxylate or phenylisocyanate, since only the trisubstituted isomer is reactive toward these reagents. The results obtained parallel those found by NMR analysis and indicate that neither a spontaneous equilibrium is present, nor does equilibration occur between the more or less substituted forms, at least under the conditions already reported.[1,2] Ethyl azodicarboxylate has been used to analyse the composition of the enamine mixtures obtained from the reactions between cyclohexanone enamines and electrofilic olefins.[3]

We report the chemical behaviour of 2-substituted-cyclohexanone enamines in which the substituent is not an alkyl but an electron withdrawing group that can be conjugated with the enaminic N atom, through the C=C double bond. We have found that the reactions of these enamines with the aforementioned reagents give results which are not in agreement with the percentages of the more or less substituted isomers found by NMR analysis.

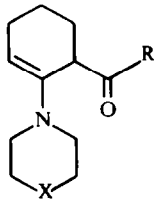
The examined enamines were 2-carbomethoxy- (I–III), 2-carbethoxy- (IV–VI), 2-acetyl- (VII–IX), 2-benzoyl- (X–XII) and 2-phenylcarbamyl-cyclohexanone (XIII–XV) derivatives (Table 1). Their structures were established by NMR and IR spectroscopy. The percentages of more or less substituted isomers, determined by integration of vinyl proton signals, are listed in Table 1. Morpholino-enamine mixtures contained the less substituted form in amounts varying from 59% for 2-phenylcarbamyl- to 78% for 2-carbethoxy derivative. The percentages of this form, found in the piperidino-enamines, ranged from 33% for 2-phenylcarbamyl- to 73% for 2-carbethoxy compound. Whichever the substituent, only small amounts, 10–25%, of the less substituted isomer, were always found for the pyrrolidino-enamines.

The IR spectroscopic data (Table 1) supported the structures assigned by NMR analysis. Actually, when considerable amounts of both more or less substituted isomers were present, we found the bands of the conjugated system N—C=C—C=O[4] and those of the N—C=C and C=O groups of the trisubstituted form. Thus, for instance, the IR spectrum of 1-N-morpholino-2(and 6)-carbomethoxy-cyclohex-1-ene (I) showed a strong band at 1740 cm^{-1} and a weak band at 1650 cm^{-1}, attributable respectively to the C=O and N—C=C groups of the less substituted form. Other bands at 1685 cm^{-1} and at 1580 cm^{-1}, characteristic of the conjugated system N—C=C—C=O, indicated the presence of the more substituted isomer. On the other hand, the IR spectrum of 1-N-pyrrolidino-2-carbomethoxycyclohex-1-ene (III), containing only about 10% of the trisubstituted isomer, showed absorption bands at 1681 cm^{-1} and at 1535 cm^{-1} (N—C=C—C=O), whereas C=O and N—C=C bands were not present.

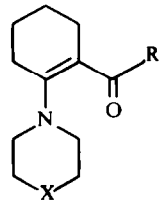
Enamines III[5], VII[6, 7, 8], VIII[6, 7], IX[7], X[8, 9], XIII[10] and XV[7] are reported in the literature. The structure of the more substituted isomer assigned to III, IX and X is in agreement with our data, whereas for the enamines VII, VIII, XIII[10a] and XV, our results are not in agreement with those found in the literature.

The fact that 2-methylcyclohexanone morpholino- and piperidino-enamines exist as mixtures of about equal amounts[1, 11] or more or less substituted isomers has been explained[11] on the basis of the slight importance of the conjugation of the heterocyclic N atom with the C=C double bond. This does not depend on the basicity of the N atom, but it is due to the low stability of the resonance structures having a double bond *exo* to two 6-membered rings.[12] This postulate, indeed, is in accordance with the relative stability of enamines of 1-azabicycloalkanes,[13] in which are missing the steric factors that could affect the N—C=C conjugation. Hence the position of the double bond is controlled by the same factors that are responsible for the relative stability of simple cyclic olefins.[12]

In the more substituted enamines **B**, reported in Table 1, the condition of planarity of the N—C=C—C=O system is not completely fulfilled. Therefore a full interaction of the π-electrons of the two double bonds with the free electron pair of the N atom is not possible. This situation is not very different from that of the 2-methylcyclohexanone-enamines. This holds, for instance for morpholino- and piperidino-enamine derivatives, in which R=OMe, OEt, Me and NHPh, that exist as mixtures of more or less substituted isomers **A** and **B**:



A



B

X = O. CH_2 R = OMe. OEt. Me. NHPh

In these cases, however, besides steric factors there are also electronic ones controlling the composition of isomeric mixtures, that is the base strength and the electron withdrawing character of the carbonyl O atom.

Actually, our findings indicate that the percentages of the conjugated form **B** are higher in the piperidino than in the morpholino derivatives. Moreover, the amount of **B** for each enamine depends also on the nature of R, which competes with the N atom in conjugating with C=O. Hence the percentage of **B** is reduced in favour of that of **A**:

The greater the + R resonance effect of the R group (OMe > CH_3 > NH—Ph > Ph), the less the conjugation N—C=C—C=O. Because of steric hindrances the phenyl group is somewhat distorted out of the plane of the C=O group and therefore the conjugation Ph—C=O is greatly reduced. This could account for the fact that enamines X and XI exist almost exclusively in the form **B**. In this connection attention must be turned to the fact that 1-N-morpholino-2-formylcyclohex-1-ene[14] (R=H) exists just as **B** isomer. Its NMR spectrum shows a singlet at 2·74 τ (1H) for the formyl proton and multiplets at 6·45 τ (8H), 7·65 τ (4H) and at 8·30 τ (4H), while vinyl proton signal is not present. In the IR spectrum the bands of the N—C=C—C=O group at 1642 cm^{-1} and at 1540 cm^{-1} are clearly evident.

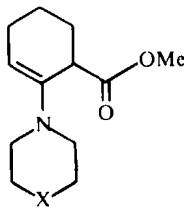
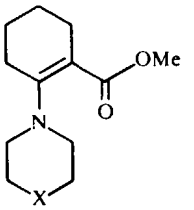
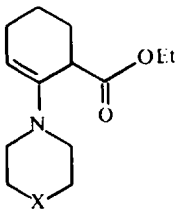
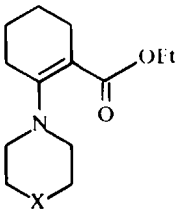
A completely different situation was observed in the pyrrolidino-enamines III, VI, IX, XII and XV (Table 1), with respect to the corresponding 2-methylcyclohexanone derivative. Actually, the former exist largely (80–95%) as **B** isomers, whereas the latter exists almost completely (90%) as the less substituted isomer.[1, 11, 14] This opposite situation depends, however, on the same factors. The pyrrolidino N atom requires the most extended conjugation, both for its basicity and for the stability of the double bond *exo* to a 5-membered ring.[12] The most extended conjugation is present in the trisubstituted form of the 2-methylcyclohexanone enamine, whereas in enamines III, VI, IX, XII and XV it occurs when they are in the structure **B**.

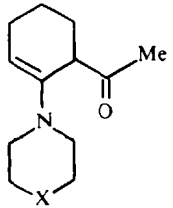
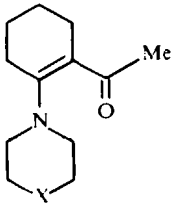
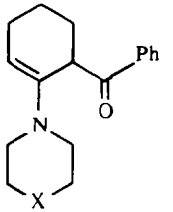
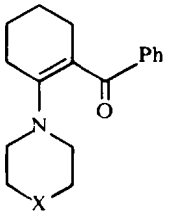
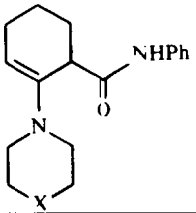
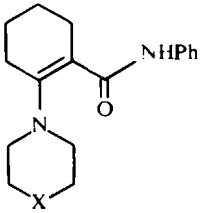
As far as the reactivity of enamines I–XV is concerned, the most remarkable fact we have observed was their behaviour towards both ethyl azodicarboxylate and phenylisocyanate. Actually, the results of these reactions when carried out under the conditions reported [1, 2] for 2-methylcyclohexanone enamines, did not reflect the isomeric compositions of I–XV found by NMR analysis, but seemed to indicate that these enamines existed almost exclusively as **A** isomers.

In fact, the percentages of 2,6-disubstituted products, isolated as enamines **C** and **E** or as cyclohexanone derivatives **D** and **F**, after hydrolysis of the reaction mixtures, were always much higher than those expected (Table 1).

Noteworthy is the behaviour of 1-N-pyrrolidino-2-carbomethoxycyclohex-1-ene (III) that reacts, under the standard conditions,[1, 2] with both ethyl azodicarboxylate and phenylisocyanate leading to the enamines XVIII and XXXVII in 85% and

TABLE 1. PERCENTAGES OF ISOMERIC ENAMINES DETERMINED BY NMR ANALYSIS AND FROM THE REACTION YIELDS OF THE LESS SUBSTITUTED ISOMER A WITH ETHYL AZODICARBOXYLATE AND PHENYLISOCYANATE

Enamine mixtures A	B		NMR τ[a]	NMR A%	NMR B%[b]	Reaction with $EtO_2C-N=N-CO_2Et$ %	Reaction with PhNCO %	IR Absorption bands C=O	IR Absorption bands N C=C	IR Absorption bands C=O	IR Absorption bands C=C
									wave numbers (cm^{-1})		
		I : X = O	5·10	70	30	95[c]	86[d]	1740	1685-1580		1650
		II : X = CH_2	5·14	51	49	71[c]	80[d]	1738	1685-1565		1648
		III : X = —	5·56	10	90	85[c]	95[c]		1681-1535		
		IV : X = O	5·08	78	22	88[c]	80[d]	1740	1686-1575		1647
		V : X = CH_2	5·15	73	27	90[c]	—	1737	1686-1570		1645
		VI : X = —	5·56	15	85	65[d]	92[c]		1678-1558		

		VII : X = O	5·07	60	40	80[d]	—	1704	1620–1540	1642
		VIII : X = CH_2	5·11	40	60	70[d]	—	1705	1615–1580	1640
		IX : X = —	5·50	10	90	59[d]	80[c]		1610–1492	
		X : X = O	5·01	5	95	83[c]	—		1620–1571	
		XI : X = CH_2	5·02	10	90	65[c]	—		1642–1565	
		XII : X = —	5·71	5	95	90[c]	81[c]		1618–1538	
		XIII : X = O	4·94	59	41	93[c]	90[e]	1688	1595–1545	1656
		XIV : X = CH_2	4·95	33	67	74	80[d]	1688	1595–1542	1650
		XV : X = —	5·32	25	75	—	68[d]	—	—	—

[a] Signal of vinylic proton:
[b] Obtained by difference (100-A%):
[c] Isolated as 2.6-disubstituted enamine **C** or **E**:
[d] Isolated as 2.6-disubstituted cyclohexanone **D** or **F**, after *hydrolysis* of the reaction mixture:
[e] Obtained in refluxing benzene

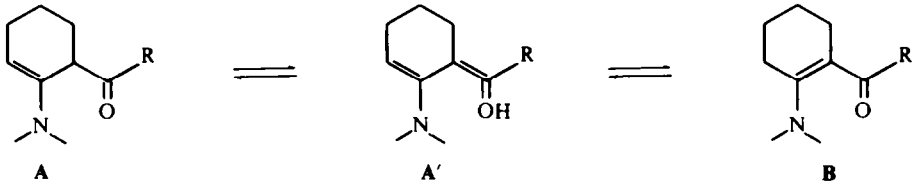
95% yields, respectively. The results obtained from the reactions of the other enamines I–XV with the aforementioned reagents are summarized in Table 1.

All the spectra of the 2,6-disubstituted enamines **C** show, at 4·9–5·0 τ (1H) the signal of the proton linked at the C atom bearing the —N(COOEt)NHCOOEt grouping. This clearly indicates that enamines **C** have the structure of vinylogous amides N—C=C—C=O.

In the NMR spectra of the corresponding 2,6-disubstituted cyclohexanones **D**, the signal of the same proton is slightly shifted upfield.

In the NMR spectra of enamines **E**, the signals of the protons linked at C-2 and C-6 atoms appear at very close τ values, so that a broad and unresolved multiplet (1H) is observed. Therefore the assignment of the C=C double bond position was not possible. In our opinion, however, as the enaminic N atom can be conjugated with both C=O of the —COR and CONHPh groups, enamines **E** very probably exist as mixtures of C=C double bond isomers.

Since our reaction conditions are nonequilibrating,[1,2] we must assume that in these enamines, in which the **B** isomers are, after all, α,β-unsaturated ketones, there is a spontaneous equilibrium between the forms **A** and **B**, through the common enols **A'**



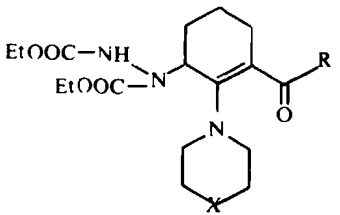
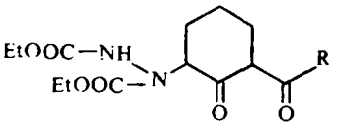
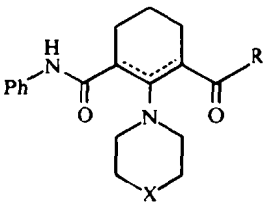
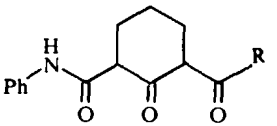
A **A'** **B**

In this way all the enamines I–XV react with ethyl azodicarboxylate as well as with phenylisocyanate through the corresponding **A** isomers and this can account for the high reaction yields, whatever is the effective percentage of **A** in the mixtures.

We were not able to evidence the enolic form **A'** in the equilibrium. Nevertheless, in some cases, analogous compounds have been isolated;

Thus, for instance, 1-N-morpholino-2-nitroso-cyclohex-1-ene is the initial product of the reaction of 1-N-morpholinocyclohex-1-ene with nitrosyl chloride. But it is very unstable and changes immediately into the corresponding more stable oximino isomer,[15] which can be regarded as its enolic form.

TABLE 2

	C	D	E	F
				
R = OMe	XVI : X = O XVII : X = CH_2 XVIII : X = —	XXX	[XXXV : X = O] XXXVI : X = CH_2 XXXVII : X = —	XLV
R = OEt	XIX : X = O XX : X = CH_2 [XXI : X = —]*	XXXI	[XXXVIII : X = O] — XXXIX : X = —	XLVI
R = Me	[XXII : X = O] [XXIII : X = CH_2] [XXIV : X = —]	XXXII	— — XL : X = —	XLVII
R = Ph	XXV : X = O XXVI : X = CH_2 XXVII : X = —	XXXIII	— — XLI : X = —	XLVIII
R = NHPh	XXVIII : X = O XXIX : X = CH_2	XXXIV	XLII : X = O [XLIII : X = CH_2] [XLIV : X = —]	XLIX

* The compounds in brackets were not isolated

EXPERIMENTAL

All m.ps are uncorrected. The IR spectra were recorded with a Perkin-Elmer 225 double beam spectrophotometer and the NMR spectra with a Jeol JNM-C-60HL spectrometer with TMS as internal standard. for $CDCl_3$ solns. unless otherwise noted. Plates for analytical TLC were spread with Silica Gel G (Merck) and developed with benzene–acetone 90:10. Chromatographic columns were prepared by using extra pure SiO_2 Merck (70–325 mesh ATMS) as stationary phase and employing gradient elution of benzene–acetone.

1. 1-N-*morpholino*-2 (*and* 6)*carbomethoxycyclohex*-1-*ene* (I)

Methylchloroformate (18·5 g. 0·25 moles) was added dropwise to a soln of 1-N-morpholino-cyclohex-1-ene (83 g. 0·50 moles) in dry benzene (200 ml). The mixture was heated under reflux and stirring. for 30 hr. After 12 hr. some more methylchloroformate (11 g. 0·14 moles) was added. After cooling. dry ether (150 ml) was added and the ppt of enamine hydrochloride filtered off. Removal of the solvent left an oil which was twice distilled. b.p. 160–168° (14 mm). (Found: C. 63·60: H. 8·33; N. 6·24. $C_{12}H_{19}NO_3$ requires: C. 63·98; H. 8·50: N. 6·21%): IR spectrum (neat): 1740 cm^{-1} ($COOCH_3$): 1650 cm^{-1} (N—C=C) 1685. 1580 cm^{-1} (N—C=C—C=O): NMR spectrum: 5·10 τ (C=C<u>H</u>): 6·36 τ ($OC\underline{H}_3$: $C\underline{H}_2$—O—$C\underline{H}_2$).

2. *Reaction of* 1-N-*morpholino*-2 (*and* 6) *carbomethoxycyclohex*-1-*ene* (I) *with ethyl azodicarboxylate*

(a) 1-N-*Morpholino*-2-*carbomethoxy*-6-(N.N′-*dicarbethoxy*)*hydrazino cyclohex*-1-*ene* (XVI). Ethyl azodicarboxylate (2·3 g, 13 mmoles) in dry ether (5 ml) was added dropwise and under stirring, to the soln of I (3·0 g. 13 mmoles) in the same solvent (15 ml). cooling with an ice bath. in order to prevent the temp from rising above 5–10°. The mixture was kept in the refrigerator for 72 hr.* The solvent was removed under red press and left XVI (5·0 g. 95%) m.p. 118–120°. (Found: C. 53·30: H. 7·50: N. 10·60. $C_{18}H_{29}N_3O_7$ requires: C. 53·93; H. 7·31; N. 10·52%): IR spectrum (nujol): 3324 cm^{-1} (NH): 1744. 1702. 1677 cm^{-1} (CO): 1618 cm^{-1} (N—C=C—C=O): NMR spectrum: 3·80 τ (N<u>H</u>): 4·97 τ (C<u>H</u>—N—NH): 5·84 τ ($C\underline{H}_2CH_3$); 6·26 τ ($OC\underline{H}_3$); 6·42 τ ($C\underline{H}_2$—O—$C\underline{H}_2$); 7·07 τ ($C\underline{H}_2$–N—$C\underline{H}_2$); 8·73 τ (CH_2—$C\underline{H}_3$).

(b) 2-*Carbomethoxy*-6-(N.N′-*dicarbethoxy*)*hydrazino-cyclohexanone* (XXX). To a suspension of XVI (1·0 g. 2·5 mmoles) in water. HCl 10% (10 ml) was added. The soln was stirred for 48 hr and gave XXX. m.p. 80–86°. from ligroin. (Found: C. 50·90: H. 6·71: N. 8·48. $C_{14}H_{22}N_2O_7$ requires: C. 50·97: H. 6·76: N. 8·45%): IR spectrum (nujol): 3280 cm^{-1} (NH): 1750. 1721. 1708. 1690 cm^{-1} (COOEt: CO): NMR spectrum: 3·33 τ (N<u>H</u>); 4·97 τ (C<u>H</u>—N—NH): 5·85 τ ($C\underline{H}_2$—CH_3); 6·25 τ ($OC\underline{H}_3$); 6·52 τ ($C\underline{H}COOCH_3$); 8·74 τ (CH_2—$C\underline{H}_3$).

3. *Reaction of* 1-N-*morpholino*-2(*and* 6)*carbomethoxy-cyclohex*-1-*ene* (I) *with phenylisocyanate*)

2-*Carbomethoxy*-6-*phenylcarbamyl-cyclohexanone* (XLV). Phenylisocyanate (1·59 g. 13 mmoles) in dry ether (10 ml) was added dropwise to a soln of I (3·0 g. 13 mmoles) in the same solvent (10 ml) under stirring and cooling with an ice bath in order to prevent the temp from rising above 5–10°. The mixture was kept in the refrigerator for 72 hr.† The solvent was distilled under red press and the viscous oily residue was dissolved in EtOH and *hydrolised* with HCl 10% (15 ml). The soln was stirred for 48 hr. giving XLV (3 15 g. 86%) m.p. 126–128°. (Found: C. 65·50: H. 6·25: N. 5·17. $C_{15}H_{18}NO_4$ requires: C. 65·20: H. 6·57: N. 5·07%): IR spectrum (nujol): 3287. 3135 cm^{-1} (NH): 1732. 1715. 1704. 1670. 1655. 1546 cm^{-1} (COOEt: CONH): NMR spectrum (DMSO d_6): 0·16 τ (N<u>H</u>): 2·65 τ (Ph): 6·27 τ ($OC\underline{H}_3$: C<u>H</u>—$COOCH_3$: C<u>H</u>—CONHPh) (5H).

4. 1-N-*piperidino*-2(*and* 6)*carbomethoxycyclohex*-1-*ene* (II)

The enamine II was prepared as described in section 1 and purified by two distillations. b.p. 140–145° (7 mm). (Found: C. 70·80: H. 9·81: N. 6·17. $C_{13}H_{21}NO_2$ requires: C. 69·92: H. 9·48: N. 6·27%). IR spectrum (neat): 1738 cm^{-1} ($COOCH_3$): 1648 cm^{-1} (N—C=C): 1685. 1565 cm^{-1} (N—C=C—C=O): NMR spectrum: 5·14 τ (C<u>H</u>=C): 6·46 τ ($OC\underline{H}_3$).

* Unless otherwise specified, all the reactions with ethyl azodicarboxylate were carried out in the conditions of solvent temp and time above noted

† Unless otherwise specified, all the reactions with phenylisocyanate were carried out in the conditions of solvent, temp and time, above noted

5. *Reaction of* 1-N-*piperidino*-2(*and* 6)*carbomethoxycyclohex*-1-*ene* (II) *with ethyl azodicarboxylate*

(a) 1-N-*Piperidino*-2-*carbomethoxy*-6-(N.N'-*dicarbethoxy*)*hydrazino-cyclohex*-1-*ene* (XVII). From ethyl azodicarboxylate (1·37 g. 7·9 mmoles) and II (1·75 g. 7·9 mmoles). after removal of the solvent. XVII was obtained as viscous oil which solidified in light petroleum (2·20 g. 71%). m.p. 80–82°. (Found: C. 57·8: H. 7·72: N. 10·90. $C_{19}H_{31}N_3O_6$ requires: C. 57·4: H. 7·86: N. 10·58%); IR spectrum (nujol) 3290 cm^{-1} (NH): 1750. 1705 cm^{-1} (CO): 1688. 1602. 1523 cm^{-1} (N—C=C—C=O); NMR spectrum: 3·67 τ (NH): 4·95 τ (CH—N—NH): 6·28 τ (OCH_3).

(b) The compound XVII. hydrolysed with HCl 10% gave XXX. identical to the analytical sample.

6. *Reaction of* 1-N-*piperidino*-2(*and* 6)*carbomethoxycyclohex*-1-*ene* (II) *with phenylisocyanate*

(a) 1-N-*Piperidino*-2(*and* 6)*carbomethoxy*-6(*and* 2)*phenylcarbamylcyclohex*-1-*ene* (XXXVI). From phenyl-isocyanate (0·93 g. 7·9 mmoles) and II (1·75 g. 7·9 mmoles). after removal of the solvent. an oil was obtained. which solidified in light petroleum (2·15 g. 80%). m.p. 87–93° (Found: C. 70·0: H. 7·64: N. 8·32. $C_{20}H_{26}N_2O_3$ requires: C. 70·15: H. 7·65: N. 8·18%); IR spectrum (nujol): 3245 cm^{-1} (CO): 1645. 1610. 1534 cm^{-1} (N—C=C—C=O); 1591. 1495 cm^{-1} (Ph): NMR spectrum: − 2·01 τ (NH); 6·26 τ ($O—CH_3$); 6·43 τ (CH—CO).

(b) The compound XXXVI. hydrolysed with HCl 10% gave XLV.

7. 1-N-*Pyrrolidino*-2(*and* 6)*carbomethoxycyclohex*-1-*ene* (III).

The enamine III was prepared as described in section 1. and purified by distillation. b.p. 120–125° (0·1 mm). The product solidified on standing or by scratching m.p. 71–73° [lit. 76–78°]. from light petroleum (Found: C. 68·34: H. 9·42: N. 6·6. $C_{12}H_{19}NO_2$ requires: C. 68·87: H. 9·15: N. 6·69%); IR spectrum (nujol): 1681, 1662, 1558, 1535 cm^{-1} (N—C=C—C=O); NMR spectrum: 5·56 τ (CH=C); 6·34 τ (OCH_3); 6·74 τ ($CH_2—N—CH_2$).

8. *Reaction of* 1-N-*pyrrolidino*-2(*and* 6)*carbomethoxycyclohex*-1-*ene* (III) *with ethyl azodicarboxylate*

(a) 1-N-*Pyrrolidino*-2-*carbomethoxy*-6-(N.N'-*dicarbethoxy*)*hydrazinocyclohex*-1-*ene* (XVIII). Ethyl azo-dicarboxylate (1·74 g. 9·8 mmoles) and III (2·0 g. 9·8 mmoles) gave a crystalline XVIII (3·1 g. 85%). m.p. 106–109°. (Found: C. 56·29: H. 7·42: N. 10·97. $C_{18}H_{29}N_3O_6$ requires: C. 56·38: H. 7·62: N. 10·96%); IR spectrum (nujol): 3308 cm^{-1} (NH): 1754. 1692 cm^{-1} (COOEt): 1672. 1602 cm^{-1} (N—C=C—C=O): NMR spectrum: 3·65 τ (NH): 5·06 τ (CH—N—NH): 6·32 τ (OCH_3).

(b) The compound XVIII, hydrolysed with HCl 10%, gave XXX, identical to the analytical sample.

9. *Reaction of* 1-N-*pyrrolidino*-2(*and* 6)*carbomethoxycyclohex*-1-*ene* (III) *with phenylisocyanate*

(a) 1-N-*Pyrrolidino*-2(*and* 6)*carbomethoxy*-6(*and* 2)*phenylcarbamylcyclohex*-1-*ene* (XXXVII). Phenyliso-cyanate (1·17 g. 9·8 mmoles) reacted with III (2·0 g. 9·8 mmoles) to give XXXVII (2·93 g. 95%). m.p. 157 158 . from benzene. (Found: C. 69·70: H. 7·47; N. 8·36. $C_{19}H_{24}N_2O_3$ requires: C. 69·49: H. 7·38: N. 8·53%); IR spectrum (nujol): 3320 cm^{-1} (NH): 1729 cm^{-1} (CO): 1634. 1609. 1508 cm^{-1} (N—C=C—C=O); 1590 cm^{-1} (Ph); NMR spectrum: 2·75 τ (Ph; NH); 6·26 τ (OCH_3): 6·32 τ (CH—CO).

(b) The compound XXXVII. treated with HCl 10%. gave XLV. identical to the analytical sample.

10. 1-N-*Morpholino*-2(*and* 6)*carbethoxycyclohex*-1-*ene* (IV)

Ethylchloroformate (14·4 g, 0·12 moles) was added dropwise to a soln of 1-N-morpholino-cyclohex-1-ene (4·0 g. 0·24 moles) in dry benzene (200 ml). The mixture was heated under reflux with stirring for 10 hr. After cooling. dry ether (150 ml) was added and the ppt of enamine hydrochloride filtered off. Removal of the solvent left an oil which was twice distilled. b.p. 95–105° (0·1 mm). (Found: C. 64·80: H. 8·85: N. 5·87. $C_{13}H_{21}NO_3$ requires: C. 65·24: H. 8·85: N. 5·85%); IR spectrum (neat): 1740 cm^{-1} (CO): 1686. 1575 cm^{-1} (N—C=C—C=O): 1647 cm^{-1} (N—C=CH): NMR spectrum: 5·08 τ (CH=C): 5·85 τ ($CH_2—CH_3$): 6·32 τ ($CH_2—O—CH_2$): 8·74 τ ($CH_2—CH_3$).

11. *Reaction of* 1-N-*morpholino*-2(*and* 6)*carbethoxycyclohex*-1-*ene* (IV) *with ethyl azodicarboxylate*

(a) 1-N-*Morpholino*-2-*carbethoxy*-6-(N.N'-*dicarbethoxy*)*hydrazinocyclohex*-1-*ene* (XIX). Ethyl azodi-carboxylate (1·95 g. 13 mmoles) reacted with IV (2·7 g. 13 mmoles) to give. after removal of the solvent. an oil which crystallized by scratching (4·1 g. 88%) m.p. 92–94°. from benzene and light petroleum. (Found: C. 55·36: H. 7·49: N. 10·10. $C_{19}H_{31}N_3O_7$ requires: C. 55·18: H. 7·56: N. 10·16%); IR spectrum (nujol): 3300 cm^{-1} (NH): 1746. 1699 cm^{-1} (CO): 1675. 1594 cm^{-1} (N—C=C—C=O): NMR spectrum: 3·67 τ (NH): 4·94 τ (CH—N—NH): 5·82 τ ($CH_2—CH_3$): 6·42 τ ($CH_2—O—CH_2$): 7·08 τ ($CH_2—N—CH_2$): 8·72 τ ($CH_2—CH_3$).

(b) 2-*Carbethoxy*-6-(N.N'*dicarbethoxy*)*hydrazinocyclohexanone* (XXXI). The compound XIX. treated with HCl 10%. gave a solid (XXXI) m.p. 69–71°. from aqueous MeOH. in quantitative yield. (Found: C. 52·12; H. 7·10; N. 8·09. $C_{15}H_{24}N_2O_7$ requires: C. 52·31; H. 7·03; N. 8·14%); IR spectrum (nujol) 3278 cm^{-1} (NH); 1751. 1738. 1719. 1680 cm^{-1} (CO); NMR spectrum 3·42 τ (N<u>H</u>); 5·20 τ (C<u>H</u>—N—NH); 5·84 τ ($C\underline{H}_2$—CH_3); 6·62 τ (C<u>H</u>—COOEt); 8·72 τ (CH_2—$C\underline{H}_3$).

12. *Reaction of* 1-N-*morpholino*-2(*and* 6)*carbethoxycyclohex*-1-*ene* (IV) *with phenylisocyanate*

2-*Carbethoxy*-6-*phenylcarbamylcyclohexanone* (XLVI). Phenylisocyanate (1·0 g. 8·4 mmoles) reacted with IV (2·0 g. 8·4 mmoles). to give a viscous oil which was hydrolysed with HCl 10% under cooling and stirring. for 48 hr. A solid XLVI was obtained (1·0 g). m.p. 97–98°. from aqueous EtOH. The mother liquors were extracted with benzene; the benzene soln. after concentration. was chromatographed to give a further 0·60 g of XLVI. total yield 80%. (Found: C. 66·97; H. 6·59; N. 4·87. $C_{16}H_{19}NO_4$ requires: C. 66·42; H, 6.62; N, 4·84%); IR spectrum (nujol); 3285, 3250, 3195, 3138 cm^{-1} (NH); 1740, 1730, 1712, 1670, 1652 cm^{-1} (CO); 1602, 1595 cm^{-1} (Ph); NMR spectrum; −4·05 τ, −1·27 τ (—O<u>H</u>—C═C); 0·78 τ, 1·27 τ, 1·63 τ (N<u>H</u>): 2·75 τ (Ph); 5·82 τ ($C\underline{H}_2$—CH_3); 6·57 τ (C<u>H</u>—CO); 8·74 (CH_2—$C\underline{H}_3$).

13. 1-N-*Piperidino*-2(*and* 6)*carbethoxycyclohex*-1-*ene* (V)

The enamine V was prepared as described in section 10 and purified by two distillations. b.p. 120° (1·5 mm). (Found: C. 71·80; H. 9·29; N. 6·08. $C_{14}H_{23}NO_2$ requires: C. 70·85; H. 9·77; N. 5·90%); IR spectrum (neat); 1737 cm^{-1} (CO); 1686. 1570 cm^{-1} (N—C═C—C═O). 1645 cm^{-1} (N—C═CH); NMR spectrum: 5·15 τ (C<u>H</u>═C); 5·89 τ ($C\underline{H}_2$—CH_3); 8·75 τ (CH_2—$C\underline{H}_3$).

14. *Reaction of* 1-N-*piperidino*-2(*and* 6)*carbethoxycyclohex*-1-*ene* (v) *with ethyl azodicarboxylate*

(a) 1-N-*Piperidino*-2-*carbethoxy*-6-(N.N'-*dicarbethoxy*)*hydrazino*-*cyclohex*-1-*ene* (XX). Ethyl azodicarboxylate (1·5 g. 8·4 mmoles) reacted with V (2·0 g. 8·4 mmoles) to give, after removal of the solvent, a spongy solid (3·15 g. 90%). which crystallized by scratching in light petroleum. m.p. 70–72°. (Found: C. 58·60; H. 8·01; N. 10·40. $C_{20}H_{33}N_3O_6$ requires: C. 58·37; H. 8·07; N. 10·21%); IR spectrum (nujol): 3276 cm^{-1} (NH); 1745. 1704. 1678 cm^{-1} (CO); 1595 cm^{-1} (N—C═C—C═O); NMR spectrum: 3·72 τ (N<u>H</u>); 4·95 τ (C<u>H</u>—N—NH); 5·82 τ ($C\underline{H}_2$—CH_3); 8·71 τ (CH_2—$C\underline{H}_3$).

(b) Acidic hydrolysis of XX with HCl 10% gave XXXI. identical to the analytical sample.

15. 1-N-*Pyrrolidino*-2(*and* 6)*carbethoxycyclohex*-1-*ene* (VI)

The enamine VI was prepared as described in section 10 and purified by two distillations. b.p. 148–152° (4 mm). The product crystallized by scratching. m.p. 53–54°. (Found: C. 70·80; H. 9·81; N. 6·16. $C_{13}H_{21}NO_2$ requires: C. 69·90; H. 9·48; N. 6·27%); IR spectrum (neat): 1740 (CO); 1678. 1558 cm^{-1} (N—C═C—C═O); 1615 cm^{-1} (N—C═C); NMR spectrum: 5·56 τ (C<u>H</u>═C); 5·91 τ ($C\underline{H}_2$—CH_3); 8·76 τ (CH_2—$C\underline{H}_3$).

16. *Reaction of* 1-N-*pyrrolidino*-2(*and* 6)*carbethoxycyclohex*-1-*ene* (VI) *with ethyl azodicarboxylate*

Ethyl azodicarboxylate (1·56 g. 9·0 mmoles) reacted with VI (2·0 g. 9·0 mmoles). to give. after removal of the solvent. a viscous oil which hydrolysed with HCl 10%. under cooling and stirring. for 48 hr. The mixture was extracted with ether and benzene. The organic extracts. concentrated and chromatographed on silica gel. gave XXXI (1·96 g. 65%). identical to the analytical sample.

17. *Reaction of* 1-N-*pyrrolidino*-2(*and* 6)*carbethoxycyclohex*-1-*ene* VI *with phenylisocyanate*

(a) 1-N-*Pyrrolidino*-2(*and* 6)*carbethoxy*-6(*and* 2)*phenylcarbamylcyclohex*-1-*ene* (XXXIX). Phenylisocyanate (1·6 g. 13·5 mmoles) reacted with VI to give XXXIX as a crystalline product (4·25 g. 92%). m.p. 135–138°. (Found: C. 70·70; H. 7·86; N. 8·35. $C_{20}H_{26}N_2O_3$ requires: C. 70·14; H. 7·66; N. 8·18%); IR spectrum (nujol): 3318 cm^{-1} (NH); 1740 cm^{-1} (COOEt); 1634. 1610. 1515 cm^{-1} (N—C═C—C═O); NMR spectrum: 0·52 τ. 2·27 τ (N<u>H</u>COPh); 5·84 τ ($C\underline{H}_2$—CH_3); 6·46 τ (C<u>H</u>—CO); 8·71 τ (CH_2—$C\underline{H}_3$).

(b) The product XXXIX was hydrolysed with HCl 10%. giving XLVI. identical to the analytical sample.

18. 1-N-*Morpholino*-2(*and* 6)*acetylcyclohex*-1-*ene* (VII)[7]

Acetylcyclohexanone (10·0 g. 0·07 moles) and morpholine (13·0 g. 0·14 moles) were heated in refluxing benzene (35 ml) for 96 hr. The solvent was removed and the residue distilled b.p. 88–90° (0·1 mm): IR spectrum (neat): 1704 cm^{-1} (CO); 1642 cm^{-1} (N—C═CH); 1620. 1540 cm^{-1} (N—C═C—C═O); NMR spectrum: 5·07 τ (C<u>H</u>═C); 6·4 τ ($C\underline{H}_2$—O—$C\underline{H}_2$); 7·73 τ (C═C—CO$C\underline{H}_3$); 7·91 τ (CH—CO$C\underline{H}_3$).

19. *Reaction of* 1-N-*morpholino-2(and 6)acetylcyclohex-1-ene* (VII) *with ethyl azodicarboxylate*

2-*Acetyl-6-(N.N'-dicarbethoxy)hydrazinocyclohexanone* (XXXII). Ethyl azodicarboxylate (1·67 g. 9·6 mmoles) reacted with VII (2·0 g. 9·6 mmoles) to give, after removal of the solvent, a viscous oil which was hydrolysed with HCl 10%. under stirring for 48 hr. The mixture was extracted with benzene. The concentrated benzene soln was chromatographed on column and left XXXII (2·9 g. 80%) m.p. 88–89°. from aqueous MeOH. (Found: C. 53·86; H. 6·98; N. 8·93. $C_{14}H_{22}N_2O_6$ requires: C. 53·49; H. 7·05; N. 8·91%); IR spectrum (nujol); 3265 cm^{-1} (NH); 1752, 1700 cm^{-1} (CO); 1605 cm^{-1} (C═C—OH...OC^-); NMR spectrum ($CDCl_3$ + CCl_4): − 1·24 τ (C═C—OH..OC—) 3·33 τ (N<u>H</u>); 5·22 τ (C<u>H</u>—N—NH); 5·85 τ ($C\underline{H}_2$—CH_3); 7·87 τ ($COC\underline{H}_3$); 8·41 τ (CH_2—$C\underline{H}_3$).

20. 1-N-*Piperidino-2(and 6)acetylcyclohex-1-ene* (VIII)

The enamine VIII was prepared as described in section 19. and purified by distillation. b.p. 108–110° (0·3 mm); IR spectrum (neat): 1705 cm^{-1} (CO); 1640 cm^{-1} (N—C═CH); 1615. 1580 cm^{-1} (N—C═C—C═O); NMR spectrum: 5·11 τ (C<u>H</u>═C—N); 7·79 τ (C═C—$COC\underline{H}_3$); 8·0 τ (CH—CO—$C\underline{H}_3$).

21. *Reaction of* 1-N-*piperidino-2(and 6)acetylcyclohex-1-ene* (VIII) *with ethyl azodicarboxylate*

Ethyl azodicarboxylate (1·34 g. 7·7 mmoles) reacted with VIII (1·6 g. 7·7 mmoles) to give a viscous oil which was hydrolysed with HCl 10%. under stirring for 72 hr. The mixture was extracted with ether. The extracts gave XXXII (1·7 g. 70%) by column chromatography.

22. 1-N-*Pyrrolidino-2(and 6)acetylcyclohex-1-ene* (IX)

The enamine IX was prepared according to the method described.[7] namely by acetylation of 1-N-pyrrolidinocyclohex-1-ene with acetylchloride. in presence of $(Et)_3N$. The ppt. of base hydrochloride was filtered off and the residue distilled. b.p. 120–130° (0·1 mm). The product crystallized by scratching in light petroleum. m.p. 74–76°; IR spectrum (nujol): 1610. 1492 cm^{-1} (N—C═C—C═O); NMR spectrum: 5·50 τ (C<u>H</u>—C—N); 6·80 τ ($C\underline{H}_2$—N—$C\underline{H}_2$); 7·90 τ (C═C—CO—CH_3).

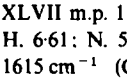
23. *Reaction of* 1-N-*pyrrolidino-2(and 6)acetylcyclohex-1-ene* (IX) *with ethyl azodicarboxylate*

Ethyl azodicarboxylate (2·08 g. 11·9 mmoles) reacted with IX (2·3 g. 11·9 mmoles) to give. after the removal of the solvent. an oil which was hydrolysed with HCl 10%. under stirring for 48 hr. The compound XXXII was obtained. The mother liquors were extracted with benzene. chromatographed in column. and furnished 0·850 g of XXXII. total yield 59%.

24. *Reaction of* 1-N-*pyrrolidino-2(and 6)acetylcyclohex-1-ene* (IX) *with phenylisocyanate*

(a) 1-N-*Pyrrolidino-2(and 6)acetyl-6(and 2)-phenylcarbamylcyclohex-1-ene* (XL). Phenylisocyanate (1·26 g. 10·6 mmoles) reacted with IX (2·0 g. 10·6 mmoles) to give crystalline XL (2·57 g. 80%). m.p. 169–170° [lit. 169–170°[7]] (Found: C. 72·92; H. 7·74; N. 8·97. $C_{19}H_{24}N_2O_2$ requires: C. 73·04; H. 7·86; N. 9·01%); IR spectrum (nujol): 3240. 3180. 3120 cm^{-1} (NH); 1682. 1580. 1549 (N—C═C—C═O); 1599 cm^{-1} (Ph).

(b) 2-*Acetyl-6-phenylcarbamylcyclohexanone* (XLVII). Acidic hydrolysis of XL gave quantitatively XLVII m.p. 113–114°. from ligroin. (Found: C. 69·34; H. 6·58; N. 5·46. $C_{15}H_{17}NO_3$ requires: C. 69·48; H. 6·61; N. 5·40%); IR spectrum (nujol): 3280. 3250. 3195 cm^{-1} (NH); 1660. 1546 cm^{-1} (CO—NH); 1615 cm^{-1} (C═C—OH..O═C); 1599, 1500 cm^{-1} (Ph); NMR spectrum (DMSO d_6): −5·8 τ



: −0·11 τ (N<u>H</u>—CO); 2·7 τ (Ph); 6·44 τ (C<u>H</u>—CONHPh); 7·81 τ ($COC\underline{H}_3$).

25. 1-N-*Morpholino-2(and 6)benzoylcyclohex-1-ene* (X)

Benzoylcyclohexanone (10·0 g. 0·05 moles) and morpholine (13·06 g 0·15 moles) in dry benzene. were heated under reflux for 7 days. Removal of the solvent left an oil which was distilled b.p. 170–180° (0·6 mm). The product solidified in ether. m.p. 77·5–79° [lit. 77–78°[9]]. (Found: C. 75·0; H. 7·98; N. 5·15. $C_{17}H_{21}NO_2$ requires: C. 75·2; H. 7·70; N. 5·10%); IR spectrum (nujol): 1620. 1571 cm^{-1} (N—C═C—C═O); 1591 cm^{-1} (Ph); NMR spectrum: 2·45 τ (Ph); 5·01 τ (C<u>H</u>═C).

26. *Reaction of* 1-N-*morpholino-2(and 6)benzoylcyclohex-1-ene* (X) *with ethyl azodicarboxylate*

(a) 1-N-*Morpholino-2-benzoyl-6-(N.N'-dicarbethoxy)hydrazinocyclohex-1-ene* (XXV). Ethyl azodicarboxylate (2·0 g. 11·4 mmoles) reacted with X (3·09 g. 11·4 mmoles) in a mixture of dry ether and benzene

(10 ml). to give a solid (4·2 g. 83%). m.p. 140–142°. from benzene and ligroin. (Found: C. 61·30; H. 6·85; N. 9·37. $C_{23}H_{31}N_3O_6$ requires: C. 61·91; H. 7·00. N. 9·42%): IR spectrum (nujol): 3275 cm^{-1} (NH); 1740. 1690 cm^{-1} (CO); 1675. 1619. 1572 cm^{-1} (N—C═C—C═O); NMR spectrum: 2·52 τ (Ph); 3·82 τ (NH); 4·80 τ (CH—N—NH); 5·82 τ (CH_2—CH_3); 6·76 τ (CH_2—O—CH_2); 8·72 τ (CH_2—CH_3).

(b) *2-Benzoyl-6-(N.N'dicarbethoxy)hydrazinocyclohexanone* (XXXIII). Acidic hydrolysis of XXV gave quantitatively XXXIII. m.p. 142–143°. from benzene and ligroin (Found: C. 60·05; H. 6·50; N. 7·26. $C_{19}H_{24}N_2O_6$ requires: C. 60·63; H. 6·43; N. 7·44%); IR spectrum (nujol): 3278 cm^{-1} (NH); 1745. 1703. 1681 cm^{-1} (CO); 1594. 1578 cm^{-1} (Ph); NMR spectrum: 2·50 τ (Ph); 3·45 τ (NH); 5·0 τ (CH—N—NH); 5·86 τ (CH_2—CH_3); 8·76 τ (CH_2—CH_3).

27. 1-N-*Piperidino-2(and 6)benzoylcyclohex-1-ene* (XI)

The enamine XI was prepared as described in section 25. and purified by distillation. b.p. 158–160° (0·1 mm). The product crystallized from light petroleum. m.p. 52–55°. (Found: C. 80·30; H. 8·55; N. 4·91. $C_{18}H_{23}NO$ requires: C. 80·26; H. 8·61; N. 5·20%); IR spectrum (nujol): 1642. 1565 cm^{-1} (N—C═C—C═O); 1595. 1578 cm^{-1} (Ph); NMR spectrum: 2·50 τ (Ph); 5·02 τ (N—C═CH).

28. *Reaction of* 1-N-*piperidino-2(and 6)benzoylcyclohex-1-ene* (XI) *with ethyl azodicarboxylate*

(a) 1-N-*Piperidino-2-benzoyl-6-(N.N'-dicarbethoxy)hydrazinocyclohex-1-ene* (XXVI). Ethyl azodicarboxylate (1·29 g. 7·4 mmoles) and XI (2·0 g. 7·4 mmoles). in a mixture of dry ether and benzene (10 ml). gave a crystalline product (1·6 g) m.p. 111–113° from light petroleum. (Found: C. 65·00; H. 7·47; N. 9·49. $C_{24}H_{33}N_3O_5$ requires: C. 64·99; H. 7·50; N. 9·47%); IR spectrum (nujol): 3325 cm^{-1} (NH); 1745. 1692 cm^{-1} (COOEt); 1652. 1635 cm^{-1} (N—C═C—C═O); 1597. 1579 cm^{-1} (Ph); NMR spectrum: 2·48 τ (Ph); 3·48 τ (NH); 4·82 τ (CH—N—NH); 5·83 τ (CH_2—CH_3); 8·74 τ (CH_2—CH_3). The mother liquors were treated with HCl 10%. under stirring for 24 hr. and left XXXIII identical to the analytical sample. yield 65%.

(b) The product XXXVI. hydrolysed with HCl 10%. gave XXXIII.

29. 1-N-*Pyrrolidino-2(and 6)benzoylcyclohex-1-ene* (XII)

The enamine XII was prepared as described in section 25 and purified by distillation. b.p. 165–166° (0·1 mm). The product solidified by scratching. m.p. 87–89°. from light petroleum. (Found: C. 79·90; H. 8·24; N. 5·21. $C_{23}H_{21}NO$ requires: C. 80·00; H. 8·20; N. 5·40%); IR spectrum (nujol): 1600. 1586 cm^{-1} (Ph); 1618. 1538 cm^{-1} (N—C═C—C═O); NMR spectrum: 2·62 τ (Ph); 5·71 τ (CH═C—N); 6·88 τ (CH_2—N—CH_2).

30. *Reaction of* 1-N-*pyrrolidino-2(and 6)benzoylcyclohex-1-ene* (XII) *with ethyl azodicarboxylate*

(a) 1-N-*Pyrrolidino-2-benzoyl-6-(N.N'-dicarbethoxy)hydrazinocyclohex-1-ene* (XXVII). Ethyl azodicarboxylate (2·0 g. 11·3 mmoles) and XII (2·9 g. 11·3 mmoles) in a mixture of dry ether and benzene (10 ml). gave a yellow product. XXVII m.p. 91–93°. from light petroleum. (Found: C. 64·00; H. 7·34; N. 9·67. $C_{23}H_{31}N_3O_5$ requires: C. 64·32; H. 7·26; N. 9·78%); IR spectrum (nujol): 3245 cm^{-1} (NH); 1747. 1695 cm^{-1} (COOEt); 1685. 1622. 1559 cm^{-1} (N—C═C—C═O); 1596. 1588 cm^{-1} (Ph); NMR spectrum: 2·57 τ (Ph); 3·70 τ (NH); 4·97 τ (CH—N—NH); 5·84 τ (CH_2—CH_3); 7·08 τ (CH_2—N—CH_2); 8·74 τ (CH_2—CH_3).

(b) The product XXVII. hydrolysed with HCl 10%. gave (XXXIII).

31. *Reaction of* 1-N-*pyrrolidino-2(and 6)benzoylcyclohex-1-ene* (XII) *with phenylisocyanate*

(a) 1-N-*Pyrrolidino-2(and 6)benzoyl-6(and 2)-phenylcarbamylcyclohex-1-ene* (XLI). Phenylisocyanate (0·93 g. 7·8 mmoles) reacted with XII (2·0 g. 7·8 mmoles) to give a yellow product XLI (2·6 g. 81%). m.p. 193–194°. (Found: C. 77·33; H. 7·20; N. 7·38. $C_{24}H_{26}N_2O_2$ requires: C. 76·97; H. 7·00; N. 7·48%); IR spectrum (nujol): 3295–3136 cm^{-1} (NH); 1671. 1619. 1552 cm^{-1} (N—C═C—C═O); 1601. 1581 cm^{-1} (Ph).

(b) *2-Benzoyl-6-phenylcarbamylcyclohexanone* (XLVIII). Acidic hydrolysis of XLI gave XLVIII, m.p. 153–155°. from aqueous MeOH. (Found: C. 74·32; H. 5·90; N. 4·29. $C_{20}H_{19}NO_3$ requires: C. 74·74; H. 5·96; N. 4·36%); IR spectrum (nujol): 3283. 3200 (NH). 1697. 1678. 1665. 1546 cm^{-1} (CO; CONH); 1594. 1581 cm^{-1} (Ph); NMR spectrum (DMSO d_6): 0·17 τ (NH); 2·5 τ (Ph); 5·20 τ (CHCOPh); 6·15 τ (CH—CONHPh).

32. 1-N-*Morpholino-2(and 6)phenylcarbamylcyclohex-1-ene* (XIII)

Phenylisocyanate (2·85 g. 24 mmoles) in dry ether (5 ml) was added dropwise to a soln of 1-N-morpholinocyclohex-1-ene (4·0 g. 24 mmoles) in the same solvent (15 ml). A solid was obtained (5·8 g. 85%). m.p. 123–126° [lit. 125–126°[10a, b]]. from acetonitrile. (Found: C. 70·64; H. 7·64; N. 9·69. $C_{17}H_{22}N_2O_2$ requires: C. 71·30; H. 7·74; N. 9·78%); IR spectrum (nujol): 3240–3120 cm^{-1} (NH); 1688 cm^{-1} (CO); 1595. 1545 cm^{-1} (N—C═C—C═O); 1656 cm^{-1} (N—C═CH); NMR spectrum: − 2·92 τ. 0·21 τ (N<u>H</u>—CO); 2·74 τ (Ph); 4·94 τ (C<u>H</u>═C); 6·21 τ (C<u>H</u>$_2$—O—C<u>H</u>$_2$).

33. *Reaction of* 1-N-*morpholino-2(and 6)phenylcarbamylcyclohex-1-ene* (XIII) *with ethyl azodicarboxylate*

(a) 1-N-*Morpholino-2-phenylcarbamyl-6-(N.N'-dicarbethoxy)hydrazinocyclohex-1-ene* (XXVIII). Ethyl azodicarboxylate (1·32 g. 7·6 mmoles) reacted with XIII (2·2 g. 7·6 mmoles). in a mixture of dry ether and acetonitrile. Removal of the solvent left an oil which solidified by scratching. m.p. 124–127°. from benzene and light petroleum (3·3 g. 93%). (Found: C. 59·83; H. 6·84; N. 12·10. $C_{23}H_{32}N_4O_6$ requires: C. 59·98; H. 7·00; N. 12·17%); IR spectrum (nujol): 3308 cm^{-1} (NH); 1743. 1688. 1657. 1538 cm^{-1} (N—C═C—C═O; COOEt; CONH); NMR spectrum (DMSO d_6): 0·2 τ (N<u>H</u>CO); 1·02 τ (N<u>H</u>); 2·65 τ (Ph); 5·05 τ (C<u>H</u>—N—NH); 5·90 τ (C<u>H</u>$_2$—CH$_3$); 6·55 τ (C<u>H</u>$_2$—O—C<u>H</u>$_2$); 7·07 τ (C<u>H</u>$_2$—N—C<u>H</u>$_2$); 8·78 τ (CH$_2$—C<u>H</u>$_3$).

(b) 2-*Phenylcarbamyl-6-(N.N'-dicarbethoxy)hydrazinocyclohexanone* (XXXIV). The compound XXVIII was treated with HCl 10%. under stirring for 36 hr. giving XXXIV. m.p. 175–176°. from MeOH. (Found: C. 57·91; H. 6·26; N. 10·76. $C_{19}H_{25}N_3O_6$ requires: C. 58·30; H. 6·40; N. 10·70%); IR spectrum (nujol): 3250. 3180 cm^{-1} (NH); 1752. 1725. 1690. 1672. 1538 cm^{-1} (COOEt; CONH); NMR spectrum: 1·11 τ (N<u>H</u>COPh); 2·68 τ (Ph); 3·17 τ (N<u>H</u>—N); 5·12 τ (C<u>H</u>—N—NH); 5·86 τ (C<u>H</u>$_2$—CH$_3$); 6·65 τ (C<u>H</u>—CONH); 8·75 τ (CH$_2$—C<u>H</u>$_3$).

34. *Reaction of* 1-N-*morpholino-2(and 6)phenylcarbamylcyclohex-1-ene* (XIII) *with phenylisocyanate*

(a) 1-N-*Morpholino-2.6-diphenylcarbamylcyclohex-1-ene* (XLII). A quantitative yield of XLII. m.p. 194–196°. from MeOH could be obtained only when the reaction was carried out in refluxing benzene. (Found: C. 70·33; H. 6·70; N. 10·08. $C_{24}H_{27}N_3O_3$ requires: C. 71·08; H. 6·71; N. 10·36%); IR spectrum (nujol): 3280–3130 cm^{-1} (NH); 1650. 1550 cm^{-1} (CONH); 1640. 1534 cm^{-1} (N—C═C—C═O); NMR spectrum: (DMSO d_6) − 0·24 τ. 0·00 τ (N<u>H</u>); 2·7 τ (Ph); 6·34 τ (C<u>H</u>—CONHPh); 6·56 τ (C<u>H</u>$_2$—O—C<u>H</u>$_2$); 7·12 τ (C<u>H</u>$_2$—N—C<u>H</u>$_2$).

(b) 2.6-*Diphenylcarbamylcyclohexanone* (XLIX). Acidic hydrolysis of XLII with HCl 10% gave quantitatively XLIX. m.p. 234–238° [lit. 254°[10a, b]]. from aqueous dioxan. (Found: C. 71·10; H. 6·13; N. 8·24. $C_{20}H_{20}N_2O_3$ requires: C. 71·40; H. 5·99; N. 8·33%); IR spectrum (nujol): 3285–3140 cm^{-1} (NH); 1702. 1688. 1648. 1546 cm^{-1} (CO; CONH).

35. 1-N-*Piperidino-2(and 6)phenylcarbamylcyclohex-1-ene* (XIV)

Phenylisocyanate (2·8 g. 24 mmoles) reacted with 1-N-piperidinocyclohex-1-ene (4·0 g. 24 mmoles) in dry ether (15 ml). A solid compound was isolated (5·3 g. 78%) m.p. 102–103°. from acetonitrile. (Found: C. 76·15; H. 8·61; N. 9·92. $C_{18}H_{24}N_2O$ requires: C. 76·01; H. 8·51; N. 9·85%); IR spectrum (nujol): 3230–3118 cm^{-1} (NH); 1684 cm^{-1} (CONH); 1595. 1542 cm^{-1} (N—C═C—C═O); 1650 cm^{-1} (N—C═CH); NMR spectrum: − 2·82 τ. − 0·45 τ (N<u>H</u>); 2·40 τ (Ph); 4·95 τ (C<u>H</u>═C); 7·31 τ (C<u>H</u>$_2$—N—C<u>H</u>$_2$).

36. *Reaction of* 1-N-*piperidino-2(and 6)phenylcarbamylcyclohex-1-ene* (XIV) *with ethyl azodicarboxylate*

(a) 1-N-*Piperidino-2-phenylcarbamyl-6-(N.N'-dicarbethoxy)hydrazinocyclohex-1-ene* (XXIX). Ethyl azodicarboxylate (1·24 g. 7·04 mmoles) reacted with XIV (2·02 g. 7·04 mmoles) to give a crystalline product (1·5 g). m.p. 138–140°. (Found: C. 62·16; H. 7·31; N. 11·9. $C_{22}H_{34}N_4O_5$ requires: C. 62·86; H. 7·47; N. 12·22%); IR spectrum (nujol): 3310 cm^{-1} (NH); 1745. 1735. 1690 cm^{-1} (CO); 1657. 1535 cm^{-1} (CONH); NMR spectrum: − 0·35 τ (N<u>H</u>CO); 2·6 τ (Ph); 3·25 τ (N<u>H</u>—COOEt); 4·82 τ (C<u>H</u>—N—NH); 5·78 τ (C<u>H</u>$_2$—CH$_3$); 7·05 τ (C<u>H</u>$_2$— N C<u>H</u>$_2$); 8·70 τ (CH$_2$—C<u>H</u>$_3$). The mother liquors. hydrolysed with HCl 10% gave further 0·810 g of XXXIV. identical to the analytical sample. yield 74%.

(b) Acidic hydrolysis of XXIX with HCl 10% gave quantitatively XXXIV.

37. *Reaction of* 1-N-*piperidino-2(and 6)phenylcarbamylcyclohex-1-ene* (XIV) *with phenylisocyanate*

Phenylisocyanate (1·0 g. 8·4 mmoles) in dry benzene (10 ml) was added to a soln of XIV (2·4 g. 8·4 mmoles) in the same solvent (10 ml). Removal of the solvent left a crude product which was treated with HCl 10%. under cooling and stirring. The compound XLIX (2·26 g. 80%) was isolated.

38. *Reaction of* 1-N-*pyrrolidinocyclohex*-1-*ene with phenylisocyanate*

Numerous attempts were made in order to obtain 1-N-pyrrolidino XV[7] as pure product. but they all failed. Therefore we carried out the same reaction using $CDCl_3$ as solvent and preventing the temp from rising above 25°. After 30 min. a little portion of it was analysed by NMR. No change was observed after 24 hr: NMR spectrum: 0·08 τ. 0·26 τ. 1·2 τ (NH: 1H): 2·76 τ (Ph: 5H): 5·32 τ (CH=C: 0·25 H): 6·4 τ (CH—CONHPh): 6·83 τ (CH_2—N—CH_2: 4H).

39. *Reaction of* 1-N-*pyrrolidinocyclohex*-1-*ene with phenylisocyanate* (1 : 2)

Phenylisocyanate (3·12 g, 26 mmoles) in dry ether (5 ml) was added to a soln of 1-N-pyrrolidino-cyclohex-1-ene (2·0 g. 13 mmoles) in the same solvent (10 ml). After removal of the solvent. the crude product was hydrolysed with HCl 10% under stirring for 24 hr. The compound XLIX (3·15 g, 68%) was isolated.

Acknowledgement—This work was supported by a grant from the Consiglio Nazionale delle Ricerche (Rome).

REFERENCES

1 Part X. F. P. Colonna. M. Forchiassin. G. Pitacco. A. Risaliti and E. Valentin. *Tetrahedron* **26**. 5289 (1970)

2 F. P. Colonna. M. Forchiassin. A. Risaliti and E. Valentin. *Tetrahedron Letters* 571 (1970)

3 [a] A. Risaliti and L. Marchetti. *Boll. Sci. fac. chim. ind. BO Italy* **22**. 61 (1964);
[b] A. Risaliti. L. Marchetti and M. Forchiassin. *Ann. Chim. (Italy)*. **56**. 317 (1966);
[c] A. Risaliti. S. Fatutta and M. Forchiassin. *Tetrahedron* **23**. 1451 (1967);
[d] A. Risaliti. S. Fatutta. M. Forchiassin and C. Russo. *Ric. Sci.*. **38**. 827 (1968);
[e] A. Risaliti. M. Forchiassin and E. Valentin. *Tetrahedron* **24**. 1889 (1968);
[f] F. P. Colonna. S. Fatutta. A. Risaliti and C. Russo. *J. Chem. Soc.* (C). 2377 (1970)

4 J. Dabrowski and K. Kamieńska-Trela. *Spectrochim. Acta* **22**. 211 (1966)

5 A. Halleux and G. Viehe. *J. Chem. Soc.* (C). **881** (1970)

6 G. Opitz and F. Zimmerman. *Liebigs. Ann.*. **662**. 178 (1963)

7 G. Opitz and E. Tempel. *Ibid.* **699**. 74 (1966)

8 R. Jacquier. C. Petrus. F. Petrus and M. Valentin. *Bull. Soc. Chim. Fr.* 2678 (1970)

9 R. Helmers. *Acta Chem. Scand.* **19**. 2139 (1965)

10 [a] R. Fusco. G. Bianchetti and S. Rossi. *Gazz. Ital.* **91**, 825 (1961);
[b] G. Bertchold. *J. Org. Chem.* **26**. 3043 (1961)

11 W. D. Gurowitz and M. A. Joseph. *J. Org. Chem.* **32**. 3289 (1967)

12 [a] H. C. Brown. J. H. Brewster and H. Shechter. *J. Am. Chem. Soc.* **76**. 467 (1954);
[b] H. C. Brown. *J. Org. Chem.* **21**. 439 (1957)

13 M. G. Reinecke and L. R. Kray. *Ibid.* **31**. 4215 (1966)

14 A. Risaliti. *Boll. Sci. fac. chim. ind. BO Italy* **19**. 173 (1961)