Tetrahedron. Vol. 24, pp. 1889 to 1898. Pergamon Press 1968 Printed in Great Britain

VINYLAMINES—VIII[1]

THE REACTION OF CYCLOHEXANONE ENAMINES WITH 1- AND 2-NITROPROPENE

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(*Received in the UK* 23 *July* 1967; *accepted for publication* 21 *August* 1967)

Abstract—Enamines containing a trisubstituted double bond were obtained by reaction of morpholine, piperidine and pyrrolidine enamines of cyclohexanone with 1-nitropropene. Different results were obtained in the reaction of the same enamines with 2-nitropropene. A cycloaddition reaction occurred between 1-N-morpholino-cyclohexene and 2-nitropropene in ether at 0°, leading to an oxazine derivative. The structures of the products were determined by spectral and chemical evidence. In acetonitrile at 0° or in ether at room temperature the same enamine reacted with 2-nitropropene to give an enaminic mixture, where the less substituted alkylated isomer appeared to be the minor component. Analogous behaviour was shown by piperidine and pyrrolidine enamines. The mechanism and the stereochemistry of these reactions have been discussed. The formation of diadducts of a different nature from morpholine and pyrrolidine enamines with excess 2-nitropropene is also reported.

THE selective formation of isomeric products in the reaction of cyclohexanone enamines with electrophilic unsaturated reagents, depends on the structure of the latter. Thus, with reagents bearing hindering groups at the electrophilic center, new less substituted enamines were obtained,[2] while opposite results[1] were found when no substituents were linked to such a center. These findings have been interpreted in terms of relative conformational and rotational stability of the dipolar intermediates formed in the reactions.

In this connection, a comparison has been made between the reactions of cyclohexanone enamines with 1- and 2-nitropropene—two simple electrophilic isomeric olefins differing from one another only in the above mentioned steric requirements. In this paper, the results of these reactions[3] are discussed and the possibility of nitro group participation in the formation of heterocyclic derivatives containing O and N is atoms considered.

RESULTS

The reaction of 1-N-morpholino-cyclohexene (Ia) with 1-nitropropene (Chart 1) in petroleum ether at 0° gave 1-N-morpholino-6-(β-nitroisopropyl)cyclohex-1-ene (IIa) in 85% yield. The structure of IIa followed from analytical, spectral and chemical data. The NMR spectrum of IIa showed signals at 4·98 τ (area 1) and 5·58 τ (area 2) corresponding to the vinyl and nitromethylenic protons respectively. In the IR spectrum of IIa absorption bands at 1642 cm^{-1} for enaminic double bond and 1550 cm^{-1} for nitro group were evident. IIa upon hydrolysis with dilute aqueous hydrochloric acid gave 2-(β-nitroisopropyl)cyclohexanone (IV) and by reaction with ethyl azodicarboxylate led to 1-N-morpholino-2-(N,N′-dicarbethoxyhydrazino)-6-(β-nitroisopropyl)cyclohex-1-ene (IIIa) in 90% yield. The IR spectrum of IIIa showed

strong bands at 3280 cm^{-1} (NH) and at 1652 cm^{-1} (C=C—N). No signals at about 5 τ were seen in the NMR spectrum of IIIa, while one signal at 5·13 τ for the proton attached to the ring carbon atom bearing the dicarbethoxyhydrazinic group was present in the NMR spectrum of 2-(N,N'-dicarbethoxyhydrazino)-6-(β-nitroisopropyl)cyclohexanone (V), obtained on acidic hydrolysis of IIIa. These spectral data indicate the correct position of enaminic double bond in IIIa.

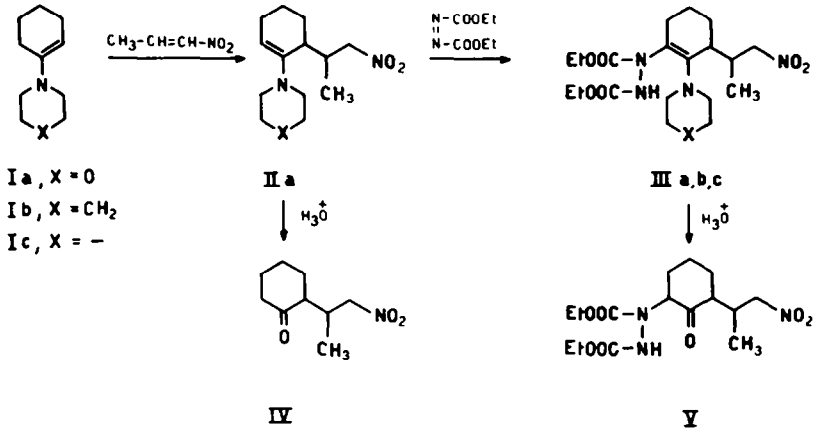


CHART 1

The behaviour of 1-N-piperidino- (Ib) and 1-N-pyrrolidino-cyclohexene (Ic) in the reaction with 1-nitropropene is similar to that of Ia (Chart 1). We were unable to isolate from Ib and Ic the corresponding reaction products II, but the structure similar to IIa, was demonstrated by reaction with ethyl azodicarboxylate. Actually, when this reagent was added to a soln of the reaction product from Ic and 1-nitropropene, 1-N-pyrrolidino-2-(N,N'-dicarbethoxyhydrazino)-6-(β-nitroisopropyl)cyclohex-1-ene (IIIc) was obtained in 85% yield. Similarly, from Ib through IIIb, V was formed in 76% yield. The structures of the disubstituted enamines IIIb and IIIc were assigned on the basis of their IR and NMR spectra.

When 1-N-morpholino-cyclohexene (Ia) reacted with 2-nitropropene (Chart 2) in dry ether at 0°, a white solid was formed within a few minutes. This product (80% yield) showed in the IR spectrum a strong band at 1628 cm^{-1}, but no significant absorption for NO_2 stretching. Its NMR spectrum revealed a signal at 7·95 τ as singlet (area 3) corresponding to the Me group and no signals in the region of 4–6 τ, as would be expected if vinyl or nitromethylenic protons were present. These spectral data, together with the analytical figures, indicate the structure of 3-methyl-9-N-morpholino-5,6,7,8,9,10-hexahydro-[1.2.4*H*]benzoxazine-N-oxide (VIIa). The band at 1628 cm^{-1} in the IR spectrum can be attributed[4] to the ring $C{=}N\overset{O}{\diagdown}$. In fact the same group in the furoxan ring has been found[5] to absorb at 1625–1600 cm^{-1}. Moreover VIIa was unreactive toward ethyl azodicarboxylate.

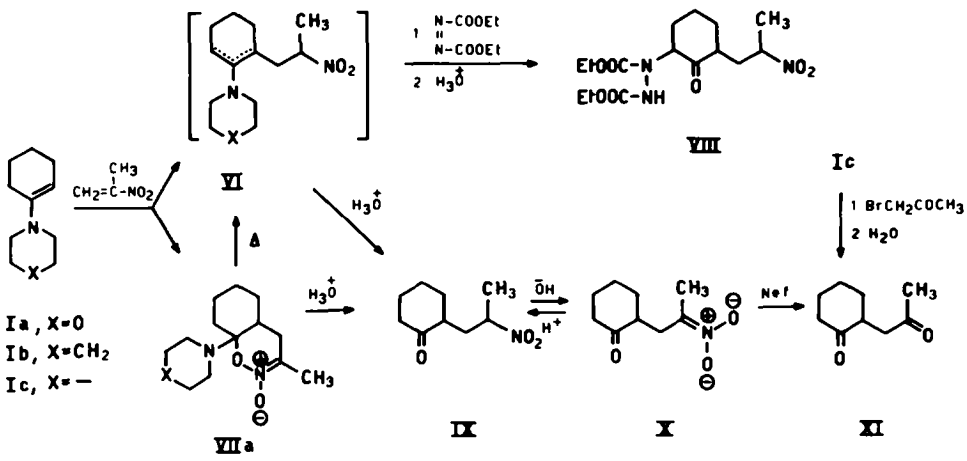


CHART 2

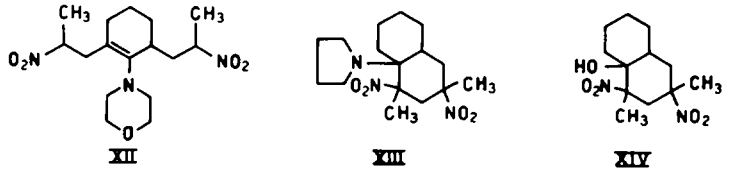
Compound VIIa was very unstable and had to be stored below 0°. On warming to room temperature, it gradually turned into a semi-solid material which showed in the IR spectrum strong bands at 1640 cm^{-1} and 1552 cm^{-1}, and no band at 1628 cm^{-1}. Interpreting these absorptions as evidence for the C=C—N and NO_2 groups respectively, we can conclude that VIIa was converted into a mixture of enamines VIa.

The same mixture of compounds (VIa) instead of VIIa, was obtained when the reaction of Ia with 2-nitropropene was carried out either in acetonitrile below 0° or in ether at 25–30°. This was revealed by the IR spectra of the reaction solutions. In every case, the mixtures VIa on treatment with ethyl azodicarboxylate and subsequent hydrolysis gave only 20–30% of 2-(β-nitropropyl)-6-(N,N'-dicarbethoxyhydrazino)-cyclohexanone (VIII). Considering that enamines II (Chart 1), like all the less substituted enamines,[2] react with ethyl azodicarboxylate to give the corresponding 2,6-disubstituted derivatives in 80–90% yield, we can assume that in the mixture VIa the less substituted isomer was always the minor component.

Both compounds VIIa and VIa by acidic hydrolysis or even by exposure to atmospheric moisture were easily converted into 2-(β-nitropropyl)cyclohexanone (IX). By GC and TLC analyses, IX appeared to be a mixture (1 : 1) of two isomers, which were identified as the diastereoisomers relevant to the ring and side chain asymmetric carbon atoms. Actually, on destroying one of the two asymmetric centers, the two isomers of the mixture IX were converted into the same compound. In fact, the sodium salt X formed from IX, gave by Nef reaction only 2-acetonyl-cyclohexanone (XI). This was identical in all respects with a sample obtained by alkylation of Ic with bromoacetone and subsequent hydrolysis. Also the compound VIII appeared to consist of two isomers. These, worked up as the nitroketone IX, were converted into an unique compound. This result also possibly suggests diastereoisomerism.

The reactions of 2-nitropropene with 1-N-piperidino- (Ib) and 1-N-pyrrolidino-cyclohexene (Ic) in ether solution at 0°, followed by hydrolysis, led to the diastereoisomeric mixture of 2-(β-nitropropyl)cyclohexanone (IX) in 80–90% yield. If ethyl azodicarboxylate was added to the solutions of these products before hydrolysis,

VIII was obtained in 35–40% yield (Chart 2). This indicates that also in the case of piperidine and pyrrolidine enamines, the monoalkylated less substituted enamine in the mixture VI was not the main product of the reaction with 2-nitropropene.



XII XIII XIV

CHART 3

From the reactions of 1-N-morpholino- and 1-N-pyrrolidino-cyclohexene (1 mole) with excess of 2-nitropropene (2 moles), diadducts in small yields (4% and 10% respectively) were isolated. These products however had different structures. The morpholine derivative showed in the IR spectrum absorptions at 1658 cm^{-1} and 1552 cm^{-1} giving evidence for C=C—N and NO_2 groups respectively. The NMR spectrum of this compound revealed a multiplet (area 2) at 5·1 τ which can be ascribed to protons linked to carbon atoms bearing a nitro group, and doublets at 8·44 τ and 8·46 τ corresponding to two nonequivalent Me groups. In contrast, in the IR spectrum of the pyrrolidine derivative, absorption bands were missing in the 2800–1550 cm^{-1} region, but a band was seen at 1538 cm^{-1} (NO_2). Moreover, no signals were found in the 4–6 τ region of its NMR spectrum, while signals due to two nonequivalent Me groups appeared as singlets. These data would indicate the structures of 1-N-morpholino-2,6-bis(β-nitropropyl)cyclohex-1-ene (XII) and 1,3-dimethyl-1,3-dinitro-9-N-pyrrolidino-decalin (XIII) for the above compounds, (Chart 3).

Compound XIII in aqueous solvents underwent rapid hydrolysis to give the hydroxy derivative XIV (Chart 3). The structure of the latter was consistent with its NMR and IR spectra that resembled those of XIII. The only significant difference was the appearance in NMR of a singlet at 7·47 τ and in IR of a band at 3510 cm^{-1}, both being distinctive features for the OH group.

All attempts to form analogous 2,6-dialkylated enamines or decalin derivatives by reaction of Ia, b, c with 1-nitropropene were unsuccessful.

DISCUSSION

The difference in chemical behaviour between 1- and 2-nitropropene in the reactions with cyclohexanone enamines, evidently depends on the position at which the Me group is bonded in the α,β-unsaturated nitro compound. In our opinion this structural feature plays an important role in defining the favorable conformation of the dipolar intermediate, on which, in turn, depends the nature of the final products.

When the Me group is linked to the electrophilic carbon atom of the olefinic reagent, as in 1-nitropropene, the result of the reaction with cyclohexanone enamines (I) is similar to that observed[2b] for β-nitrostyrene and the steric course of the reaction is similarly interpreted (Chart 4).

Assuming a two step mechanism with formation of a dipolar intermediate, the most stable conformation of the latter appears to be XV, in which the substituent in 2 position of the cyclohexane ring chair form is axially oriented. The alternative chair conformation with this substituent equatorially oriented is indeed strongly destabilized by the large $A^{(1,3)}$ strain[6] between the equatorial substituent and the

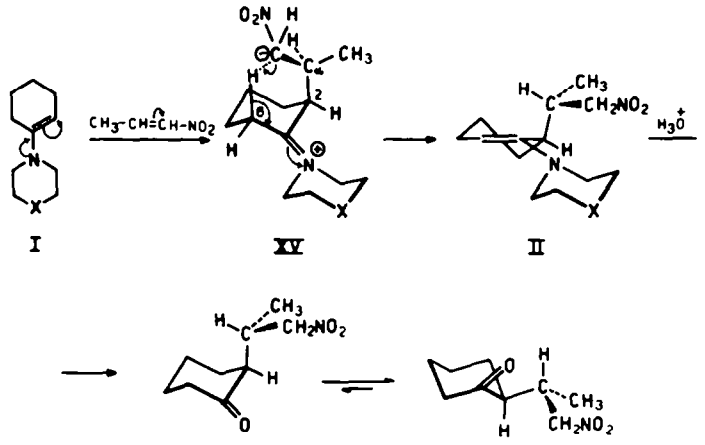


CHART 4

α-methylenic group on the nitrogen atom of the heterocyclic ring. Furthermore, in XV the rotation around the axial C_2–C_α bond is somewhat restricted and in the most stable rotomer the methyl group attached to C_α atom must be pointed outside the cyclohexane ring. As a result, the carbon atom bearing the negative charge points inside the ring, near to the axial hydrogen at the 6 position. Thus, by intramolecular transfer of this hydrogen to the negative carbon atom, the less substituted enamine II, in the quasi-axial half-chair conformation to avoid the $A^{(1,2)}$ strain,[6] is then formed from the intermediate XV.

This mechanism also determines the configuration of both C_2 and C_α atoms and, of the two possible diastereoisomers, only the *erythro* derivative is expected for the enamine II and, of course, for its hydrolysis product IV. Accordingly, a sole isomer was obtained from this reaction, as found by GC analysis of the hydrolysis product. Since these results are identical with those of the reaction of cyclohexanone enamines with β-nitrostyrenes yielding only *erythro* derivatives,[7,*] a similar configuration may be assigned to the compounds II and IV (Chart 4).

The most stable conformation for the dipolar intermediate of the reaction between cyclohexanone enamines (I) and 2-nitropropene, is again that with the substituent in 2 position axially oriented (XVI) (Chart 5). In this case, however, the rotation around the axial C_2—C_α bond is not hindered, so that both rotomers with $-\overset{\ominus}{C}(CH_3)NO_2$ at C_α atom turned outside (XVI A) or inside (XVI B) the cyclohexane ring, are possible.

From the rotomer XVI A, by intramolecular transfer of the equatorial hydrogen from the C_2 of the ring to the negative carbon atom, through a 6-membered cyclic transition state, the more substituted enamine VI A can be formed *via* the aci-nitro tautomer. Nevertheless, as the abstraction of an equatorial proton to form a cyclohexene double bond is difficult because of unfavourable stereoelectronic factors,[8]

* The *erythro* configuration of 2-(α-*p*-bromophenyl-β-nitroethyl)cyclohexanone, obtained from the reaction of *p*-bromo-β-nitrostyrene with 1-N-morpholino-cyclohexene, followed by hydrolysis, has been demonstrated by X-ray crystal structure determination.

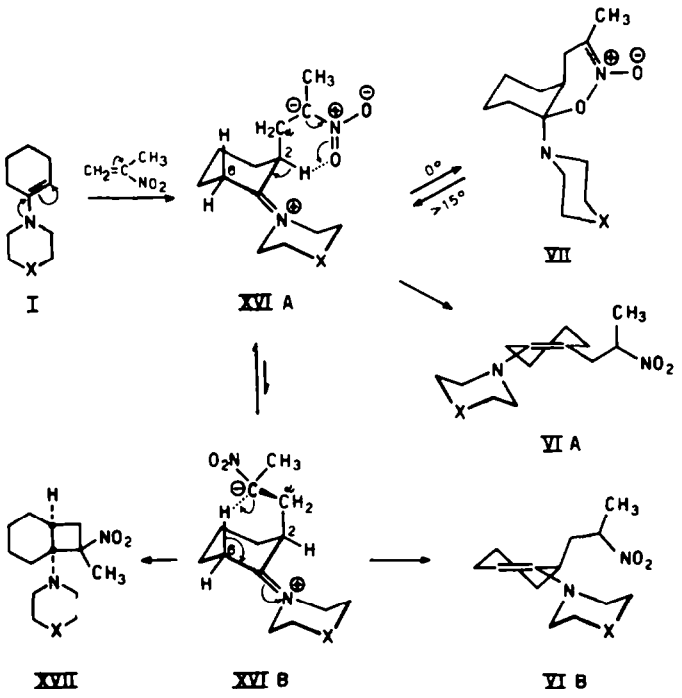


CHART 5

the intermediate XVI A may rearrange along another pathway to give the cyclic product VII. Heterocyclic compounds analogous to VII are formed for instance from enamines with α,β-unsaturated aldehydes[9] and from methyl vinyl ketone.[10] Compound VII is however unstable and at room temperature is converted, probably through XVI A, into the enamine VI A. Thus, according to reaction conditions, the rotomer XVI A can lead either to more substituted enamines VI A or heterocyclic compounds VII.

On the contrary, from the rotomer XVI B, by a similar mechanism (Chart 4) for the intermediate XV of the reaction with 1-nitropropene, the less substituted enamines VI B would be formed. It may be inferred that the rotomer XVI B, being more crowded, is less favoured than XVI A. This can account for the observed low yields of VI B, by reaction of cyclohexanone enamines with 2-nitropropene.

Finally, the intermediate XVI B, as well as XV (Chart 4), could collapse to the cyclobutane adduct XVII (Chart 5). Actually, products of this type have been found in several cases[11] by reaction of enamines with electrophilic olefins. In particular, a cyclobutane adduct has been reported[12] to be formed from 1-N-morpholino-cyclohexene and nitroethylene when the reaction is carried out in apolar solvents. Nevertheless cyclobutane derivatives were not isolated from the reactions with either 1- or 2-nitropropene even when working under analogous conditions.

EXPERIMENTAL

All m.ps are uncorrected. The IR spectra were recorded with a Perkin–Elmer Model 13 double beam IR Spectrophotometer and the NMR spectra with a Varian DP-60 NMR Spectrometer at 56·4 Mc, with

TMS as internal standard. Gas chromatographic analyses were carried out on a C.Erba Fractovap Model C with flame ionization detector, using a 1 meter column of 10% SE 30 methyl silicon-Chromosorb W on 80–100 mesh.

1. *Reaction of* 1-N-*morpholino-cyclohexene with* 1-*nitropropene.*

(a) 1-N-*Morpholino*-6-(β-*nitroisopropyl*)*cyclohex*-1-*ene* (IIa). 1-Nitropropene[13] was prepared by dehydration of 1-nitro-2-propanol.[14] The nitro olefin (2·1 g, 24 mmoles) in pet. ether (5 ml) was added dropwise under stirring to a soln of 1-N-morpholino-cyclohexene (4 g, 24 mmoles) in the same solvent (5 ml), keeping the temp at about 0° with an ice bath. After standing in refrigerator for 24 hr, IIa (5·1 g, 85% yield) was filtered off and recrystallized from pet. ether as white prisms, m.p. 51–53°. (Found: C, 61·39; H, 9·30; N, 11·12. $C_{13}H_{22}N_2O_3$ requires: C, 61·39; H, 8·79; N, 11·01%); IR spectrum (KBr): 1642 cm^{-1} (C=C—N); 1550 cm^{-1} (NO_2); NMR spectrum (Chf): 4·98 τ (H—C=C); 5·58 τ (CH_2—NO_2); 6·27 τ (CH_2—O—CH_2); 7·17 τ (CH_2—N—CH_2); 9·12 τ (CH—CH_3).

(b) 2-(β-*Nitroisopropyl*)*cyclohexanone* (IV). To a soln of IIa (5·1 g, 20 mmoles) in EtOH (10 ml) 10% HCl (50 ml) was added under cooling. After allowing the mixture to stand at room temp for 12 hr, the solvent was removed at reduced press and the residue was extracted with ether. The ethereal extract by evaporation left crude IV as brown oil (3 g, 80% yield) which was purified by distillation—pale yellow oil, b.p. 128–130° (0·8 mm), n_D^{25} 1·4808. The product was unstable and darkened after short storage. (Found: C, 59·14; H, 8·39; N, 7·45. $C_9H_{15}NO_3$ requires: C, 58·36; H, 8·16; N, 7·56%); IR spectrum (neat): 1710 cm^{-1} (CO); 1550 cm^{-1} (NO_2). IV showed a single GC peak. On TLC the substance migrated as one spot. IV gave a *semicarbazone*, m.p. 148–149°. (Found: C, 50·10; H, 7·46; N, 23·25. $C_{10}H_{18}N_4O_3$ requires: C, 49·57; H, 7·49; N, 23·13%.)

(c) 1-N-*Morpholino*-2-(N,N′-*dicarbethoxyhydrazino*)-6-(β-*nitroisopropyl*)*cyclohex*-1-*ene* (IIIa). Ethyl azodicarboxylate (2·1 g, 12 mmoles) in dry ether (5 ml) was added dropwise to a well cooled soln of IIa (3·05 g, 12 mmoles) in dry ether (10 ml). After standing in refrigerator for 72 hr the white solid was filtered off (4·62 g, 90% yield). Purification from benzene–pet. ether afforded white crystals of pure IIIa, m.p. 120°. (Found: C, 53·71; H, 7·88; N, 13·00. $C_{19}H_{32}N_4O_7$ requires: C, 53·26; H, 7·53; N, 13·08%); IR spectrum (KBr): 3280 cm^{-1} (NH); 1754 cm^{-1} and 1694 cm^{-1} (CO); 1652 cm^{-1} (C=C—N); 1550 cm^{-1} (NO_2); NMR spectrum (Chf): 3·27 τ (NH); 5·58 τ (CH_2—NO_2); 5·78 τ (CH_2—CH_3); 6·29 τ (CH_2—O—CH_2); 7·08 τ (CH_2—N—CH_2); 8·73 τ (CH_2—CH_3); 9·03 τ (CH—CH_3).

(d) 2-N,N′-*Dicarbethoxyhydrazino*)-6-(β-*nitroisopropyl*)-*cyclohexanone* (V). Compound IIIa (2·15 g, 5 mmoles) was dissolved in acetone (50 ml) and to this soln 5% HCl (40 ml) was added portionwise and under cooling in order to maintain the temp below 10°. After standing at room temp for 72 hr, the solvent was removed and the mixture yielded 1·54 g (86%) of V as white crystals (from benzene–pet. ether), m.p. 115–116°. (Found: C, 50·16; H, 7·22; N, 11·83. $C_{15}H_{25}N_3O_7$ requires: C, 50·13; H, 7·17; N, 11·69%); IR spectrum (KBr): 3255 cm^{-1} (NH); 1760 cm^{-1} and 1706 cm^{-1} (CO); 1552 cm^{-1} (NO_2). NMR spectrum (Chf): 3·24 τ (NH); 5·13 τ (CH—N—NH); 5·80 τ (CH_2—NO_2); 5·92 τ (CH_2—CH_3); 8·73 τ (CH_2—CH_3); 8·93 τ (CH—CH_3).

2. *Reaction of* 1-N-*piperidino-cyclohexene with* 1-*nitropropene*

(a) 1-Nitropropene (2·6 g, 30 mmoles) in pet. ether (3 ml) was added dropwise to a stirred soln of 1-N-piperidino-cyclohexene (5·1 g, 30 mmoles) in 5 ml of the same solvent at 0°. After 24 hr the solvent was distilled off at reduced press and the oily residue was diluted with EtOH (5 ml) and then treated with 10% HCl (20 ml). Work up, followed by distillation of the residue from ether afforded IV, b.p. 128–130° (0·8 mm), n_D^{25} 1·4806. GC and TLC analyses, and IR spectrum indicated the compound was identical with that obtained on hydrolysis of IIa.

(b) 1-N-*Piperidino*-2-(N,N′-*dicarbethoxyhydrazino*)-6-(β-*nitroisopropyl*)*cyclohex*-1-*ene* (IIIb). 1-Nitropropene (2·6 g, 30 mmoles) and 1-N-piperidino-cyclohexene (5·1 g, 30 mmoles) were allowed to react as described in section 2(a). After 24 hr, ethyl azodicarboxylate (5·2 g, 30 mmoles) in pet. ether (5 ml) was added and the soln was kept in refrigerator for further 72 hr. Removal of the solvent under reduced press gave a crude viscous oil which solidified on refluxing with ligroin (b.p. 70–110°). The solid recrystallized from benzene–pet. ether gave IIIb as white crystals, m.p. 103–105°. (Found: C, 55·37; H, 8·00; N, 12·80. $C_{20}H_{34}N_4O_6$ requires: C, 55·03; H, 7·85; N, 12·83%); IR spectrum (KBr): 3270 cm^{-1} (NH); 1750–1690 cm^{-1} (CO); 1630 cm^{-1} (C=C—N); 1550 cm^{-1} (NO_2); NMR spectrum (Chf): 5·60 τ (CH_2—NO_2); 5·80 τ (CH_2—CH_3); 8·73 τ (CH_2—CH_3); 9·02 τ (CH—CH_3).

(c) In another experiment carried out on the same amounts of reagents and under reaction conditions

as reported in 2(b), the crude product was dissolved in acetone (75 ml) and treated with 5% HCl (20 ml). After 72 hr the solvent was removed and 8 g (76%) of V were obtained, m.p. 115–116°, with no depression in m.p. on admixture of the compound obtained on hydrolysis of IIIa.

3. *Reaction of* 1-N-*pyrrolidino-cyclohexene with* 1-*nitropropene*

(a) The reaction between 1-nitropropene and 1-N-pyrrolidino-cyclohexene, followed by hydrolysis, was carried out as described for the piperidine enamine. The ketone IV was obtained and identified by GC, TLC analyses and IR spectrum.

(b) 1-N-*Pyrrolidino*-2-(N,N'-*dicarbethoxyhydrazino*)-6-(β-*nitroisopropyl*)*cyclohex*-1-*ene* (IIIc). The reaction soln of 1-nitropropene (1·9 g, 21 mmoles) with 1-N-pyrrolidino-cyclohexene (3·15 g, 21 mmoles) was treated with ethyl azodicatboxylate (3·75 g, 21 mmoles) under the conditions described for IIIb. Compound IIIc (7·32 g, 84%), m.p. 105–106°, was obtained after recrystallization from benzene–pet. ether. (Found: C, 55·44; H, 7·84; N, 13·71. $C_{19}H_{32}N_4O_6$ requires: C, 55·32; H, 7·82; N, 13·59%); IR spectrum (KBr): 3260 cm^{-1} (NH); 1764–1694 cm^{-1} (CO): 1650 cm^{-1} (C═C—N); 1549 cm^{-1} (NO_2). NMR spectrum (Chf): 3·24 τ (NH); 5·65 τ (CH_2—NO_2); 5·77 τ (CH_2—CH_3); 8·74 τ (CH_2—CH_3); 8·91 τ (CH—CH_3).

(c) The acidic hydrolysis of IIIc afforded V, identical in all respects (m.p., mixed m.p. and IR spectrum) with that obtained from IIIa or IIIb.

4. *Reaction of* 1-N-*morpholino-cyclohexene with* 2-*nitropropene.*

(a) 3-*Methyl*-9-N-*morpholino*-5,6,7,8,9,10-*hexahydro*-[1.2.4*H*] *benzoxazine*-N-*oxide* (VIIIa). 2-Nitropropene[13] was prepared by dehydration of 2-nitropropanol.[15] 2-Nitropropene (2·8 g, 32 mmoles) in dry ether (5 ml) was added dropwise and under vigorous stirring to a well cooled soln of 1-N-morpholino-cyclohexene (5·5 g, 32 mmoles) in the same solvent (5 ml). The reaction was very exothermic and it was necessary to cool the mixture in an ice–salt bath to prevent the temp from rising above 5°. Within few min after the nitro olefin was added, VIIa (6·5 g, 80%) separated as a crystalline solid, m.p. 64–65°. The product had to be filtered off as quickly as possible, washed with dry ether, dried by suction and stored in desiccator *in vacuo* at 0°. (Found: C, 60·88; H, 8·39; N, 10·91. $C_{13}H_{22}N_2O_3$ requires: C, 61·39; H, 8·79; N, 11·01%);

IR spectrum (Nujol): 1628 cm^{-1} (C═N<(O)); some CO and NO_2 absorptions were present due to partial hydrolysis; NMR spectrum ($CDCl_3$): triplet (4H) at 6·33 τ (CH_2—N—CH_2); singlet (3H) at 7·95 τ (CH_3); multiplets at 7·24 τ (5H) and 8·41 τ (10H) were also present.

At room temp, even in desiccator, compound VIIa gradually changed into a semi-solid product (VIa). IR spectrum (neat): 1640 cm^{-1} (C═C—N); 1552 cm^{-1} (NO_2). VIIa by exposure to the air moisture rapidly hydrolysed to 2-(β-nitropropyl)cyclohexanone (IX). VIIa in dry benzene at 0–5° did not react with ethyl azodicarboxylate.

(b) 2-(β-*Nitropropyl*)-6-(N,N'-*dicarbethoxyhydrazino*)*cyclohexanone* (VIII). A repeat of the reaction 4(a) using acetonitrile instead of dry ether, VIa was obtained. In fact, IR spectrum of a small portion of the reaction soln showed absorption bands at 1640 cm^{-1} (C═C—N) and 1550 cm^{-1} (NO_2). To this soln ethyl azodicarboxylate (5·6 g, 32 mmoles) in acetonitrile (5 ml) was added. After standing at 0° for 5 days, the solvent was removed under reduced press and the dark reddish brown oily residue was dissolved in EtOH (50 ml) and treated with 5% HCl (20 ml). After 24 hr the EtOH was evaporated, the mixture was extracted with benzene and chromatographed on alumina (Merck, acc. to Brockmann). Elution with benzene–$CHCl_3$–acetone (4·5:4·5:1), testing every fraction on TLC, gave: VIII (3·45 g, 30%), XI, 2,6-bis(N,N'-dicarbethoxyhydrazino)cyclohexanone,[2a] ethyl hydrazodicarboxylate and traces of unidentified products. VIII crystallized from aqueous MeOH, as white crystals, m.p. 111°. (Found: C, 50·80; H, 7·21; N, 11·57. $C_{15}H_{25}N_3O_7$ requires: C, 50·13; H, 7·17; N, 11·69%); IR spectrum (KBr): 3260 cm^{-1} (NH); 1760–1700 cm^{-1} (CO); 1550 cm^{-1} (NO_2); NMR spectrum (CCl_4—$CHCl_3$): multiplet (2H) at 5·27 τ (CH—NO_2 and CH—N(COOEt)—NHCOOEt).

The mixture of enamines VIa obtained either by allowing VIIa to warm to room temp or by reaction of Ia with 2-nitropropene in excess of dry ether at 25–30°, upon treatment with ethyl azodicarboxylate afforded the same results (20–30% of VIII). Compound VIII showed on TLC two spots, which evidently were corresponding to two isomers. These, by conversion into their sodium salt and subsequent acidification, gave a product that showed on TLC an unique spot of different R_f with respect to those of VIII and in its IR spectrum NO_2 bands were missing.

(c) 2-(β-*Nitropropyl)cyclohexanone* (IX). Compound VIIa (5·1 g, 20 mmoles) was dissolved in EtOH (5 ml) and treated with 5% HCl (15 ml) under stirring and cooling to keep the temp at about 10°. The oil which separated by removal of the organic solvent, was extracted with ether. Distillation of the ether extracts gave 2·8 g (75%) of crude IX. This was purified by distillation under reduced press—pale yellow oil, b.p. 118–120° (1 mm), n_D^{25} 1·4705. (Found: C, 58·29; H, 8·12; N, 7·56. $C_9H_{15}NO_3$ requires: C, 58·36; H, 8·16; N, 7·60%); IR spectrum (neat): 1716 cm^{-1} (CO); 1552 cm^{-1} (NO_2). IX gave a *semicarbazone*, m.p. 150°. (Found: C, 49·36; H, 7·40; N, 23·62. $C_{10}H_{18}N_4O_3$ requires: C, 49·57; H, 7·49; N, 23·13%.) The same compound IX was obtained also upon hydrolysis of the mixture VIa.

Compound IX on TLC over silica gel G (Merck, acc. to Stahl) using benzene–acetone (9:1) as eluent showed two spots which were detected by spraying with a suitable indicator. GC analysis at 150° and a N_2 flow of 12 ml/min gave two peaks having retention times 4·5 and 6·0.

(d) 2-*Acetonyl-cyclohexanone* (XI). The diastereoisomeric mixture IX (3·7 g, 20 mmoles), freshly distilled, was added dropwise to a soln of NaOH (0·5 g, 22 mmoles) in abs EtOH (30 ml). The soln was reduced *in vacuo* at room temp to one third of its initial volume and then dry ether was added until separation of the Na salt (X) as white crystals, m.p. 93–95°; IR spectrum (KBr): 1710 cm^{-1} (CO); 1596 cm^{-1} (C=N<O). The salt X was dissolved in water and on acidification with 10% HCl a transient blue colour appeared. After standing overnight, the colourless mixture was extracted with ether. Removal of the solvent left an oil that was analysed on TLC and GC under the same conditions used for the ketone IX. TLC and GC analyses showed the presence of a major product, identified as XI, and only traces of IX. XI distilled as pale yellow oil, b.p. 91–93° (1 mm), n_D^{25} 1·4618 (lit.[16]: n_D^{25} 1·4615). (Found: C, 69·73; H, 9·27. Calc. for $C_9H_{14}O_2$: C, 70·10; H, 9·15%); IR spectrum (neat): 1712 cm^{-1} (CO). *Bis-semicarbazone*, m.p. 192–194° dec (lit.[17]: m.p. 195–199° dec). An authentic sample of XI for comparison was prepared by reaction of Ic with bromoacetone, followed by hydrolysis.[17]

(e) 1-N-*Morpholino-2,6-bis*(β-*nitropropyl)cyclohex-1-ene* (XII). When 1-N-morpholino-cyclohexene (11 g, 66 mmoles) in dry ether (10 ml) was added dropwise under stirring and cooling to a soln of 2-nitropropene (11 g, 130 mmoles) in the same solvent (10 ml), after standing overnight in refrigerator, XII (0·9 g, 4%) as white solid separated. This was filtered off and recrystallized from MeOH, m.p. 117–118°. (Found: C, 56·04; H, 7·67; N, 12·25. $C_{16}H_{27}N_3O_5$ requires: C, 56·30; H, 7·97; N, 12·31%); IR spectrum (KBr): 1658 cm^{-1} (C=C—N); 1546 cm^{-1} (NO_2); NMR spectrum (Chf): multiplet (2H) at 5·1 τ (2 C<u>H</u>—NO_2); triplet (4H) at 6·24 τ (CH_2—O—C<u>H</u>$_2$); triplet (4H) at 7·20 τ (CH_2—N—C<u>H</u>$_2$); two doublets at 8·44 τ and 8·46 τ (2 CH_3).

5. *Reaction of* 1-N-*piperidino-cyclohexene with* 2-*nitropropene.*

(a) 2-Nitropropene (2·6 g, 30 mmoles) in dry ether (5 ml) was added dropwise to a stirred soln of 1-N-piperidino-cyclohexene (5·1 g, 30 mmoles) in 5 ml of the same solvent, at 0°. After standing in refrigerator for 24 hr, the solvent was distilled off under reduced press and the oily residue was dissolved in EtOH (5 ml) and then treated with 5% HCl (20 ml). Removal of the alcohol, extraction with ether and evaporation of the extract gave crude IX (4·5 g, 80%). By distillation pure IX, b.p. 118–120° (1 mm), n_D^{25} 1·4705, was obtained. It was identical in all respects with that formed on hydrolysis of VIIa.

(b) 2-Nitropropene (2·6 g, 30 mmoles) reacted with 1-N-piperidino-cyclohexene (5·1 g, 30 mmoles) as described in 5(a). After 24 hr, ethyl azodicarboxylate (5·2 g, 30 mmoles) in dry ether (10 ml) was added and the soln was kept in refrigerator for further 72 hr. The solvent was removed *in vacuo* and the dark reddish oil obtained was diluted with EtOH (20 ml) and then treated with 5% HCl (20 ml). The alcohol was distilled off and the residue was extracted with benzene. The benzene soln was dried over Na_2SO_4 and then, after concentration, chromatographed on Al_2O_3 (Merck, acc. to Brockmann). Elution with benzene–acetone (9:1), testing every fraction on TLC, gave VIII (4 g, 35%) and a mixture of IX, XI, 2,6-bis(N,N'-dicarbethoxyhydrazino)cyclohexanone[2a] and ethyl hydrazodicarboxylate.

6. *Reaction of* 1-N-*pyrrolidino-cyclohexene with* 2-*nitropropene.*

(a) The reaction of 2-nitropropene with 1-N-pyrrolidino-cyclohexene, followed by hydrolysis, was carried out as described for the piperidine enamine. In this case the nitro olefin had to be added very slowly to avoid the formation of the diadduct XIII. The crude ketone IX was obtained in 88% yield and, after purification, it was identified by GC, TLC analyses and IR spectrum.

(b) The enaminic mixture obtained from the reaction between Ic and 2-nitropropene, as reported in

6(a), by treatment with ethyl azodicarboxylate in the usual manner, led to VIII (40%) separated by chromatography on alumina.

(c) 1,3-*Dimethyl*-1,3-*dinitro*-9-N-*pyrrolidino*-*decalin* (XIII). 1-N-Pyrrolidino-cyclohexene (3·3 g, 22 mmoles) dissolved in dry ether (4 ml) was added dropwise to a well stirred soln of 2-nitropropene (3·9 g, 44 mmoles) in the same solvent (4 ml). The reaction temp was maintained at about 0°. Within few min a pale yellow crystalline product corresponding to XIII (0·83 g, 10%) separated. It was filtered off and carefully washed with dry ether, m.p. 114–116°. (Found: C, 59·58; H, 8·55; N, 12·11. $C_{16}H_{27}N_3O_4$ requires: C, 59·05; H, 8·36; N, 12·91%); IR spectrum (KBr): no absorption bands in the 2800–1550 cm^{-1} region; strong band at 1538 cm^{-1} (NO_2); NMR spectrum ($CDCl_3$): no signals below 6 τ; broad line at about 7·1 τ ($C\underline{H}_2$—N—$C\underline{H}_2$); singlet at 8·39 τ ($C\underline{H}_3$ at 1 position); singlet at 8·52 τ ($C\underline{H}_3$ at 3 position).

(d) 1,3-*Dimethyl*-1,3-*dinitro*-9-*hydroxy*-*decalin* (XIV). Compound XIII was dissolved in aqueous EtOH and the soln was allowed to stand overnight at room temp. XIV separated quantitatively as white crystals that, after recrystallization from EtOH, had m.p. 147°. (Found: C, 52·62; H, 7·33; N, 10·15. $C_{12}H_{20}N_2O_5$ requires: C, 52·93; H, 7·40; N, 10·29%); IR spectrum (KBr): 3510 cm^{-1} (OH); no bands between 2800 cm^{-1} and 1550 cm^{-1}; 1538 cm^{-1} (NO_2); NMR spectrum ($CDCl_3$): no signals below 6 τ; singlet (1H) at 7·47 τ (O$\underline{H}$); singlet at 8·39 τ (CH_3 at 1 position); singlet at 8·52 τ ($C\underline{H}_3$ at 3 position).

Acknowledgements—This work was supported by a grant from the Consiglio Nazionale delle Ricerche (Rome). The authors are indebted to Dr. F. Taddei, Faculty of Industrial Chemistry, Bologna University, for recording and interpreting NMR spectra.

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