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CYCLIC NITRONIC ESTERS

SYNTHESIS OF SUBSTITUTED 5,6-POLYMETHYLENE-5,6-DIHYDRO-4H-1,2-OXAZINE 2-OXIDES BY REACTION OF ENAMINES WITH NITROOLEFINS

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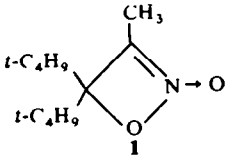
Abstract—The role of structure in the reaction between enamines and nitroolefins has been evaluated. A synthetic method is presented for preparing substituted cyclic nitronic esters incorporating a 6-membered ring. Reaction of cyclopentanone, cyclohexanone and cycloheptanone enamines derived from pyrrolidine and morpholine with 2-nitro-1-phenylpropene, 2-nitro-1-phenyl-1-butene and α-nitrostilbene in hexane solvent at 0–25° led to 3-methyl-, 3-ethyl-, or 3-phenyl-4-phenyl-5,6-polymethylene-5,6-dihydro-4H-1,2-oxazine 2-oxides **9a–j** (31–94% yield). Spectral data support the assigned structures and establish stereochemistry. The reaction is limited to α-substituted nitroolefins and enamines derived from cycloalkanones having fewer than eight ring members. Enamines derived from aldehydes and acyclic ketones failed to produce nitronic esters. Alkaline hydrolysis of nitronic esters **9a–j** by treatment with aqueous ethanolic potassium hydroxide, followed by acidification with acetic acid, leads to products whose structure is determined by the nature of substituents and ring size of the 5,6-polymethylene group. Esters **9d** and **9e** derived from cyclohexanone gave 8a-hydroxy-3-methyl-4-phenyl-4a,5,6,7,8,8a-hexahydro-4*H*-1,2-benzoxazine 2-oxide (**4**), found to be identical with the product of Michael addition of cyclohexanone to 2-nitro-1-phenylpropene. Ester **9h** derived from cycloheptanone gave the Nef product, 2-(1-phenylacetonyl)cycloheptanone (**19**). Esters **9g, j** having 3,4-diphenyl substituents produced 3,4,5-triphenylisoxazole. The results of the present investigation provide additional examples of nucleophilic addition of nitronate oxygen to carbon-hetero atom double bonds; addition occurs intramolecularly on carbon of an iminium ion in the zwitterion intermediate **6**.

CYCLIC nitronic esters incorporating 4-, 5-, and 6-membered rings are known (**1, 2, 3**); none incorporating larger rings have been described. Only the 5-membered ring



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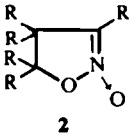

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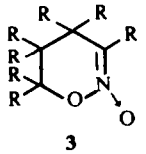

3

2-isoxazoline 2-oxides (**2**) are well known.[1–5] They are readily prepared by reaction of 3-halo-1-nitroalkanes or 1,3-dinitroalkanes with base, and are stable, crystalline solids. One 4-membered ring nitronic ester has been reported—compound **1**, also a stable crystalline compound.[6] Two examples of 6-membered cyclic nitronic esters are known—crystalline hexahydro-4*H*-1,2-benzoxazine 2-oxides **4**[7,8] and **5**.†[9] Compound **5** is unstable at 25°.

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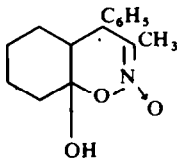
† Compound **5** was reported while the present study was in progress. (ref. 9).



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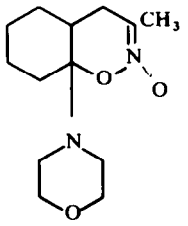

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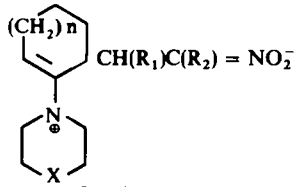
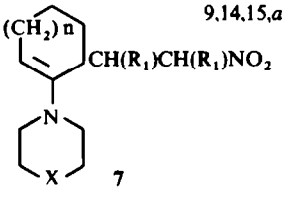
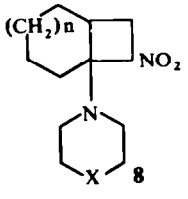
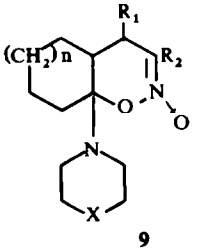
TABLE 1. REACTIONS OF 1:1 CYCLOALKANONE-NITROOLEFIN ZWITTERION INTERMEDIATE ADDUCT (6) IN APROTIC SOLVENTS



6 (X = O, —)

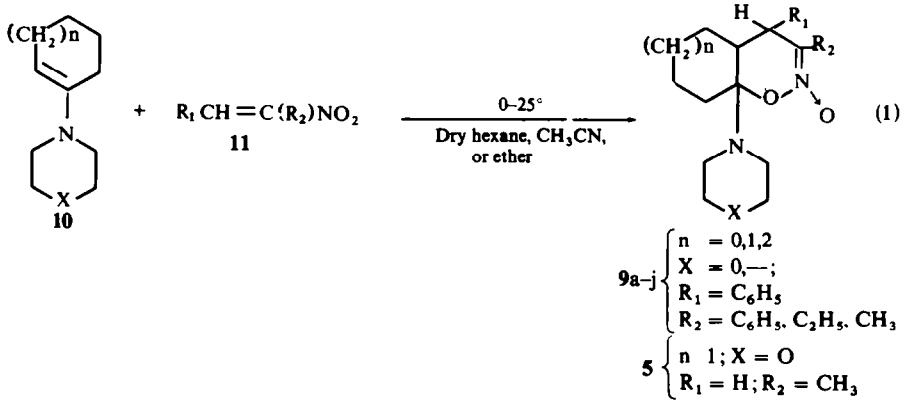
Substituent in 6		n	Aprotic Solvent Type	Reaction Type	Product	Ref.
R_1	R_2					
Aryl, alkyl, H	H	n	Polar	C Protonation	 7	9,14,15,*a*
Aryl, alkyl, H	Aryl, alkyl	>2	Polar or Non-polar	C Protonation	7	a
H	H	0,1[b]	Non-polar	Intramolecular C Alkylation	 8	13
Aryl, alkyl, H	Aryl, alkyl	0,1,2	Polar or Non-polar	Intramolecular O Alkylation	 9	9,*a*

[a] This work; [b] Not studied for n > 1

In the present study we have found the reaction of certain enamines with suitably substituted nitroolefins to provide a synthetic route to substituted 6-membered cyclic nitronic esters. Cyclic nitronic esters are relatively stable compared to acyclic ones. Most acyclic nitronic esters decompose within a few hours at room temperature.[10, 11] From the limited data available the stability order of nitronic esters (with comparable substituents) would appear to decrease in the order: cyclic 5-ring > 4-ring > 6-ring > 7-ring and acyclic.

The reaction of enamines with nitroolefins has been studied.[9, 12–15] Three types of 1:1 adducts have now been observed with cycloalkanone derived enamines and nitroolefins. These are illustrated in Table 1 for reactions leading from the initial zwitterionic intermediate **6** in aprotic solvents. With *beta*-substituted nitroolefins lacking an *alpha* substituent, C protonation, which is usually observed in polar solvents such as acetonitrile, leads to a substituted acyclic nitroalkane (**7**). In nonpolar solvents such as hexane intramolecular reactions are favored. Only with nitroethylene does C alkylation in **6** lead to a bicyclic nitrocyclobutane (**8**). In the present work it has been found that *alpha*-substituted nitroolefins with enamines from cycloalkanones of less than eight ring members, in polar or nonpolar aprotic solvents (hexane, acetonitrile, ether), lead to a zwitterion which undergoes intramolecular O alkylation to a cyclic nitronic ester (**9**). The role of concentration in determining the reaction fate of **6** has not been completely evaluated.

Reaction of C_5–C_7 cycloalkanone morpholine and pyrrolidine derived enamines (**10**) with ω-substituted ω-nitrostyrenes (**11**, R_1 = Ph) in dry hexane at 0–25° (dry N_2 atmosphere) leads to a red-orange solution, followed by a rapid disappearance of color and crystallization of the cyclic nitronic ester (**9**); Eq 1. Data are summarized



(1)

in Table 2. The reaction also occurs in acetonitrile, but the products do not crystallize out unless the solvent is removed and replaced with hexane. The formation of related compound **5** occurs in ether.[9] The new cyclic nitronic esters **9a–j** may be recrystallized from hexane or benzene-hexane and are white, crystalline solids, most of which may be stored at 25° for several weeks, or at lower temperatures for longer periods. Cyclohexanone pyrrolidine enamine reacts fastest and produces the best yields (85–94% of **9e–g** within 2–3 hr).

TABLE 2. FORMATION OF CYCLIC NITRONIC ESTERS (9) FROM CYCLOALKANONE ENAMINES AND NITROOLEFINS, $C_6H_5CH{=}C(R_2)NO_2$ (Eq. 1)

No.	n	X	R_2	Yield %	M.p., °C	Molecular formula	Elemental analyses							
							Calculated				Found			
							%C	%H	%N	Mol wt	%C	%H	%N	Mol wt[a]
9a	0	0	CH_3	63	108–110	$C_{18}H_{24}N_2O_3$	68·33	7·65	8·85	316·4	68·51	7·65	8·53	290
9b	0	0	C_2H_5	62	87–89	$C_{19}H_{26}N_2O_3$	69·06	7·93	8·48	330·4	68·84	7·72	8·27	280
9c	0	0	C_6H_5	42	94–97	$C_{23}H_{26}N_2O_3$	72·99	6·93	7·40	378·5	72·83	6·93	7·22	386
5	1	0	CH_3[b]	80[b]	64–65[b]	$C_{13}H_{22}N_2O_3$	61·39	8·72	11·02	254·3	60·88[b]	8·39[b]	10·91[b]	—
9d	1	0	CH_3	53	107–108	$C_{19}H_{26}N_2O_3$	69·06	7·93	8·48	330·4	69·60	8·01	8·42	330[c]
9e	1	—	CH_3	91	108–110	$C_{19}H_{26}N_2O_2$	72·58	8·34	8·91	314·4	72·63	8·11	8·73	307
9f	1	—	C_2H_5	94	108–111	$C_{20}H_{28}N_2O_2$	73·13	8·59	8·53	328·4	73·19	8·75	8·37	323
9g	1	—	C_6H_5	85	104–107	$C_{24}H_{28}N_2O_2$	76·56	7·50	7·44	376·5	76·62	7·38	7·36	386
9h	2	0	CH_3	52	96–98	$C_{20}H_{28}N_2O_3$	69·74	8·19	8·13	344·4	70·09	7·85	8·20	331
9i	2	0	C_2H_5	31	98–101	$C_{21}H_{30}N_2O_3$	70·36	8·44	7·82	358·5	70·15	8·32	7·73	334
9j	2	0	C_6H_5	72	118–123	$C_{25}H_{30}N_2O_3$	73·86	7·44	6·89	406·5	74·11	7·55	6·64	412

[a] Molecular weight determinations by vapor osmometry in benzene or chloroform solvent.

[b] Data of Risaliti *et al*, ref. 9; R_1 in **9** = H, R_2 = CH_3(from $CH_2 = C(CH_3)NO_2$).

[c] Mass spectrum molecular weight.

TABLE 3. SPECTRA OF 5,6-POLYMETHYLENE-5,6-DIHYDRO-4H-1,2-OXAZINE 2-OXIDES

Compd.	5,6-Poly-methylene ring size	IR (KBr) C=N band cm^{-1}	UV (95% EtOH) λ_{max} (mμ) (ε_{max})	NMR Signals ($CDCl_3$; TMS internal standard)[a] C-3 Substituent R	C-3 Substituent τ (J, Hz)	C-4 Benzyl H τ (J, Hz)
9a	5	1610	238 (5800)[b]	CH_3	8·18d (1·5)[b,c]	6·17d (4)
9b	5	1590	240 (8700)[b,d]	$C\underline{H}_3CH_2$	9·02t (7)	6·15d (4)
9c	5	1560	---------[b]	C_6H_5	2·60s	5·70d (3)
		1580				
5	6	1628[e,f]	---------[f]	CH_3	7·95s[f]	------
9d	6	1605	237 (9500)[g]	CH_3	7·94d (1·5)	------[h]
9e	6	1605	238 (9500)	CH_3	8·18d (1·5)	6·42d (10)
4	6	1610	228 (17,000)	CH_3	8·18d (1·5)	6·53d (10)
9f	6	1600	240 (12,400)	$C\underline{H}_3CH_2$	9·02t (7)	6·41d (9)
17	6	1595	---------[i]	CH_3CH_2	------[i]	------[i]
9g	6	1570	220 (10,000)	C_6H_5	2·82s	5·92d (8)
		1590	276 (7900)			
9h	7	1610	239 (10,100)[j]	CH_3	8·24d (1·5)	------[h]
9i	7	1590	241 (10,500)	$C\underline{H}_3CH^2$	9·05t (7)[b]	6·13d (4)[b]
9j	7	1550	239 (8900)	C_6H_5	2·62s	5·88d (5)
		1575	284 (6900)			

[a] All 4-phenyl compounds show aryl signals near 2·7 τ; N-pyrrolidinyl compounds **9e–g** show a CH_2NCH_2 signal (4 protons) of triplet shape at τ 6·96 J = 5–7); N-morpholinyl compounds show a similar signal at τ 6·35 in addition to a CH_2OCH_2 signal (4 protons) of triplet shape near τ 7·0; bridgehead methine and methylene signals appear as a complex multiplet at τ 7·2–8·8.

[b] Sample decomposes in soln.

[c] Sample decomposes in soln with appearance of a Me doublet signal at τ 8·63 (J = 7 Hz).

[d] After 12 hr the initial extinction coefficients of 8700 at 240 mμ had decreased to 7600 (ca. 13% decomposition). In hexane soln: λ_{max} 247 mμ (ε 8000) for freshly prepared soln.

[e] Measurement in Nujol mull.

[f] Data of Risaliti *et al.* (Ref. 9); UV spectrum not reported.

[g] After 24 hr the initial extinction coefficient of 9500 at 237 mμ had decreased to 8700 after 24 hr (ca. 8·5% decomposition).

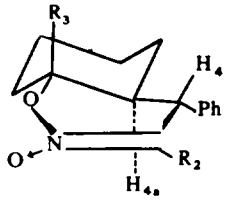
[h] The signal for the C-4 benzyl proton is hidden under the morpholinyl group proton signals.

[i] UV and NMR spectra not determined.

[j] After 48 hr the extinction coefficient of 10,100 at 239 mμ had decreased to 6200 (ca. 39% decomposition).

Spectral data support the nitronic ester structure of products **9a–j** (Table 3). Characteristic nitronic ester infrared C=N bands are found near 1600 cm^{-1}, and nitroalkane bands, usually appearing near 1540 cm^{-1}, are absent.[10] Strong UV absorption near 240 mμ, typical of α,α-dialkl substituted nitronic esters, is observed.[8] NMR spectra are also in agreement with the structures. For example, the 3-Me substituted compounds **9a, 9d, 9e,** and **9h** reveal a Me doublet (J = 1·5 Hz) signal near τ 8·0, caused by coupling with the adjacent C-4 benzyl proton.

The stereochemistry of the 5,6-tetramethylene compounds **9e–g** is like that of the related **8a**-hydroxy compound **4** established previously,[8] in which a *trans* ring juncture is assumed and the C-4 Ph group was shown to be pseudoequatorial. The C-4 benzyl proton appears as a doublet (J = 8–10 Hz) near τ 6 due to coupling with the adjacent bridgehead proton at 4a. In **4** the C-4 proton doublet appears at τ 6·53



4; R_2 = Me; R_3 = OH
9e–g; R_2 = Me, Et, Ph; R_3 = $N(CH_2)_4$

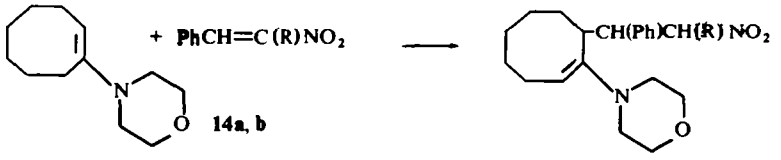
(J = 10 Hz). In the 5,6-trimethylene and pentamethylene compounds **9a–c** and **9h–j** the C-4 benzyl proton signals also appear as doublets near τ 6 (J = 4 Hz); cf. Table 3. The C-4 phenyl group is believed to be pseudoequatorial in these compounds. In **9a, d, e, h** the C-4 proton doublet signal is broadened due to unresolved fine structure caused by coupling with the C-3 Me protons.

The scope of the reaction of Eq 1 with respect to structural limitations on the nitroolefin, $R_1CH{=}C(R_2)NO_2$ (**11**) can be defined. An *alpha* substituent must be present (R_2 may be alkyl or aryl, but not H; Table 1). For example, ω-nitrostyrene (**12**) —under conditions whereby **9** was formed from ω-substituted ω-nitrostyrenes—was found to react in hexane with 1-(N-pyrrolidinyl)cyclohexene and 1-(N-morpholinyl)-cyclopentene to produce only the known C protonated nitroalkanes (**7**, Table 1).[13, 14] The nmr spectra of these products reveal a vinyl proton signal near τ 5 in agreement with the less-substituted olefin structure. There would appear to be no severe limitation on the nature of the *beta* substituent R_1 in the nitroolefin since the reaction succeeds when R_1 = Ph or H; although not as yet tested, the reaction should occur if R_1 is alkyl. It has been reported that 2-methyl-1-nitropropene fails to react with 1-(N-morpholinyl)cyclohexene.[13] This result suggests that suitable nitroolefins leading to **9** would not include those in which both *beta* substituents were groups other than hydrogen.

Intramolecular O alkylation leading to cyclic nitronic ester **9** from zwitterion **6** is believed favored owing to the relatively slower rate of C-protonation (to form **7**) in the *alpha*-substituted intermediate. Highly substituted nitronate anions are known to C protonate very slowly.[10]

The scope of the reaction of Eq 1 is limited to cycloalkanone enamines having fewer than eight ring members (cyclobutanone derived enamines were not investigated).

1-(N-Morpholinyl)cyclooctene (**13**) reacts with ω-methyl- and ω-ethyl-ω-nitrostyrene (**14a, b**) to yield the acyclic adducts **15a, b** (Eq 2). Structures **15a, b** are supported by their spectra, including characteristic nitroalkane absorption near 1540 cm^{-1} (KBr) and vinyl proton signals near τ 5.



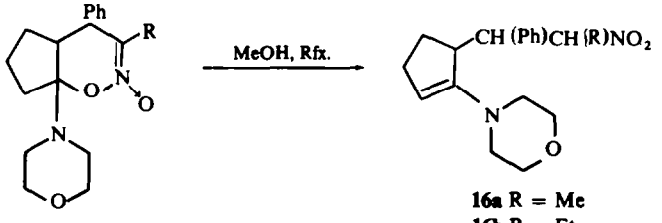
(2)

13

15a R = Me
15b R = Et

Acyclic enamines do not react with nitroolefins to produce cyclic nitronic esters. With α-substituted α-nitroolefins no C—C addition occurred. The morpholine enamine of desoxybenzoin failed to react in hexane with 1-phenyl-2-nitropropene (**14a**, R = Me) and was recovered. The reaction also failed when isobutyraldehyde morpholine enamine was treated with 1-phenyl-2-nitropropene; the product was the amine Michael adduct, 1-(N-morpholinyl)-1-phenyl-2-nitropropane. However, ω-nitrostyrene itself reacts with these and related acyclic enamines to produce substituted nitroalkanes and nitrocyclobutanes (acyclic analogs of **7** and **8**; Table 1).[12,13] The ynamine, $C_6H_5C{\equiv}CN(C_2H_5)_2$,[16] failed to react with 1-phenyl-2-nitropropene in hexane.

Tautomerization of cyclic nitronic esters **5**, **9a–j** to the related acyclic nitroalkanes (**7**; Table 1) occurs at a rate determined by ester structure. Absence of a 4-substituent (as in **5**) speeds tautomerization. The zwitterion **6** is involved in the C protonation (Eq 4), and the stereochemistry and mechanism of the intramolecular proton transfer process has been discussed.[9,14] The reaction is irreversible. It may occur slowly in the absence of solvents,[9] or rapidly in hot alcohol solvents (intermolecular proton transfer). For example, heating nitronic esters **9a–c** under reflux in methanol led to

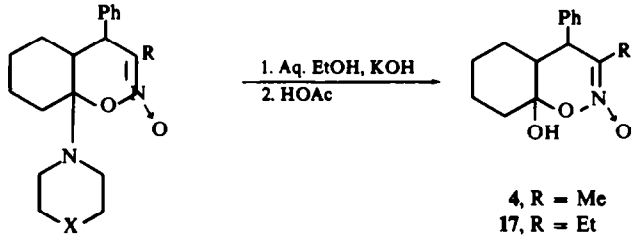


9a–c

16a R = Me
16b R = Et
16c R = Ph

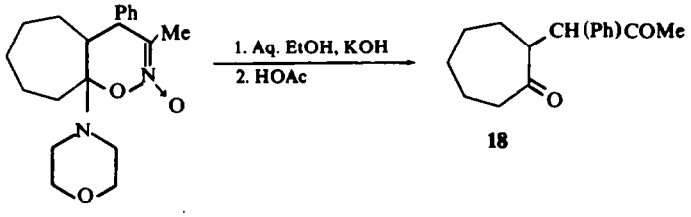
nitroalkanes **16a–c**. At 25° in 95% ethanol esters **9a–j** were found to decompose at the rate of ca. 5–25% in 24 hr as indicated by a decrease in the intensity of the characteristic nitronic ester UV absorption bands. Tautomerization was also observed in deuteriochloroform solvent with **9a**; the Me signal singlet of **9a** at τ 8·18 rapidly changes to the doublet observed in **16a** (τ 8·63, J = 7 Hz). Observations of the rate of change of the **9a–j** nitronic ester spectra in solution indicate a decreasing stability according to size of the 5,6-polymethylene ring in the order: 6 > 7 > 5.

Alkaline hydrolysis products of cyclic nitronic esters **9a–j** varied according to substituents and ring size of the 5,6-polymethylene substituent. The more stable 3-alkyl-5,6-tetramethylene compounds **9d–f** derived from cyclohexanone could be converted to the 8a-hydroxy derivatives **4** and **17** by treatment with aqueous potassium hydroxide at 25°, followed by acidification with acetic acid (78–89% yield). Compound **4** was also prepared by addition of cyclohexanone to 2-nitro-1-phenylpropene.[7,8]



4, R = Me
17, R = Et

Alkaline hydrolysis of cyclic nitronic esters derived from cyclopentanone (**9a–c**) and cycloheptanone (**9h–j**) did not lead to bridgehead hydroxy compounds (homologs of **4** and **17**). Reaction of the 5,6-pentamethylene compound **9h** with aqueous ethanolic potassium hydroxide at 25°, followed by treatment with acetic acid, gave the Nef product **18**. Under the same conditions the 5,6-trimethylene compounds **9a–c** produced no crystalline products.



18

9h

Hydrolysis of the 3,4-diphenyl cyclic nitronic ester derivatives **9g, j** by treatment with aqueous ethanolic potassium hydroxide at 25°, followed by addition of acetic acid, led to precipitation of 3,4,5-triphenylisoxazole. Ester **9c** should behave similarly. Triphenylisoxazole forms from the derived retrogression products α-nitrostilbene and phenylmethanenitronate anion, in reactions known to produce triphenylisoxazole in alkaline medium.[5]

Acid hydrolysis of nitronic esters **9a–j** (methanolic hydrochloric acid) gave yellow or blue oils, or tars, but no crystalline products. This behavior contrasts with that of nitroalkane enamines (**7**) which hydrolyze readily in methanolic hydrochloric acid (pH 4) to produce nitro ketones in high yield.[13,14]

Results of the present study support our previous conclusions on formation of isolable products by intramolecular nucleophilic addition of nitronate oxygen to double bonds.[5,8,18] Such additions can occur on carbon of carbon-hetero atom double bonds (C=O, C=N), but not to electrophilic olefinic double bonds. In the present study, nitronate oxygen addition occurs intramolecularly on carbon of an

iminium ion (C=N$^+$) in the zwitterion intermediate **6**. A photochemically induced intramolecular addition of nitronate oxygen to an iminium ion, leading to a reaction intermediate, has been described.[19]

EXPERIMENTAL

M.ps were determined on a Kofler block and are corrected. UV spectra were determined on a Cary Model 11 or Perkin–Elmer Model 202 spectrophotometer, IR spectra on a Perkin–Elmer Model 137 spectrophotometer, and NMR spectra on a Varian A-60 spectrometer. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee.

Reagents. Enamines 1-(N-morpholinyl)cyclopentene, 1-(N-morpholinyl) cycloheptene, 1-(N-morpholinyl)cyclooctene, and 1-(N-pyrrolidinyl)cyclohexene were prepared by the method of Kuehne,[20] distilled under reduced press, and stored at 0° under N_2. α-(N-Morpholinyl)stilbene was prepared by the method of Benzing.[21] Nitroolefins were prepared by known methods: ω-nitrostyrene;[22] α-nitrostilbene;[23] 2-nitro-1-phenylpropene,[24] (NMR of the latter ($CDCl_3$): τ 1·92 (d, J = 1, 1, = CH); 2·57 (s, 5, Ph); 7·57 (d, J = 1,3,Me).

2-Nitro-1-phenyl-1-butene (**14b**).[24] A soln of 1-nitropropane (50 ml), benzaldehyde (50 ml), and 5 ml 1-aminobutane in 200 ml xylene was heated under reflux until 9·0 ml water was removed in a Dean–Stark trap (4 days). The soln was distilled under reduced press to remove xylene and yield 78 g (89%) of **14b**, b.p. 110° (2 mm); lit.[25] b.p. 125–129° (10 mm).

Preparation of substituted 5,6-polymethylene-5,6-dihydro-4H-1,2-oxazine 2-oxides

General procedure—reaction of 1-(N-Pyrrolidinyl)cyclohexene with 2-nitro-1-phenylpropene to form 3-methyl-4-8a-(N-pyrrolidinyl)4a,5,6,7,8,8a-hexahydro-4H-1,2-benzoxazine 2-oxide (**9e**). To a soln of 2-nitro-1-phenylpropene (2·0 g, 0·0123 mole) in 100 ml dry hexane, cooled to 0° in an ice bath (dry N_2 atmosphere maintained throughout the reaction), was added dropwise during a few min 2·0 g (0·0132 mole) freshly distilled 1-(N-pyrrolidinyl)cyclohexene. The soln rapidly turned brownish orange in color and changed to a yellow color within 10 min when white, crystalline **9e** began to separate from the soln. After allowing to come to room temp (2 hr total reaction time) the mixture was filtered to yield 3·49 g (91%) of **9e**, m.p. 100–110°; the product was recrystallized by dissolving in warm benzene, followed by addition of hexane until turbidity was observed; m.p. 108–110°. Spectral properties are summarized in Table 3, elemental analyses in Table 2.

In a parallel experiment in which 10 ml acetonitrile solvent was employed in place of hexane, no ppt was observed after 4 hr reaction time at 25°; chilling to − 15° failed to precipitate the product. The solvent was removed under reduced press at 30° and the oily residue triturated with hexane to precipitate 1·6 g (41%) crude **9e**, m.p. 90–96°.

The above procedure used in the preparation of **9e** (hexane solvent, ca. 2% soln of each reactant, 25°, 2–3 hr, N_2 atmosphere) was employed in the preparation of **9f,g**. Preparation of the other esters listed in Tables 2 and 3 required slight modifications in procedure. The reaction to form the derivatives **9a–d** proceeded at 25° for 24 hr when the precipitated product was filtered and recrystallized from hexane. In the preparation of the cycloheptanone enamine derived products **9h–j** the reaction was conducted in 1:4 benzene-hexane solvent with a reaction time of 24 hr for **9h**, 36 hr for **9j** and 4 days for **9i**. The product **9i** failed to precipitate after 4 days; the solvent was evaporated at 30° and the residue diluted with hexane and chilled to − 15° to precipitate the product.

2-(N-Morpholinyl)-3-(2-nitro-1-phenylpropyl)cyclooctene (**15a**). 2-Nitro-1-phenylpropene (2 g, 0·0123 mole) and 2 g (0·0102 mole) 1-(N-morpholinyl)cyclooctene were dissolved in 30 ml hexane at 40°. The soln was allowed to stand at 25° overnight to deposit crystals which were removed by filtration. Recrystallization from hexane gave 1·5 g (42%) of **15a**, m.p. 134–136°. (Found: C, 70·57, H, 8·23; N, 7·70; mol wt, 346 (osmometry, $CHCl_3$); $C_{21}H_{30}N_2O_3$ requires: C, 70·36; H, 8·44; N, 7·82%; mol wt, 358·47); ν (KBr) 1545 cm^{-1} (NO_2), 1640 (C=CN); NMR ($CDCl_3$): τ 2·78 (m, 5, C_6H_5); 4·5–5·0 (m, 2, =CH and $CHNO_2$); 5·7–6·5 (m, 5, $C_6H_5C\underline{H}$ and CH_2NCH_2); 6·6–9·0 [m, 15, $CH(CH_2)_5$ and CH_2OCH_2]; 8·70 (d, J = 6·5, 3, CH_3).

2-(N-Morpholinyl)-3-(2-nitro-1-phenylbutyl)cyclooctene (**15b**). The procedure employed above in the preparation of **15a** gave with 2-nitro-1-phenyl-1-butene (0·65 g) and 1-(N-morpholinyl)cyclooctene (0·98 g) in hexane (25 ml) a clear soln after standing at 25° for one week. The solvent was evaporated and the residue triturated with MeOH to precipitate the product. Recrystallization from MeOH gave 0·75 g (55%) of

15b, m.p. 145–146°. (Found: N, 7·43; $C_{22}H_{32}N_2O_3$ requires: N, 7·56%); ν (KBr) 1540 cm^{-1} (NO_2), 1630 (C=CN); NMR ($CDCl_3$): τ 2·58 (m, 5, C_6H_5); 4·6–5·0 (m, 2, =CH and $CHNO_2$); 5·9–6·4 (m, 5, $C_6H_5C\underline{H}$ and CH_2NCH_2); 6·5–9·0 (m, 17, $CH_3C\underline{H}_2$, $CH(CH_2)_5$ and CH_2OCH_2); 9·15 (t, J = 7, 3, $C\underline{H}_3CH_2$.

1-(N-*Morpholinyl*)-2-*nitro*-1-*phenylpropane*

A. *Reaction of* 2-*nitro*-1-*phenylpropene with* 2-*methyl*-1-(N-*morpholinyl*)*propene.* A soln of 2-nitro-1-phenylpropene (2·0 g, 0·0123 mole) and 2-methyl-1-(N-morpholinyl)propene (1·8 g, 0·0128 mole) in 20 ml benzene, after standing at 25° for 24 hr, was diluted with hexane (30 ml). After standing for one week at 25° the soln deposited 0·65 g (21%) crude 1-(N-morpholinyl)-2-nitro-1-phenylpropane, m.p. 120–125°; recrystallization from MeOH gave crystals, m.p. 146–147°.

B. *Addition of morpholine to* 2-*nitro*-1-*phenylpropene.* A soln of 2-nitro-1-phenylpropene (0·5 g, 0·031 mole) and morpholine (0·3 g, 0·035 mole) in 10 ml MeOH was heated under reflux for 5 min. The crystals which separated were recrystallized from MeOH; 0·5 g (65%), m.p. 146–147°. (Found: C, 62·17; H, 7·17; N, 10·95; $C_{13}H_{18}N_2O_3$ requires: C, 62·38. H, 7·25; N, 11·19%). IR and NMR spectra were identical to those of the sample prepared by method A, above; ν (KBr) 1540, 1550 cm^{-1} (NO_2); NMR ($CDCl_3$): τ 2·4–3·0 (m, 5, Ph); 4·4–5·0 (m, 1, $CHNO_2$); 6·01 (d, J = 11·5, 1, $C_6H_5C\underline{H}$); 6·38 (t, J = 5, 4, CH_2NCH_2); 7·2–8·0 (m, 4, CH_2OCH_2); 8·66 (d, J = 6, 3, Me).

1-(N-*Morpholinyl*)-2-*nitro*-1-*phenylbutane.* A soln of 2-nitro-1-phenyl-1-butene (0·5 g, 0·0028 mole) in morpholine (0·4 g, 0·0046 mole) was allowed to stand for one week at 25°. Trituration with EtOH gave a solid which was recrystallized from MeOH; 0·6 g (80%), m.p. 94–95°. (Found: C, 63·70; H, 7·44; N, 10·45; $C_{14}H_{20}N_2O_3$ requires: C, 63·61; H, 7·63; N, 10·60%); ν (*Nujol*) 1540 cm^{-1} (NO_2).

2-(N-*Morpholinyl*)-3-(2-*nitro*-1-*phenylpropyl*)*cyclopentene* (**16a**). A soln of **9a** (1·0 g) in 10 ml MeOH was heated under reflux for 0·5 hr and cooled to yield crystalline **16a**, m.p. 120–122°. (Found: C, 68·51; H, 7·56; N, 8·73. $C_{18}H_{24}N_2O_3$ requires: C, 68·33; H, 7·65; N, 8·85%); ν (KBr) 1540 (NO_2) 1640 cm^1 (C=CN); NMR ($CDCl_3$): τ 2·82 (s, 5, C_6H_5); 4·4–5·1 (m, 1, $C\underline{H}NO_2$); 5·1–5·8 (m, 1, =CH); 6·0–6·6 (m, 5, CH_2NCH_2 and $C_6H_5C\underline{H}$); 7·0–9·0 (m, 9, CH_2OCH_2 and CH_2CH_2CH); 8·63 (d, J = 7, 3, CH_3).

In a parallel experiment with **9c** there was obtained a 60% yield of a product believed to be 2-(N-*morpholinyl*)-3-(1,2-*diphenyl*-2-*nitroethyl*)*cyclopentene*, m.p. 102–103°; ν (KBr) 1540 (NO_2); 1630 cm^{-1} (C=CN). Nitronic ester **9b** under these conditions gave an oil which failed to crystallize.

8a-*Hydroxy*-3-*methyl*-4-*phenyl*-4a,5,6,7,8,8a-*hexahydro*-4H-1,2-*benzoxazine* 2-*oxide* (**4**). A 1·0-g sample of **9e** was dissolved in 10 ml 10% KOH aq. After standing 1 hr at 25° the soln was added to a soln of 20 ml AcOH in 50 ml water to slowly precipitate **4**, 0·65 g (78%), m.p. 105–110°; recrystallization from EtOH gave colorless prisms, m.p. 136–138° (dec); lit[7,8] m.p. 137–139° (dec); mixture m.p., 136–138; IR and NMR spectra identical with those of an authentic sample.[8] Nitronic ester **9d**, under the same reaction conditions, also produced **4**, m.p. 135–137°, before recrystallization; IR spectrum identical to that of authentic **4**; mixture m.p. not depressed.

8a-*Hydroxy*-3-*ethyl*-4-*phenyl*-4a,5,6,7,8,8a-*hexahydro*-4H-1,2-*benzoxazine*-2-*oxide* (**17**). A 1·0 g sample of **9f** dissolved in 10ml EtOH was treated with 50 ml 1% KOH aq. After standing for 20 min at 25° AcOH (4 ml) was added until the soln became cloudy. After standing 24 hr the mixture was filtered to yield 0·74 g (89%) of **17**, m.p. 110–112°. (Found: C, 70·06; H, 7·69; N, 4·94; $C_{16}H_{21}NO_3$ requires: C, 69·79; H, 7·69; N, 5·09%); ν (KBr) 1595 cm^1 (C=N), 3100 (OH).

2-(1-*Phenylacetonyl*)*cycloheptanone* (**18**). A 0·20 g sample of **9h** was dissolved by addition of 5 ml each EtOH and 10% KOH aq. After standing 1 hr at 25°, a soln of 5 ml AcOH in 25 ml MeOH was added. After standing at 25° for 1 week, the mixture was concentrated to a small volume under reduced press, and the resulting ppt collected by filtration. Recrystallization from MeOH gave **18**; 0·11 g (77%), m.p. 86–88°. (Found: C, 78·51; H, 8·17; $C_{16}H_{20}O_2$ requires: C, 78·65, H, 8·25%); ν (KBr) 1685, 1700 cm^{-1} (C=O); NMR ($CDCl_3$): τ 2·70 (s, 5, Ph); 5·92 (d, J = 11, 1, $PhC\underline{H}$); 6·2–6·7 (m, 1, CH); 6·8–9·0 [m, 10, $(CH_2)_5$]: 7·92 (s, 3, MeCO).

3,4,5-*Triphenylisoxazole.* A 0·30 g sample of **9j** was dissolved by addition of 10 ml each of EtOH and 10% KOH aq. After standing for 2 hr at 25° the soln was added to a soln of 10 ml AcOH in 50 ml MeOH. Concentration under reduced press gave a ppt of triphenylisoxazole which was removed by filtration; 0·10 g (91%), m.p. 212°; lit[5] m.p. 210–212°; when mixed with an authentic sample the m.p. was not depressed. In a parallel experiment **9g** also produced triphenylisoxazole; m.p. 212° (38%).

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