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1,3,4-OXADIAZINE DERIVATIVES FROM CYCLOHEXANONE ENAMINES AND ASYMMETRIC DIIMIDES

POSSIBILITY OF RING-CHAIN TAUTOMERISM IN SUCH HETEROCYCLIC SYSTEM

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Abstract—1,3,4-oxadiazine derivatives, in equilibrium with their corresponding trisubstituted enamine isomers, are obtained in a regiospecific way from cyclohexanone enamines and ethoxycarbonyl aroyl diimides. Such an equilibrium is not present in analogous oxadiazine systems, derived from aryl aroyl diimides.

IT IS well known that aminocyclohexenes **1**, **2** react with symmetric diimides such as RO_2C–N=N–CO_2R and Ar–CO–N=N–CO–Ar to give trisubstituted enamine[1] and 1,3,4-oxadiazine derivatives,[2] respectively. In a previous communication[3] we have reported that also asymmetric diimides of type Ar–N=N–CO–Ar' **3** do react with the same substrates, but the results are partially different. In fact in some cases, depending on the reaction conditions and the basic moiety of enamines, the above reactions proceed with formation of tetrasubstituted enamine derivatives **4** which easily isomerise into oxadiazine derivatives **5**, as depicted in Scheme 1.

This outcome, doubly unusual as far as both type of the obtained products **4** and their subsequent easy isomerization into **5** are concerned, made us investigate the behaviour of two other asymmetrically substituted diimides, i.e. Ar–N=N–CO_2Et **7** and Ar–CO–N=N–CO_2Et **9**.

RESULTS AND DISCUSSION

(a) *Reactions with* Ar–N=N–CO_2Et. With these electrophiles, our attempts to isolate any 1:1 addition product from the mixtures failed. However, on acidic hydrolysis of the crudes and subsequent column chromatography, the corresponding 2-substituted cyclohexanones **8** were isolated, although in rather low yields (Scheme 2).

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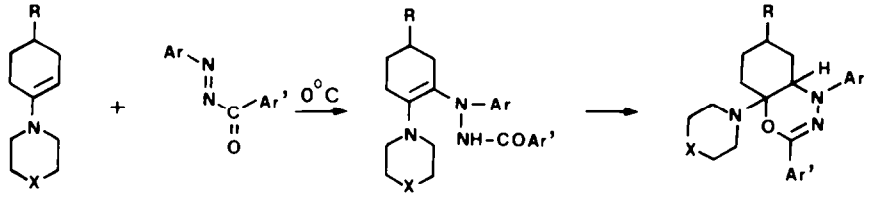
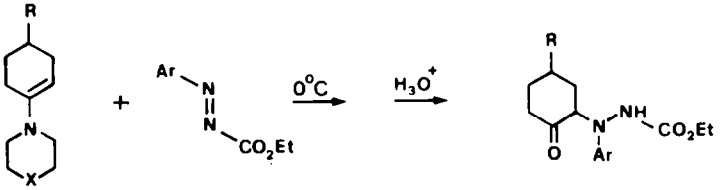


1 X=O 2 X=- 3 4 X=O 5 X=O 6 X=-

a: R=H b: R=Bu^t c: Ar=Ar'=C_6H_5 d: Ar=p-NO_2-C_6H_4, Ar'=C_6H_5
e: Ar=C_6H_5, Ar'=p-NO_2-C_6H_4

Scheme 1



1 X=O 2 X=- 7 8

a: R=H b: R=Bu^t c: Ar=C_6H_5 d: Ar=p-NO_2-C_6H_4

Scheme 2

In fact from the reaction between **1a** and **7c** the ketone **8ac** was obtained in 10% yield, operating as usual at 0° in ether. Starting from the more reactive pyrrolidine enamine **2a** the same ketone was obtained in 45% yield only. Analogous behaviour was shown by enamine **1b** that furnished the ketone **8bc** (39%). With **7d** as electrophile both **1a** and **2a** furnished after hydrolysis the corresponding ketone **8ad** in 45 and 50% yield, respectively. These disappointing results made us not to take into consideration further reactions with aryl ethoxycarbonyl diimides.

(b) *Reactions with* Ar–CO–N=N–CO_2Et. Ethoxycarbonyl aroyl diimides **9** add to enamines **1a**, **1b** and **2b** giving exclusively 1,3,4-oxadiazine derivatives **10** or **11**. IR spectral characteristics (lack of NH bands and presence of only one strong CO absorption band together with a weak one corresponding to the C=N stretching) agreed with such a type of structure and allowed to rule out at the same time both enamine and diazetidine structures. In some cases small amounts of the 2,6-disubstituted cyclohexanones **12** were isolated from mother liquors, after acidic hydrolysis (Scheme 3).

When the reaction was carried out with pyrrolidinocyclohexene **2a**, all attempts to isolate 1:1 adducts **11** failed and only the corresponding 2-substituted cyclohexanones, together with traces of ketone **12**, could be obtained, after hydrolysis of the mixtures.

Owing to the presence of two similarly electron withdrawing groups[4] linked to the –N=N–system in the diimides **9**, *a priori* both N atoms could behave as electrophilic sites and attack the nucleophilic C-2 of enamines, leading therefore to the formation of different oxadiazine derivatives, i.e. **10**, **11** and/or **10'**, **11'**. In spite of this possibility, the reaction occurred in a regiospecific way, and to the single (TLC) regioisomers structures **10**, **11** were assigned on the basis of the solid state IR spectra. In fact all heterocyclic adducts showed a weak band at 1620–1630 cm^{-1}, corresponding to the C=N stretching of an Ar–C=N system; furthermore a strong absorption band was present at 1680–1695 cm^{-1}, related to the CO of the N–CO_2Et group. Structures like **10'** and **11'** (Scheme 3) would show in their IR spectra weak bands at 1660–1680 cm^{-1} (C=N stretchings) and strong bands at 1635–1650 cm^{-1} (CO), as verified in compounds having N=C–OR[5] and Ar–CO–N[2] features. In the ^{1}H NMR spectra of all derivatives **10** and **11** the signal related to the C–4a proton appeared as an unresolved multiplet downfield but partially overlapped with the ester methylene protons; for **10ad**, **10bd** and **11bd** integration of the related area gave 3H. Oxadiazines **10ac**, **10bc** and **11bc** showed at lower field an additional broadened multiplet attributable to protons both linked to an enaminic double bond and geminal to substituted hydrazine groups.

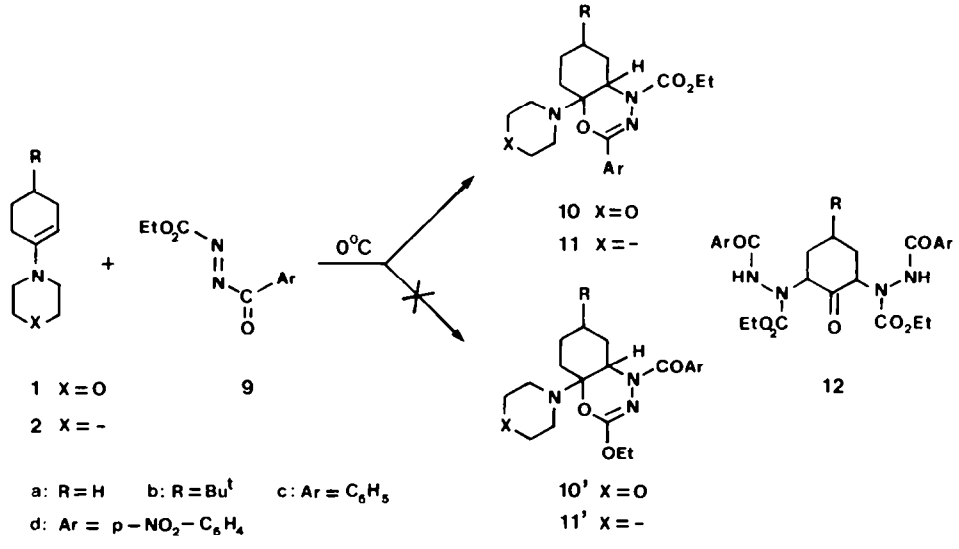
The latter signal indicated that small amounts of trisubstituted enamine isomers **10''ac**, **10''bc** and **11''bc** (Scheme 4) were present in the probe. Estimation of such amounts by ^{1}H NMR spectrometry was not very easy since the latter proton resonances partly underlie the C–4a proton absorptions. Integration of all signals in the range 4–5.15δ, however, always gave values corresponding roughly to 3.2–3.4 H.

It is worth noting that in the latter cases after removal of the solvent, the residue gave an IR spectrum superimposable in all parts to that one of the starting oxadiazine derivative.

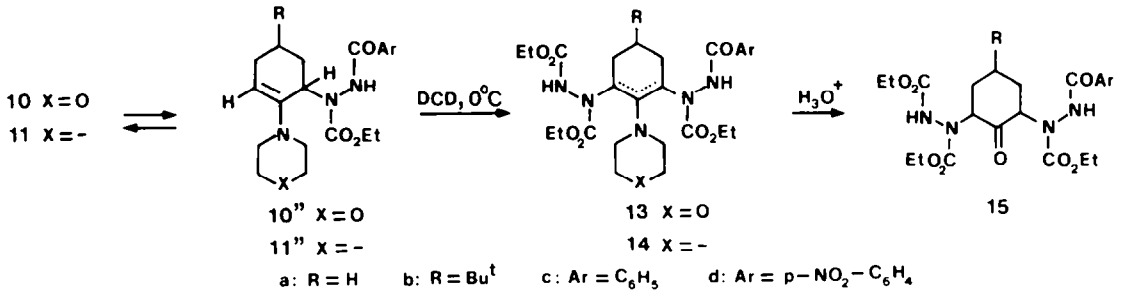
(c) *Ring-chain tautomerism in* 1,3,4-*oxadiazine derivatives*. These spectral data suggested that a ring⇆chain tautomeric equilibrium, although lying well over to the cyclic form, existed in solution. Since an equilibrium of this type had been already observed for oxazine[6] and apparently also oxadiazine derivatives,[2] the question then arising was whether or not all our oxadiazine systems, previously reported[3] and under present investigation, could be in equilibrium with their corresponding open chain tautomers, the presence of which was detectable by neither IR nor ^{1}H NMR spectroscopy.

To solve this problem on the basis of indirect evidence, all adducts **5**,**6**,**10** and **11** were allowed to react with diethoxycarbonyl diimide (DCD) which can act as a trap for the trisubstituted enamine forms.[7]

No reaction was observed with compounds **5** and **6**, while under the same conditions most oxadiazines **10** and **11** furnished the corresponding enamine diadducts **13** and **14**, quantitatively from which 2,6-disubstituted cyclohexanones **15** were obtained on acidic hydrolysis (Scheme 4).



Scheme 3



Scheme 4

These results established beyond doubt that only the oxadiazine derivatives obtained from aroyl ethoxycarbonyl diimides **9** are in equilibrium with the trisubstituted enamine tautomers. This fact accounts also for the formation of cyclohexanones **12**. The complete resistance of compounds **5** and **6** to conversion into trisubstituted enaminic forms, in comparison with other heterocyclic adducts obtained also from enamines and various electrophiles[6,8] is a rather surprising result, but it is difficult to provide an explanation to fit, at present.

(d) *Stereochemical aspects of* 1,3,4-*oxadiazine derivatives.* In the ^{1}H NMR spectra of oxadiazine derivatives **5** and **6** the C–4a proton resonances always appeared as unresolved multiplets, the half height widths (15 ÷ 20 Hz) of which indicated axial protons.[3] For these compounds a structure with the two rings *cis* fused and the bulky amine group equatorially oriented can be assigned, by analogy with other oxadiazine[2] or hexahydronaphthopyrane systems,[9] the stereochemistry of which was proved by X-ray analysis. As for oxadiazine derivatives **10** and **11**, the partial overlap of the C–4a and ester methylene proton signals does not allow the correct stereochemical assignment at C–4a to be made. We think, however, that also these compounds can be assumed to present the same steric assessment on the basis of the results of hydrolysis. In fact under non epimerising conditions t-Bu susbstituted oxadiazine derivatives **10** and **11** always led exclusively to ketone **16** which did not further epimerise and where the C–2 substituents were assigned an equatorial position from the pattern and W_H values of the proton signals at the same C–2 (Table 3).

(e) *Hydrolysis of* 1,3,4-*oxadiazine derivatives.* This dis not always afford 2-substituted cyclohexanones **16A**, but sometimes 8a-hydroxy-1,3,4-oxadiazines **16B** were obtained, or mixtures of **A** and **B** tautomers (see the solid state IR spectra reported in Table 3). In $CHCl_3$ solution, however, all hydrolysis products existed as acyclic tautomers **A**, apart from compounds **16ad** and **16bd** for which an equilibrium between **A** and **B** was rapidly established under the same conditions. In the latter cases, the only apparent rationalisation for the relative stability of the cyclic forms **B** could be the extended conjugation going from the N atom at 4-position as far as the p-nitro proup. In fact, when an electron attracting group like CO_2Et is linked at the N-4 atom, so that the extension of such a conjugation is reduced, also derivatives like **16ag** and **16bg** undergo complete ring opening.

Table 1. Oxadiazine derivatives **10** and **11**

Entry no. Formula	Elemental analysis Found (Calc.) C	H	N	M.p.(°C)	Yield(%)	IR (cm^{-1}) CO_2Et	C=N	^{1}H NMR (δ)
10ac $C_{20}H_{27}N_3O_4$	64.38 (64.32)	7.22 (7.29)	11.3 (11.25)	103-4[a]	84	1690	1625	4.0 -5.15[f]
10ad $C_{20}H_{26}N_4O_6$	57.3 (57.41)	6.30 (6.26)	13.38 (13.39)	134-5[b]	36	1685	1620	4.1 -4.8[g]
10bc $C_{24}H_{35}N_3O_4$	67.1 (67.11)	8.36 (8.21)	9.73 (9.78)	146-8[c]	41	1685	1630	4.05-5.15[f]
10bd $C_{24}H_{34}N_4O_6$	60.5 (60.74)	7.25 (7.22)	11.75 (11.81)	162-4[b]	55	1695	1625	4.0 -4.75[g]
11bc $C_{24}H_{35}N_3O_3$	69.5 (69.70)	8.46 (8.53)	10.1 (10.16)	134-5[d]	50	1680	1630	4.0 -5.1[f]
11bd $C_{24}H_{34}N_4O_5$	62.8 (62.86)	7.50 (7.47)	12.3 (12.22)	136[e]	37	1695	1620	4.05-4.7[g]

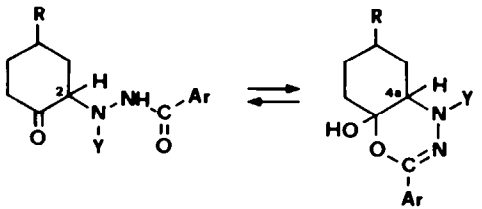
[a]From ligroin. [b]Bright yellow crystals, from 99% ethanol. [c]From 99% ethanol. [d]Triturated with anhydrous ether. [e]Dark yellow powder, triturated with 99% ethanol. [f]In the range are included the $C_{(4a)}$-H and CO_2CH_2 signals, together with the signals related to the C-2 vinyl proton and the C-6 proton of the enamine isomers 10" or 11". [g]In the range are included the $C_{(4a)}$-H and CO_2CH_2 signals.

Table 2. Enamines diadducts 13 and 14 and 2,6-dissubstituted cyclohexanones 15

Entry no. Formula	Elemental analysis Found (Calc.) C	H	N	M.p.(°C)	Yield(%)	IR(cm^{-1}) NH	CO_2Et and CO	N-C=C
13ac[a] $C_{26}H_{37}N_5O_8$	57.08 (57.03)	6.88 (6.81)	12.7 (12.79)	70-5[b]	100	3400,3280	1760,1710br	1650sh[c]
13ad[a] $C_{26}H_{36}N_6O_{10}$	52.55 (52.69)	6.17 (6.12)	14.1 (14.18)	50-60[b]	96	3400,3280	1760,1710br	1650sh[c]
13bc[a] $C_{30}H_{45}N_5O_8$	59.6 (59.69)	7.46 (7.51)	11.55 (11.60)	70-90[b]	100	3400,3290	1760,1710br	1635sh[c]
13bd $C_{30}H_{44}N_6O_{10}$	55.5 (55.54)	6.86 (6.83)	12.8 (12.96)	183-4[d]	77	3260	1750,1715,1675	1630
14ac $C_{26}H_{37}N_5O_7$	58.6 (58.74)	7.01 (7.02)	13.2 (13.17)	154-6[e]	58	3290,3260	1745,1700,1670	1640
14ad $C_{26}H_{36}N_6O_9$	54.05 (54.15)	6.18 (6.29)	14.53 (14.58)	125-8[f]	50	3290	1760,1750sh,1690sh	1650
14bc[a] $C_{30}H_{45}N_5C_7$	61.28 (61.31)	7.80 (7.72)	11.85 (11.92)	60-80[b]	95	3260	1760,1710br	1650[c]
14bd $C_{30}H_{44}N_6O_9$	56.75 (56.95)	7.05 (7.0)	13.25 (13.28)	85-90[b]	90	3400,3290	1760,1710br	1650sh[c]
15ac $C_{22}H_{30}N_4O_8$	55.0 (55.22)	6.41 (6.32)	11.75 (11.71)	196[g]	90	3270	1755,1710,1680	—
15ad $C_{22}H_{29}N_5O_{10}$	50.39 (50.48)	5.55 (5.58)	13.31 (13.38)	185-8[f]	90	3280,3240	1755,1740,1690	—
15bc $C_{26}H_{38}N_4O_8$	58.4 (58.41)	7.20 (7.16)	10.4 (10.48)	229[g]	90	3270	1750,1740,1710,1680	—
15bd $C_{26}H_{37}N_5O_{10}$	54.0 (53.88)	6.48 (6.43)	12.06 (12.08)	185-6[f]	90	3360-3290	1760,1740,1710,1685	—

[a] Glass-like product, homogeneous on t.l.c. (ethyl acetate-ligroin 3:2). [b] Triturated with light petroleum. [c] In CCl_4 solution. [d] Triturated with 99% ethanol. [e] From benzene-ligroin 1:1. [f] Triturated with anhydrous ether. [g] From 99% ethanol.

Table 3. 2-Substituted cyclohexanones **16**

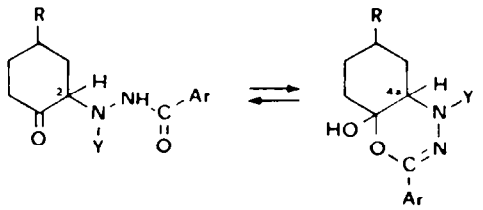


16A **16B**

	Y	Ar
a R = H		
b R = Bu^t		
c	C_6H_5	C_6H_5
d	C_6H_5	p-NO_2-C_6H_4
e	p-NO_2-C_6H_4	C_6H_5
f	CO_2Et	C_6H_5
g	CO_2Et	p-NO_2-C_6H_4

Entry no. Formula	Elemental analysis Found (Calc.) C	H	N	M.p. (°C)	IR (cm^{-1}) Nujol	$CHCl_3$	^{1}H NMR (δ) NH	$C_{(2)}$-H (W_H)^h	$C_{(4a)}$-H
16ac $C_{19}H_{20}N_2O_2$	73.9 (74.0)	6.48 (6.54)	9.10 (9.08)	170-3[a]	1680 ($CO-C_6H_5$) 1710 (C=O) 3380 (N-H)	1685 ($CO-C_6H_5$) 1715 (C=O) 3370 (N-H)	8.45	4.65(20)	—
16bc $C_{23}H_{28}N_2O_2$	75.9 (75.79)	7.80 (7.74)	7.69 (7.69)	65-85[b]	1620 (C=N) 1670 ($CO-C_6H_5$) 1720 (C=O) 3140-3500 (N-H/O-H)	1685 ($CO-C_6H_5$) 1720 (C=O) 3370 (N-H)	8.40	4.65(18)	—
16ad $C_{19}H_{19}N_3O_4$	64.6 (64.58)	5.41 (5.42)	11.85 (11.89)	131-4[c]	1620 (C=N) 3460 (O-H)	1620 (C=N) 1680 ($CO-C_6H_4$-) 1715 (C=O) 3200-3560 (N-H/O-H)	8.65	4.6	4.1
16bd $C_{23}H_{27}N_3O_4$	67.6 (67.46)	6.67 (6.65)	10.2 (10.26)	156-8[c]	1620 (C=N) 3515 (O-H)	1620 (C=N) 1690 ($CO-C_6H_4$-) 1715 (C=O) 3360 (N-H) 3515 (O-H)	8.65	4.7	4.1
16ae $C_{19}H_{19}N_3O_4$	64.5 (64.58)	5.44 (5.42)	11.8 (11.89)	150-1[d]	1680 ($CO-C_6H_5$) 1720 (C=O) 3300 (N-H)	1690 ($CO-C_6H_5$) 1715 (C=O) 3380 (N-H)	8.40	4.74(19)	—

Table 3 (*Condt.*)



16A 16B

	Y	Ar
a R = H		
b R = Bu^t		
c	C_6H_5	C_6H_5
d	C_6H_5	$p\text{-}NO_2\text{-}C_6H_4$
e	$p\text{-}NO_2\text{-}C_6H_4$	C_6H_5
f	CO_2Et	C_6H_5
g	CO_2Et	$p\text{-}NO_2\text{-}C_6H_4$

Entry no. Formula	Elemental analysis Found (Calc.) C	H	N	M.p. (°C)	IR (cm^{-1}) Nujol	$CHCl_3$	^1H NMR (δ) NH	$C_{(2)}$-H (W_H)[h]	$C_{(4a)}$-H
16be $C_{23}H_{27}N_3O_4$	67.4 (67.46)	6.69 (6.65)	10.18 (10.26)	110-30[e]	1630 (C=N) 1680 ($CO\text{-}C_6H_5$) 1720 (C=O) 3200-3500 (N-H/O-H)	1690 ($CO\text{-}C_6H_5$) 1720 (C=O) 3360 (N-H)	8.27	4.75 (18)	—
16af $C_{16}H_{20}N_2O_4$	63.35 (63.14)	6.68 (6.62)	9.14 (9.20)	135-7[f]	1670 ($CO\text{-}C_6H_5$) 1708 (C=O) 1730 (CO_2Et) 3270 (N-H)	1705br (C=O/CO_2Et) 3410 (N-H)	8.25	4.95 (20)	—
16bf $C_{20}H_{28}N_2O_4$	66.61 (66.64)	7.88 (7.83)	7.69 (7.77)	117-8[g]	1680 ($CO\text{-}C_6H_5$) 1705 (C=O) 1720 (CO_2Et) 3255 (N-H)	1710br (C=O/CO_2Et) 3400 (N-H)	8.05	4.95 (21)	—
16ag $C_{16}H_{19}N_3O_6$	55.1 (55.01)	5.47 (5.48)	12.0 (12.03)	136-7[a]	1670 ($CO\text{-}C_6H_5$) 1690-1710 (C=O/CO_2Et) 3290 (N-H)	1710br (C=O/CO_2Et) 3400 (N-H)	8.2	5.05 (23)	—
16bg $C_{20}H_{27}N_3O_6$	59.3 (59.25)	6.72 (6.71)	10.3 (10.36)	148[a]	1688 ($CO\text{-}C_6H_5$) 1700-1730 (C=O/CO_2Et) 3330 (N-H)	1710br (C=O/CO_2Et) 3400 (N-H)	8.3	4.9 (23)	—

[a] From ethanol. [b] Triturated with light petroleum. [c] Red crystals, from ligroin. [d] Yellow crystals, from benzene-light petroleum. [e] Orange red crystals, triturated with light petroleum. [f] Triturated with water. [g] From ligroin. [h] W. values are given in Hz.

EXPERIMENTAL

M. ps are uncorrected and were determined on capillary tubes on a W.Büchi apparatus. IR spectra were recorded for Nujol mulls, unless otherwise noted, with a Perkin–Elmer 257 double beam spectrometer with polystyrene calibration. ^{1}H NMR spectra were obtained at 60 MHz in $CDCl_3$ solutions (TMS as internal standard, at 20°) with Jeol JNM spectrometer. Microanalyses were carried out on a Hewlett–Packard 185 instrument. Analytical TLC plates were prepared by using Merk silica gel G.

Hexahydro-4H-1,3,4-benzoxadiazine derivaties **5** and **6** were prepared as described elsewhere.[3] Enamines **1** and **2** were prepared by azeotropic removal of water[10] from the appropriate ketone and three-fold excess amine in refluxing benzene, with p-toluenesulphonic acid as a catalyst.

Diimides **7** *and* **9**. Compounds **7c**[11] and **7d**[12] were prepared by oxidation of the corresponding hydrazine derivatives with 0.2M $KMnO_4$ in anhyd AcOH.[11] Compounds **9c**[13] and **9d** were prepared by oxidation of the corresponding N,N'-disubstituted hydrazines with N-bromosuccinimide. N-p-nitrobenzoyl-N'-ethoxycarbonylhydrazine was prepared from ethyl chloroformate and p-nitrobenzhydrazide, by the method reported[13] for the unsubstituted N-benzoyl derivative.

N-p-nitrobenzoyl-N'-ethoxycarbonyl hydrazine (66%), m.p. 195° from EtOH. (Found: C,47.3; H, 4.40; N,16.51; $C_{10}H_{11}N_3O_5$ requires: C,47.43; H,4.38; N,16.59%). IR cm^{-1}, 3350 and 3250 (NH), 1720 (CO_2Et), 1670 (COPh).

Compound **7d** (70%), dark red oil thermally very sensitive. (Found: C,47.79; H,3.70; N,16.68; $C_{10}H_9N_3O_5$ requires: C,47.82; H,3.61; N,16.73%). IR (film) cm^{-1}, 1765 (CO_2Et), 1720 (COPh).

Reactions of enamines **1** *and* **2** *with aryl ethoxycarbonyl diimides* **7**. A soln of diimide (11 mmoles) in anhyd ether (15 ml) was added under N_2 and over 20 min to a stirred soln of 10% excess enamine in the same amount of solvent, chilled in an ice-bath. The mixture was set aside at 0° for 48 hr. Removal of the solvent under reduced press and at room temp left a dark red sticky mass which resisted all attempts of crystallization. It was then dissolved in EtOH and hydrolysed with 10% HCl. After 48 hr at room temp, the solvent was removed under reduced press and the resulting viscous residue was diluted with water, neutralized with $NaHCO_3$ and extracted with ether. The extract was dried (Na_2SO_4), filtered, and evaporated to leave a semi-solid residue that was shown by TLC to be a mixture of essentially enamine ketone and product, so it was chromatographed on silica gel (Merk, 70–230 mesh ASTM). After elution of parent cyclohexanone with benzene, **8** was eluted with benzene–acetone 98:2.

Compound **8ac** (10% from **1a** and **7c**; 43% from **2a** and **7c**), white crystals m.p. 113–4° from ligroin. (Found: C, 65.0; H, 7.09; N,10.2; $C_{15}H_{20}N_2O_2$ requires: C, 65.20; H,7.30; N,10.14%) IR cm^{-1}, 3380 (NH), 1750 (CO_2Et), 1710 (CO); ^{1}H NMRδ, 4.66 (m, W_H 15 Hz, CH–N).

Compound **8ad** (45% from **1a** and **7d**; 50% from **2a** and **7d**), bright yellow crystals m.p. 158–60° from benzene–ligroin. (Found: C,56.0; H,6.0; N,13.14; $C_{15}H_{19}N_3O_4$ requires: C,56.07 H,5.96; N,13.08%). IR cm^{-1}, 3370 (NH), 1752 (CO_2Et), 1725 (CO); ^{1}H NMR δ, 4.8 (m, W_H 19 Hz, CH–N).

Compound **8bc** (39%)), m.p. 68–70°; IR ($CHCl_3$) cm^{-1}, 3380 (NH), 1745 (CO_2Et), 1720 (CO); this glass-like product could not be purified and gave an unsatisfactory elemental analysis; it was identified through its 2,4-dinitrophenyl-hydrazone, m.p. 112–5°. (Found: C,59.80; H, 6.19; N,8.42; $C_{25}H_{31}N_3O_8$ requires: C,59.87; H,6.23; N,8.38%).

Reactions of enamines **1** *and* **2** *with aroyl ethoxycarbonyl diimides* **9**. A soln of **9** (20 mmoles) in anhyd ether (15 ml) was added dropwise and under N_2 to a stirred soln of 10% excess enamines in the same amount of solvent, cooled in an ice-bath. The mixture was allowed to stand at 0° for 48 hr. The precipitated **10** or **11** were filtered off (single spot on TLC, EtOAc-ligroin 1:1). The solvent was removed from the filtrate and the oily residue, diluted with acetone, was hydrolysed with 10% HCl. After standing 2 days at room temp, **12** separated as a white solid. Authentic samples of **12** for comparison were prepared by reaction of **2** with **9** in 1:2 molar ratio, followed by hydrolysis. Yields, physical, analytical and spectral data of **10** and **11** are reported in Table 1. When **2a** was reacted, no ppt was observed; attempts to precipitate the product (chilling to −10°, removal of the solvent and trituration of the oily residue with light petroleum) failed. Acidic hydrolysis of the mixtures furnished the corresponding **16** (Table 3), together with small amounts of **12**.

Compound **12ac** (2% from **2a** and **9c**), m.p. 204–5° from EtOH. (Found: C,61.0; H,5.95; N,10.95; $C_{26}H_{30}N_4O_7$ requires: C,61.17; H,5.92; N,10.97%). IR cm^{-1}, 3370, 3280 (NH), 1730, 1710sh, 1700–1690 (CO_2Et, COPh and CO).

Compound **12ad** (1% from **2a** and **9d**), m.p. 230° from EtOH. (Found: C,52.1; H,4.68; N,14.2; $C_{26}H_{28}N_6O_{11}$ requires: C, 52.0; H,4.70; N,14.0%). IR cm^{-1}, 3370, 3310 (NH), 1730sh, 1710–1700, 1690, 1680 (CO_2Et, COPh and CO).

Compound **12bc**, (8% from **1b** and **9c**, 12% from **2b** and **9c**), m.p. 249° from EtOH. (Found: C,63.4; H, 6.76; N,9.96; $C_{30}H_{38}N_4O_7$ requires: C,63.59; H,6.76; N,9.89%). IR cm^{-1}, 3260 (NH), 1740, 1730, 1710, 1680 (CO_2Et, COPh and CO).

Compound **12bd** (5% from **2b** and **9d**), m.p. 219–20°C from EtOH. (Found: C,55.0; H,5.60; N,12.8; $C_{30}H_{36}N_6O_{11}$ requires: C,54.87; H,5.52; H,12.79%). IR cm^{-1}, 3350 (NH), 1730, 1710, 1690, 1675 (CO_2Et, COPh and CO).

Reactions of oxadiazine derivatives **10** *and* **11** *with diethoxycarbonyl diimide*. To a cooled soln of **10** or **11** in anhyd benzene, an equimolar amount of DCD in the same solvent was added dropwise. After standing at 0° for 48 hr, the solvent was removed under reduced press and **13** or **14** were obtained. When the oxadiazine derivative could not be isolated as in the reactions between enamine **2a** and diimides **9c** or **9d**, DCD was added directly to the reaction soln. In this case after the usual work up, diadducts **14ac** or **14ad** were isolated. M.ps, yields, analytical and spectral data of derivatives **13** and **14** are reported in Table 2.

Derivatives **5** and **6** did not react with DCD under similar conditons to furnish the corresponding diadducts. Work up as described above gave dark oils from which, on acidic hydrolysis N,N'-diethoxycarbonylhydrazine, N-aryl-N'-aroyl-hydrazine, 2-substituted ketones **16** were isolated, together with minor amounts of uncharacterised oily products (TLC).

Hydrolysis of oxadiazine derivatives **5**,**6**,**10**,**11** *and enamine diadducts* **13**,**14**. To a stirred soln of the title compounds in acetone at room temp, 10% HCl was added until acidity. After 48 hr, the soln was neutralised with $NaHCO_3$. Removal of acetone, extraction with ether, drying and evaporation of the extract at reduced press gave the corresponding **15**, **16** almost quantitatively. Owing to the hydrolysis conditions, all derivatives **15** and **16** (R = Bu^t) were obtained as the thermodynamic isomers; in fact they did not epimerise on heating under reflux in EtOH in the presence of p-toluenesulphonic acid or HCl as catalysts. Hydrolysis of **10** and **11** (R = Bu^t) carried out under non epimerising conditions, i.e. with equimolar amounts of AcOH, afforded the **16** in the more stable epimeric form with the substituent at C-2 in equatorial orientation.

Physical, analytical and spectral data of **15** and **16** are reported in Tables 2 and 3, respectively.

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