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FUNCTIONALIZED ENAMINES—XIV[1]

REACTION OF α-TETRALONE ENAMINES WITH CARBENES

INFLUENCE OF THE NATURE OF CARBENE AND THE BASE-COMPONENT OF THE ENAMINE ON THE REACTION PATTERN

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Abstract—Enamine **1a**, derived from 6-methoxy-1-tetralone and morpholine, reacts with carbenes† **2a** and **2b** to give (1:1) adducts **3a**, and a mixture of **3b** and **3c**, respectively. The pyrrolidine enamine **1b**, on the other hand, reacts with carbene **2b**, to give, beside the (1:1) adduct **3e**, benzylidene-derivative **4b**. Reaction of enamine **1b** with carbene **2a** does not yield a 1:1 adduct; instead, two products were isolated which have been identified as **4a** and **5**. Both morpholine and pyrrolidine enamines **1a,b** react with carbene **2c** to give one and the same product **6**. Possible mechanisms for the formation of the reaction products are discussed.

Reactions of enamines with carbenes, in general, lead to aminocyclopropanes as primary products;[3] however, dependence of the course of reaction on the nature of the enamine-base has been recently observed in this laboratory.[4] In connection with our continued interest in the chemistry of conjugated enamines[1,5] we have examined the reaction of α-tetralone enamines **1a,b** with carbenes **2a–c** (Scheme 1). α-Tetralone enamines possess the unusual feature that their dipolar resonance structures are subject to steric inhibition by the peri-proton (C_8-H) of the tetralin ring.[6]

Enamines **1a.b** were prepared by the method described by Van der Vlugt.[7] The carbenes **2a**,[8] **2b**[9] and **2c**[10] were generated by procedures reported in the literature.

Reaction of the morpholine enamine of 6-methoxy-1-tetralone (**1a**) with dichlorocarbene (**2a**) gave a single product, namely, the 1:1 adduct **3a**, m.p. 104–107°, in good yield. The same enamine, however, reacted with phenylchlorocarbene (**2b**) to give a mixture of the stereoisomeric (1:1) adducts, **3b** and **3c** which could not be separated into its components. The isomeric ratio **3b/3c** was derived from the NMR spectrum of the mixture. *Endo*-phenyl adduct **3b** exhibits a considerable shielding of the C_5-, C_7-, C_8- and the OMe group protons as compared with the corresponding protons in **3c** (Experimental). Furthermore, in adduct **3c**, while the protons of the tetralin system resonate at "normal" δ values, the morpholine methylene protons are, on the other hand, considerably shielded, (δ 3·23 centre, m: $—CH_2—O—CH_2—$; the corresponding protons in **3b** resonate at "normal" δ values: 2·87 centre, m: $—CH_2—N—CH_2—$; δ 3·71 centre, m: $—CH_2—O—CH_2—$). These results are consistent with a *cis*-stereochemistry of the phenyl and the morpholine rings.[9] The **3b/3c** ratio was determined to be 7:3; which is in agreement with a more hindered approach of phenylchlorocarbene to the enamine double bond in the transition-state leading to the formation of isomer **3c**.

Reaction of enamine **1b** with dichlorocarbene (**2a**) led, after hydrolysis, to products, which emphasize the special character of the enamines utilizing pyrrolidine as the base-component. After column-chromatography, two products, **4a** (m.p. 52–58°) and **5** (m.p. 70–72°) could be isolated. The structure of **4a** followed from its spectral data; IR($CHCl_3$) 1660 cm^{-1} (α,β-unsaturated CO) and NMR ($CDCl_3$) δ 7·37 s (C_9–H). The latter chemical shift assignment for the C_9-proton is in agreement with the expected anisotropic influence of the C_1–CO and is also consistent with considerations to be presented later. Possible mechanisms for the formation of **4a** are presented in Scheme II. According to route A (Scheme II) enamine **1b** is assumed to express its reactivity via the dipolar ion **1b'**, which would contribute significantly to the ground state of the molecule in view of the stabilization of an exocyclic double bond in polar resonance structures of pyrrolidine enamines.[4]

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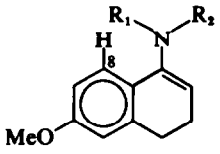
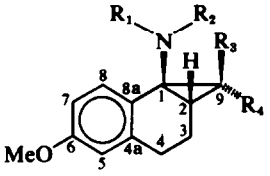
†Although clearly **2c**[17] and presumably **2b**[18] are carbenoid reagents rather than free carbenes, the word carbene will be used for convenience.



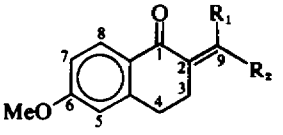
1a: $R_1R_2 = -(CH_2)_2-O-(CH_2)_2-$
b: $R_1R_2 = -(CH_2)_4-$

$R_1-\ddot{C}-R_2$

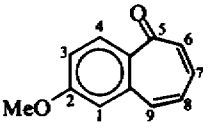
2a: $R_1 = R_2 = Cl$
b: $R_1 = Cl, R_2 = \phi$
c: $R_1 = H, R_2 = COOEt$



3a: $R_1R_2 = -(CH_2)_2-O-(CH_2)_2-$ $R_3 = R_4 = Cl$
b: $R_1R_2 = -(CH_2)_2-O-(CH_2)_2-$ $R_3 = Cl, R_4 = \phi$
c: $R_1R_2 = -(CH_2)_2-O-(CH_2)_2-$ $R_3 = \phi, R_4 = Cl$
d: $R_1R_2 = -(CH_2)_4-$ $R_3 = R_4 = Cl$
e: $R_1R_2 = -(CH_2)_4-$ $R_3 = Cl, R_4 = \phi$



4a: $R_1 = H, R_2 = Cl$
b: $R_1 = H, R_2 = \phi$
c: $R_1 = \phi, R_2 = H$



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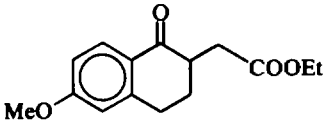
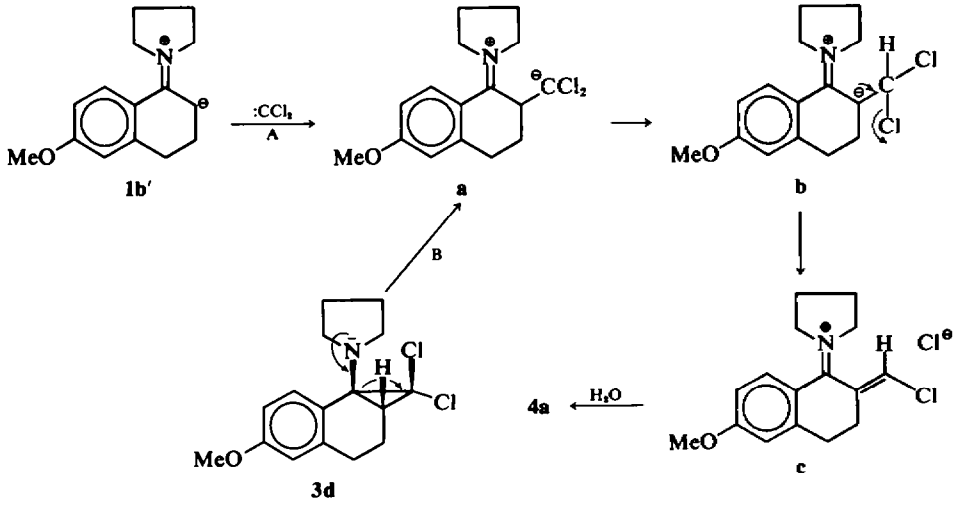


6

SCHEME 1



SCHEME 2

A nucleophilic attack by the dipolar ion on the carbene leads initially to intermediate **a**, which yields intermediate **b** (enamine in its dipolar form) via a proton transfer. Loss of a chloride ion from **b** gives the iminium salt **c**, which hydrolyses to ketone **4a**. Intermediate **a** can also be visualized as arising by an "*quasi*-enamine" reaction of **3d** (route B). Circumstantial evidence for the latter path may be derived from the isolation of adduct **3e** and the consequent implication of **3d** itself in the reaction leading to **5** (Scheme III). Although direct evidence distinguishing between A and B is lacking at the present, experiments described later favour route B.

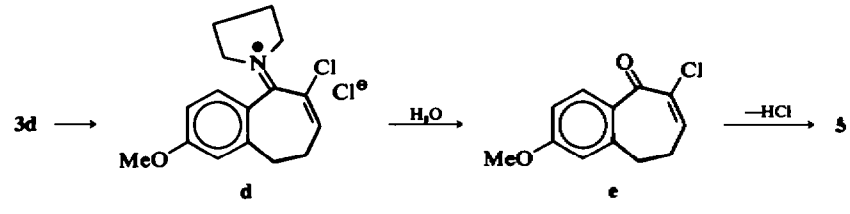
Formation of benzotropone derivative **5** is visualized as proceding via 1 : 1 adduct **3d** (Scheme III). Adduct **3d** undergoes a ring opening reaction to the intermediate iminium salt **d**, which, after hydrolysis and loss of HCl,[12] gives **5**.

Reaction of pyrrolidine enamine **1b** with phenylchlorocarbene **2b**, and subsequent hydrolysis, yielded **3e**, m.p. 152–154°, and **4b**, m.p. 95–97°. The stereochemistry of **3e** followed from its NMR spectrum; the pyrrolidine α,α'-methylene protons gave signals at "normal" δ values (2·96, centre, m: $-CH_2-N-CH_2-$), while the C_5-proton was distinctly shielded (by the phenyl group, δ 6·40, d, $J = 2{\cdot}5$ Hz); thus implying that the pyrrolidine and phenyl rings are trans in this compound. This result is not surprising in view of the expected steric hindrance to the approach of phenylchlorocarbene to the enamine double bond, so as to result in the formation of the stereoisomer of **3e**. Formation of **4b** is believed to proceed via a mechanism analogous to that proposed for **4a** (Scheme II, route B). This was confirmed by heating **3e** in a pyridine-water mixture whereupon it was converted quantitatively to **4b**, thereby demonstrating the *quasi*-enamine reactivity of the aminocyclopropane system. Stereochemistry of **4b** could be deduced from the low-field resonance signal of the C_9-proton in the NMR spectrum (δ 7·82, t, $J = 1{\cdot}5$ Hz) and the small trans allylic coupling with the C_3-protons. It was further established by synthesis and comparison of the NMR spectra of isomers **4b** and **4c** as outlined below.

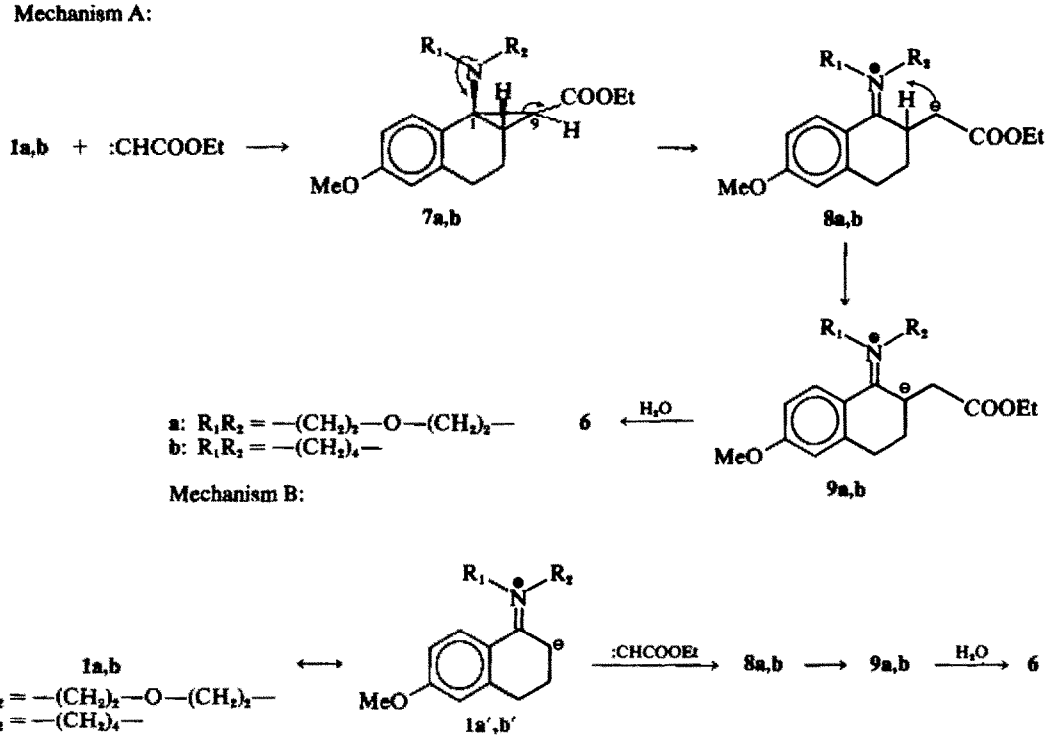
Base-catalysed condensation of 6-methoxy-1-tetralone with benzaldehyde led, in analogy to the synthesis of 2-benzylidene-1-tetralone,[13] to the formation of **4b**, in high yield. Upon irradiation of **4b** (350 nm) the product underwent isomerization to its stereoisomer **4c**. The NMR spectrum of the new isomer exhibited a signal for C_9-H at δ 6·76 (s), thereby attesting to the assigned stereochemistry of the two isomers.

Both the enamines **Ia** and **Ib** reacted with carbethoxycarbene **2c** to give one and the same product, namely **6**, in good yield. Two possible mechanisms can be postulated for the formation of **6** (Scheme IV). According to mechanism A the reaction of enamines **1a,b** is visualized as proceeding via the intermediacy of adducts **7a,b**. C_1-C_9-bond cleavage leads to the resonance stabilized intermediates **8a,b**, which, after proton transfer and hydrolysis of the resulting enamines **9a,b** (ionic structures) lead to product **6**. In an alternative mechanism (B, Scheme IV) nucleophilic attack by the dipolar structures of the enamines (**1a'** or **1b'**) on the carbene, in a fashion analogous to the attack of **1b'** on: CCl_2 (Scheme II), leads to the same dipolar intermediates **7a,b** which were postulated in mechanism A.

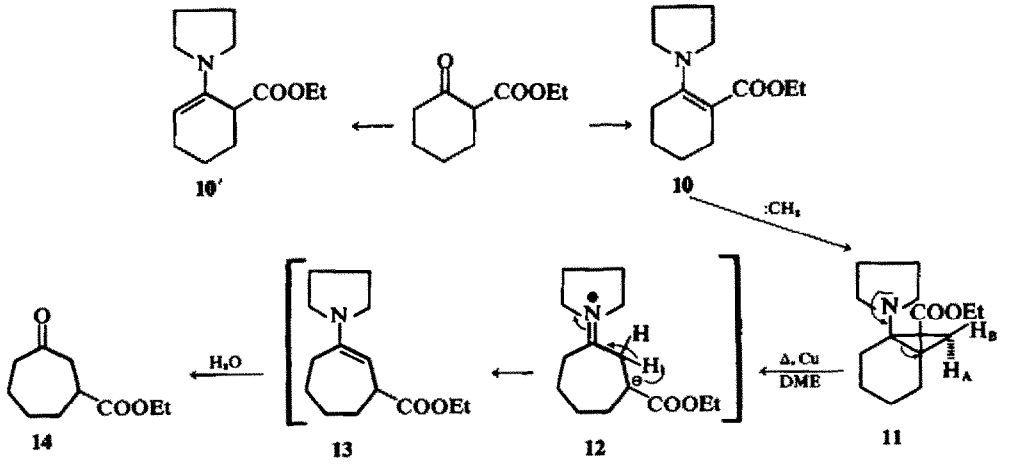
Whether the cyclopropyl adducts **7a** and **7b** (mechanism A) are involved in the reactions leading to ester **6** is a question of considerable mechanistic interest. That the morpholine enamine **1a** should react with carbene **2c** to give adduct **7a** would be amply anticipated in the light of previous results.[4,5,11,14] However, the formation of the same product from both pyrrolidine and morpholine enamines is unexpected, particularly in view of the stress that has all along been laid on their distinctive characters. This anomalous situation can, however, be resolved if one takes into account the very special nature of α-tetralone enamines, especially those containing pyrrolidine as the base component. Considerable evidence now exists which suggests that the dipolar structures of enamines derived from α-tetralone are subject to steric inhibition owing to interaction between the peri hydrogen (C_8–H) of the tetralin system and the α-methylene protons of the amine. The suppression of such an ionic structure would have significant consequences on the reactivity pattern of the pyrrolidine-enamine of α-tetralone; in general, decreasing the reactivity of the latter as a nucleophilic reagent would make its behaviour approximate to that of enamines derived from other



SCHEME 3



SCHEME 4



SCHEME 5

bases. Seen in this background, the similarity in behaviour of **1a** and **1b** towards **3c** does not appear to be contradictory. It may be recalled that in contrast to reactions of other pyrrolidine enamines with carbenes, **1b** is the only one which gives a cyclopropyl adduct (**3e**).

The intermediacy of **7a,b**, in the reactions of the enamines (**1a,b**) leading to formation of **6**, was provided convincing support by the following experiment. Enamine ester **10**, prepared from 2-carbethoxycyclohexanone and pyrrolidine, was converted to the cyclopropyl derivative **11** (Scheme V). When **11** was treated with copper powder in DME under the conditions used for reaction of the enamines with **3c**, the main product isolated, after hydrolysis and chromatography, was keto ester

14. The structure of 14 was attested to by its IR (1705 and 1735 cm^{-1}) and NMR spectra; the latter showed no cyclopropyl or pyrrolidine ring hydrogens. This result is in complete accordance with mechanism A, which, by analogy, would suggest the quasi-enamine ring opening of 11 to 12 and its further conversion via 13 to 14.

The abovementioned results, along with the recently reported ring-opening of 2-aminocyclopropylsulfoxides,[15] provide further support for the concept of *quasi*-enamine reactivity of aminocyclopropanes.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Analyses were carried out by Mr. H. Pieters of the Microanalytical Department of this laboratory. IR spectra were recorded on a Unicam SP 200 spectrometer and NMR spectra were run in $CDCl_3$ on Varian Association Model A-60 D and HA-100 instruments, using TMS as an internal standard (except for cyclopropyl compounds where benzene was used as internal standard). All reactions were carried out with dry reagents in dried apparatus under a nitrogen atmosphere.

Reaction of morpholine enamine **1a** *with dichlorocarbene* **2a**. A soln of **1a** (2·45 g, 0·01 mole) in 20 ml 1,2-dimethoxy-ethane (DME) was added dropwise to a warm (50°), stirred soln of sodium trichloroacetate (7·4 g, 0·04 mole) in 100 ml DME. After the addition was complete, the mixture was allowed to reflux for 2 hr, after which the NaCl formed was removed and the solvent evaporated under reduced pressure. The residue was dissolved in a mixture of 60 ml CH_2Cl_2 and 40 ml of 2% HCl/H_2O. This mixture was heated to reflux for 30 min after which it was neutralised with $NaHCO_3$. The organic layer was separated, washed successively with water, sat NaCl aq and dried over $MgSO_4$. Removal of the solvent gave a brown oil, which was chromatographed on a silicagel column. Elution with $CHCl_3$/EtOAc 6:1 gave product **3a**, yield (after recrystallisation fom MeOH) 2·12 g (65%), m.p. 104–107°; IR (KBr) 1610, 1580 and 1510 cm^{-1} (arom), 1110 cm^{-1} (—CH_2—O—CH_2—); NMR δ 2·70, centre, m (4H, —CH_2—N—CH_2—) 3·66 centre, m (4H, —CH_2—O—CH_2—), 3·76, s (3H, —OMe), 6·65, d, $J_{5,7}$ = 2·5 Hz (1H, H_5), 6·79, d × d, $J_{7,5}$ = 2·5 Hz, $J_{7,8}$ = 8·5 Hz (1H, H_7), 7·23, d, $J_{8,7}$ = 8·5 Hz (1H, H_8). (Found: C, 58·6; H, 5·7; N, 4·2; Cl, 21·7. Calc. for $C_{16}H_{19}NO_2Cl_2$: C, 58·54; H, 5·83; N, 4·27; Cl, 21·60%).

Reaction of morpholine enamine **1a** *with phenylchlorocarbene* **2b**. To a stirred and cooled (−20°) soln of **1a** (2·45 g, 0·01 mole) and benzalchloride (1·61 g, 0·01 mole) in 20 ml DME, was slowly (1 hr) added a soln of t-BuOK (1·57 g, 0·014 mole) in 12 ml DME. After the addition was complete the mixture was allowed to come to room temp and stand for 72 hr. Following the addition of 10 ml of 10% HCl/H_2O stirring was continued for another 24 24 hr the mixture was neutralised with $NaHCO_3$ and the solvent removed under reduced pressure. The residue was dissolved in $CHCl_3$, washed with water (twice), sat NaCl aq and dried over $MgSO_4$. Removal of the solvent gave 3·60 g of a brown oil which, upon addition of MeOH, gave 1·73 g (47%) of light yellow crystals (mixture **3b** + **3c**). Softening at 147–148°, followed by decomp; IR (KBr) 1600, 1570 and 1500 cm^{-1} (arom), 1110 cm^{-1} (—CH_2—O—CH_2—); NMR (**3b**) δ 2·80–2·95, m (4H, —CH_2—N—CH_2—), 3·65–3·77, m (4H, —CH_2—O—CH_2—), 3·67, s (3H, —OMe), 6·43, d, $J_{5,7}$ = 2·5 Hz (1H, H_5), 6·72, d × d, $J_{7,8}$ = 8·5 Hz, $J_{7,5}$ = 2·5 Hz (1H, H_7), 7·05–7·40, m (Ar-protons of **3b** and **3c**), 7·52, d, $J_{8,7}$ = 8·5 Hz (1H, H_8); NMR (**3c**) δ 3·07–3·40, m (4H, —CH_2—O—CH_2—), 3·78, s (3H, —OMe), 6·74, d, $J_{5,7}$ = 2·5 Hz (1H, H_5), 6·81, d × d, $J_{7,8}$ = 9 Hz, $J_{7,5}$ = 2·5 Hz (1H, H_7), 7·64, d, $J_{8,7}$ = 9 Hz (1H, H_8). (Found: C, 71·3; H, 6·6; N, 3·7; Cl, 9·7. Calc. for $C_{22}H_{24}NO_3Cl$: C, 71·43; H, 6·54; N, 3·79; Cl, 9·59%).

Reaction of pyrrolidine enamine **1b** *with dichlorocarbene* **2a**. The same procedure as described for reaction with **1a** was followed. Starting with **1b** (2·29 g, 0·01 mole) and sodium trichloroacetate (7·4 g, 0·04 mole) and subsequent chromatography of the mixture over a silicagel column, two products were obtained. They were rechromatographed through a florisil column and the separated products **4** and **5** were further purified by sublimation, yield of **4a**: 508 mg (23%), m.p. 52–58°; IR ($CHCl_3$) 1660 cm^{-1} (C=O), 1600 cm^{-1} (arom); NMR δ 2·93, s (4H, $2H_3$ and $2H_4$), 3·84, s (3H, —Me_4, 6·71, d, $J_{5,7}$ = 2·5 Hz (1H, H_5), 6·85, d × d, $J_{7,8}$ = 8·5 Hz, $J_{7,5}$ = 2·5 Hz (1H, H_7), 7·37, s (1H, H_9), 8·05, d, $J_{8,7}$ = 8·5 Hz (1H, H_8), yield of **5** 232 mg (12·5%), m.p. 70–72°; IR (KBr) 1660 cm^{-1} (C=O), 1630 cm^{-1} (C=C), 1600 and 1570 cm^{-1} (arom); NMR δ 3·87, s (3H, —OMe), 6·49–6·73, m (1H, H_6), 6·78–7·06, m (3H, H_1, H_7 and H_9), 7·17, d × d, $J_{3,4}$ = 9 Hz, $J_{3,1}$ = 2 Hz (1H, H_3), 7·18, 3 × d, $J_{6,7}$ = 11 Hz, $J_{6,8}$ = 1 Hz (1H, H_6), δ 8·47, d, $J_{4,3}$ = 9 Hz (1H, H_4). (Found: C, 77·2; H, 5·5; O, 17·3. Calc. for $C_{12}H_{10}O_2$: C, 77·40; H, 5·41; O, 17·19).

Reaction of pyrrolidine enamine **1b** *with phenylchlorocarbene* **2b**. The same procedure as described for reaction with **1a** was followed. In this reaction **1b** (2·29 g, 0·01 mole), benzalchloride (1·61 g, 0·01 mole) and t-BuOK (1·57 g, 0·014 mole) were used. After working up the mixture a brown syrup was obtained, from which, upon addition of MeOH, adduct **3e** crystallized as colourless crystals, yield 1·18 g (36·5%), m.p. 152–154° (dec); IR (KBr) 1600, 1575 and 1500 cm^{-1} (arom); NMR δ 2·78–3·15, m (4H, —CH_2—N—CH_2—), 3·66, s (3H, —OMe), 6·40, d, $J_{5,7}$ = 2·5 Hz (1H, H_5), 6·70, d × d, $J_{7,8}$ = 9 Hz, $J_{7,5}$ = 2·5 Hz (1H, H_7), 7·04–7·37, m (5H, Ar-protons), 7·49, d, $J_{8,7}$ = 9 Hz (1H, H_8). (Found: C, 74·7; H, 6·9; N, 3·9; Cl, 10·1. Calc. for $C_{22}H_{24}NOCl$: C, 74·66; H, 6·84; N, 3·96; O, 4·52; Cl, 10·02%). The filtrate was concentrated and chromatographed over a silicagel column (eluent CH_2Cl_2/EtOAc 6:1), whereupon (after an additional purification on TLC) 173 mg of **4b** was obtained (6·5%), m.p. 95–97°; IR (KBr) 1660 cm^{-1} (C=O), 1610, 1590 and 1500 cm^{-1} (C=C and arom); NMR δ 2·78–2·98, m (2H, $2H_4$), 3·00–3·20, m (2H, $2H_3$), 3·83, s (3H, —OMe), 6·69, d, $J_{5,7}$ = 2·5 Hz (1H, H_5), 6·88, d × d, $J_{7,8}$ = 9 Hz, $J_{7,5}$ = 2·5 Hz (1H, H_7), 7·28–7·50, m (5H, Ar-protons), 7·82, t, $J_{9,3}$ = 1·5 Hz (1H, H_9), 8·11, d, $J_{8,7}$ = 9 Hz (1H, H_8). (Found: C, 81·6; H, 6·2. Calc. for $C_{18}H_{16}O_2$: C, 81·79; H, 6·10; O, 12·11%).

Synthesis of trans- *and* cis-2-*benzylidene*-1-*tetralone* (**4b**, **4c**). 6-Methoxy-1-tetralone (8·8 g, 0·05 mole) and benzaldehyde (5·3 g, 0·05 mole) were dissolved in 50 ml of 4% KOH/EtOH. After 15 min product **4b** precipitated as almost colourless crystals. After a reaction time of 1·5 hr the mixture was neutralised with AcOH, and some water was added to complete the precipitation of **4b**. The product was filtered off and washed with water/EtOH, yield 10·43 g (82%).

trans-**4b** (1 g) was dissolved in 100 ml MeOH and this

soln was irradiated with light of 350 nm over a period of 72 hr. On evaporation of the solvent a light yellow syrup was obtained. The degree of conversion into the *cis* isomer **4c** (88%) followed from its NMR spectrum. Product **4c** was crystallized from MeOH; m.p. 75·5–76·5°; IR (KBr) 1665 cm^{-1} (C=O), 1600, 1570 and 1495 cm^{-1} (C=C and arom); NMR δ 2·74–2·94 and 2·97–3·17, m (4H, $2H_3$ and $2H_4$), 3·97, s (3H, —OMe), 6·68, d, $J_{5,7} = 2·5$ Hz (1H, H_5), 6·76, s (1H, H_9), 6·82, d × d, $J_{7,8} = 8·5$ Hz, $J_{7,5} = 2·5$ Hz (1H, H_7), 7·21–7·60, m (5H, Ar-protons), 8·06, d, $J_{8,7} = 8·5$ Hz (1H, H_8). (Found: C, 81·9; H, 6·1. Calc. for $C_{18}H_{16}O_2$: C, 81·79; H, 6·10; O, 12·11%).

Reaction of morpholine enamine **1a** *with carboethoxycarbene* **2c**. To a refluxing solution of **1a** (2·45 g, 0·01 mole) in 30 ml DME, with Cu powder (0·5 g) as catalyst, was added dropwise over a 2 hr period a soln of diazoacetic ester (2·28 g, 0·02 mole) in 20 ml DME. After the addition was complete, the refluxing was continued for another 2 hr. The Cu powder was removed by filtration and some water added to the filtrate and this mixture was refluxed for an additional 4 hr. The solvent was removed, the residue dissolved in $CHCl_3$, washed with water, sat NaCl aq and then dried over $MgSO_4$. On evaporation of the solvent a brown oil was obtained. The fumaric and maleic esters formed during the reaction were distilled off at 0·1 mm. The residual oil was distilled at 158–178°/1·75 . 10^{-5} mm to yield **6**, yield 1·85 g (71%); IR ($CHCl_3$) 1725 cm^{-1} (sat. ester), 1680 cm^{-1} (C=O), 1600 and 1580 cm^{-1} (arom); NMR δ 1·27, t, J = 7 Hz (3H, —O—CH_2—Me), 3·84, s (3H, —OMe), 4·18, quart, J = 7 Hz (2H, —O—CH_2—), 6·68, d, $J_{5,7} = 2·5$ Hz (1H, H_5), 6·83, d × d, $J_{7,8} = 8·5$ Hz, $J_{7,5} = 2·5$ Hz (1H, H_7), 8·00, d, $J_{8,7} = 8·5$ Hz (1H, H_9). (Found: C, 68·5; H, 6·8; O, 24·6. Calc. for $C_{15}H_{18}O_4$: C, 68·68; H, 6·92; O, 24·40%).

Reaction of pyrrolidine enamine **1b** *with carbethoxycarbene* **2c**. The abovementioned procedure was followed. Starting with **1b** (2·38 g, 0·0104 mole), diazoacetic ester (2·28 g, 0·02 mole) and Cu powder (0·5 g), after working up the mixture and distillation under high-vacuum, 1·12 g light yellow product **6** (48%) was obtained.

Synthesis of 1-*pyrrolidino*-2-*carbethoxycyclohexane*-1 (**10**). 2-Carbethoxycyclohexanone (8·5 g, 0·05 mole) and pyrrolidine (5·3 g, 0·075 mole) were dissolved in 180 ml dry benzene. After the addition of a small quantity of *p*-toluenesulphonic acid, the soln was heated to reflux under N_2 for 114 hr, the water formed being removed by means of a circulation apparatus filled with freshly calcinated molecular sieves type 4A.[5] Removal of the solvent afforded an oil, which upon distillation gave a light yellow oily distillate which crystallized. This consisted of the desired enamine **10** (70%) and its 1,6-double bond isomer **10'** (30%). Total yield 9·25 g (83%); IR of the mixture **10** and **10'** ($CHCl_3$) 1720 cm^{-1} (ester of **10'**), 1650 cm^{-1} (ester of **10**), 1645 cm^{-1} (N—C=C); NMR of **10**: δ 1·24, t, J = 7 Hz (3H, —O—C—Me), 3·25, m, centre (4H, —CH_2—N—CH_2—), 4·12, quart, J = 7 Hz (2H, —O—CH_2—).

Synthesis of the methylene adduct **11**. This reaction was carried out according to the method of Muck and Wilson.[16] Enamine **10** (2·33 g, 0·01 mole) was dissolved in 10 ml of dry ether and cuprous chloride (0·25 g) was added. While stirring, a soln of diazomethane (1 g) in 35 ml ether was slowly added over a 1 hr period. After filtration of the mixture and evaporation of the solvent, a light green oil resulted, which was chromatographed over a silicagel column. Besides hydrolysed enamine (2-carbethoxycyclohexanone) and addition product originating from enamine **10'**, 0·47 g of adduct **11** (27%) was obtained as a yellow oil; IR ($CHCl_3$) 1725 cm^{-1} (ester); NMR δ 0·27, d, J = − 5·7 Hz (1H, H_A[16]), 1·27, t, J = 7·5 Hz (3H, —O—Me), 2·77, m, centre (4H, —CH_2—N—CH_2—), 4·22, quart, J = 7·5 Hz (2H, —O—CH_2—).

Heating of adduct **11** *in refluxing DME*. Adduct **11** (0·45 g, 0·0018 mole) was dissolved in 15 ml DME. After addition of Cu powder (0·1 g), the soln was heated to reflux for 4 hr. The Cu powder was filtered off and the filtrate was diluted with 5 ml water. This mixture was refluxed for another 4 hr and this solvent was removed, the residue was dissolved in $CHCl_3$ and this soln was washed with water, sat NaCl aq and dried over $MgSO_4$. After the removal of the solvent, 0·38 g of a dark brown oil was obtained which was chromatographed over a silicagel column. This gave 60 mg of **14** (18%); IR ($CHCl_3$) 1735 cm^{-1} (sat. ester), 1710 cm^{-1} (sat. ketone); NMR δ 1·30, t, J = 7 Hz (3H, —O—CH_2—Me), 3·50, m, centre (1H, CH–COOEt), 4·31, quart, J = 7 Hz (2H, —O—CH_2—).

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