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Amine catalyzed ring opening of (2+2) cycloadducts derived from enamines of cyclic ketones and methyl propynoate

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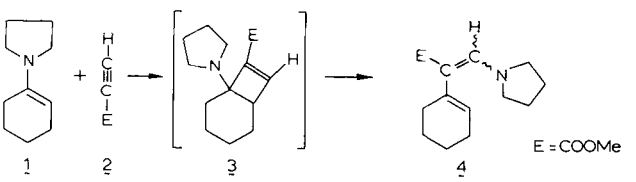
Abstract. The (2 + 2) cycloadducts **3**, **6**, **10** and **13**, derived from pyrrolidine enamines of cyclic ketones and methyl propynoate **2**, react, under the influence of pyrrolidine via the α-[(1-pyrrolidinyl)methylene]cycloalkeneacetates (*Z*)-**4**, (*Z*)-**7**, (*Z*)-**11** and (*Z*)-**14**, to give the corresponding *E* isomers. The structure of (*E*)-**7** has been unequivocally established by X-ray analysis. The formation of (*E*)-**4**, (*E*)-**7**, (*E*)-**11** and (*E*)-**14** can be explained by the sequence: Michael addition, elimination, conrotatory ring opening, followed by *Z*/*E* isomerization. In the cases involving a relatively slow reaction (**10**, **13**) and, in addition, the presence of an excess of pyrrolidine, the enamines **9**, **16** and the propenoate **12** could also be detected. The formation of **12** can be rationalized by a Michael addition of pyrrolidine to methyl propynoate (**2**), formed by a *retro* (2 + 2) cycloaddition.

Introduction

Since the development of the enamines in the early sixties they have appeared to be a very important class of compounds[1,2]. One of the frequently used reactions involves the formation of fused cyclobutenes by (2 + 2) cycloaddition of enamines of cyclic ketones with electron-deficient acetylenes in an apolar solvent. Thermal rearrangement of this type of cyclobutenes is an established and useful method in organic synthesis for ring enlargement with two C atoms. Previously, we have shown that this reaction proceeds via a conrotatory ring opening with formation of a *cis,trans*-cycloalkadiene, eventually followed by a thermal [1,5] hydrogen shift to the corresponding *cis,cis*-cycloalkadiene[3,4]. Another interesting reaction involves the smooth conversion of 1-(1-pyrrolidinyl)cyclobutenes into pyrrolizine derivatives using a protic polar solvent[3]. These pyrrolizines can also be obtained directly by reaction of pyrrolidine enamines with dimethyl acetylenedicarboxylate in a protic polar solvent[5,6]. A deviation from the normal pathway has been reported by *Brannock* et al.[7] for the reaction of enamines derived from cyclohexanone, *e.g.* **1** with methyl propynoate (**2**) in an apolar solvent. Instead of the expected cyclobutenes, *e.g.* **3** or ring-opened products, they obtained α-methylene-1--cyclohexeneacetates, *e.g.* **4**, the stereochemistry of which has not yet been assigned.

We have recently studied this reaction in more detail and have also included reactions of other enamines. This work was restricted to pyrrolidine enamines (the most reactive type) on account of the lower reactivity of methyl propynoate (**2**) as compared with dimethyl acetylenedicarboxylate. The results of this investigation are the subject of the present paper.

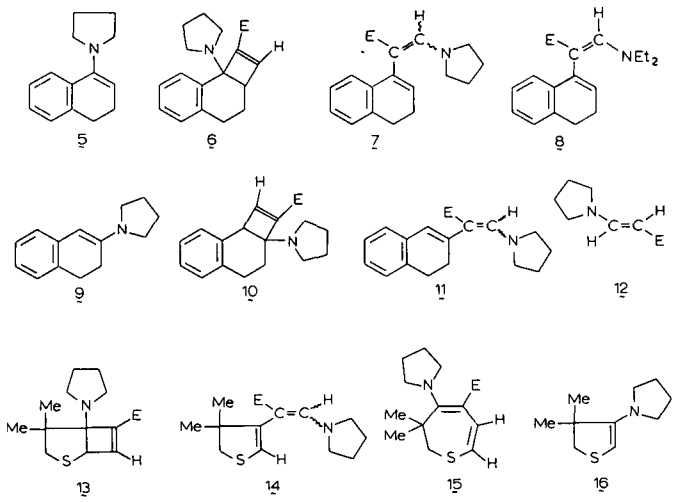


1 2 3 4

Scheme 1

Results

Firstly, we have reinvestigated the reaction of 1-(1-cyclohexenyl)pyrrolidine (**1**) with methyl propynoate (**2**) in diethyl ether at 25–35 °C, as described by *Brannock* et al.[7]. In the ^{1}H NMR spectra of aliquots of the reaction mixture, an intermediate could be detected with characteristic absorptions at δ 6.60 (s) and 5.55–5.3 (m). In the ^{13}C NMR spectrum, characteristic signals of the intermediate were present at δ 143.5 (d), 137.7 (s) and 123.2 (d). After prolonged reaction time, these signals disappeared and ultimately, in the ^{1}H NMR spectrum among others, absorptions of the main product were present at δ 7.48 (s) and 5.55–5.25 (m). These values correspond with those reported by *Brannock* et al.[7] for methyl α-[(1-pyrrolidinyl)methylene]--1-cyclohexeneacetate (**4**). The reason that *Brannock* et al.[7] did not observe the intermediate product must be the higher work-up temperatures employed. We found that, at higher temperatures, the intermediate isomerizes very rapidly. By comparing the spectroscopic data of both isomers with those of the corresponding α-methylene-1-naphthaleneacetates **7** *(vide infra)* we have assigned the *Z* stereochemistry



to the intermediate and the *E* stereochemistry to the final product.

Reaction of the structurally related 1-(3,4-dihydro-1-naphthalenyl)pyrrolidine[8] (**5**) with methyl propynoate (**2**) in hexane afforded, after trituration, the solid (2 + 2) cycloadduct **6** in 59% yield and no trace of a ring-opened product could be detected. However, monitoring a deuteriochloroform ($CDCl_3$) solution of **6** by ^1H NMR spectroscopy revealed a slow conversion ($t_{0.5}$ ~3 h) into another compound which exhibited characteristic signals at δ 7.79 (s) and 5.86 (t, *J* 4.4 Hz). When the same experiment was performed in the presence of pyrrolidine, the rearrangement was much faster ($t_{0.5}$ ~22 min) while, in addition, transient signals were present at δ 6.72 (s) and 5.87 (t, *J* 4.6 Hz). On a preparative scale using chloroform as a solvent, the intermediate product could be isolated after 20 min reaction time in 60% yield. Heating a solution of this compound in chloroform at reflux temperature for 10 min gave the other isomer in 94% yield. This isomer could also be obtained upon stirring overnight or by the heating at 61 °C for 30 min of a solution of **6** in chloroform. On the basis of the spectroscopic data, we assigned to both isomers the methyl 3,4-dihydro-α-[(1-pyrrolidinyl)methylene]-1-naphthaleneacetate structure (**7**). Evidence for the stereochemistry was obtained by single-crystal X-ray analysis of the ultimately formed isomer which proved that this compound has the *E* configuration (Fig. 1, Table I).

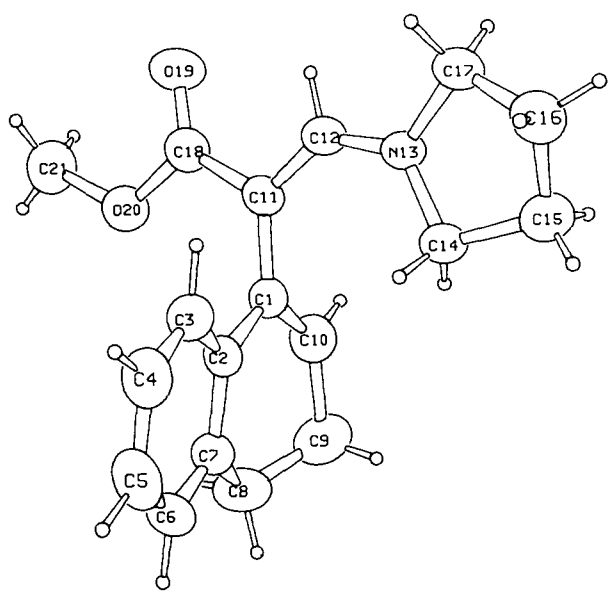


Fig. 1. X-Ray crystal structure of (E)-7.

Table I Positional parameters and their estimated standard deviations of (E)-7.

Atom	*x*	*y*	*z*
O19	0.3178(2)	0.11076(8)	0.4154(1)
O20	0.3995(2)	0.14461(8)	0.2494(1)
N13	0.3431(2)	0.33029(9)	0.5558(1)
C1	0.3926(2)	0.3004(1)	0.2868(2)
C2	0.5680(2)	0.32202(9)	0.3016(2)
C3	0.7010(2)	0.3046(1)	0.4147(2)
C4	0.8632(2)	0.3273(1)	0.4295(2)
C5	0.8959(2)	0.3671(1)	0.3325(2)
C6	0.7665(3)	0.3846(1)	0.2197(2)
C7	0.6023(2)	0.3625(1)	0.2026(2)
C8	0.4615(3)	0.3788(1)	0.0783(2)
C9	0.2966(3)	0.3920(1)	0.1005(2)
C10	0.2681(2)	0.3340(1)	0.1928(2)
C11	0.3600(2)	0.2447(1)	0.3801(2)
C12	0.3380(2)	0.2625(1)	0.4947(2)
C14	0.3809(2)	0.4062(1)	0.5142(2)
C15	0.3378(3)	0.4606(1)	0.6061(2)
C16	0.3676(3)	0.4162(1)	0.7273(2)
C17	0.3314(3)	0.3338(1)	0.6871(2)
C18	0.3546(2)	0.1618(1)	0.3541(2)
C21	0.4004(3)	0.0635(1)	0.2201(2)
H3	0.679(2)	0.278(1)	0.481(2)
H4	0.959(3)	0.314(1)	0.516(2)
H5	1.011(2)	0.381(1)	0.343(2)
H6	0.787(2)	0.411(1)	0.150(2)
H8A	0.451(2)	0.330(1)	0.018(2)
H8B	0.486(2)	0.424(1)	0.028(2)
H9A	0.206(3)	0.388(1)	0.017(2)
H9B	0.290(2)	0.443(1)	0.139(2)
H10	0.153(2)	0.321(1)	0.187(2)
H12	0.314(2)	0.218(1)	0.543(2)
H14A	0.314(2)	0.417(1)	0.424(2)
H14B	0.497(3)	0.409(1)	0.520(2)
H15A	0.202(6)	0.446(3)	0.607(4)
H15B	0.386(3)	0.507(1)	0.609(2)
H16A	0.508(6)	0.423(3)	0.766(4)
H16B	0.311(2)	0.435(1)	0.785(2)
H17A	0.220(3)	0.314(1)	0.684(2)
H17B	0.411(3)	0.297(1)	0.746(2)
H21A	0.419(3)	0.059(2)	0.137(2)
H21B	0.465(3)	0.033(1)	0.298(2)
H21C	0.293(4)	0.043(2)	0.205(3)

Two major planes can be seen in the molecule (plane 1: C1...C8; plane 2: C11, C12, N13, C18, O19, O20, C21). The maximum deviation of the atoms from the planes is 0.07 Å for plane 2. The dihedral angle of the two planes is 96.6°, indicating the absence of conjugation between the two planar parts of the molecule. The lack of conjugation can also be demonstrated by the length of the C1–C11 bond: 1.491(3) Å, a value close to the length of a single C–C bond. The C1–C10 [1.333(2) Å] and C11–C12 [1.360(3) Å] bonds can be described as double bonds. The C11–C18 [1.458(3) Å] and C1–C2 [1.486(3) Å] bonds are somewhat shorter than a single C–C bond (1.54 Å).

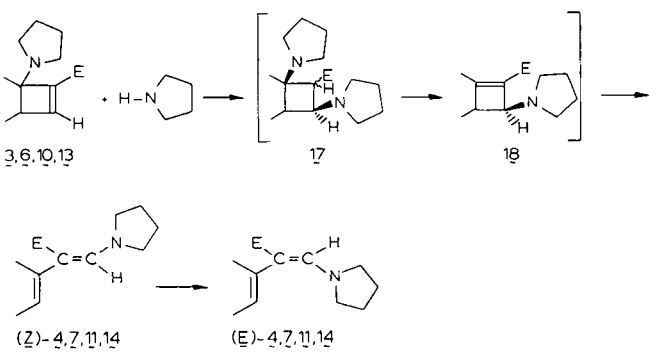
Solutions of the (2 + 2) cycloadduct **6** in acetone, acetonitrile, hexane and dimethyl sulfoxide appeared to be stable for at least two days at room temperature. However, upon addition of pyrrolidine, a fast rearrangement did take place with the ultimate formation of (*E*)-**7**. In order to investigate the possible influence of other amines, a solution of **6** in $CDCl_3$ in the presence of a large excess of diethylamine was heated for 2 h at 61 °C. According to the ^1H NMR spectrum, both (*E*)-**7** and the diethylamino compound **8** [^1H NMR δ 7.61 (s) and 5.94 (t, *J* 4.6 Hz)] were formed in an approximate 1:1 ratio.

Starting from 1-(3,4-dihydro-2-naphthalenyl)pyrrolidine[9] (**9**) and methyl propynoate (**2**), the (2 + 2) cycloadduct **10** was obtained as an oil in quantitative yield. Heating of a solution of **10** in chloroform at 61 °C for 15 min afforded methyl (*E*)-3,4-dihydro-α-[(1-pyrrolidinyl)methylene]-2-naphthaleneacetate [(*E*)-**11**] which was isolated in 75% yield (calculated on **9**). The *E* stereochemistry was-dihydro assigned by comparison of the ^{1}H NMR signals at δ 7.61 (s) and 6.14 (bs) with those of (*E*)-**7** *(vide supra)*. When the reaction was monitored by ^{1}H NMR spectroscopy at room temperature, a slow conversion was observed ($t_{0.5}$ ~4 d), however, the isomeric (*Z*)-**11** could not be detected. Addition of pyrrolidine accelerated the reaction but also in this case in the ^{1}H NMR spectrum no signals of (*Z*)-**11** could be detected. After completion of the reaction, after *ca.* 2 days, a mixture of (*E*)-**11**, the enamine **9** [^{1}H NMR δ 5.11 (s, 1H, N–C=CH)][10] and methyl (*E*)-3-(1-pyrrolidinyl)-2-propenoate (**12**) was present in a ratio of about 1:1:1. The structural assignment of the latter is based on the characteristic vinylic signals in the ^{1}H NMR spectrum at δ 7.63 (d, *J* 13.0 Hz) and 4.47 (d, *J* 13.0 Hz)[11].

Subsequently, the behaviour of methyl 4,4-dimethyl-5-(1-pyrrolidinyl)-2-thiabicyclo[3.2.0]hept-6-ene-6-carboxylate (**13**)[12] was studied. In $CDCl_3$ solution, **13** rearranged slowly via (*Z*)-**14** [^{1}H NMR δ 6.51 (s) and 5.75 (s, SCH=)] to the thermodynamically more stable isomer methyl (*E*)-4,5-dihydro-4,4-dimethyl-α-[(1-pyrrolidinyl)methylene]-3-thiopheneacetate [(*E*)-**14**] [^{1}H NMR δ 7.70 (s) and 5.76 (s)]. On a preparative scale, **13** was converted completely into (*E*)-**14** within 4 weeks at room temperature. However, performing the reaction at 45 °C, in order to accelerate it, afforded a mixture of the expected (*E*)-**14** and the "normal" ring-expanded compound **15**[12] in a ratio of 1:2. Addition of pyrrolidine resulted in the complete conversion of **13** within 25 h into a mixture of (*E*)-**14**, **12** and the enamine **16** [^{1}H NMR δ 4.50 (s, 1H, N–C=CH)][12] in an approximate 1:1:1 ratio. Although after short reaction time (*Z*)-**14** is present in excess, it could not be isolated in a pure state.

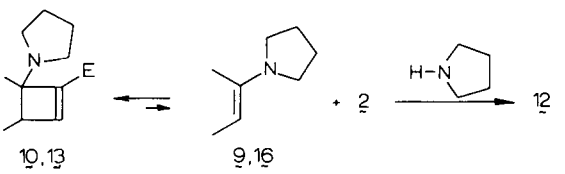
Discussion

The formation of the ring-opened compounds (*E*)-**4**, (*E*)-**7**, (*E*)-**11** and (*E*)-**14** can be rationalized as depicted in Scheme 2. This mechanism is only in general lines analogous to that described for the formation of **4**[7]. The presence of free pyrrolidine is a prerequisite for the reaction to proceed. In contrast to *Brannock* et al.[7], we were able to isolate two (2 + 2) cycloadducts (**6**, **13**) as pure solids which proved to be stable in inert solvents such as acetone, acetonitrile, hexane and dimethyl sulfoxide. Therefore, we assume that, in chloroform solution, a slow decomposition of the (2 + 2) cycloadducts occurs, which is responsible for the presence of a small amount of free pyrrolidine.



Scheme 2

The first step in the reaction comprises a Michael addition of free pyrrolidine to the (2 + 2) cycloadducts **3**, **6**, **10** and **13**. Since Dreiding models show that in these compounds the cyclobutene ring is almost perpendicularly fused with the adjacent ring (dihedral angle ~100°), the attack can only take place at the same face as the other pyrrolidinyl moiety. Subsequent elimination of pyrrolidine gives the cyclobutenes **18** whereupon a fast symmetry-allowed conrotatory ring-opening affords the *Z* isomers of **4**, **7**, **11** and **14**, which isomerize to the corresponding thermodynamically more stable *E* isomers. Addition of pyrrolidine to the reaction mixture accelerates the first step of the reaction sequence and results in a temporary accumulation of the *Z* isomers. The experiment with diethylamine shows that, despite the excess used, a considerable amount of (*E*)-**7** is also formed which may be explained by the larger nucleophilicity of pyrrolidine compared with that of diethylamine[13].



Scheme 3

In the cases where, even in the presence of pyrrolidine, the conversion of the cyclobutenes takes a relatively long time, the addition product of pyrrolidine and methyl propynoate (**2**) has also been detected. The formation of **12** can be explained assuming an equilibrium between the (2 + 2) cycloadducts **10**, **13** and the enamines **9**, **16** and methyl propynoate (**2**) from which the latter reacts further by a Michael addition with pyrrolidine to **12** (Scheme 3). This mechanism can be considered as a unique example of a *retro* (2 + 2) cycloaddition[14] of a cyclobutene system under mild conditions. To the best of our knowledge, there are in the literature only a few examples of *retro* (2 + 2) cycloadditions which, however, only proceed either photochemically[15] or on using very high temperatures[16]. Previously[4] we reported that during the reaction of pyrrolidine enamines with **2** and the subsequent ring enlargement, propenoate **12** was obtained as a very troublesome side-product. In this case, the formation of **12** may be explained in a similar way. A more general study of *retro* (2 + 2) cycloaddition reactions is in progress.

In chloroform solution at 61 °C, the (2 + 2) cycloadducts **6**, **10** rearranged specifically to (*E*)-**7**, (*E*)-**11**, while in the case of **13**, even at 45 °C, the "normal" ring-enlarged species **15** is the major product. The activation energy for ring enlargement of **13** is probably lower compared with that of **6** and **10** because of the presence of a sulfur atom adjacent to the bridgehead in **13**[17].

Experimental

Melting points were determined using a Reichert melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded using a Bruker WP-80 spectrometer and ^{13}C NMR spectra using a Nicolet MT 200 spectrometer in $CDCl_3$ unless otherwise stated (Me_4Si as an internal standard). Mass spectra were obtained using a Varian MAT 311A spectrometer and IR spectra using a Perkin-Elmer 257 spectrophotometer. Elemental analyses were carried out by *A. Christenhusz* of the Laboratory of Chemical Analysis of the University of Twente.

All reactions were carried out under a nitrogen atmosphere.

Petroleum ether refers to the fraction with b.p. 60–80°C, unless stated otherwise. Diethyl ether, methanol and hexane were dried by distillation from sodium. Methanol was stored over 3 Å molecular sieves; all other solvents were stored under nitrogen over 4 Å molecular sieves.

The pyrrolidine enamines **1**[7], **5**[8], **9**[9] and **16**[12] derived from cyclohexanone, α-tetralone, β-tetralone and tetrahydro-4,4-dimethyl-3(2*H*)-thiophenone, respectively, were prepared according to the literature. The (2 + 2) cycloadduct **13** was prepared as described[12]. Methyl propynoate was obtained from Janssen Chimica.

Methyl (Z)-α-[(1-pyrrolidinyl)methylene]-1-cyclohexeneacetate [(*Z*)-**4**]

To a solution of **1** (1.00 g, 6.6 mmol) in 10 ml of diethyl ether was added methyl propynoate (**2**, 0.56 g, 6.6 mmol) at room temperature. The reaction temperature increased to 25–35°C. After stirring for 15 min, an aliquot was evaporated at room temperature. From the ^{1}H NMR spectrum it could be concluded that the starting material had disappeared and that (*Z*)-**4** had been formed. ^{1}H NMR: δ 6.60 (s, 1H, =CHN), 5.55–5.3 (m, 1H, =C<u>H</u>–CH_2) and 3.67 (s, 3H, OCH_3). ^{13}C NMR: δ 143.5 (d, =CHN), 137.7 (s, =C–CE) and 123.2 (d, =<u>C</u>H–CH_2). After stirring for 5 h, (*Z*)-**4** had isomerized to (*E*)-**4**, the product described by *Brannock* et al.[7].

Methyl 2a,3,4,8b-tetrahydro-8b-(1-pyrrolidinyl)cyclobuta[a]naphthalene-1-carboxylate (**6**)

A solution of enamine **5** (10.0 g, 50 mmol) and methyl propynoate (**2**, 4.2 g, 50 mmol) in 250 ml of hexane was stirred for 1 week at room temperature. After 3 days, an extra portion of **2** (1 g, 12 mmol) was added. After removal of the solvent at room temperature, the resulting solid was triturated with diisopropyl ether to give **6**; yield 59%; m.p. 110–112°C (dec) (diisopropyl ether). $C_{18}H_{21}NO_2$ (283.373) calcd.: C 76.29, H 7.47, N 4.94; found: C 76.48, H 7.55, N 4.88%. ^{1}H NMR: δ 8.2–7.9 (m, 1H, ArH), 7.4–6.9 (m, 3H, ArH), 6.94 (d, 1H, *J* 1.0 Hz, =CH), 3.59 (s, 3H, OCH_3), 3.4–3.15 (bs, 1H, HC–C=) and 3.0–1.5 (m, 12H, NCH_2 and CH_2). ^{13}C NMR: δ 161.1 (s, C=O), 146.9 (d, =CH), 66.8 (s, –C–N), 51.0 (q, OCH_3), 47.4 (t, NCH_2) and 40.4 (d, H<u>C</u>–C=). IR: 1720 cm^{-1} (CO). MS: accurate mass theor. 283.157 for $C_{18}H_{21}NO_2$; exp. 283.154.

Methyl (Z)-3,4-dihydro-α-[(1-pyrrolidinyl)methylene]-1-naphthaleneacetate [(*Z*)-**7**]

To a solution of **6** (0.95 g, 3.4 mmol) in 10 ml of chloroform was added pyrrolidine (0.75 g, 10.0 mmol) at room temperature. After stirring for 20 min, the solvent was removed under reduced pressure at room temperature. The resulting solid was recrystallized from diisopropyl ether to give pure (*Z*)-**7**; yield 60%; m.p. 76–89°C. $C_{18}H_{21}NO_2$ (283.373) calcd.: C 76.29, H 7.47, N 4.94; found: C 76.70, H 7.60, N 4.92%. ^{1}H NMR: δ 7.10 (s, 4H, ArH), 6.72 (s, 1H, =CHN), 5.87 (t, 1H, *J* 4.6 Hz, =C<u>H</u>–CH_2), 3.47 (s, 3H, OCH_3), 3.5–3.2 (m, 4H, NCH_2) and 2.9–2.6 (m, 2H, $ArCH_2$). ^{13}C NMR: δ 167.6 (s, C=O), 146.8 (d, =CHN), 98.6 (s, =CE), 52.7 (t, NCH_2), 50.7 (q, OCH_3) and 28.2 (t, $ArCH_2$). MS: accurate mass theor. 283.157 for $C_{18}H_{21}NO_2$; exp. 283.158.

Methyl (E)-3,4-dihydro-α-[(1-pyrrolidinyl)methylene]-1-naphthaleneacetate [(*E*)-**7**]

A solution of **6** (0.95 g, 3.4 mmol) in 10 ml of chloroform was either heated for 10 min at 61°C or stirred overnight at room temperature. After evaporation of the solvent, the resulting solid was recrystallized from diethyl ether to give pure (*E*)-**7**; yield 68%; m.p. 106–107°C. $C_{18}H_{21}NO_2$ (283.373) calcd.: C 76.29, H 7.47, N 4.94; found: C 76.62, H 7.67, N 4.90%. ^{1}H NMR: δ 7.79 (s, 1H, =CHN), 7.11 (s, 4H, ArH), 5.86 (t, 1H, *J* 4.4 Hz, =C<u>H</u>–CH_2), 3.57 (s, 3H, OCH_3) and 3.6–2.65 (m, 6H, NCH_2 and $ArCH_2$). ^{13}C NMR: δ 170.7 (s, C=O), 146.6 (d, =CHN), 96.3 (s, =CE), 50.9 (q, OCH_3) and 50.8 (t, NCH_2). MS: accurate mass theor. 283.157 for $C_{18}H_{21}NO_2$; exp. 283.158.

Methyl 2a,3,4,8b-tetrahydro-2a-(1-pyrrolidinyl)cyclobuta[a]naphthalene-2-carboxylate (**10**)

A solution of enamine **9** (1.0 g, 5.0 mmol) and methyl propynoate (**2**, 0.42 g, 5.0 mmol) in 25 ml of hexane was stirred for 1 week at room temperature. Evaporation of the solvent at room temperature gave **10** as an unstable oil which was used directly for further reactions. ^{1}H NMR: δ 7.3–6.7 (m, 4H, ArH), 6.67 (d, 1H, *J* 1.2 Hz, =CH), 3.9–3.8 (bs, 1H, HC–C=), 3.77 (s, 3H, OCH_3) and 3.4–3.1 (m, 2H, $ArCH_2$). ^{13}C NMR: δ 162.2 (s, C=O), 145.4 (d, =CH), 71.3 (s, –C–N), 51.3 (q, OCH_3), 47.9 (t, NCH_2) and 46.9 (d, H<u>C</u>–C=). MS: accurate mass theor. 283.157 for $C_{18}H_{21}NO_2$; exp. 283.158.

Methyl (E)-3,4-dihydro-α-[(1-pyrrolidinyl)methylene]-2-naphthaleneacetate [(*E*)-**11**]

A solution of crude **10** (1.42 g) in 10 ml of chloroform was heated for 15 min at 61°C. After removal of the solvent under reduced pressure, the resulting solid was recrystallized from diisopropyl ether to give pure (*E*)-**11**; yield 75% (calculated on **9**); m.p. 93–94°C. $C_{18}H_{21}NO_2$ (283.373) calcd.: C 76.29, H 7.47, N 4.94; found: C 76.61, H 7.56, N 4.94%. ^{1}H NMR: δ 7.61 (s, 1H, =CHN), 7.2–6.8 (m, 4H, ArH), 6.14 (bs, 1H, ArCH=), 3.67 (s, 3H, OCH_3), 3.45–3.1 (m, 4H, NCH_2) and 3.0–2.6 (m, 2H, $ArCH_2$). ^{13}C NMR: δ 170.1 (s, C=O), 145.5 (d, =CHN), 100.0 (s, =CE), 51.5 (t, NCH_2) and 50.9 (q, OCH_3). MS: accurate mass theor. 283.157 for $C_{18}H_{21}NO_2$; exp. 283.156.

Methyl (E)-4,5-dihydro-4,4-dimethyl-α-[(1-pyrrolidinyl)methylene]-3-thiopheneacetate [(*E*)-**14**]

A solution of **13** (0.50 g, 1.9 mmol) in 10 ml of chloroform was stirred for 4 weeks at room temperature. Evaporation of the solvent under reduced pressure afforded (*E*)-**14** as an oil in quantitative yield. ^{1}H NMR: δ 7.70 (s, 1H, =CHN), 5.76 (s, 1H, =CHS), 3.63 (s, 3H, OCH_3), 3.5–3.2 (m, 4H, NCH_2), 3.07 (s, 2H, SCH_2) and 1.14 (s, 6H, CH_3). ^{13}C NMR: δ 170.9 (s, C=O), 147.2 (d, =CHN), 137.6 (s, SC=<u>C</u>), 123.9 (d, =CHS), 92.2 (s, =CE), 51.5 (t, NCH_2), 50.7 (q, OCH_3), 49.7 [s, <u>C</u>$(CH_3)_2$], 47.1 (t, SCH_2), 25.7 (q, CH_3) and 25.3 (t, NCH_2–<u>C</u>H_2). MS: accurate mass theor. 267.129 for $C_{14}H_{21}NO_2S$; exp. 267.128.

X-Ray crystal structure analysis of (*E*)-**7**

Crystals of (*E*)-**7** belong to the monoclinic space group $P2_1/n$, with a = 8.459(2), b = 17.270(7), c = 10.924(2) Å, β = 109.50(3)°, Z = 4, d_{calc} = 1.24 g·cm^{-3}, μ(MoKα) = 0.8 cm^{-1}. Measurements were performed on a CAD 4 single crystal diffractometer (MoKα radiation, graphite monochromator). Intensities were measured in the ω/2θ scan mode (3 < θ < 25°). Structure solution (MULTAN[18]) and refinement (full-matrix least squares) were based on 1872 reflections with $I > 3\sigma(I)$. The number of parameters refined was 275 [scale factor, extinction parameter, positional parameters of all atoms and thermal parameters (isotropic for hydrogen atoms, anisotropic for others)]. The final R factor was 3.9%. All calculations were carried out using SDP[19].

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