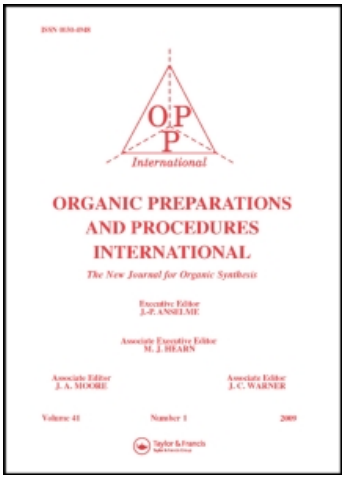


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

Synthesis of Various 2,8-Cyclooctadiene-1,2-dicarboxylates

Ayse Uzgoren-Baran[a]; Nazan Tunoglu[a]; Gurol Okay[a]
[a] Department of Chemistry, Faculty of Science, Hacettepe University, Beytepe, Ankara, Turkey

Online publication date: 07 April 2010

To cite this Article Uzgoren-Baran, Ayse , Tunoglu, Nazan and Okay, Gurol(2010) 'Synthesis of Various 2,8-Cyclooctadiene-1,2-dicarboxylates', Organic Preparations and Procedures International, 42: 2, 143 — 150
To link to this Article: DOI: 10.1080/00304941003680269
URL: http://dx.doi.org/10.1080/00304941003680269

Organic Preparations and Procedures International, 42:143–150, 2010

ISSN: 0030-4948 print
DOI: 10.1080/00304941003680269

Synthesis of Various 2,8-Cyclooctadiene-1,2-dicarboxylates

Ayse Uzgoren-Baran, Nazan Tunoglu, and Gurol Okay

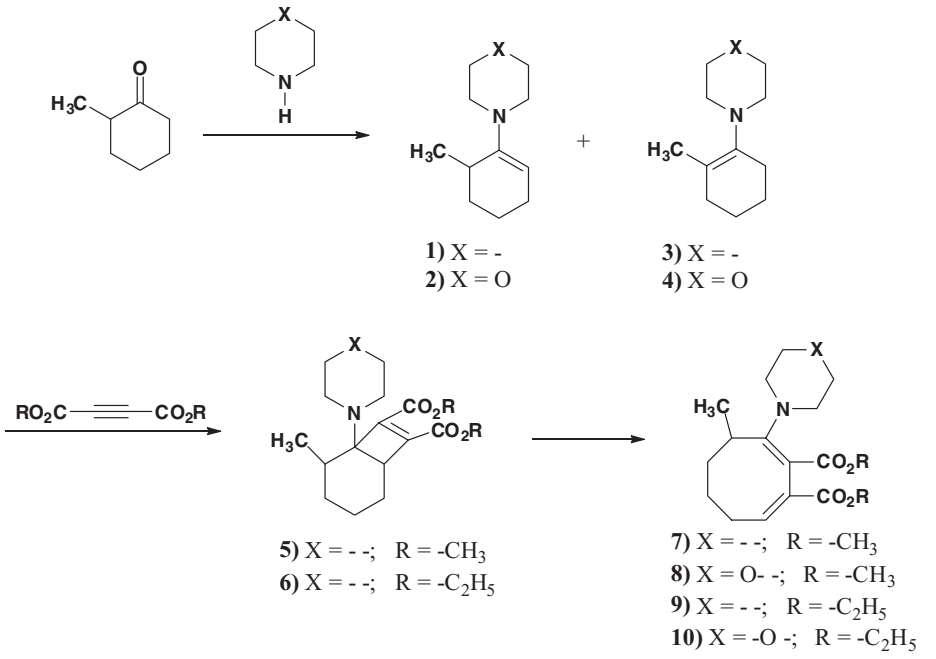
Department of Chemistry, Faculty of Science, Hacettepe University Beytepe, Ankara, Turkey

Reactions of enamines with electrophilic acetylenes such as dimethyl acetylenedicarboxylate (DMAD), diethyl acetylenedicarboxylate (DEAD), methyl propiolate and dicyanoethylene have been extensively studied in the literature.[1,2] The two carbon ring expansions which involve [2 + 2] cycloaddition of enamines of cyclic ketones and electron deficient acetylenes followed by thermal rearrangement of the resulting fused cyclobutenes is an established and useful method in organic synthesis. These ring enlargement reactions have been successfully used in the synthesis of medium-sized heterocycles,[3–5] azulenes,[6] and several natural products including muscone,[7] steganone, and velleral.[8,9]

The mechanism of the reaction of enamine with acetylene derivatives has been thoroughly investigated.[1,10–13] It was found that enamine reactions with acetylene derivatives can be affected by many factors. First, a solvent has a remarkable effect on the course of the reactions of acetylene derivatives with enamines. In non-polar solvents, [2 + 2] cycloaddition takes place while in polar solvents pyrrolizines are formed by reaction of the initially formed linear Michael adducts of enamine and acetylene derivatives.[13–15] Secondly, the amine moiety on the enamine also affects the rate of reaction and the formation of products as well. The [2 + 2] cycloadducts with the more effective π-electron donating 1-pyrrolidinyl group undergo a thermal rearrangement at room temperature while the analogues with 1-pyrrolidinyl or 4-morpholinyl substituent at the bridgehead sp^3-hybridized carbon are thermally stable at room temperature.[16]

When 2-methylcyclohexanone was subjected to enamine formation reaction with pyrrolidine or morpholine, isomeric mixtures were obtained in each case as reported in the literature.[17] 6-Methyl-1-(1-pyrrolidinyl)-1-cyclohexene (**1**) and 2-methyl-1-(1-pyrrolidinyl)-1-cyclohexene (**3**) were obtained in 87% yields in a ratio of 10:90%. Furthermore 6-methyl-1-(4-morpholinyl)-1-cyclohexene (**2**) and 2-methyl-1-(4-morpholinyl)-1-cyclohexene (**4**) were formed in 79% yield in a 48:52% ratio. We obtained the same results. The [2 + 2] cycloaddition reactions occured with only isomers **1** and **2** which is

Received June 19, 2009; in final form January 22, 2010.
Address correspondence to Uzgoren-Baran, Department of Chemistry, Faculty of Science, Hacettepe University, TR-06800 Beytepe, Ankara, Turkey. E-mail: uzgoren@hacettepe.edu.tr



Scheme 1

presumably due to the steric hindrance of methyl groups attached to the double-bonded carbon of compounds **3** and **4** (*Scheme 1*).

6-Methyl-1-(1-pyrrolidinyl)-1-cyclohexene (**1**) reacted with DMAD in toluene and gave a mixture of cyclobutene derivatives, dimethyl 2-methyl-1-(1-pyrrolidinyl)bicyclo[4.2.0]octene-7,8-dicarboxylate (**5**) in 11% yield and thermal isomerization product, dimethyl 7-methyl-8-(1-pyrrolidinyl)-2,8-cyclooctadiene-1,2-dicarboxylate (**7**) in 40% yield. When compound **1** reacted with a different electrophilic acetylene, DEAD, in the same solvent, the cyclobutene derivative, diethyl 2-methyl-1-(1-pyrrolidinyl)bicyclo[4.2.0]octene-7,8-dicarboxylate (**6**), could be isolated alone and it was readily isomerized to cyclic 1,3-dienamine, diethyl 7-methyl-8-(1-pyrolidinyl)-2,8-cyclooctadiene-1,2-dicarboxylate (**9**) after refluxing in dioxane for 2 hours. However, the reactions of compound **1** with the same electrophilic acetylenes, DMAD and DEAD, in a polar solvent, such as methanol, yielded cycloisomerization products (**7** and **9**) directly, and the cyclobutene derivatives could not be isolated. The electrophilicity of DEAD is lower than that of DMAD which accounts for the lower reactivity of DEAD.[10] Hence, the less electrophilic DEAD gave only the cyclobutene product in toluene and then it was converted to the cyclooctadiene product in a subsequent reaction, but the more electrophilic DMAD gave a faster reaction to yield both the cyclobutene adduct and the 1,3-dienamine.

Proton NMR indicated that both cycloadducts (**5** and **6**) were produced as mixtures of *endo* and *exo* isomers (**5a** and **5b**; **6a** and **6b**). The existence of isomers **5a** and **5b** together was proved by extra signals corresponding to $-OCH_3$ protons. Even though two singlets were expected for the ester $-OCH_3$ protons, three singlet protons at δ 3.77, δ 3.79 and δ 3.82 were observed in the ^1H NMR spectrum of compound **5**. The same result was

observed for the DEAD product, thus, in the ^{1}H NMR spectrum of isomers **6a** and **6b** included extra peaks corresponding to both -OCH_2 and -CH_3 groups. The -CH_3 signals appeared at δ 1.13, δ 1.18, δ 1.24 and δ 1.30, respectively. When the single crystal X-ray structure determination of a similar cycloadduct was examined by Özbey and Tunoğlu both endo and exo products have been observed for the [2+2] cycloadducts obtained by the reactions of morpholine enamine of α-tetralone with DMAD. The cyclobutene moiety was positioned both up and down relative to the fused cyclohexene ring to produce endo and exo products.[18]

In the case of the morpholine enamine of 2-methylcyclohexanone, 6-methyl-1-(4-morpholinyl)-1-cyclohexene (**2**), the [2 + 2] cycloaddition reactions with both DMAD and DEAD in toluene or in methanol yielded 1,3-dienamines, (**8**) and (**10**), respectively (*Scheme 1*). Even though the cyclobutene adduct was isolated in some pyrrolidine enamine reactions, a quite different result was observed with the [2 + 2] cycloaddition reaction of the morpholine enamine of 2-methylcyclohexanone (**2**), that is, no trace of cyclobutene derivatives with either DMAD or DEAD was observed. Besides the effect of the electrophilic acetylenes and the solvent used, the morpholine group might be more effective in the direct synthesis of 1,3-dienamines without isolation of cyclobutene. Morpholine is less nucleophilic than pyrrolidine which may account for the slower reaction of the enamine with electrophilic acetylene if the dipolar intermediate was formed in the reaction process.

The ability of the pyrrolidine group to supply electrons is greater than that of morpholine making the β-carbon atom of the enamine more nucleophilic towards the triple bond of the electron-deficient acetylene.[10] Thus, the cycloaddition reaction of 6-methyl-1-(4-morpholinyl)-1-cyclohexene (**2**) with DMAD or DEAD required a longer time than the reaction of 6-methyl-1-(1-pyrrolidinyl)-1-cyclohexene (**1**) under the same conditions (see *Table 1*).

The higher basicity of the pyrrolidine group compared with the morpholine group affected the yields of the reactions of the corresponding enamines. Hence, the formation of compound **9** (yield: 67%) from the pyrrolidine enamine occurred in higher yield than the formation of compound **10** (yield: 49%) from the morpholine enamine.

When the IR spectra of pyrrolidine substituted cyclobutene adducts (**5** and **6**) and the corresponding 1,3-dienamines (**7** and **9**) were compared, the carbonyl band of the

Table 1
Yields, mps, Reaction Times and Temperature

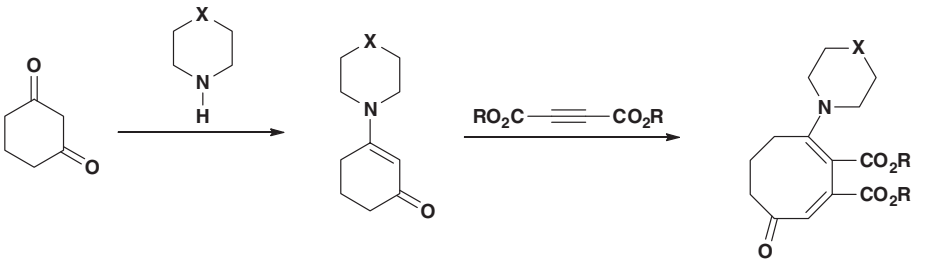
Cmpd	Time (solvent)	Temp (°C)	mp. (°C)	Yield (%)
5	48 h (toluene)	RT	142.0–143.1	11
6	48 h (toluene)	RT	137.0–137.8	57
7	48 h (toluene) 24 h (methanol)	RT	144.0–144.9	40
9	24 h (methanol)	RT	102.3–102.6	67
8	72 h (toluene)	RT	143.4–143.9	42
10	72 h (toluene)	RT	124.6–125.7	49

ester groups was at 1738 cm^{-1} for compound **5**, 1733 cm^{-1} for compound **6**, 1719 cm^{-1} for compound **7** and 1704 cm^{-1} for compound **9**. The different locations of ester C=O bands in the cyclobutene adducts and the 1,3-dienamines allowed us to determine that the cycloadducts were successfully isomerized to 1,3-dienamines. The same comparison was possible with the C=C bands of cycloadducts and cycloisomerization products. The C=C band of pyrrolidine substituted cyclobutene adducts appeared at 1550 cm^{-1} for compound **5** and 1528 cm^{-1} for compound **6** due to ring strain of cyclobutene whereas the conjugated C=C bands for compounds **7** and **9** appeared at higher wavenumbers, 1621 cm^{-1} and 1619 cm^{-1}, respectively. Even though, there is conjugation in the 1,3-dienamine structures, there is much less angle strain in the cyclooctadiene ring compared to the cyclobutene so that the C=C band in the IR spectra appeared at its normal value.

The conversion of compounds **5** and **6** to the corresponding 1,3-dienamines, **7** and **9**, could also be ascertained by the characteristic proton peaks in the ^1H NMR spectra. Thus, the bridgehead protons at δ 4.21 for compound **5** and δ 4.25 for compound **6** completely disappeared in the corresponding ^1H NMR spectra of **7** and **9**. Instead of the bridgehead protons, the vinylic protons at δ 6.44 for compound **7** and δ 6.71 for compound **9** were observed. Even though there was no significant difference in the location of bridged protons in the spectra of **5** and **6**, the vinylic protons of **7** and **9** appeared in quite different areas (δ 6.44 for **7** and δ 6.71 for **9**) relative to each other. This result may be due to the effect of conjugation of the vinylic protons with the methyl and ethyl ester moieties. Since, the electron donating effect of the ethyl group is higher than that of the methyl group, the vinylic proton of the methyl ester appeared at lower field.

The second ketone investigated, 1,3-cyclohexanedione, also reacted with pyrrolidine and morpholine to yield 3-(1-pyrrolidinyl)-2-cyclohexene-1-one (**11**) and 3-(4-morpholinyl)-2-cyclohexene-1-one (**12**) in 99% and 85% yields, respectively as reported in the literature, because of conjugation of the enamine double bond with the carbonyl group.[19] In subsequent reactions, [2+2] cycloaddition and then thermal isomerization, only the 1,3-dienamine structures, (**13**) and (**14**) were synthesized with DMAD. None of the cycloadducts could be isolated during the course of the reaction. This result can be attributed to the increased conjugation in the 1,3-dienamine structures arising from extra carbonyl groups. Compared to the simple enamines, the reactions occurred at high rates, probably due to the same reason. The reaction of both enamines with DEAD gave the same result to yield the corresponding 1,3-dienamines, (**15**) and (**16**) (*Scheme 2*). The reactions with the morpholine enamine were slower than those of the pyrrolidine enamines, and lower yields were observed in these reactions (see *Table 2*). The polarity of the solvent did not alter the reaction course and the same product was obtained either with toluene or methanol in each case.

In the ^1H NMR spectra of compounds **13**, **14, 15** and **16** the vinylic proton appeared in a very narrow range between δ 6.43–6.46, δ 6.43 for compound **13**, δ 6.45 for compound **15**, δ 6.46 for compound **14** and δ 6.46 for compound **16**. Even though the chemical shift of the vinylic proton ranged from δ 6.44–6.96 for the dienamines **7**, **8**, **9** and **10** because of the conjugation with the diester groups, the chemical shifts for the vinylic protons of 5-oxo-1,3-dienamines (**13, 14, 15** and **16**) were nearly identical. The reason is that the effect of the 5-oxo group of each compound on this vinylic proton is higher when compared with the effect of ester groups. The vinylic protons signals for the 5-oxo-1,3-dienamines appeared as singlets due to adjacent carbonyl groups where the same signals for methyl substituted-1,3-dienamines appeared as triplets due to adjacent -CH_2 groups.



11) X = -
12) X = O

13) X = - -; R = -CH_3
14) X = O- -; R = -CH_3
15) X = - -; R = -C_2H_5
16) X = -O -; R = -C_2H_5

Scheme 2

The structure determination of compounds **13** and **15** were also determined by single crystal X-ray analysis in order to establish the configuration of the octadiene moiety. These compounds consist of substituted 2,8-cyclooctadiene and pyrrolidine moieties. The configuration of eight-membered ring was observed as a *cis*, *cis*. The confirmation of the pyrrolidine ring was observed as a twist.[20,21]

Experimental Section

^{1}H-NMR (400 MHz) spectra were recorded with a Bruker instrument DPX-400, 400 MHz High Performance Digital FT-NMR Spectrometer in $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at 25°C. Chemical shifts are expressed in terms of parts per million (δ) and the coupling constants are given in Hz. IR spectra were obtained as KBr pellets using a Mattson 1000 FT-IR spectrometer. Melting points were determined in a capillary tube on a Gallenkamp apparatus and are uncorrected. Reactions were monitored by thin layer chromatography (silica gel 60 F254). Purification of solvents was performed according to standard methods.

General Procedure for the Reaction of Enamines with DMAD and DEAD

A solution of the enamine (10 mmol) in anhydrous toluene under a nitrogen atmosphere was cooled to 0–5°C with an ice bath. A solution of the acetylenedicarboxylate (in 5 mL

Table 2
Yields, mps, Reaction Times and Temperature

Cmpd	Time (solvent)	Temp (°C)	mp. (°C)	Yield (%)
13	2 h (toluene)	0–5	161.0–161.9	53
14	48 h (toluene)	RT	125.5–125.9	41
15	2 h (toluene)	0–5	120.5–121.7	64
16	72 h (toluene)	RT	131.1–132.5	47

toluene; 10 mmol) was added slowly with stirring at such a rate that the temperature never rose above 30°C. When all of acetylenedicarboxylate had been added, the mixture was stirred at room temperature for several hours. The solvent was removed and the products were purified by column chromatography (silica gel, chloroform). Each was recrystallized from methanol.

Dimethyl 2-methyl-1-(1-pyrrolidinyl)bicyclo[4.2.0]octene-7,8-dicarboxylate (5). IR: ν 2946, 1738, 1550, 1434, 1257, 1187, 1118 cm^{-1};^{1}H NMR: δ 1.79 (d, 3 H, J = 4.7 Hz), 1.95 (m, 4 H), 2.15 (m, 2 H), 2.45 (m, 2 H), 2.93 (m, 2 H), 3.28 (m, 2 H), 3.66 (m, 1 H), 3.77 (s, 3 H, isomer a), 3.79 (s, 6 H, isomer a and b), 3.82 (s, 3 H, isomer b), 4.21 (t, 1 H, J = 2.3 Hz); MS (70 eV), *m/z*: 166.7 (M^+-$C_6H_4O_4$), 153.8 (M^+-$C_7H_5O_4$), 94.0 (M^+-$C_{10}H_{15}NO_4$), 70.1 (M^+-$C_{13}H_{17}O_4$); mp. 142.0–143.1°C.

Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.38; H, 8.24; N, 4.57.

Diethyl 2-methyl-1-(1-pyrrolidinyl)bicyclo[4.2.0]octene-7,8-dicarboxylate (6). IR: ν 2981, 1733, 1528, 1434, 1258, 1119 cm^{-1}; ^{1}H NMR: δ 0.89 (d, 3 H, J = 7.0 Hz), 0.95 (t, 2 H, J = 7.1 Hz), 1.13 (t, 3 H, J = 7.1 Hz, isomer a), 1.18 (t, 3 H, J = 7.1 Hz, isomer b), 1.24 (t, 3 H, J = 7.0 Hz, isomer a), 1.30 (t, 3 H, J = 7.1 Hz, isomer b), 1.71 (m, 4 H), 1.88 (m, 2 H), 3.02 (m, 2 H), 3.25 (m, 1 H, J = 7.0 Hz), 3.54 (m, 2 H), 3.87 (m, 2 H), 4.08–4.25 (m, 9 H, isomer a and b); MS (70 eV), *m/z*: 335.4 (M^+), 262.3 (M^+-$CO_2CH_2CH_3$), 234.2 (M^+-$C_5H_9O_2$), 205.3 (M^+-$C_6H_{14}O_4$), 167.2 (M^+-$C_8H_8O_4$), 97.1 (M^+-$C_{12}H_{16}NO_4$), 82.8 (M^+-$C_{13}H_{19}NO_4$); mp. 137.0–138.0°C.

Anal. Calcd for $C_{19}H_{29}NO_4$: C, 68.03; H, 8.71; N, 4.18. Found: C, 68.06; H, 8.74; N, 4.20.

Dimethyl 7-methyl-8-(1-pyrolidinyl)-2,8-cyclooctadiene-1,2-dicarboxylate (7). IR: ν 2930, 1719, 1682, 1621, 1523, 1436 cm^{-1}; ^{1}H NMR: δ 0.89 (d, 3 H, J = 4.4 Hz), 1.25 (m, 2 H), 1.73 (m, 4 H), 1.93 (m, 2 H), 2.37 (m, 1 H), 3.07 (m, 2 H), 3.27 (m, 1 H), 3.53 (s, 3 H), 3.61 (m, 2 H), 3.67 (s, 3 H), 3.68 (m, 1 H), 6.44 (m, 1 H); MS (70 eV), *m/z*: 309.1 (M^++2), 307.5 (M^+), 276.3 (M^+-OCH_3), 248.4 (M^+-CO_2CH_3), 232.2 (M^+-$C_3H_6O_2$), 188.3 (M^+-$C_4H_6O_4$), 70.1 (M^+-$C_{13}H_{17}O_4$), 58.96 (M^+-$C_{15}H_{22}NO_2$); mp. 144.0–144.9°C.

Anal. Calcd for $C_{17}H_{25}NO_4$: C, 66.43; H, 8.20; N, 4.56. Found: C, 66.47; H, 8.25; N, 4.60.

Dimethyl 7-methyl-8-(4-morpholinyl)-2,8-cyclooctadiene-1,2-dicarboxylate (8). IR: ν 2924–2846, 1712, 1551, 1257, 1111 cm^{-1}; ^{1}H NMR: δ 1.12 (d, 3 H, J = 7.0 Hz), 1.55 (m, 2 H), 1.71 (m, 1 H), 1.84 (m, 2 H), 2.07 (m, 1 H), 2.67 (m, 1 H), 3.30 (m, 4 H), 3.74 (m, 2 H), 3.91 (s, 3 H), 3.92 (m, 2 H), 3.96 (s, 3 H), 6.96 (m, 1 H); MS (70 eV), *m/z*: 324.8 (M^++1), 323.5 (M^+), 292.5 (M^+-OCH_3), 264.5 (M^+-CO_2CH_3), 249.6 (M^+-$C_3H_6O_2$), 233.7 (M^+-$C_3H_6O_3$), 206.6 (M^+-$C_4H_5O_4$), 120.4 (M^+-$C_8H_{13}NO_5$), 105.3 (M^+-$C_9H_{16}NO_5$); mp. 143.4–143.9°C.

Anal. Calcd for $C_{17}H_{25}NO_5$: C, 63.14; H, 7.79; N, 4.33. Found: C, 63.17; H, 7.75; N, 4.30.

Diethyl 7-methyl-8-(1-pyrolidinyl)-2,8-cyclooctadiene-1,2-dicarboxylate (9). IR: ν 2977, 2877, 1704, 1673, 1619, 1519, 1249, 1103 cm^{-1}; ^{1}H NMR: δ 1.19 (d, 3 H, J = 7.0 Hz), 1.41 (t, 3 H, J = 7.1 Hz), 1.49 (t, 3 H, J = 7.1 Hz), 1.56 (m, 2 H), 2.02 (m, 4 H), 2.20 (m, 2 H), 2.64 (m, 1 H), 3.35 (m, 2 H), 3.55 (m, 1 H), 3.93 (m, 2 H), 4.26 (m, 1 H), 4.41 (m, 4 H), 6.71 (m, 1 H); MS (70 eV), *m/z*: 336.8 (M^++1), 335.5 (M^+), 306.5

(M^+-CH_2CH_3), 290.4 (M^+-OCH_2CH_3), 262.5 (M^+-$CO_2CH_2CH_3$), 234.4 (M^+-$C_5H_{10}O_2$), 216.4 (M^+-$C_5H_{11}O_3$), 188.3 (M^+-$C_6H_{11}O_4$), 70.00 (M^+-$C_{15}H_{21}O_4$); mp. 102.3–102.6°C.

Anal. Calcd for $C_{19}H_{29}NO_4$: C, 68.03; H, 8.71; N, 4.18. Found: C, 68.06; H, 8.67; N, 4.23.

Diethyl 7-methyl-8-(1-morpholinyl)-2,8-cyclooctadiene-1,2-dicarboxylate (10). IR: ν 2970–2854, 1705, 1551, 1257, 1111 cm^{-1}; ^1H NMR: δ 0.82 (d, 3 H, J = 7.0 Hz), 1.16 (t, 3 H, J = 7.2 Hz), 1.19 (t, 3 H, J = 7.1 Hz), 1.41 (m, 2 H), 1.54 (m, 2 H), 1.76 (m, 1 H), 2.38 (m, 1 H), 2.93 (m, 2 H), 3.02 (m, 1 H), 3.47 (m, 2 H), 3.67 (m, 4 H), 4.04 (m, 2 H), 4.11 (m, 2 H), 6.62 (t, 1 H, J = 7.6 Hz); MS (70 eV), *m/z*: 353.1 (M^++2), 351.1 (M^+), 336.2 (M^+-CH_3), 322.2 (M^+-CH_2CH_3), 306.0 (M^+-OCH_2CH_3), 278.1 (M^+-$C_3H_3O_2$), 262.9 (M^+-$C_4H_6O_2$), 249.1 (M^+-$C_5H_8O_2$), 232.9 (M^+-$C_5H_8O_3$), 204.9 (M^+-$C_6H_8O_4$), 119.8 (M^+-$C_{10}H_{16}NO_5$); mp. 124.6–125.7°C.

Anal. Calcd for $C_{19}H_{29}NO_5$: C, 64.94; H, 8.32; N, 3.99. Found: C, 64.91; H, 8.34; N, 3.96.

Dimethyl 3-(1-pyrrolidinyl)-7-oxo-2,8-cyclooctadiene-1,2-dicarboxylate (13). IR: ν 2989–2877, 1725, 1693, 1562, 1139 cm^{-1}; ^1H NMR: δ 1.79 (m, 2 H), 2.00 (t, 4 H, J = 6.1 Hz), 2.58 (m, 4 H), 3.14 (m, 2 H), 3.52 (m, 2 H), 3.55 (s, 3 H), 3.70 (s, 3 H), 6.43 (s, 1 H); MS (70 eV), *m/z*: 308.1 (M^++1), 276.1 (M^+-OCH_3), 248.1 (M^+-CO_2CH_3), 232.1 (M^+-$C_3H_7O_2$), 188.0 (M^+-$C_4H_7O_4$), 72.10 (M^+-$C_{12}H_{11}O_5$); mp. 161.0–161.9°C.

Anal. Calcd for $C_{16}H_{21}NO_5$: C, 62.53; H, 6.89; N, 4.56. Found: C, 62.58; H, 6.91; N, 4.53.

Dimethyl 3-(4-morpholinyl)-7-oxo-2,8-cyclooctadiene-1,2-dicarboxylate (14). IR: ν 2987–2859, 1727, 1698, 1562, 1126 cm^{-1}; ^1H NMR: δ 1.98 (m, 2 H), 2.40 (d, 2H, J = 10.7 Hz), 2.58 (d, H, J = 12.7 Hz), 2.81 (m, 2 H), 3.20 (m, 2 H), 3.42 (m, 2 H), 3.58 (s, 3 H), 3.69 (s, 3 H), 3.72 (m, 4 H), 6.46 (s, 1 H); MS (70 eV), *m/z*: 325.1 (M^++2), 324.20 (M^++1), 178.6 (M^+-$C_6H_{11}NO_3$); mp. 125.5–125.9°C.

Anal. Calcd for $C_{16}H_{21}NO_6$: C, 59.43; H, 6.55; N, 4.33. Found: C, 59.45; H, 6.52; N, 4.38.

Diethyl 3-(1-pyrrolidinyl)-7-oxo-2,8-cyclooctadiene-1,2-dicarboxylate (15). IR: ν 2985–2904, 1722, 1697, 1562, 1128 cm^{-1}; ^1H NMR: δ 1.22 (t, 3 H, J = 7.1 Hz), 1.32 (t, 3 H, J = 7.1 Hz), 1.84 (m, 2 H), 2.06 (m, 4 H), 2.66 (m, 4 H), 3.22 (m, 2 H), 3.58 (m, 2 H), 4.05 (q, 2 H, J = 7.1 Hz), 4.20 (q, 2 H, J = 7.0 Hz), 6.45 (s, 1 H); MS (70 eV), *m/z*: 337.2 (M^++2), 336.1 M^++1, 221.2 (M^+-$C_5H_6O_3$), 220.1 (M^+-$C_5H_7O_3$), 219.1 (M^+-$C_5H_8O_3$); mp. 120.5–121.7°C.

Anal. Calcd for $C_{18}H_{25}NO_5$: C, 64.46; H, 7.51; N, 4.18. Found: C, 64.49; H, 7.47; N, 4.19.

Diethyl 3-(4-morpholinyl)-7-oxo-2,8-cyclooctadiene-1,2-dicarboxylate (16). IR: ν 2981–2854, 1714, 1681, 1556, 1122 cm^{-1}; ^1H NMR: δ 1.15 (t, 3 H, J = 7.1 Hz), 1.23 (t, 3 H, J = 7.2 Hz), 1.94 (m, 2 H), 2.42 (d, 1 H, J = 11.1 Hz), 2.57 (d, 1 H, J = 12.0 Hz), 2.81 (m, 2 H), 3.22 (m, 2 H), 3.43 (m, 2 H), 3.71 (m, 4 H), 4.03 (q, 2 H, J = 7.1 Hz), 4.13 (q, 2 H, J = 7.0 Hz), 6.46 (s, 1 H); MS (70 eV), *m/z* 353.0 (M^++2), 352.1 (M^++1), 336.1 [M^+-CH_3), 306.1 (M^+-OCH_2CH_3), 220.20 (M^+-$C_6H_{11}O_4$), 178.6 (M^+-$C_8H_{15}NO_3$); mp. 131.1–132.5°C.

Anal. Calcd for $C_{18}H_{25}NO_6$: C, 61.53; H, 7.17; N, 3.99. Found: C, 61.57; H, 7.14; N, 4.04.

Acknowledgements

We are grateful to Hacettepe University Research Fund (project no. HU-03G082 and project no. HU-0302601003) for financal support.

References

1. C. F. Huebner, L. Dorfman, M. M. Robison, E. Donoghue, W. G. Pierson, and P. L. Strachan, *J. Org. Chem.*, **28**, 3134 (1963).
2. N. Tunoğlu and G. Okay, *Synth. Commun*, **26**, 3151 (1996).
3. V. Snieckus and M. S. Lin, *J. Org. Chem.*, **36**, 645 (1971).
4. D. N. Reinhoudt and C. G. Kouwenhoven, *Tetrahedron*, **30**, 2431 (1974).
5. D. N. Reinhoudt and C. G. Kouwenhoven, *Tetrahedron*, **30**, 2093 (1974).
6. K. Hafner, H. G. Klaes and M. C. Böhm, *Tetrahedron Lett.*, **21**, 41 (1980).
7. G. Stork and T. L. Macdonald, *J. Am. Chem. Soc.*, **97**, 1264 (1975).
8. T. Fex, J. Froborg, G. Magnusson, and S. Thoren, *J. Org. Chem.*, **41**, 3518 (1976).
9. J. Froborg, and G. Magnusson, *J. Am. Chem. Soc.*, **100**, 6728 (1978).
10. N. Tunoğlu and N. Uludağ, *Org. Prep. Proc. Int.*, **29**, 541 (1997).
11. N. Tunoğlu and G. Okay, *Org. Prep. Proc. Int.*, **32**, 584 (2000).
12. D. N. Reinhoudt, J. Geevers and W. P. Trompenaars, *Tetrahedron Lett.*, 1351 (1978).
13. W. Verboom, G. W. Visser, W. P. Trompenaars, D. N. Reinhoudt, S. Harkema and G. J. van Hummel, *Tetrahedron*, **37**, 3525 (1981).
14. D. N. Reinhoudt, J. Geevers, W. P. Trompenaars, S. Harkema and G. J. van Hummel, *J. Org. Chem.*, **46**, 424 (1981).
15. D. N. Reinhoudt, G. W. Visser, W. Verboom, P. H. Benders and M. L. M. Pennings, *J. Am. Chem. Soc.*, **105**, 4775 (1983).
16. F. Effenberger, P. Fischer, W. W. Schoeller and W. D. Stohrer, *Tetrahedron*, **34**, 2409 (1978).
17. W. D. Gurowitz and M. A. Joseph, *J. Org. Chem.*, **32**, 3289 (1967).
18. S. Ozbey and N. Tunoğlu, *Analytical Sciences*, **15**, 1 (1999).
19. T. Ishıkawa, E. Uedo, R. Tani, and S. Saito, *J. Org. Chem.*, **66**, 186 (2001).
20. T. Hökelek, A. Uzgören, Y. Ergün, N. Tunoğlu and G. Okay, *Acta Crystallographica Section E*, **E59**, 1220 (2003).
21. T. Hökelek, A. Uzgören, Y. Ergün, N. Tunoğlu and G. Okay, *Acta Crystallographica Section E*, **E60**, 48 (2004).