Pergamon

Tetrahedron, Vol. 53, No. 5, pp. 1813-1822, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(96)01107-6

Novel Heterocycles : A Convenient Synthesis of Pyrrolo[2,3-d]pyrazole; Cycloaddition Reaction of N-Aryl(methyl)pyrrol-2,3-Diones to Diazomethane and Olefins

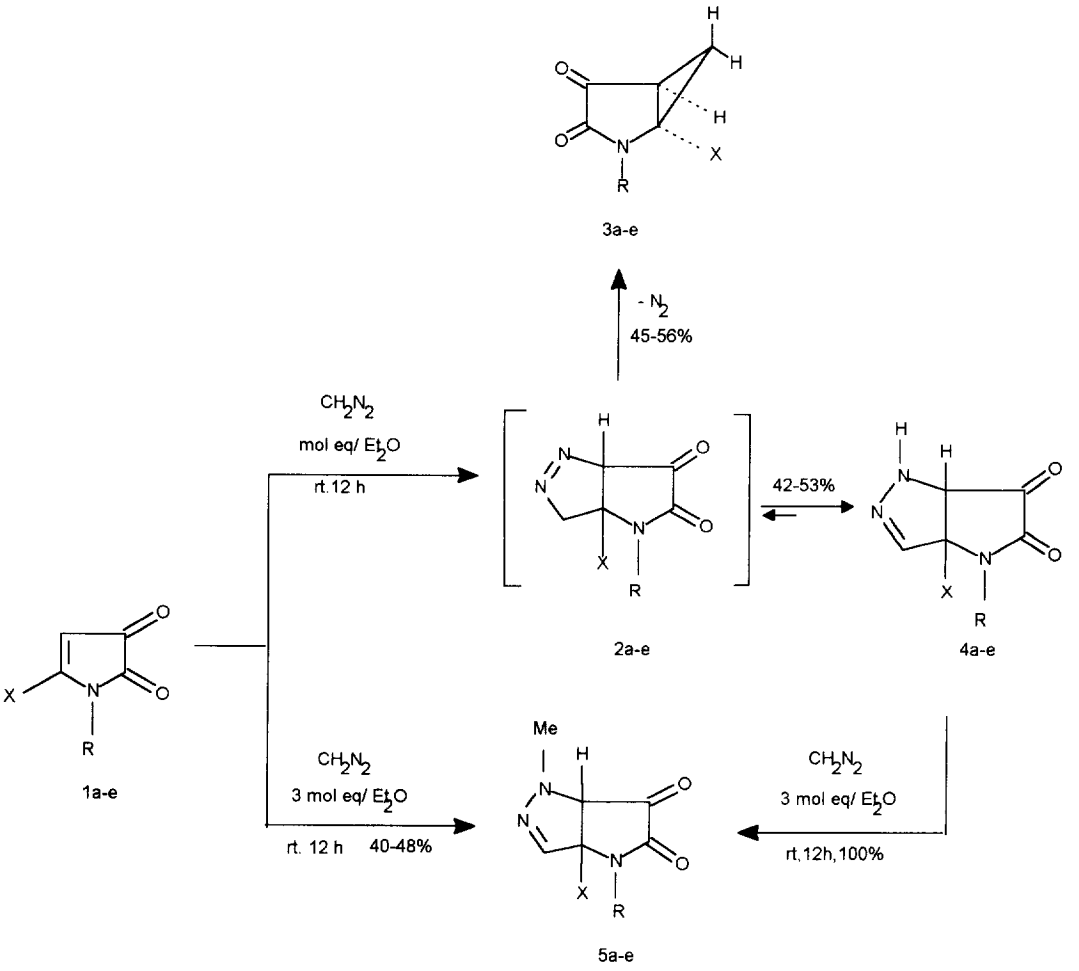
Hisham A. Abd El-Nabi*

Chemistry Department , Faculty of Science, El-Minia University, El-Minia A. R. EGYPT

Abstract : The cycloaddition reaction of the pyrrol-2,3-diones **1a-e** to equimolar amount of diazomethane gave 2-aryl(methyl)-2-azabicyclo[3.1.0]hexane **3a-e** together with 5.6-dioxo-1H-pyrrolo[2,3-d]pyrazole derivatives **4a-e**. While **1a-e** reacted with an excess of diazomethane to give the corresponding N-methyl derivatives **5a-e** with a minor amount of **3a-e**. Treatment of **4a-e** with excess of diazomethane gave **5a-e** quantitatively. Photocycloaddition reaction of pyrrol-2.3-diones **1a** to olefins **8a-d** gave two diastereoisomers **9a,b** and **10a-d** .

Pyrrol-2,3-diones have proved to be versatile synthons for a variety of heterocycles. Diels-Alder reaction of dioxopyrroline with butadienes gave hydroindoles,[1] providing the key step in syntheses of Amaryllidaceae [2] and Erythrina [3] alkaloids. We have recently reported that 5-methoxy-N-arylpyrrol-2,3-dione [4] and 4-ethoxycarbonyl-5-phenyl-pyrrol-2,3-dione [5] easily reacted with nitrones to afford pyrrolo[2,3-d]isoxazole derivatives. [6] In continuation of our interest on the reactivity of five membered heterocyclic-2,3-diones, [7,8] the behaviour of pyrrol-2,3-diones **1a-e** towards diazomethane, as a simple model of a 1,3-dipole, and olefins **8a-d** were reported.

Thus, it has been found that, when 5-methoxy-N-aryl-pyrrol-2,3-dione [4] and 5-methyl-thio-N-phenyl(methyl)-pyrrol-2,3-dione [9] **1a-e** were allowed to react with an equimolar amount of diazomethane in ether at room temperature, and the resulting reaction mixture was resolved by flash chromatography, the bicyclic cyclopropane derivatives **3a-e** together with the new ring system **4a-e** were isolated in moderate yield (Scheme 1). Structures **3** and **4** were firmly established on the basis of the analytical and spectral data which are in full agreement with the proposed structures. The IR spectrum of **3a** displays characteristic absorption bands at 1745 and 1730 cm^{-1} for two CO groups, while ^{1}H-NMR shows signals at δ 1.65 (dd, 2H, J=1.5, 7.5 Hz, H-6), 3.95 (s,3H,OMe), 4.85 (dd,1H, J=1.5, 7.5Hz,H-5),7.25-7.78(m,5H,arom.); ^{13}C-NMR shows signals at 19.4 (t,C-6), 52.8 (q,OCH_3), 80.1 (d,C-5), 82.9 (s,C-1),162.9 (s,C-3), 176.2 (s,C-4) which in particular support the suggested structure.



1,3,4,5	X	R
a	OMe	Ph
b	OMe	p-CH_3-C_6H_4
c	OMe	p-CH_3O-C_6H_4
d	SMe	Ph
e	SMe	Me

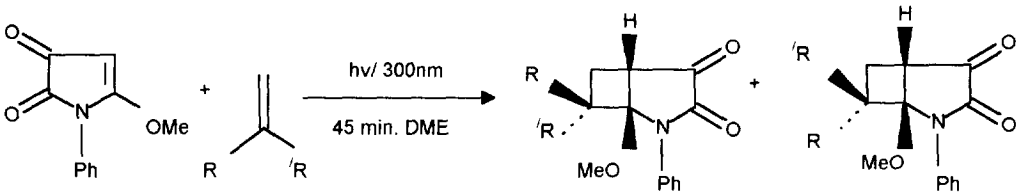
Scheme 1

The formation of **3a-e**, whose structure based on the analytical and spectral evidence (see Experimental part), can be accounted for on the basis of a regioselective 1,3-dipolar cycloaddition of the diazomethane on C(4)-

C(5) pyrrol-2,3-diones double bond of **1a-e**, followed by loss of nitrogen from the cycloadduct **2** . The primary cycloadduct **2** may tautomerize into **4** which explains the isolation of pyrrolo[2,3-d]pyrazole derivatives **4a-e** as a second product (Scheme 1).

Interaction of pyrrol-2,3-diones **1a-e** with an excess of diazomethane (3 mol eq.) in diethyl ether at RT gave compounds **5a-e** directly in 40-48% yield, together with a minor amount of (8-16% yield) **3a-e** which appears rather unstable under these reaction conditions. Treatment of **4a-e** with diazomethane in ether at RT gave the corresponding N-methyl derivatives **5a-e** quantitatively.

On the other hand, photocycloaddition reaction of pyrrol-2,3-dione **1a** to olefins **8a-d** was investigated too. Thus, it has been found that, irradiation of a solution of the pyrrol-2,3-dione **1a** to electron rich olefins **8a-d** in dimethoxyethane (DME) with >=300 nm light gave two diastereoisomeric cyclobutane adducts the exo- and endo-isomers **9a,b** and **10a-d** , respectively (Scheme 2).



8,9,10	R	'R
a	Ph	H
b	OEt	H
c	OPh	H
d	OC_6H_{11}	H

Scheme 2

The ratio of the two isomeric products were determined by chromatographic isolation or by inspection of the C_7-H signal in the ^{1}H-NMR spectrum of the product mixture.[10] ^{1}H-NMR spectra of the exo-isomers **9a,b** (major product) resonate at higher field (4.17 and 4.18) than that of the endo-isomer **10a,b** (4.75 and 4.55) minor product. ^{13}C-NMR chemical shift of C-7 also differentiates the two isomers in that the exo-isomer resonates at lower field than that of the endo-isomer. The C-7 signals of the sole isolable adducts from

olefins **8c,d** appeared at lower field, comparable to those of **10a,b**. Thus they were concluded to be the endo-isomers **10c,d** .

The structure and stereochemistry of the [2+2] cycloadducts **9** and **10** based on the elemental analysis and spectral data are in a good agreement to the proposed structure (Scheme 2), and similar to the products obtained from photocycloaddition of N-4'-bromo-phenyldioxopyrroline to olefins which were firmly established by X-ray crystallographic analysis.[11] On the other hand, Olefins having electron withdrawing groups e.g. 1,2-dichloroethylene irradiated with **1a** in DME for 2h did not give any cycloadducts.

Summarizing the above results, the photocycloaddition of **1a** to electron rich olefins **8a-d** easily proceeded in a highly stereoselective manner to give [2+2] cycloadducts **9** and **10** . The yield of cyclobutanes and the ratios of diastereoisomers were found to be affected by the substituent type of the olefins. Olefins carrying phenyl or ethoxy group afforded mixtures of both the exo-isomers **9a,b** (major product) and the endo-isomers **10a,b** (minor product), while olefins carrying groups such as phenoxy or cyclohexyloxy groups afforded the endo-isomers **10c,d** predominantly. Olefins possessing an electron withdrawing groups e.g. 1,2-dichloroethylene did not undergo cycloaddition to **1a** to any significant extent.

EXPERIMENTAL

All melting points were determined on a Gallenkamp Melting point apparatus and are uncorrected. Infrared spectra were measured with a Perken-Elmer Model 298 spectrophoto-meter. ^{1}H-NMR spectra were recorded on a Varian XL-200 spectrometer with $CDCl_3$ as solvent and TMS as internal reference, chemical shifts are expressed as δ ppm. Analytical data were performed on C,H,N,- Elemental analyzer Carlo Erba 1106. Silica gel 60 (Merck, 230-400 mesh) was used for flash chromatography. The photolysis solution was irradiated internally using a 300 W high-pressure mercury lamp (Eikosha Halos PIH 300) with a Pyrex filter.

Reaction of pyrrol-2,3-diones ***1a-e*** *with equimolar amount of Diazomethane; Synthesis of 2-aryl (methyl)-3,4-dioxo-2-azabicyclo[3.1.0]hexane 3a-e and 4-aryl (methyl)- 1,6a-dihydro-5,6-dioxo-pyrrolo[2,3-d]-pyrazole* ***4a-e*** *.General Procedure :*

A solution of diazomethane 2 mmol in ether (7ml) is added to pyrrol-2,3-diones **1a-e** 2 mmol in ether (30 ml), and the reaction mixture was set aside overnight at RT. By prolonged cooling of the resulting solution at -10 °C, **3a-e** were separated as colorless solids, which were collected by filtration to give 45-56% yield . Evaporation to dryness of the ethereal filtrate gave an orange residue which was purified by flash chroma-

tography, using EtOAc/toluene as eluent to give a pale yellow solid of **4a-e** in 42-53% yield.

1-Methoxy-2-phenyl-2-azabicyclo[3.1.0]hexane-3,4-dione ***(3a)***

Colorless needles, mp.112-114°C, Et_2O/ Petroleum ether (40-60) 48%; IR(KBr) 1745 and 1730 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 1.65 (dd, 2H, J=1.5,7.5 Hz, C_6-H), 3.95 (s, 3H, OCH_3), 4.85 (dd,1H, J=1.5,7.5 Hz, C_5-H), 7.25-7.78 (m, 5H, arom.); ^{13}C-NMR 19.4 (t,C-6), 52.8 (q, OCH_3) ,80.1 (d,C-5), 82.9 (s,C-1), 162.9 (s,C-3), 176.2 (s,C-4).Anal. Calcd. for $C_{12}H_{11}NO_3$ (217.21) C 66.35 H 5.10 N 6.45 Found C 66.11 H 4.98 N 6.22

1-Methoxy-2-(4-methyl phenyl)-2-azabicyclo[3.1.0]hexane-3,4-dione ***(3b)***

Colorless needles, mp.132-133°C, Et_2O/ Petroleum ether (40-60) 52%; IR(KBr) 1745 and 1725 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 1.60 (dd,2H, J=1.5,7.5 Hz,C_6-H), 2.55 (s,3H,CH_3) , 3.82 (s, 3H, OCH_3), 4.88 (dd,1H, J=1.5, 7.5 Hz, C_5-H), 7.30-7.55 (m, 4H, arom.); ^{13}C-NMR 20.6 (t,C-6), 21.4 (s,CH_3) 52.4 (q, OCH_3) , 80.4 (d,C-5), 83.3 (s,C-1), 162.6 (s,C-3), 177.0 (s,C-4); Anal. Calcd. for $C_{13}H_{13}NO_3$ (231.23) C 67.52 H 5.67 N 6.05 Found C 67.24 H 5.46 N 5.89 .

1-Methoxy-2-(4-methoxy phenyl)-2-azabicyclo[3.1.0]hexane-3,4-dione ***(3c)***

Colorless needles, mp.152-154°C, Et_2O/ Petroleum ether (40-60) 56%; IR (KBr) 1740 and 1725 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 1.58 (dd, 2H, J=2, 8 Hz,C_6-H), 3.75 (s, 3H,OCH_3) , 3.98 (s, 3H, OCH_3), 4.95 (dd,1H, J=2, 8 Hz, C_5-H), 6.98-7.68 (m, 4H, arom.); Anal. Calcd. for $C_{13}H_{13}NO_4$ (247.23) C 63.15 H 5.30 N 5.66 Found C 62.88 H 5.23 N 5.45 .

1-Methylthio-2-phenyl-2-azabicyclo[3.1.0]hexane-3,4-dione ***(3d)***

Colorless needles, mp.128-130°C, Et_2O/ n-hexane 48%; IR (KBr) 1745 and 1725 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 1.45 (dd, 2H, J=2, 8 Hz,C_6-H), 2.54 (s, 3H,SCH_3), 4.83 (dd, 1H, J=2, 8 Hz, C_5-H), 7.20-7.58 (m, 5H, arom.); Anal. Calcd. for $C_{12}H_{11}NO_2S$ (233.21) C 61.80 H 4.75 N 6.00 S 13.72 Found C 62.07 H 4.98 N 6.18 S 13.97 .

1-Methylthio-2-methyl-2-azabicyclo[3.1.0]hexane-3,4-dione ***(3e)***

Colorless needles, mp.119-121°C, Et_2O/ n-hexane 45%; IR (KBr) 1740 and 1720 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 1.50 (dd, 2H, J=1.5, 7 Hz,C_6-H), 2.50 (s, 3H,SCH_3), 3.16 (s, 3H, NCH_3), 4.85 (dd, 1H, J= 1.5, 7 Hz, C_5-H); Anal. Calcd. for $C_7H_9NO_2S$ (171.14) C 49.12 H 5.30 N 8.18 S 18.70 Found C 49.35 H 5.55 N 8.36 S 18.90 .

3a-Methoxy-4-phenyl-1,6a-dihydro-5,6-dioxo-pyrrolo[2,3-d]pyrazole ***(4a)***

Pale yellow powder, mp 173-174°C, CH_3CN 45%, IR (KBr) 3340,1755,1730 cm^{-1} for NH and two C=O groups respectively; ^{1}H-NMR ($CDCl_3$) δ 5.09 (s,1H, C_{6a}-H), 3.77 (s,3H, OCH_3), 6.89-7.45 (m, 7 H, 5 arom.,C_3-H and NH); Anal.Calcd. for $C_{12}H_{11}N_3O_3$ (245.21) C 58.77 H 4.52 N 17.13 Found C 58.53 H 4.34 N 16.96 .

3a-Methoxy-4-(4-methyl phenyl)-1,6a-dihydro-5,6-dioxo-pyrrolo[2,3-d]pyrazole ***(4b)***

Pale yellow powder, mp 143-145°C, CH_3CN 48%, IR (KBr) 3300,1750,1730 cm^{-1} for NH and two C=O groups respectively; ^{1}H-NMR ($CDCl_3$) δ 2.49 (s,3H,CH_3), 4.98 (s,1H, C_{6a}-H), 3.80 (s,3H, OCH_3), 6.95-7.50 (m, 6H, 4 arom.,C_3-H and, NH); Anal.Calcd. for $C_{13}H_{13}N_3O_3$ (259.23) C 60.23 H 5.05 N 16.20 Found C 60.02 H 5.11 N 16.00 .

3a-Methoxy-4-(4-methoxy phenyl)-1,6a-dihydro-5,6-dioxo-pyrrolo[2,3-d]pyrazole ***(4c)***

Pale yellow powder, mp 160-162°C, CH_3CN 53%, IR (KBr) 3300,1750,1730 cm^{-1} for NH and two C=O groups respectively; ^{1}H-NMR ($CDCl_3$) δ 3.80 (s,3H, OCH_3), 3.90 (s,3H, OCH_3), 4.86 (s,1H, C_{6a}-H), 7.05-7.72 (m, 6H, 4 arom.,C_3-H and NH); Anal. Calcd. for $C_{13}H_{13}N_3O_4$ (275.23) C 56.73 H 4.76 N 15.26 Found C 56.55 H 4.56 N 14.86 .

3a-Methylthio-4-phenyl-1,6a-dihydro-5,6-dioxo-pyrrolo[2,3-d]pyrazole ***(4d)***

Pale yellow powder, mp 124-126°C, CH_3CN 45%, IR (KBr) 3300,1745,1720 cm^{-1} for NH and two C=O groups respectively; ^{1}H-NMR ($CDCl_3$) δ 2.57 (s,3H, SCH_3), 4.73 (s,1H, C_{6a}-H), 7.02-7.75 (m, 7 H, 5 arom.,C_3-H and NH); Anal.Calcd. for $C_{12}H_{11}N_3O_2S$ (261.21) C 55.17 H 4.24 N 16.08 S 12.25 Found C 55.32 H 4.36 N 16.24 S12.53 .

3a-Methylthio-4-methyl-1,6a-dihydro-5,6-dioxo-pyrrolo[2,3-d]pyrazole ***(4e)***

Pale yellow powder, mp 151-152°C, CH_3CN 42%, IR (KBr) 3300,1745,1720 cm^{-1} for NH and two C=O groups respectively; ^{1}H-NMR ($CDCl_3$) δ 2.57 (s,3H, SCH_3), 3.22 (s,3H,NCH_3), 4.84 (s,1H, C_{6a}-H), 7.22 (s, 1H,C_3-H), 7.32 (sb,1H, NH); Anal.Calcd. for $C_7H_9N_3O_2S$ (199.14) C 42.21 H 4.55 N 21.09 S 16.07 Found C 41.91 H 4.44 N 20.89 S 16.33 .

Reaction of pyrrol-2,3-diones ***1a-e*** *with an excess of Diazomethane; Synthesis of 4-aryl(methyl)-1-methyl-5,6-dioxo-pyrrolo[2,3-d]pyrazole* ***5a-e*** *General Procedure:*

A solution of compound **1a-e** (1 mmol) in ether (25 ml) was treated with an excess of diazomethane (3 mmol) in ether (10ml) under the conditions described above. Removal of the solvent gave a gummy orange residue which was purified by flash chromatography, using toluene /acetone (10:3) as eluent. The first band gave the cyclopropane derivatives **3a-e** in 8-16% yield; whereas the second one was identified as **5a-e** in 40-48% yield.

*Methylation of compounds **4a-e** to **5a-e**.*

A mixture of **4a-e** (1 mmol) and diazomethane (3 mmol) in ether (25 ml) were allowed to stand overnight at RT. Removal of solvent afforded the N-methyl derivatives **5a-e**, identical (IR. and ^{1}H-NMR) with the material obtained as above, quantitatively.

*1-Methyl-3a-Methoxy-4-phenyl-6aH-5,6-dioxo-pyrrolo[2,3-d]pyrazole **(5a)***

White powder, mp 161°C, 44%, IR (KBr) 1745,1725 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 3.67 (s, 3H, NCH_3), 3.82 (s,3H, OCH_3), 4.95 (s,1H, C_{6a}-H), 7.18-7.75 (m, 6 H, 5 arom. and C_3-H); ^{13}C-NMR 42.5 (q, NCH_3), 53.3 (q, OCH_3), 79.4 (d,C-6a), 81.6 (s, C-3a), 139.8 (d,C-3), 163.2 (s, C-5), 176.6 (s, C-6); Anal.Calcd. for $C_{13}H_{13}N_3O_3$ (259.23) C 60.23 H 5.05 N 16.20 Found C 59.93 H 5.00 N 16.06 .

*1-Methyl-3a-Methoxy-4-(4-methyl phenyl)- 6aH-5,6-dioxo-pyrrolo[2,3-d]pyrazole **(5b)***

White powder, mp 152°C, 45%, IR (KBr) 1750,1730 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 2.49 (s,3H,CH_3), 3.55 (s, 3H, NCH_3), 3.75 (s,3H, OCH_3), 4.98 (s,1H, C_{6a}-H), 7.22-7.80 (m, 5H, 4 arom., and C_3-H); Anal. Calcd. for $C_{14}H_{15}N_3O_3$ (273.26) C 61.53 H 5.53 N 15.37 Found C 61.24 H 5.31 N 15.37.

*1-Methyl-3a-Methoxy-4-(4-methoxy phenyl)- 6aH-5,6-dioxo-pyrrolo[2,3-d]pyrazole **(5c)***

White powder, mp 169-170°C, 48%, IR (KBr) 1740,1720 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 3.70 (s,3H, OCH_3), 3.55 (s, 3H, NCH_3), 3.90 (s,3H, OCH_3), 4.96 (s,1H, C_{6a}-H), 7.15-7.87 (m, 5H, 4 arom., and C_3-H); Anal. Calcd. for $C_{14}H_{15}N_3O_4$ (289.26) C 58.13 H 5.23 N 14.52 Found C 58.11 H 5.21 N 14.50.

*1-Methyl-3a-methylthio-4-phenyl-6aH-5,6-dioxo-pyrrolo[2,3-d]pyrazole **(5d)***

White powder, mp 152°C, 40%, IR (KBr) 1740,1720 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 2.57 (s,3H, SCH_3), 3.50 (s, 3H, NCH_3), 4.89 (s,1H, C_{6a}-H), 7.11-7.75 (m, 6 H, 5 arom., and C_3-H); Anal.Calcd. for $C_{13}H_{13}N_3O_2S$ (275.23) C 56.73 H 4.76 N 15.26 S 11.62 Found C 56.61 H 4.59 N 15.23 S 11.48 .

*1,4-Dimethyl-3a-methylthio-6aH-5,6-dioxo-pyrrolo[2,3-d]pyrazole **(5e)***

White powder, mp 139°C, 41%, IR (KBr), 1745,1720 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 2.57 (s,3H, SCH_3), 3.35 (s,3H, NCH_3), 3.52 (s,3H, NCH_3), 4.80 (s,1H, C_{6a}-H), 7.35 (s, 1H, C_3-H), Anal.Calcd.

for $C_8H_{11}N_3O_2S$ (213.17) C 45.07 H 5.20 N 19.70 S 15.01 Found C 44.83 H 5.06 N 19.65 S 15.00

Photocycloaddition of 5-methoxy-N-phenyl-pyrrol-2,3-dione ***1a*** *to olefins* ***8a-d*** *General Procedure:*

A solution of **1a** (12 mmol) and an olefin **8** (30 mmol) in dimethoxyethane (300 ml) was irradiated for 45 min. under ice cooling. After removal of the solvent, the residue was subjected to flash chromatography using hexane-AcOEt (3:2) as eluent to separate and to purify the two diastereoisomers **9a,b** and **10a-d**.

1-Methoxy-2,7-diphenyl-2-azabicyclo[3.2.0]heptane-3,4-dione ***9a*** *(exo-isomer):*

Colorless needles mp 215-217°C, CH_2Cl_2-Et_2O 45%, IR (KBr) 1740,1720 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 1.68 (m, 2H,C_6-H), 4.83 (1H, t, J=9Hz, C_5-H), 4.17 (1H, t, J=10 Hz, C_7-H), 3.72 (s,3H, OCH_3), 6.88-7.55 (m, 10H, arom.); ^{13}C-NMR, 24.6 (t, C_6), 53.8 (d, C_7), 57.4 (d, C_5), 79.5 (s, C_1), 162.8 (s, C_3), 178.5 (s, C_4). Anal.Calcd. for $C_{19}H_{17}NO_3$ (307.33) C 74.25 H 5.57 N 4.55 Found C 73.98 H 5.34 N 4.56

1-Methoxy-2,7-diphenyl-2-azabicyclo[3.2.0]heptane-3,4-dione ***10a*** *(endo-isomer):*

Colorless needles 175-117°C CH_2Cl_2-Et_2O 15%, IR (KBr) 1745,1720 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 1.49 (m, 2H,C_6-H), 4.90 (1H,t, J=9Hz, C_5-H), 4.75 (1H, t, J=9 Hz, C_7-H), 3.85 (s,3H, OCH_3), 6.95-7.75 (m, 10H, arom.); ^{13}C-NMR, 26.2 (t, C_6), 43.8 (d, C_7), 57.9 (d, C_5), 79.9 (s, C_1), 163.4 (s, C_3), 175.2 (s, C_4). Anal.Calcd. for $C_{19}H_{17}NO_3$ (307.33) C 74.25 H 5.57 N 4.55 Found C 74.12 H 5.29 N 4.43

7-Ethoxy-1-methoxy-2-phenyl-2-azabicyclo[3.2.0]heptane-3,4-dione ***9b*** *(exo-isomer):*

Colorless needles, mp 145-147°C, CH_2Cl_2-Et_2O 18%, IR (KBr) 1735,1715 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 0.95 (t, 3H, J= 7Hz, CH_3), 1.58 (m, 2H,C_6-H), 3.15 (q, 2H,J=7Hz, CH_2), 3.72 (s, 3H, OCH_3), 4.12 (1H, t, J=8 Hz, C_7-H), 4.95 (1H, t, J=9 Hz, C_5-H), 7.15-7.45 (m, 5H, arom.); ^{13}C-NMR, 14.6 (q), 29.7 (t, C_6), 56.2 (d, C_5), 62.2 (t), 80.8 (s, C_1), 82.1 (d, C_7), 162.1 (s, C_3), 177.6 (s, C_4). Anal.Calcd. for $C_{15}H_{17}NO_4$ (275.28) C 65.44 H 6.22 N 5.08 Found C 65.18 H 5.97 N 4.84

7-Ethoxy-1-methoxy-2-phenyl-2-azabicyclo[3.2.0]heptane-3,4-dione ***10b*** *(endo-isomer):*

Colorless needles, mp 148-149°C, CH_2Cl_2-Et_2O 65%, IR (KBr) 1730,1715 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 1.12 (t, 3H, J=7 Hz, CH_3), 1.32 (m,2H, C_6-H), 3.35 (q, 2H,J=7Hz CH_2), 3.80 (s, 3H,OCH_3), 4.55 (1H, dd, J = 6, 8 Hz, C_7-H), 5.12 (1H, t, J=9 Hz C_5-H), 7.15-7.45 (m, 5H, arom.); ^{13}C-NMR, 15.0 (q), 31.5 (t, C_6), 56.3 (d, C_5), 61.9 (t), 80.3 (s, C_1), 76.6 (d, C_7), 162.7 (s, C_3), 178.4 (s, C_4). Anal.Calcd. for $C_{15}H_{17}NO_4$ (275.28) C 65.44 H 6.22 N 5.08 Found C 65.29 H 6.01 N 5.24

1-Methoxy-7-phenoxy-2-phenyl-2-azabicyclo[3.2.0]heptane-3,4-dione ***10c*** *(endo-isomer):*

Colorless needles, mp 179-181°C, CH_2Cl_2-EtOH 70%, IR (KBr) 1750,1730 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 1.39 (m,2H, C_6-H), 3.85 (s, 3H, OCH_3), 4.48 (1H, dd, J= 5, 7.5 Hz, C_7-H), 5.09 (1H, t, J=8 Hz, C_5-H), 6.65-7.73 (m, 10H, arom.); ^{13}C-NMR, 25.9 (t, C_6), 77.8 (d, C_7), 55.8 (d, C_5), 79.9 (s, C_1), 161.4 (s, C_3), 176.3 (s, C_4). Anal.Calcd. for $C_{19}H_{17}NO_4$ (323.32) C 70.57 H 5.30 N 4.33 Found C 70.32 H 5.06 N 4.34

7-Cyclohexyloxy-1-methoxy-2-phenyl-2-azabicyclo[3.2.0]heptane-3,4-dione ***10d*** *(endo-isomer):*

Colorless needles, mp 205-207°C, CH_2Cl_2-EtOH 78 %, IR (KBr) 1745,1730 cm^{-1} for two C=O groups; ^{1}H-NMR ($CDCl_3$) δ 1.10-1.85 (m, 12H, $5CH_2$ and 2H, C_6-H), 3.32 (m, 1H, OCH), 3.80 (s, 3H, OCH_3), 4.81(1H, dd, J=6, 8Hz, C_7-H), 5.03 (m,1H, C_5-H), 6.95-7.63 (m, 5H, arom.); ^{13}C-NMR, 25.9 (t, C_6), 76.4 (d, C_7), 55.8 (d, C_5), 80.3 (s, C_1), 161.4 (s, C_3), 176.3 (s, C_4) Anal.Calcd. for $C_{19}H_{23}NO_4$ (329.37) C 69.28 H 7.04 N 4.25 Found C 69.00 H 6.95 N 4.20

ACKNOWLEDGMENT

The author is deeply grateful to Prof. Dr. G. Kollenz, Institute for Organic Chemistry , Karl-Fransenz. University , Graz Austria for valuable discussions and continuos effective support.

REFERENCES

1. a)Tsuda, Y.; Isobe, K.; Ukai, A. J. Chem. Soc., Chem.Commun., **1971**,1554;
   b).Sano, T ; Tsuda, Y. Heterocycles, **1976**, **4** ,1316;
   c) Sano, T.; Toda, J.; Kashiwaba, N.; Tsuda, Y. , Heterocycles, **1981**,16,1151;
   d) Tsuda, Y.; Oshima, T.; Sano, T.; Toda, J., Heterocycles, **1982**, 19 , 2053.
2. a) Tsuda, Y.; Isobe, K.; J. Chem. Soc., Chem.Commun.,**1971**, 1555;
   b) Tsuda, Y.; Ukai, A.; Isobe, K., Tetrahedron Lett., **1972**, 3136.
3. Sano, T.; Toda, J. ; Tsuda, Y., heterocycles, **1982**, 18, 229.
4. Fulloon, B; El-Nabi, H. A. A.; Kollenz, G; Wentrup, C, Tetrahedron Lett., **1995**, 36, 6547.
5. Saalfrank, R.w.; lutz,T.; Hörner,B.; Gündel, J.; Peters, K.; H.G.von Schnering, Chem. Ber., **1991**, 124, 2289.
6. El-Nabi, H.A.A. ; J. Chem Res. (S) . **1996**, 10, 466-467.
7. Kollenz, G.; Penn, G.; Theuer, R; Fabian, W.M.F.; El-Nabi, H.A.A ; Zhang, X., Peters, K.; Peters, E.M.; H.G. von Schnering , Tetrahedron,**1996** , 52, 5427.

8. a) Kollenz, G.; Kappe, C.O.; Nabey, H. A. A , Heterocycles, **1991**, 32 , 669.
b) El-Nabi, H. A. A.; Org. Prep. and Proced. Inter. **1997**, 29(1), 41.
9. Kappe, C.O.; Kollenz, G.; Toung, R. L.; Wentrup, C.; J. Chem. Soc. Commun., **1992**, 487.
10. a) Sano, T; Horiguchi, Y; Toda, J; Imafuku, K; Tsuda, Y, Chem. Pharm. Bull., **1984**, 32, 497.
b) Sano, T; Horiguchi, Y; Tsuda, Y.; Furuhata, K.; Takayanagi, H; Ogura, H; Chem. Pharm. Bull., **1987**,35, 9.
11. Sano, T; Tsuda, Y ; Ogura, H; Furuhata, K; Litaka, Y; Heterocycles, **1976**, 4, 1233.

(*Received in UK* 30 *September* 1996; *revised* 25 *November* 1996; *accepted* 28 *November* 1996)