Asian Journal of Chemistry Vol. 20, No. 2 (2008), 954-962

Generation and Trapping of 2-Methyl-3-phenyl-4-oxoquinazolinium-1-methanide: Routes to Pyrrolo[1,2-a]quinazolinones

M. AZOUZ*, K. LAMARA, M. TEGUICHE† and R.K. SMALLEY‡
Department of Chemistry, Oum-El-Bouaghi University
Oum-El-Bouaghi 04000, Algeria
E-mail: m.azouz@mail.lagh-univ.dz

Azomethine ylide, prepared from quinazolinium salt, undergoes 1,3-dipolar cycloaddition with alkyne dipolarophiles to produce substituted pyrroles. In fact, when alkene dipolarophiles were introduced, a novel compound *i.e.*, substituted pyrrolo[1,2-a]quinazolinones have resulted from this work.

Key Words: Quinazoline, Azomethine ylides, 1,3-Dipolar cycloadditions.

INTRODUCTION

1,3-Dipolar cycloaddition of azomethine ylides has received much attention, as an entry to new five membered-nitrogen-containing rings[1]. The use of oxazoles[2], indoles[1], indolines[3], imidazoles[4] and triazoles[5-7] as a source of azomethine ylides has been well documented. To date, however, quinazolines systems have not been studied. We now report the preparation and the stereoselective [3+2] cycloadditions 2-methyl-3-phenyl-4-oxoquinazolinium azomethine ylide **3** with various dipolarophiles. The cycloaddition with dialkyl acetylenedicarboxylates gave the substituted pyrroles **5** and **6** *via* sigmatropic rearrangement of the initially formed cycloadduct **4**. Alkene dipolarophiles yielded mixtures of *exo*- and *endo*-isomers **8-13**, the cycloadduct possessing the *exo*-geometry being predominant. The cycloaddition products are novel tri- and tetracyclic structures.

EXPERIMENTAL

Melting points were measured on a Buchi melting point apparatus and are uncorrected. IR spectra of liquids were recorded as a thin film and those of solids as Nujol mulls with a Jasco 460 plus FT-IR spectrometer. NMR spectra were measured on a 300 MHz instrument (Bruker, J.F.B.

†Department of Chemistry, Guelma University, Guelma 24000, Algeria.
‡Department of Chemistry and Applied Chemistry, Salford University, Salford, U.K.

288) with tetramethylsilane as an internal reference and $CDCl_3$ or deuterioacetone as solvents. *J* values are given in Hz. The terms J_{gem} and J_{vic} refer to *geminal* and *vicinal* proton pairs, respectively. Mass spectra were measured on a Finnegan 4000 mass spectrometer. Microanalyses were measured on a Perkin-Elmer model 240 CHN analyzer. TLC. were conducted on CamLab. Polygram silica G/UV_{254} or alumina N/UV_{254} plates. Flash chromatography was carried out on silica gel 60 (Merck 9385). Medium pressure column chromatography on silica gel 60 H (Merck 7736).

Preparation of 2-methyl 3-phenylquinazolin-4-one

N,N'-Diphenylacetamidine: In a 50 mL round-bottomed flask was placed ethyl orthoacetate (8.5 g), aniline (9.3 g) and *p*-toluenesulphonic acid monohydrate (0.9 g). The mixture was heated and ethanol rapidly began to distilled. The distillation of ethanol then slowed down and the temperature raised from 90 to 196 °C. After 2.5 h the distillation of ethanol stopped and the reaction mixture was kept overnight at 107 °C. Aniline and N-phenylacetamidate were removed by steam distillation. The dark residue obtained was crystallized from aqueous-ethanol to give brown needles of N,N'-diphenylacetamidine (10 g, 45 % yield); m.p. 134-135 °C (lit., m.p. 134.5-136 °C).

2-Methyl-3-phenylquinazolin-4-one: A mixture of equimolar amounts of anthranilic acid (1.37 g) and N,N'-biphenylacetamidine (2.1 g) was heated under air at reflux (150 °C) for 45 min using an oil bath. The reaction occurred upon complete fusion of the mixture and a condensate appeared in the upper part of the flask. The dark residue was dissolved in dichloromethane, washed with water (30 mL) and then with a 2 N NaOH solution (2 × 30 mL). The solvent was dried over $MgSO_4$ and evaporated to give a brown residue which purified by flash chromatography on silica with light petrol-ethyl acetate (7:3, v/v) as an eluant to give 2-methyl 3-phenylquinazolin-4-one as a yellow solid (1.4 g, 63 % yield), m.p. 144-145 °C (lit., m.p. 148-149 °C)[8].

CYCLOADDITIONS

With alkynes dipolarophiles

General method: To a solution of 2-methyl-3-phenylquinazolin-2-one (0.22 g) in dry dichloromethane (3 mL) under a nitrogen atmosphere, was added trimethylsilylmethyltriflate (0.20 mL). The mixture was stirred at room temperature for 15 h. After removal of the solvent, the residual iminium salt was dissolved in dry acetonitrile (5 mL). Dialkyl acetylenedicarboxylate (0.98 mmol) and CsF (0.15 g, 0.98 mmol) were added and the mixture was stirred for 1h. The solvent was evaporated, 10 % NaOH (10 mL) was added and the mixture was extracted with CH_2Cl_2 (2 × 15 mL). The extracts were combined, washed with water (2 × 15 mL) and dried

over $MgSO_4$. Removal of the solvent gave a brown residue, which was chromatographed on silica with CH_2Cl_2-ethyl acetate (9.5:0.5; v/v) as an eluant, affording cycloadducts **6** and **7** (70 and 61 % yield, respectively).

2-[3',4'-*Bis*(methoxycarbonyl)-2'-methyl-1'-pyrrolyl]-N-phenyl-benzamide (6): Orange syrup (70 % yield). ν_{max}(nut)/(cm^{-1}) 3311 (NH), 1728 (ester C=O), 1655 (amide C=O); δ_H (ppm, $CDCl_3$) 2.13 (3H, s, CH_3-C-2'), 3.69 (3H, s, OMe), 3.74 (3H, s, OMe), 7.03 (1H, m, aromatic), 7.19 (2H, m, aromatic), 7.21 (1H, s, 5'-H), 7.28 (2H, d, aromatic), 7.52 (3H, m, 3,4,5-H), 7.61 (1H, s, N-H), 7.83 (1H, dd, 6-H); δ_C (ppm, $CDCl_3$) 51.5 and 51.8 (MeO), 165.2 and 162.9 (ester C=O), 165.2 (amide C=O), 140.8, 139.2, 131.5, 125.2, 110.8 and 110.0 (quaternary C), 118.7 (pyrrole C-5'), 132.5, 128.7, 127.9, 125.4, 124.1, 120.4, 120.3 (aromatic CH), 11.8 (CH_3-C-2'); m/z (CI, NH_3) 409 MNH_4^+); 393 (MH^+); (found: MH^+ 393.1440. $C_{22}H_{20}N_2O_5$ requires: 393.1450).

2-[3',4'-*Bis*(ethoxycarbonyl)-2'-methyl-1'-pyrrolyl]-N-phenyl-benzamide (7): Yellow syrup (61%). ν_{max}(nut)/cm^{-1} 3336 (NH), 1725 (ester C=O), 1650 (amide C=O); δ_H (ppm, $CDCl_3$) 1.32-1.46 (6H, m, $2CH_3$), 2.16 (3H, s, CH_3- C-2'), 3.68-3.82 (4H, m, $2CH_2$), 7.06 (1H, m, aromatic), 7.17 (2H, m, aromatic), 7.21 (1H, s, 5'-H), 7.28 (2H, d, aromatic), 7.52 (3H, m, 3,4,5-H), 7.68 (1H, s, N-H), 7.80 (1H, dd, 6-H); δ_C (ppm, $CDCl_3$) 11.6 and 12.0 (CH_3), 51.2 and 51.8 (CH_2), 165.0 and 162.5 (ester C=O), 165.2 (amide C=O), 140.8, 139.0, 131.3, 125.2, 111.0 and 110.0 (quaternary C), 118.5 (pyrrole C-5), 132.5, 128.5, 128.0, 125.6, 124.0, 120.4, 120.2 (aromatic CH), 11.8 (CH_3-C-2); m/z (CI, NH_3) 438 MNH_4^+), 421 (MH^+), (found: MH^+ 421.1760. $C_{24}H_{24}N_2O_5$ requires: 421.1763).

With alkenes dipolarophiles

General method: A solution of 2-methyl 3-phenylquinazolin-2-one (0.22 g) and trimethylsilylmethyltriflate (0.20 mL) in dry dichloromethane (3 mL) under a nitrogen atmosphere was stirred at room temperature for 15 h. The solvent was removed and to the residual immonium salt was added dry acetonitrile or dichloromethane (5 mL), N-maleimide (0.98 mmol) and CsF (0.15 g), the mixture was stirred for 2 h at 60 °C and then worked up as described in the above procedure. Chromatographic separation on silica with light petrol-ethyl acetate (7:3; v/v) as an eluant afforded the corresponding mixture of cycloadducts. Repeated chromatography on silica with CH_2Cl_2-ethyl acetate (9.5:0.5; v/v) as an eluant gave cycloadducts **8-10**. Further elution gave cycloadduct **11-13**.

6a,8-Dimethyl-6-phenyl-6a,6b,9a,10-tetrahydro-6H-6,8,10a-triaza-pentaleno[2,1-a]naphthalene-5,7,9-trione (8): White crystals (37 % yield), m.p. 175-177 °C (from light petrol-CH_2Cl_2). ν_{MAX}(Nujol mull)/(cm^{-1}) 1711 (maleimide C=O), 1653 (amide C=O); δ_H (ppm, d^6 acetone) 7.78, 7.75-7.72, 7.13, 6.93 and 6.55 (9H, aromatic protons), 4.60 (1H, dd, J_{gem}

13, J_{vic} < 1, 3-H_{exo}), 4.0(1H, dd, J_{gem} 13, J_{vic} 8.0, 3-H_{endo}), 3.6-3.8 (2H, m, 1-H_a and 2-H_b overlap signals), 2.94 (3H, s, N-CH_3), 1.5 (3H, s, CH_3-C-10a); δ_C (ppm, d^6 acetone) 175.7 and 178.3 (maleimide C=O), 163.1 (amide C=O), 146.3, 140.7, 118.3 and 68.4 (quaternary C), 130.2, 128.5, 127.8, 124.3, 120.7, 115.4 and 111.6 (aromatic CH), 39.5 (C-1), 43.4 (C-2), 33.5 (C-3); 26.8 (N-CH_3), 16.4 (CH_3-C10a). Found: C, 69.70; H, 5.22; N, 13.34. $C_{21}H_{19}N_3O_3$ requires C, 69.79; H, 5.30; N, 13.28.

8-Ethyl-6a-methyl-6-phenyl-6a,6b,9a,10-tetrahydro-6H-6,8,10a-triaza-pentaleno[2,1-a]naphthalene-5,7,9-trione (9): White crystals, (33 % yield), mp 182-183 °C (from light petrol-CH_2Cl_2). ν_{max}(Nujol mull)/(cm^{-1}) 1705 (maleimide C=O), 1660 (amide C=O); δ_H (ppm, d^6-acetone) 7.78, 7.73, 7.70, 7.79, 7.40, 7.30, 7.13, 6.93 and 6.55 (9H, aromatic protons), 4.52 (1H, dd, J_{gem} 13, J_{vic} < 1, 3-H_{exo}), 3.9 (1H, dd, J_{gem} 13, J_{vic} 8.0, 3-H_{endo}), 3.4-3.7 (2H, m, 1-H_a and 2-H_b overlap signals), 2.90 (2H, q, N-CH_2CH_3), 1.67 (3H, t, N-CH_2CH_3), 1.5 (3H, s, CH_3-C-10a); δ_C (ppm, d^6 acetone) 173.5 and 177.7 (maleimide C=O), 163.1 (amide C=O), 146.3, 140.7, 118.3 and 68.4 (quaternary C), 130.2, 128.7, 127.6, 124.3, 120.5, 115.4 and 111.6 (aromatic CH), 39.5 (C-1), 43.4 (C-2), 33.3 (C-3), 34.3 (N-CH_2CH_3), 16.1 (CH_3-C10a), 12.6 (N-CH_2CH_3). Found: C, 70.28; H, 5.56; N, 13.34. $C_{22}H_{21}N_3O_3$ requires C, 70.38; H, 5.64; N, 11.25.

6a-Methyl-6,8-diphenyl-6a,6b,9a,10-tetrahydro-6H-6,8,10a-triaza-pentaleno[2,1-a]naphthalene-5,7,9-trione (10): White crystals (40 % yield), m.p. 194-195 °C (from light petrol-CH_2Cl_2. ν_{max} (Nujol mull)/ (cm^{-1}) 1716 (maleimide C=O), 1655 (amide C=O); δ_H (ppm, d^6 acetone) 7.78, 7.75-7.72, 7.13, 6.93 and 6.55 (14H, aromatic protons), 4.60 (1H, dd, J_{gem} 13, J_{vic} < 1, 3-H_{exo}), 4.0 (1H, dd, J_{gem} 13, J_{vic} 8.0, 3-H_{endo}), 3.6-3.8 (2H, m, 1-H_a and 2-H_b overlap signals), 1.5 (3H, s, CH_3-C-10a); δ_C (ppm, d^6 acetone) 175.2 and 173.4 (maleimide C=O), 163.5 (amide C=O), 146.3, 140.6, 118.3 and 68.7 (quaternary C), 130.5, 128.8, 127.6, 124.4, 120.6, 115.3 and 111.4 (aromatic CH), 40.0 (C-1), 43.9 (C-2), 33.2 (C-3), 17.0 (CH_3-C10a). Found: C, 73.61; H, 5.15; N, 9.90. $C_{26}H_{21}N_3O_3$ requires C, 73.74; H, 5.00; N, 9.92.

6a,8-Dimethyl-6-phenyl-6a,6b,9a,10-tetrahydro-6H-6,8,10a-triaza-pentaleno[2,1-a]naphthalene-5,7,9-trione (11): White crystals (19 % yield), m.p. 221-222 °C (from light petrol-CH_2Cl_2). ν_{max} (Nujol mull)/(cm^{-1}) 1716 (maleimide C=O), 1655 (amide C=O); δ_H (ppm, $CDCl_3$) 8.1, 7.55-7.2 (9H, aromatic protons), 3.86 (1H, dd, J_{gem} 10, J_{vic} 2.4, 3-H_{exo}), 3.72 (1H, dd, J_{gem} 10, J_{vic} 8.1, 3-H_{endo}), 3.60 (1H, d, J H_a, H_b 9.0 1-H_a), 3.40 (1H, m, 2-H_b), 3.02 (3H, s, N-CH_3) 1.6 (3H, s, CH_3-C-10a); δ_C (ppm, $CDCl_3$) 175.4 and 178.2 (maleimide C=O), 163.3 (amide C=O), 146.3, 140.3, 118.2 and 68.5 (quaternary C), 130.2, 128.8, 127.8, 124.2, 120.6, 115.4 and 111.2 (aromatic CH), 40.2 (C-1), 43.4 (C-2), 33.5 (C-3), 26.8 (N-CH_3), 16.9 (CH_3-C10a). Found: C, 69.85; H, 5.20; N, 13.22. $C_{21}H_{19}N_3O_3$ requires C, 69.79; H, 5.30; N, 13.28.

8-Ethyl-6a-methyl-6-phenyl-6a,6b,9a,10-tetrahydro-6*H*-6,8,10a-triaza-pentaleno[2,1-a]naphthalene-5,7,9-trione (12): White crystals, (16 % yield), m.p. 226-228 °C (from light petrol-CH_2Cl_2). ν_{max}(Nujol mull)/(cm^{-1}) 1716 (maleimide C=O), 1655 (amide C=O); δ_H (ppm, $CDCl_3$) 8.0, 7.0-8.2 (9H, aromatic protons), 3.86 (1H, dd, J_{gem} 10, J_{vic} 2.4, 3-H_{exo}), 3.72 (1H, dd, J_{gem} 10, J_{vic} 8.1, 3-H_{endo}), 3.60 (1H, d, J H_a, H_b 9.0 1-H_a), 3.40 (1H, m, 2-H_b); 1.6 (3H, s, CH_3-C-10a); δ_C (ppm, $CDCl_3$) 173.7 and 177.9 (maleimide C=O), 163.1 (amide C=O), 146.3, 140.3, 118.2 and 68.5 (quaternary C), 130.1, 128.7, 127.5, 124.2, 120.6, 115.4 and 111.2 (aromatic CH), 39.6 (C-1), 43.7 (C-2), 33.3 (C-3), 34.1 (N-CH_2CH_3), 16.5 (CH_3-C10a), 12.8 (N-CH_2CH_3). Found: C, 70.20; H, 5.68; N, 11.10. $C_{22}H_{21}N_3O_3$ requires C, 70.38; H, 5.64; N, 11.19.

6a-Methyl-6,8-diphenyl-6a,6b,9a,10-tetrahydro-6*H*-6,8,10a-triaza-pentaleno[2,1-a]naphthalene-5,7,9-trione (13): White crystals (19 % yield), m.p. 238-239 °C (from light petrol-CH_2Cl_2). ν_{max}(Nujol mull)/(cm^{-1}) 1716 (maleimide C=O), 1655 (amide C=O); δ_H (ppm, $CDCl_3$) 8.0, 7.0-8.2 (14H, aromatic protons), 3.91 (1H, dd, J_{gem} 10, J_{vic} 2.5, 3-H_{exo}), 3.8 (1H, dd, J_{gem} 10, J_{vic} 8.3, 3-H_{endo}), 3.67 (1H, d, J Ha, Hb 9.0 1-Ha), 3.53 (1H, m, 2-Hb); 1.7 (3H, s, CH_3-C-10a); δ_C (ppm, $CDCl_3$) 173.4 and 175.2 (maleimide C=O), 163.5 (amide C=O), 146.3, 140.6, 118.3 and 68.7 (quaternary C), 130.5, 128.8, 127.6, 124.4, 120.6, 115.3 and 111.4 (aromatic CH), 40.0 (C-1), 43.9 (C-2), 33.2 (C-3), 16.7 (CH_3-C10a). Found: C, 73.61; H, 5.15; N, 9.90. $C_{26}H_{21}N_3O_3$ requires C, 73.74; H, 5.00; N, 9.92.

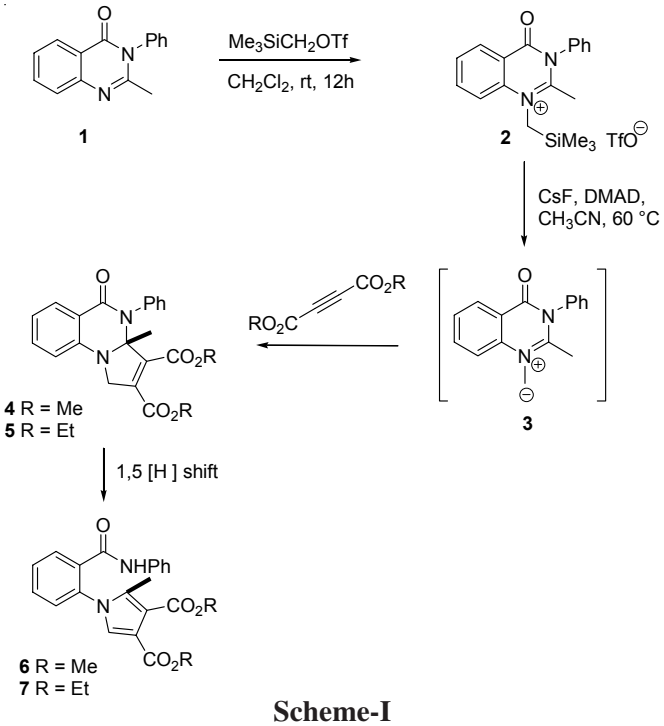
3a-Methyl-5-oxo-4-phenyl-1,2,3,3a,4,5-hexahydropyrrolo[1,2-a]quinazoline-3-carbonitrile (14): Pale yellow crystals (12 % yield) m.p. 141-142 °C (from light petrol-EtOAc). ν_{max}(Nujol mull)/(cm^{-1}) 2235 (CN), 1660 (amide C=O); δ_H (ppm, $CDCl_3$) 7.78-694 (9H, m, aromatic protons), 3.34 (2H, m, 3-CH_2), 3.03 (1H, dd, *J* 7.4, 7.4, 1-H_a), 2.32 (2H, m, 2-CH_2), 1.25 (3H, s, CH_3-C10a); δ_C (ppm, $CDCl_3$) 163.1 (amide C=O), 146.3, 140.8, 118.6 and 73.6 (quaternary C), 130.3, 128.7, 127.6, 124.1, 115.3 and 111.6 (aromatic CH), 119.2 (CN), 21.7 (C-1), 25.2 (C-2), 30.1 (C-3), 16.2 (CH_3-C10a). Found: C, 75.09, H, 5.55; N, 13.94. $C_{19}H_{17}N_3O$ requires: C. 75.23; H, 5.65; N, 13.85.

RESULTS AND DISCUSSION

The alkylation of 2-methyl-3-phenylquinazolin-4-one (**1**) was carried out with trimethylsilylmethyl trifluoromethanesulfonate in dichloromethane at room temperature for 12 h. Upon completion of the reaction (TLC analysis), the solvent was removed, affording **2** with sufficient purity to be used without further purification. Product **2** was dissolved in acetonitrile. Azomethine ylid generation was conducted using a previously described procedure[4,9] by introduction of dimethyl or diethyl acetylenedicarboxylate

followed by CsF. The mixture was then stirred at 60 °C for 1 h. After removal of solvent, sodium hydroxide was added and the mixture was extracted with dichloromethane. The combined organic extracts was concentrated by evaporation. Chromatographic purification on a silica gel (CH_2Cl_2/AcOEt) gave the unexpected products **6** and **7** in 70 and 61 % yield, respectively. The structures of compounds **6** and **7** were established from mass spectroscopy, IR, ^1H and ^{13}C NMR spectra.

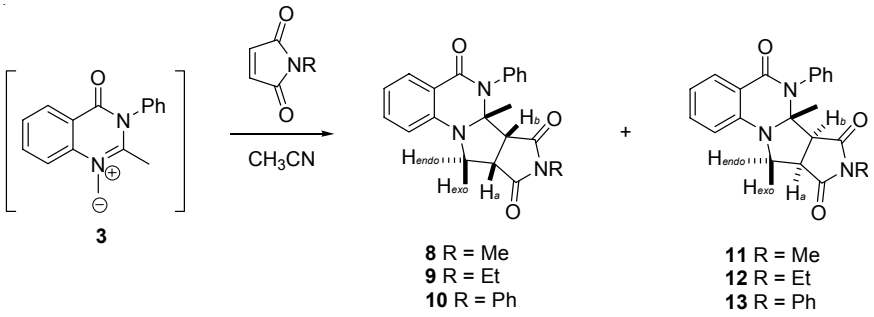
The IR spectra showed a strong (N-H) absorption at 3366-3311 cm^{-1}. More interestingly, is the presence of an exchangeable proton in the NMR spectra at 7.61 and 7.68 ppm, the presence of a singlet at 7.21 and 7.19 ppm and the absence of the methylene group around 3.00 ppm. In addition, the signal due to methyl group at C-2, expected around 1.4 ppm, suffered from a strong downfield shift of *ca.* 0.7 ppm. A satisfactory explanation of these spectroscopic datas is found in structures **6** and **7**. The reaction involves does not stop to the initial cycloadducts **4** and **5**. These latter compounds undergo a rapid ring-opening *via* a 1,5-H migration yielding substituted pyrroles **6** and **7** (**Scheme-I**).



Scheme-I

In attempts to prevent the C-2-N-3 quinazolinone bond cleavage, dipole **3** was allowed to react with other dipolarophiles. Cycloadditions of N-substituted maleimides with azomethine ylid **3** in acetonitrile gave

mixtures of cycloadducts **8-13**, in each cases the *exo*-stereochemistry being favored. To our knowledgde, compounds **8-13** are the first cycloadducts arising from dipole of type **3** with alkene dipolarophiles (**Scheme-II**).



3

8 R = Me
9 R = Et
10 R = Ph

11 R = Me
12 R = Et
13 R = Ph

Scheme-II

^{1}H NMR spectra of *exo*-cycloadducts **8-10** showed resonance of the exact number of aromatic protons at 6.55-7.85 ppm. Four atoms labelled as H_a, H_b, H_{exo} and H_{endo} stood out in the spectra and were readily assigned (Fig. 1). H_{exo} atoms appeared at 4.55-4.65 ppm and were deshielded by the dicarboxyimido group. However; its geminal partner H_{endo} was not deshielded and appeared at 3.90-4.10 ppm. These germinal pairs included the expected *J* coupling constant values of 13.0-13.3 Hz. The vicinal coupling constant of H_{exo} atoms is extremely small and was only observed in the extended spectrum. In sharp contrast the H_{endo} atoms displayed a *J* values of 7.0-8.0 Hz. The multiplet at 3.60-3.80 ppm was assigned to the overlapping signals of H_a and H_b. The angular methyl group appeared as a singlet a 1.55-1.45 ppm. Iradiation of the H_{endo} signal at 4.00 ppm affected the one of H_{exo} at 4.60 ppm, which appeared as a doublet.

^{1}H NMR spectra of *endo*-cycloadducts **11-13** showed identical aromatic protons resonances at 7.00-7.60 ppm. The doublet of doublets at 7.90-8.10 ppm was assigned to 8-H which was deshielded by the neighbouring (C_9=O) carbonyl group. The four aliphatic protons (H_a, H_b, H_{exo} and H_{endo}) were well separated (Fig. 2). H_{exo} atoms appeared at 3.86-3.91 ppm and the geminal coupling constants with H_{endo} (multiplet at 3.72-3.80 ppm) is about 10.0 Hz. H_a and H_b appeared at 3.60-3.67 and 3.40-3.53 ppm, respectively. Vicinal H_a and H_b displayed the expected *J* values of 9.0 Hz. The methyl group at C-10 appeared as a singlet and resonated at 1.70-1.76 ppm.

The reaction of acrylonitrile with dipole **3** in dichloromethane was more complicated and after a work-up, only a small quantity of the expected *endo*-isomer **14** was obtained[10]. The exclusive regiochemistry of

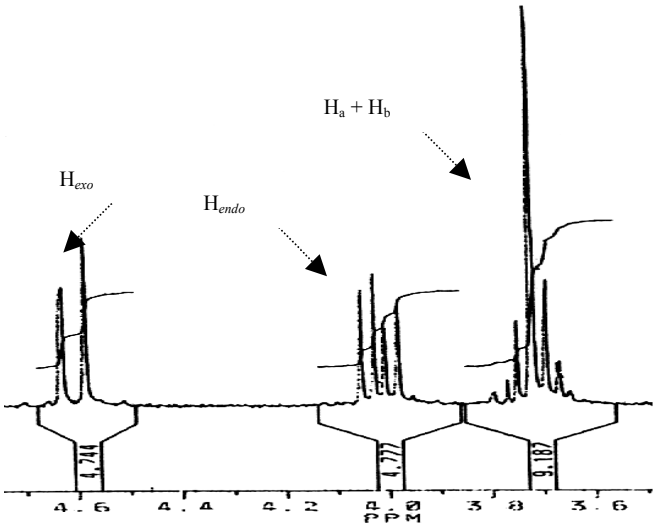


Fig. 1. ^{1}H NMR Spectra of of H_a, H_b, H_{exo} and H_{endo} of *exo*-cycloadduct **9**

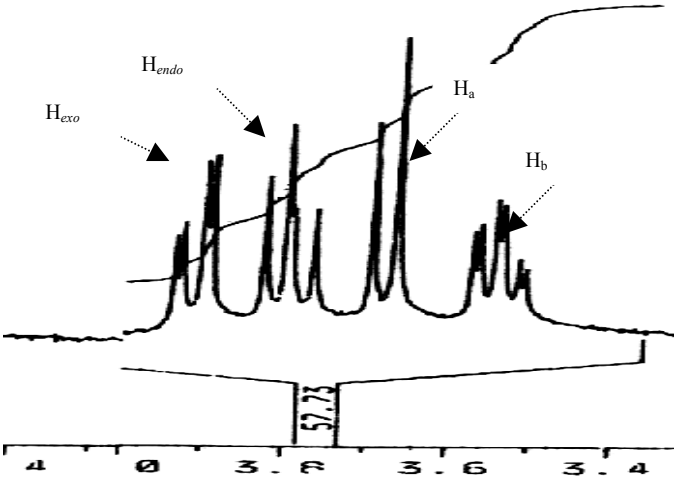
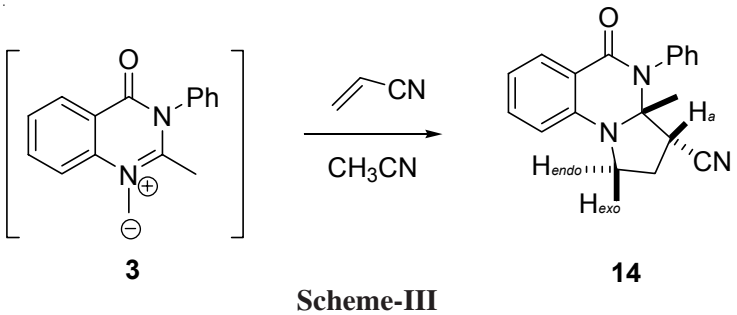


Fig. 2. ^{1}H NMR Spectra of of H_a, H_b, H_{exo} and H_{endo} of *endo*-cycloadduct **12**

this product is that expected from a dipole HOMO-dipolarophile LUMO interaction[11] where the unsubstituted methine terminus of the dipole bonds to the unsubstituted terminus of acrylonitrile. The IR spectrum showed a strong absorption at 2235 cm^{-1} corresponding to the CN stretching vibration. The amide group appeared at 1660 cm^{-1}. In ^{1}H NMR spectra H_a was a doublet of doublets at 2.97 ppm and the four protons at C-2 and C-3 appeared as multiplets at 2.28-2.35 ppm and 3.32-3.35 pmm, respectively (**Scheme-III**).



3 **14**

Scheme-III

1,3-Dipolar cycloadditions of azomethine ylides with N-substituted maleimides are highly stereoselective[1,5] and favour the formation of the isomer resulting from an *exo* transition state. Butler *et al.* have studied the *endo*/*exo* selectivities in cycloaddition reactions of substituted 1,2,3-triazolium-1-methanides, with alkene dipolarophiles. These studies included the use of N-substituted maleimides and *exo* mode of cycloadditions were observed. Based on structure models and NOE experiments, they demonstrated that the almost exclusive *exo*-mode of cycloadditions observed with maleimides dienophiles are likely due to the steric effect from the substituents of the dipole to the larger-CO-N(R)-CO-unit. With acrylonitrile as a dipolarophile the steric effect is reduced and favours the formation of the *endo*-isomer[10].

REFERENCES

1. R. Grigg, *Chem. Soc. Rev.*, **16**, 89 (1987).
2. E. Vedjs and F.G. Westmm, *Chem. Rev.*, **108**, 1104 (1986).
3. A. Padwa, U. Chiacchio and M.K. Venkatramanan, *J. Chem. Commun.*, 1108 (1985).
4. A. Padwa and J.R. Gasdaska, *J. Am. Chem. Soc.*, 1104 (1986).
5. C.W.G. Fishwick, A.D. Jones, M.B. Mitchell and C. Szantay, *Tetrahedron Lett.*, 5325 (1988).
6. R.C.F. Jones, J.R. Nichols and M.T. Cox, *Tetrahedron Lett.*, **131**, 2333 (1990)
7. R.N. Butler, P.D. McDonald, P. Ma Ardle and D. Cunningham, *J. Chem. Soc. Perkin Trans. I*, 1653 (1994).
8. R.N. Butler, F.A. Lysaght and L.A. Burke, *J. Chem. Soc. Perkin Trans. II*, 1103 (1992).
9. R.N. Butler, P.D. McDonald, P. Ma Ardle and D. Cunningham, *J. Chem. Soc. Perkin Trans. I*, 1617 (1996).
10. R.N. Butler and M.W. Leonic, *J. Chem. Soc. Perkin Trans. I*, 1778 (2001).
11. E. Vedjs, S. Lasen and F.C. West, *J. Org. Chem.*, **50**, 2970 (1985).

(*Received*: 19 December 2006; *Accepted*: 29 September 2007) AJC-5922