Reactions of three [*c*]annelated 2-aminothiophenes with electron poor olefins

E. Sopbué Fondjo[a,*] and D. Döpp[b]

[a]*Laboratory of Applied Synthetic Organic Chemistry,Department of Chemistry, Faculty of Sciences, University of Dschang, P.O.Box 067 Dschang, Republic of Cameroon*
E-mail: sopbue@yahoo.fr
[b]*Organische Chemie, Universität Duisburg-Essen, 47057 Duisburg, Germany*
E-mail: doepp@uni-duisburg.de

Dedicated to the memory of Dr. Emmanuel Nyiondi-Bonguen

Abstract

A series of electron poor alkenes [maleic acid derivatives **3a-d**, dimethyl maleate (**4**), ethyl acrylate (**5a**), phenyl vinyl sulfone (**5b**)] undergo [4+2]-cycloaddition to the thiophene moiety of benzopyrano[3,4-c]annelated 2-aminothiophenes **1a,b** and **2**. The primary adducts tend to release hydrogen sulfide, in this way the fused thiophene ring is replaced by a fused benzene ring bearing the amino group and any new substituents introduced by the dienophile. With maleic anhydride (**3a**) and dichloromaleic anhydride (**3b**) acylation of the amino group competes with the [4+2]-cycloaddition to the thiophene ring. The cycloaddition of the monosubstituted alkenes **5a,b** follows a *head-to-head* regioselectivity as predicted from FMO-considerations.

Keywords: 2-Aminothiophenes, angular annelation, Diels-Alder addition, electron poor olefins, regioselectivity

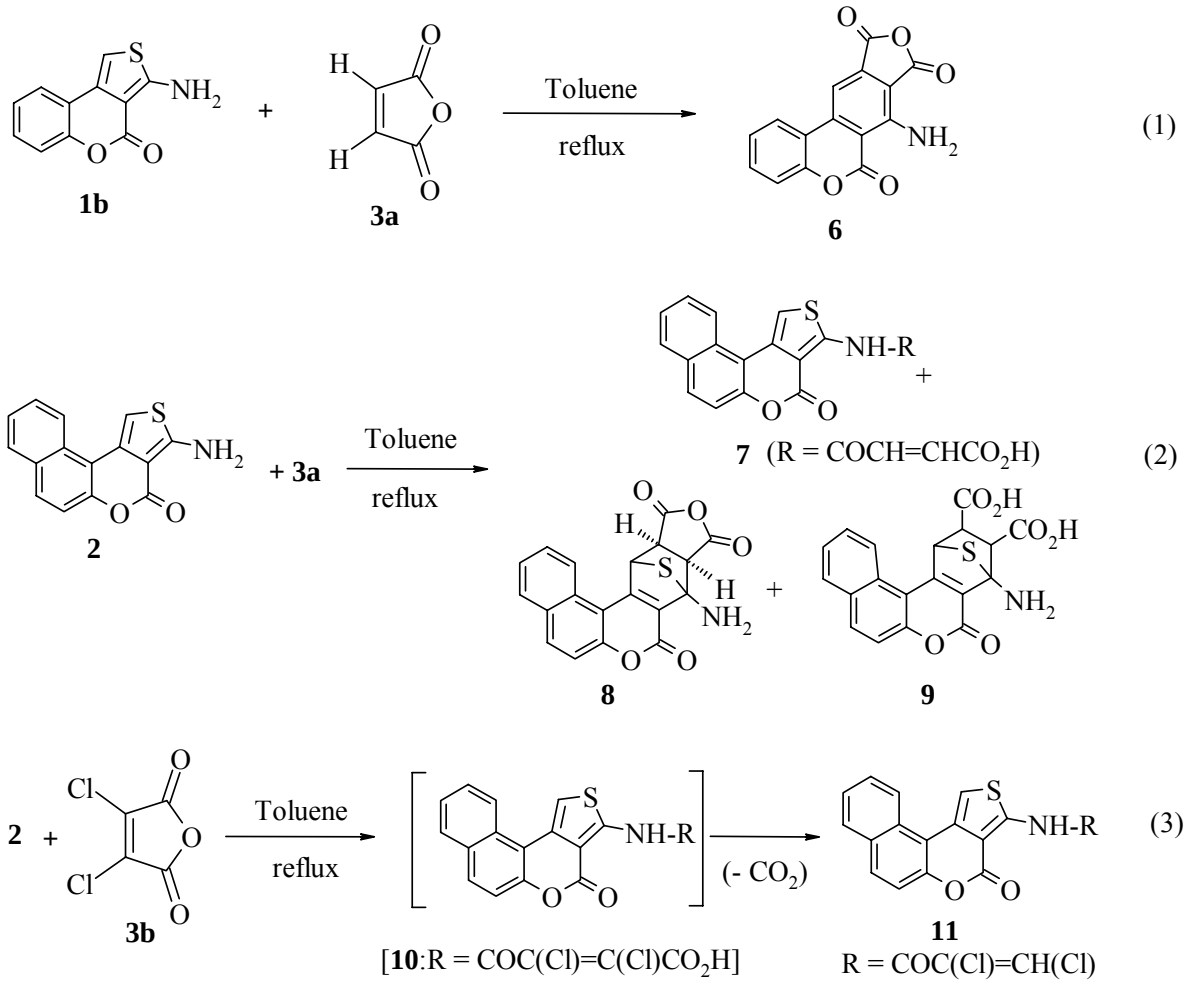
Introduction

Among the three common five-membered fully unsaturated heterocycles, furan derivatives[1,2] have been shown to readily undergo ($\pi^4+\pi^2$)-Diels-Alder additions. Pyrrole does so less readily and then usually only with electrophilic dienophiles, and sometimes Michael addition occurs instead[1,2]. Thiophene derivatives in contrast are generally more reluctant towards such cycloadditions because of their higher resonance energy[3]. The few examples of cycloadditions of certain substituted thiophenes to dienophiles refer either to reactant couples in which the thiophene compound is electron rich[1,2,4-8,10] or to cases in which the sulfur atom in the thiophene reagent is oxidized prior to or during the reaction[9,11]. Since 2-aminosubstitution does increase

the electron richness of the thiophene ring, starting materials **1a,b** and **2** were chosen for the investigation of their reactivity towards electron poor alkenes.

Results and Discussion

In refluxing toluene **1b** reacted with **3a** to give the cycloadduct **6** in quantitative yield. A similar result obtained in refluxing glacial acetic acid was recently reported by Elnagdi et al.[12]

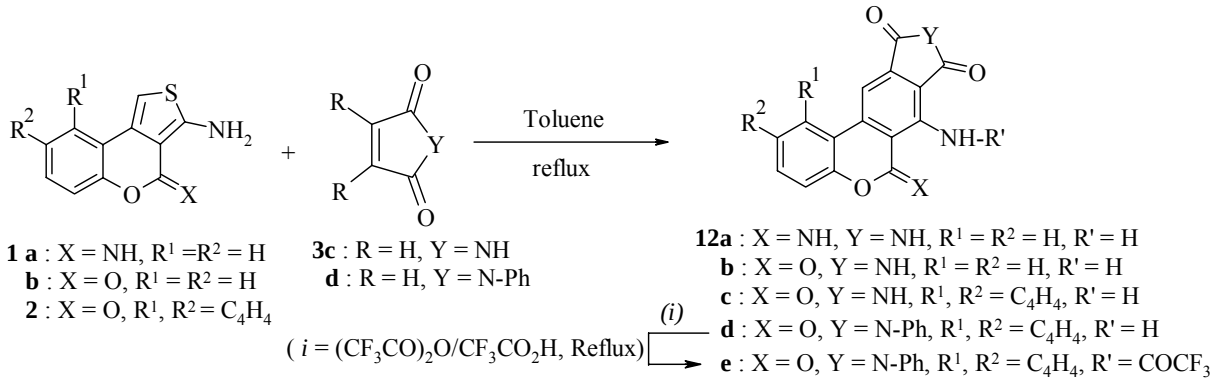


Scheme 1

From the reaction of substrate **2** with **3a** in refluxing toluene, the *N*-acylated product **7** and the mixture of the bicyclic adducts **8** and **9** (scheme 1), were obtained. The latter may result from the hydrolysis of **8**. The amide was obtained pure, whereas **8** and **9** were obtained as a mixture in the ratio 1:1.8 (on the basis of ^{1}H NMR data).

The reaction of **3b** with **2** in refluxing toluene, gave the *N*-acylated product **11** (scheme 1). The constitution of **11** was confirmed by the elemental analysis, the mass-spectrum and all the other spectroscopic data.

The reaction of substrates **1a,b** and **2** with maleimide (**3c**) and *N*-phenyl maleimide (**3d**) respectively, in boiling toluene, gave the condensed polycycles **12a-d** (scheme 2), in quantitative yields (63-96%), as results of Diels-Alder reactions of the dienophiles (**3c,d**) across the thiophene rings of the respectives thiophene reagents.



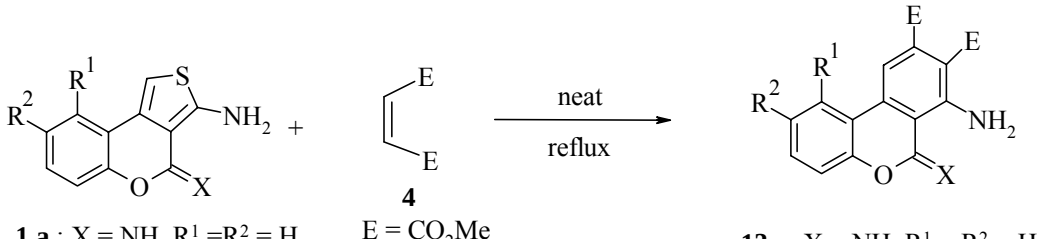
1 a : X = NH, R^1 =R^2 = H
b : X = O, R^1 = R^2 = H
2 : X = O, R^1, R^2 = C_4H_4

3c : R = H, Y = NH
d : R = H, Y = N-Ph

12a : X = NH, Y = NH, R^1 = R^2 = H, R' = H
b : X = O, Y = NH, R^1 = R^2 = H, R' = H
c : X = O, Y = NH, R^1, R^2 = C_4H_4, R' = H
d : X = O, Y = N-Ph, R^1, R^2 = C_4H_4, R' = H
e : X = O, Y = N-Ph, R^1, R^2 = C_4H_4, R' = $COCF_3$

Scheme 2

Compounds **1a,b** and **2** also add dimethyl maleate (**4**) under reflux in absence of solvent to afford the phthalate derivatives **13a-c** (scheme 3) in yields of 33-96%. The preparation, the elemental and spectroscopic data of compound **13a** were reported earlier.[8]



1 a : X = NH, R^1 =R^2 = H
b : X = O, R^1 = R^2 = H
2 : X = O, R^1, R^2 = C_4H_4

4
E = CO_2Me

13a : X = NH, R^1 = R^2 = H
b : X = O, R^1 = R^2 = H
c : X = O, R^1, R^2 = C_4H_4

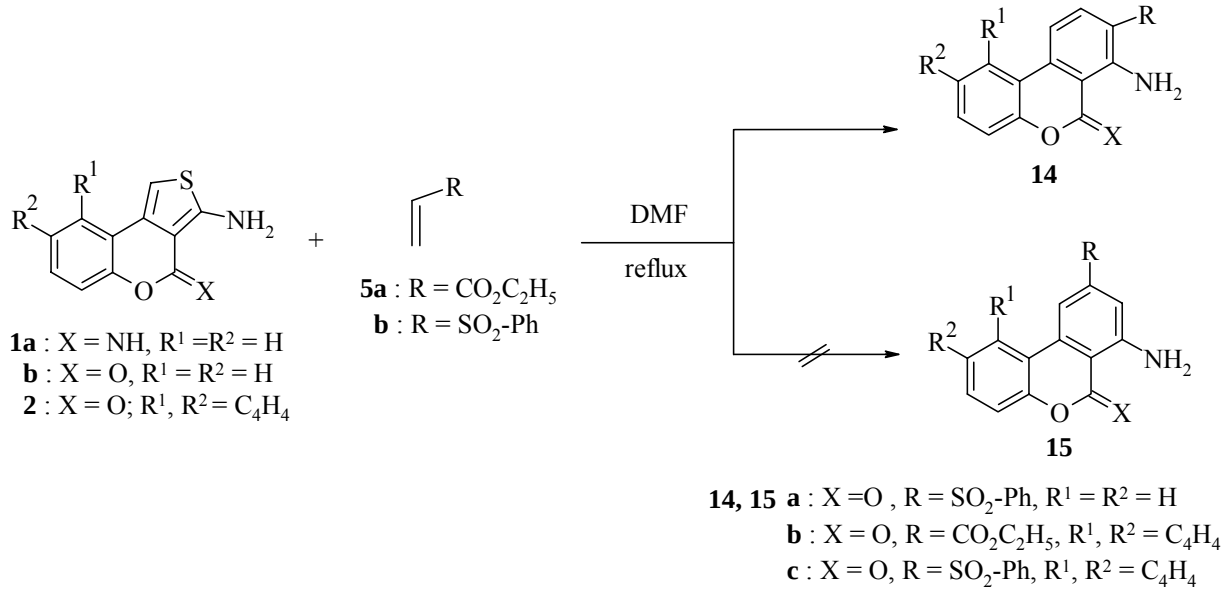
Scheme 3

Phenylvinylsulfone (**5a**) and ethylacrylate (**5b**) gave with the substrates **1a,b** and **2** in boiling *N*,*N*-dimethylformamide respectively, the addition products **14a-c** (scheme 4).

Products **14a-c** were obtained in yields of 36%, 72% and 92% respectively, as the only regioisomers. The other possible regioisomers **15a-c**, were ruled out on the basis of ^{1}H NMR experiments which clearly settled the differences with their counterparts **14** as follows. For **15**,

two more weakly coupled signals integrating for one proton each should be expected in the low field region, but two more strongly coupled (J > 8 Hz) doublets of one proton each from local AB-systems were however exhibited in this region in each case.

In the case of compound **14b**, the strong chelation of the amino protons, enhanced by the *ortho* position of the ethoxycarbonyl group is clearly exhibited in the ^{1}H NMR spectrum, which shows two broad D_2O-exchangeable signals for one proton each at δ = 8.93 and δ = 8.67 ppm. This is suggestive of a conformation in solution, in which the σ bond linking carbone-4 to the amino group is blocked. Such details can not be encountered in the isomer **15b**.



1a : X = NH, R^1 =R^2 = H
b : X = O, R^1 = R^2 = H
2 : X = O; R^1, R^2 = C_4H_4

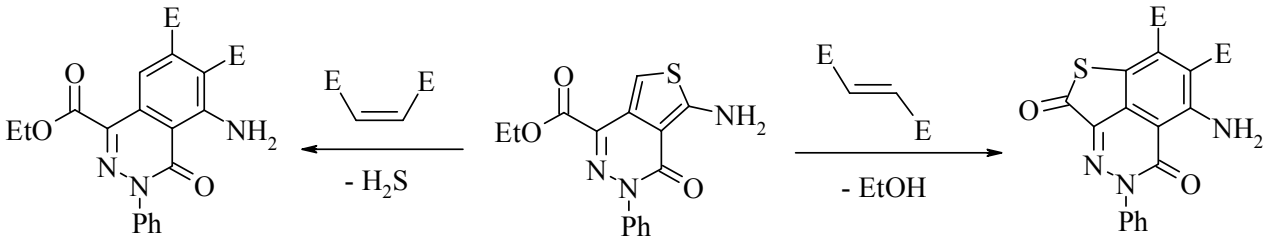
5a : R = $CO_2C_2H_5$
b : R = SO_2-Ph

14, 15 **a** : X =O , R = SO_2-Ph, R^1 = R^2 = H
b : X = O, R = $CO_2C_2H_5$, R^1, R^2 = C_4H_4
c : X = O, R = SO_2-Ph, R^1, R^2 = C_4H_4

Scheme 4

For the transformation of the annelated thiophene rings into benzene rings, a mechanism operating in at least two steps, consisting of : *(i)* [4+2]-cycloaddition to the butadiene fragment of the thiophene, *(ii)* extrusion of hydrogene sulfide, should always be envisaged. A similar process has also been suggested by Elnagdi et al[12,13a-d,14-16], for analogous transformations. It should be pointed out that both parts of the reaction can even proceed in several steps, in which :
- the concerted [4+2]-cycloaddition (scheme 5), leading to the bicyclic intermediate **20**, first takes place;
- the epithio-bridge in [4+2]-cycloadduct **20**, then opens to afford the thiolate, which subsequently undergoes H_2S-extrusion to give the final product **I** (Scheme 5).

The H_2S-extrusion is consistent with a recent observation of Elnagdi et al[16]. The addition of diethylmaleate to compound **17**, gave the product **16**, whereas the addition of diethylfumarate to the same heterocycle afforded instead the condensation product **18**.

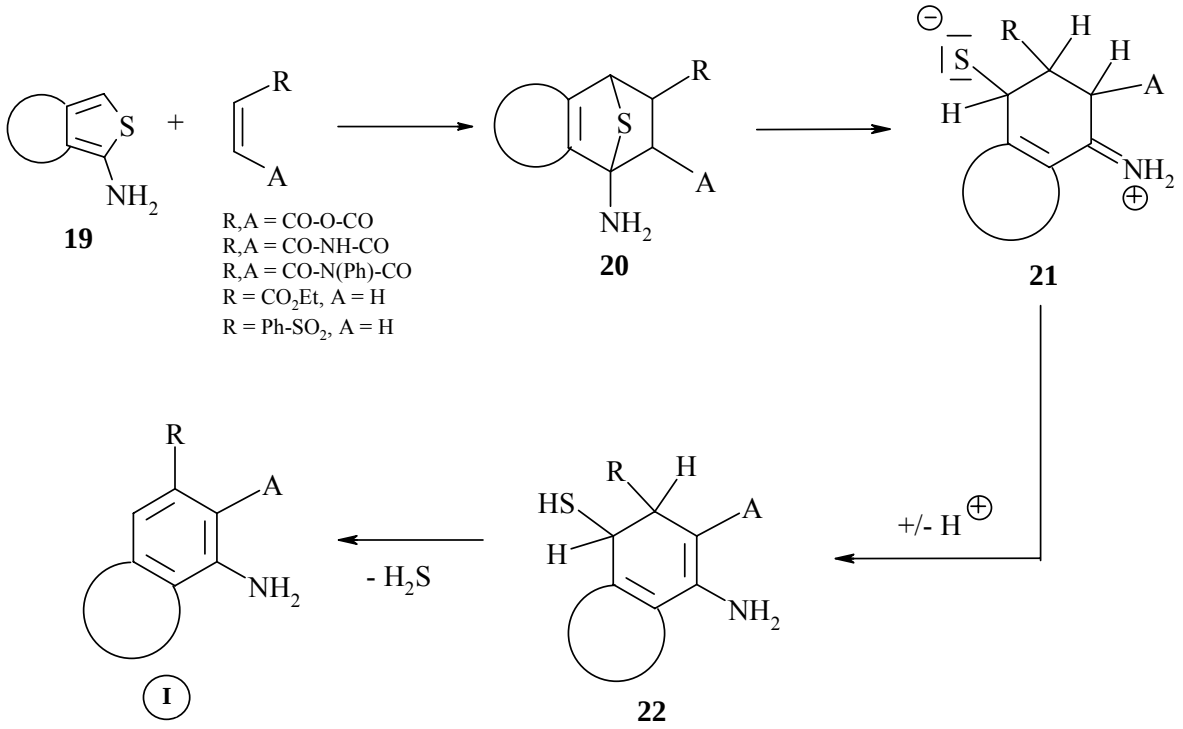


16 17 18

The formation of the latter product, proceeds by attack –SH or $–S^-$ on the ester group of the pyridazine ring. [4+2]-Cycloadditions of unsymmetrical electron poor alkenes are highly regioselective, as illustrated in this work by the formation of the products **14**. Other authors found some related examples[13a-c, 14,15].

These results are well rationalized by the Frontier-Molecular-orbital polarization and the principle of the perturbation theory[17,18]. For a [4+2]-cycloaddition reaction to even take place, a gain of conjugation should be affordable in the primary adduct. The condensed 2-aminothiophenes **1a,b** and **2** fulfill this requirement.

It should also be pointed out that the amino group lone pair in **1b** and **2** is highly delocalised due to conjugation with the pyrane C=O group and therefore this amino group is only weakly nucleophilic. This may explain why maleic anhydride does not readily react with this group, and it requires a more electrophilic anhydride (as dichloromaleic anhydride) to attack it. The C=NH in **1a** may show the same trend in abstracting electron density from the amino group, but clearly less than C=O, so it allows acylation of the amino group more readily. At the same time it is more easily replaced than the oxo group oxygen, and thus condensative dimmers may be found in some cases.[19]



Scheme 5

Experimental Section

General Procedures. All the elemental and spectroscopic analyses were performed in the chemistry department analytical center of Gerhard Mercator Universität-GH-Duisburg, Duisburg (FRG). All the melting points were determined with a Reichert Thermovar microscope and are uncorrected. The IR and the UV spectra were measured with Perkin-Elmer 983 and 554 spectrophotometers, respectively. ^{1}H and ^{13}C(^{1}H) NMR spectra were recorded on WM 300 and 500 instruments, with TMS as internal standard. Coupling constants are reported in Hertz. Mass spectra were obtained on Varian MAT 311A and AMD 604 instruments by Electron Impact Ionization (EI) at 18 eV or 70 eV, on direct inlet system. Combustion analyses were carried out with a CHN + O/S elemental analyser "CARLO ERBA'' MOD. 1106. Simulated ^{1}H and ^{13}C(^{1}H) NMR spectra were performed with an ACD NMR spectra simulation programme.

2-Aminothiophene derivatives 1a,b and **2** were prepared according to known procedures[20,21]. The analysis and the spectroscopic data were previously reported[22,23] for these substances.

7-Amino-6-oxo-6*H*-benzo[*c*](2*H*)chromen-8,9-dicarboxylic acid anhydride (6). Compound **1b** (0.44 g, 2 mmol) was treated with **3a** (0.98 g, 10 mmol) in toluene under reflux for 7 h. The resulted precipitate was crystallized from ethyl acetate to afford 494 mg (87%) of a yellow powder, mp 312-314°C (Lit[12], 194°C from ethanol). IR: ν/cm^{-1} 3457, 3344 (NH_2), 1837, 1764, 1689 (C=O). NMR data: δ_H (DMSO-d_6, 300 MHz) 7.34-7.40 (2H, m, aryl H), 7.49 (1H, s, 10-H),

7.57-7.63 (1H, m, aryl H), 8.32 (1H, m, aryl H), 8.34 (2H, broadened, NH_2). δ_C (DMSO-d_6, 75 MHz) 104.1 (C-10a), 106.8 (C-10), 110.3 (C-10b), 117.1 (C-1), 117.4 (C-6a), 124.9 (C-3), 125.1 (C-2), 132.2 (C-4), 139.3 (C-9), 143.9 (C-8), 151.3 (C-7), 152.7 (C-4a), 161.5 (C-6), 169.6, 168.2 (O=C-O-C=O). MS (EI): *m/z* 281.0242 (M^+, 100 %, $C_{15}H_7NO_5$ requires 281.0239), 238 (4), 237 (27), 44 (6), 43 (9). Anal. Calcd. for $C_{15}H_7NO_5$: C, 64.06; H, 2.49; N, 4.98. Found: C, 63.85; H, 2.77; N, 4.91.

***N*-[3-(4-oxo-4*H*-benzo[*f*]thieno[3,4-*c*](2*H*)chromenyl)]maleamic acid (7).** A mixture of **2** (0.54 g, 2 mmol) and **3a** (0.98 g, 10 mmol) in toluene was heated to reflux for 6 h. The solution was concentrated to one half of its volume under reduced pressure, and the solid precipitate was crystallized from ethyl acetate to give 422 mg (76%) of a yellow powder, mp 242-245°C. IR: ν/cm^{-1} 3445, 3227, 2582 (COOH, NH), 1716 (COOH), 1692 (C=O), 1625 (C=O). NMR data: δ_H (DMSO-d_6, 300 MHz) 6.57 (1H, d, $J_{2,3}$ 12.2 Hz, 2-H), 6.83 (1H, d, $J_{3,2}$ 12.2 Hz, 3-H), 7.54 (1H, m, aryl H), 7.61 (1H, m, aryl H), 7.75 (1H, m, aryl H), 8.05 (2H, m, aryl H), 8.24 (s, 1H, 1'-H), 8.82 (1H, m, aryl H), 11.50 (1H, broadened, COOH). δ_C (DMSO-d_6, 75 MHz) 107.9 (C-7'a), 110.8 (C-11'a), 112.6 (C-1'), 117.8 (C-3), 124.5 (C-2), 125.8 (C-7'), 128.7 (C-11'), 128.8 (C-11'c), 128.9 (C-11'b), 129.3 (C-9'), 129.5 (C-10'), 131.1 (C-3'a and C-8'), 133.1 (C-6'), 148.4 (C-5'a), 149.6 (C-3'), 158.5 (C=O), 162.8 (C=O), 167.3 (C=O). MS (EI): *m/z* 365.0397 (M^+, 3%, $C_{19}H_{11}NO_5S$ requires 365.0402), 347 (12), 321 (4), 267 (100), 45 (11), 44 (94), 43 (20). Anal. Calcd. for $C_{19}H_{11}NO_5S$: C, 62.47; H, 3.01; N, 3.84; S, 8.77. Found: C, 62.20; H, 3.10; N, 3.76; S, 8.70.

The above mother liquor was evaporated to dryness under reduced pressure. The resulted solid material was crystallized from toluene to afford 461 mg of a mixture of compounds **8** (9%) and **9** (15%) in ratio of 1 :1.8 based on ^1H NMR experiment.

2,3-Dichloro-*N*-[3-(4-oxo-4*H*-benzo[*f*]thieno[3,4-*c*]chromenyl)propenamide (11). A stirred solution of **2** (0.54 g, 2 mmol) and **3b** (1 g, 6 mmol) in toluene was heated to reflux for 1 h. The resulting solid material was crystallized from aqueous DMF to afford 728 mg (92 %) of yellow prisms, mp 279-281°C. IR: ν/cm^{-1} 3427 (NH), 1691, 1664 (C=O). NMR data: δ_H ($CDCl_3$/DMSO-d_6, 500 MHz) 7.47 (1H, m, aryl H), 7.73 (2H, m, aryl H), 7.96 (1H, m, aryl H), 7.97 (1H, m, aryl H), 7.99 (1H, s, 1'-H), 8.09 (1H, s, 3-H), 8.78 (1H, m, aryl H), 11.94 (1H, broadened, **N**H). δ_C ($CDCl_3$/DMSO-d_6, 125 MHz) 107.8 (C-7'a and C-11'a), 109.5 (C-11c), 111.1 (C-1'), 116.0 (C-9'), 122.9 (C-7'), 124.0 (C-11'), 125.2 (C-11'b), 126.9 (C-10'), 127.7 (C-8'), 128.1 (C-3'a), 129.4 (C-3), 129.8 (C-2), 130.6 (C-6'), 146.4 (C-5'a), 148.2 (C-3'), 155.8 (C=O), 158.0 (C=O). MS (EI): *m/z* 394 (M^++4, 3), 393(M^++3, 15), 392 (M^++2, 14), 391 (M^++1, 72), 390.0266 (M^+, 21%, $C_{18}H_9NO_3SCl_2$ requires 390.0274), 389 (100), 356 (9), 354 (9), 319 (5), 294 (4), 267 (21), 266 (25), 125 (15), 123 (24), 97 (6), 95 (6), 45 (3). Anal. Calcd. for $C_{18}H_9NO_3SCl_2$: C, 55.53; H, 2.31; N, 3.60; S, 8.23. Found: C, 55.47; H, 2.28; N, 3.61; S, 8.31.

7-Amino-6-imino-6*H*-benzo[*c*](2*H*)chromen-8,9-dicarboxylic imide (12a). A mixture of **1a** (0.54 g, 2.5 mmol) and **3c** (1.5 g, 15 mmol) in toluene was heated to reflux for 45 min. The precipitate was crystallized from ethyl acetate to give 513 mg (74%) of yellow powder, mp 336-339°C. IR: ν/cm^{-1} 3436, 3302, 3219 (NH_2, NH), 1759, 1727, 1657 (C=O). NMR data: δ_H

(DMSO-d_6, 300 MHz) 7.16 (1H, m, aryl H), 7.26 (1H, m, aryl H), 7.49 (1H, m, aryl H), 7.62 (1H, s, 10-H), 8.21 (1H, m, aryl H), 8.94 (1H, broadened, NH), 9.72 (1H, broadened, =NH), 11.00 (2H, broadened, NH_2). δ_C (DMSO-d_6, 75 MHz) 102.4 (C-10), 109.5 (C-6a), 110.3 (C-10b), 115.9 (C-4), 117.8 (C-10a), 123.9 (C-2), 124.9 (C-1), 131.6 (C-3), 136.7 (C-9), 139.6 (C-8), 147.2 (C-7), 151.0 (C-4a), 156.1 (C-6), 168.2 (C=O), 170.4 (C=O). MS (EI): *m/z* 279.0263 (M^+, 100 %, $C_{15}H_9N_3O_3$ requires 279.0268), 278 (8), 260 (8), 253 (4), 251 (3), 235 (10), 234 (5), 233 (7), 208 (7). Anal. Calcd. for $C_{15}H_9N_3O_3$: C, 64.52; H, 3.23; N, 15.05. Found: C, 64.52; H, 3.23; N, 15.00.

7-Amino-6-oxo-6*H*-benzo[*c*](2*H*)chromen-8,9-dicarboxylic imide (12b). A mixture of **1b** (0.54 g, 2.5 mmol) and **3c** (1.5 g, 15 mmol) in toluene was heated to reflux for 1 h. The resulted solution was concentrated to one half of its volume under reduced pressure. The combined precipitates were crystallized from ethyl acetate to afford 670 mg (96%) of yellow powder, mp 338-340°C (subl.). IR: ν/cm^{-1} 3475, 3442, 3360, 3324 (NH, NH_2), 1754 (C=O), 1696 (C=O), 1684 (C=O). δ_H (DMSO-d_6, 300 MHz) 7.35 (1H, m, aryl H), 7.38 (1H, m, aryl H), 7.60 (1H, m, aryl H), 7.70 (1H, s, 10-H), 7.72 (2H, broadened, NH_2), 8.32 (1H, m, aryl H), 11.06 (1H, broadened, NH). δ_C (DMSO-d_6, 75 MHz) 102.5 (C-10), 106.9 (C-10a), 110.4 (C-10b), 116.5 (C-1), 117.3 (C-9), 124.5 (C-3), 124.6 (C-2), 131.7 (C-4), 138.6 (C-6a), 142.5 (C-8), 148.2 (C-7), 150.6 (C-4a), 160.4 (C-6), 167.5, 169.6 (O=C-O-C=O). MS (EI): *m/z* 280.0253 (M^+, 100 %, $C_{15}H_8N_2O_4$ requires 280. 0258), 252 (5), 236 (5), 210 (24), 209 (24), 77 (4), 76 (5). Anal. Calcd. for $C_{15}H_8N_2O_4$: C, 64.29; H, 2.86; N, 10.00. Found: C, 64.22; H, 2.83; N, 10.00.

4-Amino-5-oxo-5*H*-dibenzo[*c,f*](2*H*)chromen-2,3-dicarboxamide (12c). A stirred mixture of compound **2** (401 mg, 1.5 mmol) and **3c** (1.5 g, 15 mmol) in toluene was heated to reflux for 5 h. The solution so obtained was reduced to one half of its volume, and the resulted precipitate was crystallized from ethyl acetate to give 411 mg (83%) of yellow powder, mp 339-341°C. IR: ν/cm^{-1} 3443, 3337, 3287 (NH_2, NH), 1733 (C=O), 1610 (C=O). NMR data: δ_H ($CF_3COOH/CDCl_3$, 500 MHz) 7.45 (1H, m, aryl H), 7.65 (1H, m, aryl H), 7.75 (1H, m, aryl H), 7.98 (1H, m, aryl H), 8.07 (1H, m, aryl H), 8.25 (1H, s, 1-H), 8.60 (1H, m, aryl H), 9.24 (1H, broadened, NH), 10.39 (2H, broadened, NH_2). δ_C ($CF_3COOH/CDCl_3$, 125 MHz) 108.6 (C-8a), 109.9 (C-1), 111.0 (C-12a), 116.5 (C-8), 117.8 (C-12b), 125.0 (C-12), 126.9 (C-10), 129.2 (C-12c), 129.3 (C-11), 129.9 (C-9), 132.2 (C-2), 135.3 (C-7), 138.1 (C-3), 146.3 (C-4a), 149.9 (C-4), 151.1 (C-6a), 171.3 (C-5), 169.7, 164.2 (O=C-NH-C=O). MS (EI): *m/z* 330.0314 (M^+, 100 %, requires 330.0319), 312 (3), 302 (7), 285 (9), 284 (17), 259 (10), 331 (6), 44 (3). Anal. Calcd. for $C_{19}H_{10}N_2O_4$: C, 69.09; H, 3.03; N, 8.48. Found: C, 68.90; H, 3.04; N, 8.45.

4-Amino-5-oxo-5*H*-dibenzo[*c,f*](2*H*)chromen-2,3-dicarboxylic *N*-phenylimide (12d). A mixture of compound **2** (401 mg, 1.5 mmol) and **3d** (1.73 g, 10 mmol) in toluene was heated to reflux for 5 h. The resulted solution was concentrated to one half of its volume under reduced pressure, and the resulted precipitate was crystallized from ethyl acetate to afford 381 mg (63%) of yellow powder, mp 354-356°C. IR: ν/cm^{-1} 3443, 3334 (NH_2), 2923 (C-H), 1758, 1711, 1630 (C=O). NMR data: δ_H ($CF_3COOH/CDCl_3$, 500 MHz) 7.29 (2H, broadened, NH_2), 7.42 (2H, m, aryl H), 7.54 (1H, m, aryl H), 7.58 (1H, m, aryl H), 7.59 (2H, m, aryl H), 7.71 (1H, m, aryl H),

7.83 (1H, m, aryl H), 8.06 (1H, m, aryl H), 8.16 (1H, m, aryl H), 8.50 (1H, m, aryl H), 8.76 (1H, m, aryl H). δ_C ($CF_3COOH/CDCl_3$, 125 MHz) 111.3 (C-1), 116.8 (C-8), 125.3 (C-12), 128.0 (C-10), 129.8 (C-2' and C-6'), 129.9 (C-11), 130.4 (C-9), 130.5 (C-3' and C-5'), 130.5 (C-4'), 130.7 (C-8a), 133.1 (C-12a), 136.1 (C-7), 138.3 (C-12c), 147.3 (C-12b), 150.9 (C-4a), 151.8 (C-3), 160.2 (C-2), 160.7 (C-1'), 161.2 (C-4), 162.7 (C-6a), 165.6 (C-5), 170.0, 170.8 (O=C-N(Ph)-C=O). MS (EI): *m/z* 406.0409 (M^+, 100 %, $C_{25}H_{14}N_2O_4$ requires 406.0405), 378 (6), 45 (10), 44 (10). Anal. Calcd. for $C_{25}H_{14}N_2O_4$: C, 73.89; H, 3.45; N, 6.90. Found: C, 73.50; H, 3.62; N, 6.83.

4-(Trifluoracetylamino)-5-oxo-5*H*-dibenzo[*c,f*](2*H*)chromen-2,3-dicarboxylic *N*-phenyl imide (12e). Treatment of **12d** (50 mg, 0.12 mmol) with trifluoroacetic anhydride (5 ml) in trifluoroacetic acid at reflux for 10 h, gave after the usual workup a solid material, which was crystallized from ethyl acetate to afford 38 mg of yellow prisms, mp 263-266°C. IR: ν/cm^{-1} 3443 (NH), 3075 (C-H), 1776, 1751, 1725 (C=O). NMR data: δ_H (DMSO-d_6, 300 MHz) 7.49 (3H, m, aryl H), 7.56 (2H, m, aryl H), 7.62 (1H, m, aryl H), 7.68 (1H, m, aryl H), 7.85 (1H, m, aryl H), 8.15 (1H, m, aryl H), 8.26 (1H, m, aryl H), 8.85 (1H, s, 1-H), 8.66 (1H, m, aryl H), 11.93 (1H, broadened, NH). δ_C (DMSO-d_6, 75 MHz) 111.8, 114.1 (CF_3), 116.8 (C-8a), 117.9 (C-8), 120.17 (C-12), 121.5 (C-12a), 124.42 (C-10), 126.3 (C-2' and C-6'), 127.5 (C-2' and C-6'), 128.6 (C-12c), 128.7 (C-11), 129.2 (C-9), 129.3 (C-3' and C-5'), 129.9 (C-4'), 131.5 (C-12b), 131.6 (C-4a), 134.2 (C-3), 134.7 (C-7), 136.7 (C-2), 142.4 (C-1'), 150.7 (C-5), 155.1 (C-6a), 155.6 (C=O), 157.1 (C=O), 163.9 (C=O), 165.1 (C=O). MS (EI): *m/z* 502 (M^+, 100 %, $C_{27}H_{13}N_2O_5F_3$ requires 502.0425), 435 (4), 433 (73), 77 (17), 44 (5). Anal. Calcd. for $C_{27}H_{13}N_2O_5F_3$: C, 64.54; H, 2.59; N, 5.58. Found: C, 64.64; H, 2.58; N, 5.60.

Dimethyl 7-amino-6-oxo-6H-benzo[c](2H)chromen-8,9-dicarboxylate (13b). A stirred mixture of **1b** (0.54 g, 2.5 mmol) and neat dimethyl maleate **4** (5 ml) was heated to reflux for 6 h. The solution was treated with methanol, and the resulted precipitate was crystallized from methanol to yield 588 mg (72%) of red prisms, mp 201-203°C (Lit[12], > 300°C from dioxane). IR: ν/cm^{-1} 3415, 3311 (NH_2), 2958 (C-H), 1740 (C=O), 1710 (C=O). NMR data: δ_H (DMSO-d_6, 300 MHz) 3.80 (3H, s, $COOCH_3$), 3.86 (3H, s, $COOCH_3$), 7.37 (1H, m, aryl H), 7.39 (1H, s, 10-H), 7.59 (1H, m, aryl H), 8.30 (1H, m, aryl H), 7.60 (1H, m, aryl H), 8.19 (2H, broadened, NH_2). δ_C (DMSO-d_6, 75 MHz) 52.8 ($COOCH_3$), 53.0 ($COOCH_3$), 104.9 (C-10a), 107.4 (C-10), 110.0 (C-10b), 117.1 (C-8), 117.2 (C-1), 124.9 (C-3), 125.2 (C-2), 132.4 (C-4), 139.8 (C-9), 141.1 (C-6a), 151.3 (C-4a), 152.1 (C-7), 161.4 (C=O), 166.6 (C-6), 168.1 (C=O). MS (EI): *m/z* 327.0308 (M^+, 100 %, $C_{17}H_{13}NO_6$ requires 327.0304), 238 (22), 44 (5). Anal. Calcd. for $C_{17}H_{13}NO_6$: C, 62.39; H, 3.98; N, 4.28. Found: C, 62.02; H, 3.98; N, 4.22.

Dimethyl 4-amino-5-oxo-5*H*-dibenzo[*c,f*](2*H*)chromen-2,3-dicarboxylate (13c). A solution of **1c** (0.27 g, 1 mmol) in neat dimethyl maleate **4** (5 ml) was heated to reflux for 10 h. After trituration with methanol, the resulted precipitate was crystallized from ethanol to afford 364 mg (96%) of yellow prisms, mp 183-185°C. IR: ν/cm^{-1} 3443, 3339 (NH_2), 2953 (C-H), 1735 (C=O), 1709 (C=O). NMR data: δ_H (DMSO-d_6, 300 MHz) 3.82 (3H, s, $COOCH_3$), 3.85 (3H, s, $COOCH_3$), 7.52 (1H, m, aryl H), 7.61 (1H, m, aryl H), 7.73 (1H, m, aryl H), 7.75 (1H, m, aryl H), 8.09 (2H, m, aryl H), 8.11 (2H, broadened, NH_2), 8.16 (1H, m, aryl H), 8.58 (1H, m, aryl H).

δ_C (DMSO-d_6, 75 MHz) 52.7 ($COOCH_3$), 53.1 ($COOCH_3$), 105.8 (C-8a), 110.2 (C-12a), 111.5 (C-12c), 111.8 (C-1), 116.8 (C-10), 124.4 (C-8), 125.8 (C-12), 128.4 (C-11), 128.7 (C-12b), 129.6 (C-9), 131.3 (C-2), 133.5 (C-7), 139.5 (C-3), 139.6 (C-4a), 150.6 (C-4), 151.3 (C-6a), 160.9 (C=O), 166.5 (C=O), 167.7 (C=O). MS (EI): *m/z* 377.0357 (M^+, 100 %, $C_{21}H_{15}NO_6$ requires 377.0364), 347 (5), 346 (24), 345 (9), 331 (7), 288 (12), 88 (16). Anal. Calcd. for $C_{21}H_{15}NO_6$: C, 66.84; H, 3.98; N, 3.71. Found: C, 66.65; H, 4.02; N, 3.69.

7-Amino-6-oxo-6*H*-benzo[*c*](2*H*)chromen-8-yl)phenylsulfone (14a). A mixture of **1b** (0.868 g, 4 mmol) and **5b** (1.68 g, 10 mmol) in solution in DMF was heated to reflux for 8 h. The resulted precipitate was crystallized from ethyl acetate/DMF to afford 506 mg (36%) of clear-brown prisms, mp 243-245°C. IR: ν/cm^{-1} 3449, 3429, 3322 (NH_2), 1696 (C=O), 1604, 1571, 1473, 1444, 1413, 1357 (SO_2), 1310, 1261, 1217, 1147 (SO_2). NMR data: δ_H (DMSO-d_6, 300 MHz) 7.36 (1H, dd, $J_{10,9}$ 8.7 Hz and $J_{10,1}$ 1.0 Hz, 10-H), 7.39 (1H, m, aryl H), 7.60 (1H, m, aryl H), 7.63 (2H, m, aryl H), 7.69 (1H, m, aryl H), 7.73 (1H, m, aryl H), 8.00 (2H, broadened, NH_2), 8.02 (1H, m, aryl H), 8.25 (1 H, d, $J_{9,10}$ 8.6 Hz, 9-H), 8.24 (1H, m, aryl H). δ_C (DMSO-d_6, 75 MHz) 104.5 (C-10a), 108.6 (C-4'), 116.8 (C-10), 116.9 (C-10b), 120.1 (C-6a), 124.6 (C-9), 124.9 (C-1), 126.7 (C-3' and C-5'), 129.5 (C-2' and C-6'), 132.2 (C-3), 133.7 (C-2), 136.6 (C-4), 140.7 (C-7), 141.6 (C-1'), 149.7 (C-8) 151.1 (C-4a), 161.2 (C-6). MS (EI): *m/z* 351.0799 (M^+, 78 %, requires 351.0802), 287 (35), 286 (100), 77 (8), 44 (19).

Ethyl 4-Amino-5-oxo-5*H*-dibenzo[*c,f*](2*H*)chromen-3-carboxylate (14b). A solution of **2** (0.534 g, 2 mmol) in neat **5a** (10 ml) was heated to reflux for 8 h. Evaporation to dryness gave an amorphous residue, which was dissolved in acetone and then chromatographed on SiO_2-PLC (hexan 3/ ethyl acetate 2) to afford besides the unreacted starting material, a solid material which was crystallized from ethyl acetate to yield 450 mg (79%) of yellow needles, mp 158-160°C. IR: ν/cm^{-1} 3419, 3307 (NH_2), 2983 (C-H), 1704 (C=O). NMR data: δ_H ($CDCl_3$, 300 MHz) 1.51 (3H, t, *J* 7.1 Hz, $COOCH_2CH_3$), 4.39 (2H, q, *J* 7.1 Hz, $COOCH_2CH_3$), 7.39 (1H, d, $J_{1,2}$ 9.0 Hz, 1-H), 7.52 (1H, m, aryl H), 7.60 (1H, m, aryl H), 7.65 (1H, m, aryl H), 7.90 (1H, m, aryl H), 8.30 (2H, m, aryl H), 8.68 (1H, d, $J_{2,1}$ 8.7 Hz, 2-H), 8.67 (1H, broadened, NH), 8.93 (1H, broadened, NH). δ_C ($CDCl_3$, 75 MHz) 14.4 (OCH_2CH_3), 60.8 (OCH_2CH_3), 105.3 (C-8a), 109.4 (C-12a), 112.1 (C-1), 112.8 (C-12c), 117.0 (C-10), 125.2 (C-8), 125.5 (C-12), 127.7 (C-11), 129.3 (C-9), 129.7 (C-12b), 131.6 (C-3), 132.6 (C-2), 137.8 (C-7), 141.9 (C-4a), 150.9 (C-4), 154.5 (C-6a), 162.3 (C=O), 167.3 (C=O). MS (EI): *m/z* 333.0357 (M^+, 100 %, $C_{20}H_{15}NO_4$ requires 333.0348), 305 (10), 288, 287, 261 (11), 259 (22), 244 (4). Anal. Calcd. for $C_{20}H_{15}NO_4$: C, 72.07; H, 4.50; N, 4.20. Found: C, 72.04; H, 4.49; N, 4.21.

4-Amino-5-oxo-5*H*-dibenzo[*c,f*](2*H*)chromen-3-yl)phenylsulfone (14c). A stirred mixture of **2** (0.27 g, 1 mmol) and **5b** (0.63 g, 3.75 mmol) in solution in DMF was heated to reflux for 6 h. The resulted precipitate was crystallized from ethyl acetate to afford 372 mg (92%) of brown needles, mp 243-245°C. IR: ν/cm^{-1} 3440, 3329 (NH_2), 2983 (C-H), 1702 (C=O), 1604, 1593, 1568, 1512, 1460, 1447, 1414, 1340 (SO_2), 1306, 1286, 1222, 1145 (SO_2). NMR data: δ_H (DMSO-d_6, 300 MHz) 3.40-3.32 (2H, broadened, NH_2), 7.43 (1H, m, aryl H), 7.53 (1H, m, aryl H), 7.63 (2H, m, aryl H), 7.67 (2H, m, aryl H), 7.73 (1H, d, $J_{1,2}$ 7.1 Hz, 1-H), 7.78 (1H, d, $J_{2,1}$ 8.8

Hz, 2-H), 8.01 (1H, m, aryl H), 8.07 (1H, m, aryl H), 8.08 (1H, m, aryl H), 8.28 (1H, m, aryl H), 8.59 (1H, m, aryl H). δ_C (DMSO-d_6, 75 MHz) 105.4 (C-8a), 111.7 (C-12a), 113.3 (C-1), 116.8 (C-10), 119.5 (C-12c), 125.0 (C-8), 125.8 (C-12), 127.1 (C-2' and C-6'), 128.4 (C-11), 128.9 (C-12b), 129.5 (C-9), 129.8 (C-3' and C-5'), 131.3 (C-1'), 133.7 (C-4'), 134.2 (C-2), 136.4 (C-7), 140.6 (C-4a), 142.0 (C-6a), 149.5 (C-4), 150.6 (C-3), 161.3 (C-5). MS (EI): *m/z* 401.0452 (M^+, 100 %, $C_{23}H_{15}NO_4S$ requires 401.0452), 338 (6), 337 (32), 336 (84), 77 (10), 44 (38). Anal. Calcd. for $C_{23}H_{15}NO_4S$: C, 68.83; H, 3.74; N, 3.49; S, 7.98. Found: C, 68.70; H, 3.77; N, 3.46; S, 7.88.

Acknowledgements

The authors are grateful to the Deutscher Akademischer Austauschdienst (DAAD) for granting Dr. E. Sopbué Fondjo a Ph-D fellowship (Grant N° A/96/11507). Thanks are due to the administration of Gerhard Mercator Universität-GH-Duisburg for financial and technical assistance. They also thank very sincerely through the Rector of the University of Dschang, the Ministry of higher education of the Republic of Cameroon for kindly releasing the above mentioned author, for the implementation of this work. Generous donation of chemicals by Fonds der Chemischen Industry is gratefully acknowledged.

References and Footnotes

1. Chupp J. P. *J. Heterocycl. Chem*., **1970**, *7*, 285.
2. Dauben W. G.; Krabbenhoft H. O. *J. Am. Chem. Soc*., **1976**, *98*, 1992.
3. Kloetzel M. C. *„Organic Reactions"*,Vol. 4 Ch. 1, pp 35-39.
4. Clapp D. B. *J. Am. Chem. Soc*., **1939**, *61*, 2733.
5. Allen C. F.; Gates, Jr. J. W. *ibid*., **1943**, *65*, 1283.
6. Helder R.; Wynberg H. *Tetrahedron Letters*, **1972**, 605.
7. Kuhn H. J.; Gollnick K. *ibid*., **1972**, 1909.
8. Nyiondi-Bonguen E.; Sopbué-Fondjo E.; Tanee Fomum Z.; Döpp D. *J. Chem. Soc. Perkin Trans.1*, 1994, 2191.
9. Kotsuki H.; Kitagawa S.; Nishizawa H. *J. Org. Chem*., **1978**, *43*, 1471.
10. Baker J. M.; Huddleston P. R.; Shutler S. W. *J. Chem. Soc., Perkin Trans. 1*, **1975**, 2483.
11. Torsell K. *Acta. Chem. Scand. B*, **1980**, *30*, 353.
12. Erian A. W.; Hafez E. A. A.; Darwisch E. S.; Elnagdi M. H. *Can. J. Chem.*, **1998**, *76*, 1038.

13. (a) Elnagdi M. H.; Negm A. M.; Erian A. W. *Liebigs Ann. Chem*., **1989**, 1255. (b) Elnagdi M. H.; Erian A. W. *Liebigs Ann. Chem*., **1990**, 1215. (c) Al-Awadhi H.; Al-Omran F.; Infantes L.; Forces-Forces C.; Jagerovic M.; Elguero J.; Elnagdi M. H. *Tetrahedron*, **1995**, *51*, 12745. (d) Al-Omran F.; Khalik M. M. A.; Al-Awadhi H.; Elnagdi M. H. *Tetrahedron*, **1996**, *52*, 11915.
14. Elghandour A. H. H.; Hussein A. H. M.; Elnagdi M. H.; Harb A. F. A.; Metwelly S. A.M. *J. Prakt. Chem.*, **1992**, *334*, 723.
15. Elnagdi M. H.; Negm A. M.; Hassan E. M.; El-Boreiy A. *J. Chem. Res. (S)*, **1993**, 130.
16. Abu-Shanab F. A.; Wakefield B.; Al-Omran F.; Abdel Khalek M. M.; Elnagdi M. H. *J. Chem. Res. (S)*, **1995**, 488-489; *(M)*, **1995**, 2924.
17. Lert P. W.; Trindle C. *J. Am. Chem. Soc.*, **1971**, *93*, 6392.
18. Flemming I., "Grenzorbitale und Reaktionen organischer Verbindungen", *VCH*, 1988, 1990, pp 154-172.
19. Nyiondi-Bonguen E.; Sopbué-Fondjo E.; Tanee Fomum Z.; Döpp D. *J. Heterocycl. Chem.*, **1996**, *33*, 281.
20. (a) Gewald K.; Schinke E.; Böttcher H. *Chem. Ber.*, **1996,** *99*, 94 ; *Chem. Abstr*., **1966**, *64*, 8118. (b) Gewald K. *Angew. Chem.,* **1961**, 73, 114 ; *Chem. Abstr.*, **1961**, *55*, 12383. (c) Gewald K. *Z. Chem.,* **1962**, 2, 305 ; *Chem. Abstr.*, **1963**, *58*, 6770. (d) Gewald K. *Chem. Ber.,* **1965**, 98, 3571 ; *Chem. Abstr.*, **1966**, *64*, 3451.
21. Gewald K.; Schinke E. *Chem.Ber.*, **1966**, *99*, 2712 ; *Chem. Abstr.*, **1966**, *65*, 18548.
22. Ried W.; Nyiondi-Bonguen E. *Liebigs Ann. Chem.,***1973**, *Heft 1*,134-140.
23. Sopbué-Fondjo E. *Dissertation (Dr. rer. nat.- thesis)*, **2000**, Universität-Gerhard Mercator-GH-Duisburg.
24. Sopbué-Fondjo E.; Döpp D.; Henkel G. *Tetrahedron,* submitted.