Monatshefte für Chemie 126, 1253–1256 (1995)

Monatshefte für Chemie
Chemical Monthly

[1,3]Dioxolo[5,6][1]benzothieno[2,3-*c*]-quinolin-6(5*H*)-ones†

H. K. Gakhar*,[1], R. Kaur[1], and S. B. Gupta[2]

[1] Department of Chemistry, Panjab University, Chandigarh-160014, India
[2] Department of Chemistry, Govt. College, Kalka-133302, India

Summary. The reaction of 3,4-methylenedioxycinnamic acid (**1**) with thionyl chloride resulted in the formation of 7-chlorothieno[2,3-*f*]-1,3-benzodioxole-6-carbonyl chloride (**2**) and cinnamoyl chloride (**3**). Subsequent reaction of the former with *p*-substituted anilines led to the formation of 7-chloro-N-(*p*-substituted phenyl)-thieno[2,3-*f*]-1,3-benzodioxole-6-carboxamides (**4a–c**) which on photocyclization afforded 2-substituted [1,3]dioxolo[5,6][1]benzothieno[2,3-*c*]quinolin-6(5*H*)-ones (**5a–c**) in fairly good yields and high purity. The structures have been confirmed by IR, ^{1}H NMR, and analytical methods.

Keywords. Heterocycles; ^{1}H NMR; Synthesis.

[1,3]Dioxolo[5,6][1]benzothieno[2,3-*c*]chinolin-6(5*H*)-one

Zusammenfassung. Die Reaktion von 3,4-Methylendioxyzimtsäure (**1**) mit Thionylchlorid ergab 7-Chlorothieno[2,3-*f*]-1,3-benzodioxol-6-carbonsärechlorid (**2**) und Zimtsäurechlorid (**3**). Darauffolgende Umsetzung von **2** mit substituierten Anilinen führte zur Bildung von 7-Chloro-N-(*p*-*X*-phenyl)-thieno[2,3-*f*]-1,3-benzodioxol-6-carboxamiden (**4a–c**), welche mittels Photocyclisierung in akzeptablen Ausbeuten zu 2-substituierten [1,3]Dioxolo[5,6][1]benzothieno[2,3-*c*]chinolin-6(5*H*)-onen (**5a–c**) hoher Reinheit umgesetzt wurden. Die Strukturen wurden durch spektroskopische (IR, ^{1}H-NMR) und analytische Methoden bestätigt.

Introduction

A survey of the literature reveals that the benzo[*c*] phenanthridine ankaloid Nitidine is known to possess potential antitumour activity in mice [1]. Similarly, related compounds like 2,3-dimethoxy-1,3-dioxolo[4,5-*g*]indazolo[2,3-*a*]quinoline and 1,2,3,4,13,14-hexahydro-1-oxo-1,3-dioxolo[4,5-*g*]quino[1,2-*c*]quinolinium perchlorate have been found to have antileukemic activity [2]. It was therefore thought to be of interest to synthesize a system unknown so far, [1,3]dioxolo[5,6][1]benzothieno[2,3-*c*]quinolin-6(5*H*)-one, which is of close structural resemblance with the above mentioned compounds, with the aim of testing their antitumour activity.

† Accepted for presentation at the Hong Kong International Symposium on Heterocyclic Chemistry (August 13–16, 1995)

Results and Discussion

The reaction of 3,4-methylenedioxycinnamic acid (**1**) with thionyl chloride in the presence of a catalytic amount of pyridine at 140–150° for 3 h resulted in the formation of two products, one of them being 3,4-methylenedioxycinnamoyl chloride (**3**). The second one gave positive tests for both sulfur and halogen and has been assigned the structure 7-chlorothieno[2,3-*f*]-1,3-benzodioxole-6-carbonyl chloride (**2**) on the basis of its IR and ^{1}H NMR spectra.

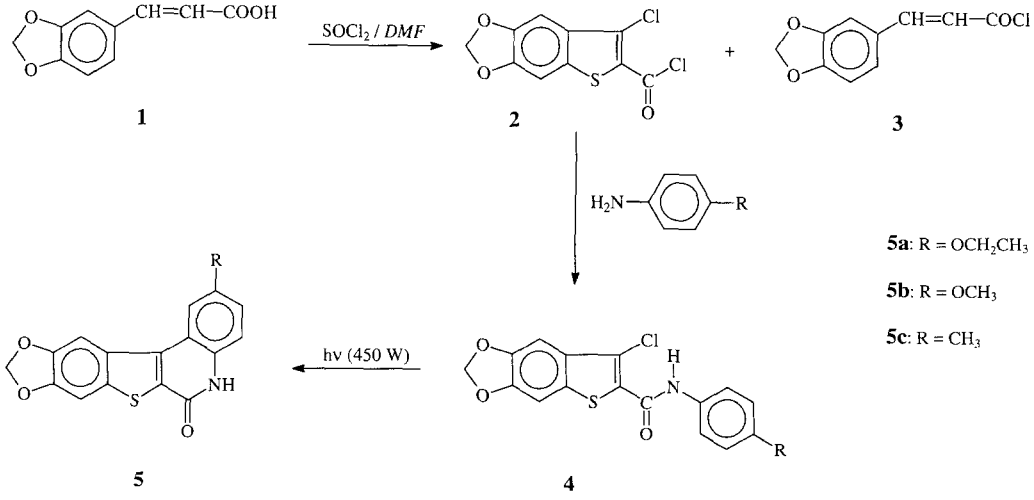
The IR spectrum of **2** shows a band at 1757 cm^{-1} due to the –COCl vibration. ^{1}H NMR spectrum of **2** (*DMSO*-d_6) shows two singlets (1H each) at 7.43 and 7.30 ppm, assignable to two aromatic protons (C_4–H and C_8–H, respectively). Besides, it exhibits another singlet (2H) at 6.20 ppm which can be attributed to the methylenedioxy protons.

The reaction of **2** with *p*-substituted anilines gave 7-chloro-N-(*p*-substituted phenyl)-thieno[2,3-*f*]-1,3-benzodioxole-6-carboxamides (**4a–c**).

4a (R = –OCH_2CH_3) shows an IR band at 3310 cm^{-1} (N–H) and one at 1634 cm^{-1} (–CO–NH–). The ^{1}H NMR spectrum of **4a** shows a quartet (2H) and a triplet (3H) at 4.23 and 1.47 ppm, respectively, assignable to the methylene and methyl protons of the ethoxy group. It also exhibits a broad signal (1H) at 9.13 ppm due to the amide proton. Besides, another singlet (2H) at 6.06 ppm can be attributed to the methylenedioxy protons. The aromatic protons appear as a multiplet (6H) at 6.90–7.67 ppm.

Dehydrochlorinative photocyclization of **4a–c** in the presence of trimethyl amine in acetone, irradiating with a Hanovia medium pressure mercury arc lamp (450 w) using a quartz filter afforded the required 2-substituted [1,3]dioxolo[5,6][1]benzothieno[2,3-*c*]quinolin-6(5*H*)-ones **5a–c**. Their structures have again been confirmed on the basis of spectral studies.

The IR spectrum of **5a** shows bands at 3250, 3132, and 1672 cm^{-1} (two N–H vibrations, one C=O vibration). The ^{1}H NMR spectrum of **5a**, besides showing a quartet (2H) and a triplet (3H) at 4.39 and 1.62 ppm assignable to the methylene and methyl protons of the ethoxy group, exhibits a singlet (2H) at 6.24 ppm which can be attributed to methylenedioxy protons. Aromatic protons appear as a multiplet (5H) at 7.20–8.03 ppm. The amide proton did not appear due to the presence of *TFA*.



Experimental

Melting points were determined in open glass capillaries using a liquid paraffin bath and are uncorrected. IR spectra were recorded in nujol (Perkin-Elmer 337); ^{1}H NMR spectra: Varian EM-390, 90 MHz, *TMS* as internal reference. The analytical values (C, H, N) agreed with the proposed structure for **2**, **4**, and **5** within experimental errors.

Reaction of 3,4-methylenedioxycinnamic acid (**1**) *with thionyl chloride*

To a mixture of 3,4-methylenedioxycinnamic acid (**1**) [3] (1 g; 0.0052 mol) and pyridine (0.1 ml), thionyl chloride (4 ml; 0.052 mol) was added dropwise with stirring. After refluxing for 4 h on a steam bath, *DMF* (0.2 ml) was added and the mixture was heated at 140–150 °C for 1 h with stirring in an oil bath. The excess of thionyl chloride was removed under reduced pressure; fractional crystallization of the residue from benzene yielded 0.6 g (42%) **2**, m.p. = 200–201 °C.

$C_{10}H_4Cl_2O_3S$; IR: $\nu_{max} = 1757\,cm^{-1}$; ^{1}H NMR (*DMSO*-$d_6$): $\delta = 7.43$ (s, 1H, aromatic C_4-H), 7.30 (s, 1H, aromatic C_8–H), 6.20 (s, 2H, $-OCH_2O-$) ppm.

On concentration, the filtrate gave 3,4-methylenedioxycinnamoyl chloride (**3**) in 55% yield.

7-Chloro-N-(*p*-substituted phenyl)-thieno[2,3-*f*]-1,3-benzodioxole-6-carboxamides (4a–c)

A mixture of **2** (0.4 g; 0.0015 mol) and *p*-substituted aniline (0.003 mol) in benzene (30 ml) was refluxed on a steam bath for 1 h. The separated solid (*p*-substituted aniline hydrochloride) was removed by filtration under suction; the benzene distilled from the filtrate under reduced pressure. The residue was crystallized from ethanol.

4a: m.p. = 206 °C; yield: 0.45 g (82%); $C_{18}H_{14}Cl\,NO_4S$; IR: $\nu_{max} = 3310,\ 1634\,cm^{-1}$; ^{1}H NMR ($CDCl_3$ + *TFA*): $\delta = 9.13$ (bs, 1H, amide), 6.90–7.67 (m, 6H, Ar–H), 6.06 (s, 2H, $-OCH_2O-$), 4.23 (q, 2H, $-OCH_2-CH_3$), 1.47 (t, 3H, $-OCH_2-CH_3$) ppm.

4b: m.p. = 188 °C; yield: (78%); $C_{17}H_{12}ClNO_4S$; ^{1}H NMR ($CDCl_3$ + *TFA*): $\delta = 9.20$ (bs, 1H, amide), 6.97–7.70 (m, 6H, Ar–H), 6.13 (s, 2H, $-OCH_2O-$) 3.97 (s, 3H, OCH_3) ppm.

4c: m.p. = 195 °C, yield: (75%); $C_{17}H_{12}ClNO_3S$; ^{1}H NMR ($CDCl_3$ + *TFA*): $\delta = 9.20$ (bs, 1H, amide), 7.00–7.67 (m, 6H, Ar–H), 6.07 (s, 2H, $-OCH_2O-$), 2.40 (s, 3H, CH_3) ppm.

2-Substituted [1,3]dioxolo[5,6][1]benzothieno[2,3-*c*]quinolin-6(5*H*)-ones (5a–c)

A solution of 7-chloro-N-(*p*-substituted phenyl)-thieno[2,3-*f*]-1,3-benzodioxole-6-carboxamide (**4a–c**) (0.0005 mol) and triethyl amine (0.3 ml) in acetone (300 ml) was irradiated with a 450 W Hanovia medium pressure mercury arc lamp for 3 h. The acetone was removed by distillation, and the residue was washed with water, dried, and crystallized from ethanol.

5a: m.p. > 300 °C; yield: 0.13 g (76%); $C_{18}H_{13}NO_4S$; IR: $\nu_{max} = 3250,\ 3132,\ 1672\,cm^{-1}$; ^{1}H NMR ($CDCl_3$ + *TFA*): $\delta = 7.20$–8.03 (m, 5H, Ar–H), 6.24 (s, 2H, $-OCH_2O-$), 4.39 (q, 2H, $-OCH_2-CH_3$), 1.62 (t, 3H, $-OCH_2-CH_3$) ppm.

5b: m.p. > 300 °C; yield: (71%); $C_{17}H_{11}NO_4S$; ^{1}H NMR ($CDCl_3$ + *TFA*): $\delta = 7.30$–7.87 (m, 5H, Ar–H); 6.33 (s, 2H, $-OCH_2O-$), 4.10 (s, 3H, OCH_3) ppm.

5c: m.p. > 300 °C; yield: (66%); $C_{17}H_{11}NO_3S$; ^{1}H NMR ($CDCl_3$ + *TFA*): $\delta = 7.17$–7.85 (m, 5H, Ar–H); 6.28 (s, 2H, $-OCH_2O-$), 2.37 (s, 3H, CH_3) ppm.

Acknowledgements

The authors thank the Head of the Chemistry Dept. for providing the necessary facilities, Mr. *L. K. Khullar* for performing the elemental analyses, and Mr. *Avtar Singh* for recording the ^{1}H NMR spectra.

References

[1] Phillips SD, Castle RN (1980) J Heterocycl Chem **17**: 1489
[2] Phillips SD, Castle RN (1980) J Heterocycl Chem **17**: 1665
[3] Gill GS, Gakhar HK, Ralhan NK, Narang KS (1965) Indian J Chem **3**: 323 and the references therein

Received April 19, 1995. Accepted April 21, 1995