

### A Novel Synthesis of Heterocyclic $\beta$ -Enaminoamides: The Reaction of Halomethyl Acet-*p*-toluidide with Isothiocyanates and with Isocyanates

Nadia Sobhy Ibrahim\*, Kamal Usef Sadek, Suzan Ibrahim Aziz, and Mohamed Hilmy Elnagdi.

Department of Chemistry, Faculty of Science, Cairo and Minia University, Giza and Minia, A. R. Egypt  
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A novel synthesis of thiophene and furan  $\beta$ -enaminoamides *via* the reaction of halomethyl acet-*p*-toluidide with isothiocyanates and isocyanates were reported.

dinitrochlorobenzene. The second product was formulated as **5** based on its identity with the cyclisation product of **3a**, *via* loss of a molecule of water, on long reflux in dioxane in presence of sodium hydride.

Compound **3b** was formed similarly using cinnamylisothiocyanate. Compounds **2a**, **b** also reacted with phenylisothiocyanate to yield the enaminothiophene derivative **3c** and another product of molecular formula  $C_{21}H_{18}N_2O_4$  (**6**). Compound **6** was also obtained when **2** was treated with sodium hydride in absence of a reagent, thus establishing that its a product of self-condensation of two molecules of **2**. The formation of **6** could be minimised to less than 10% (*cf.* Experimental Part).

Similarly, compound **2a** reacted with phenylisocyanate to yield the furan derivative **7** and also the condensation product **5**.

### Experimental

All melting points are uncorrected. IR spectra were recorded on a Beckman spectrophotometer.  $^1H$ NMR on a Varian EM-390-90 MHz spectrometer using TMS as internal indicator and chemical shifts are expressed as  $\delta$  ppm. The microanalysis were performed by the microanalytical unit at Cairo University.

#### Condensation of **2a**, **b** with isothiocyanates and phenylisocyanate: (General procedure)

Equimolecular amounts (0.01 mol) of **2a**, **b** and the appropriate isothiocyanate and phenylisocyanate in dry dioxane (50 ml) was stirred at room temperature in presence of sodium hydride (0.02 mol; 100%) for 5 h. The solid formed during stirring in case of phenylisocyanate was filtered off to afford **5** (20%). The filtrate was then poured onto water and neutralised with 2 ml concentrated hydrochloric acid (37.5%). The solid product, so formed, was collected by filtration and crystallised from the proper solvent. Compounds **3a** and **5** were obtained *via* fractional crystallisation from dioxane. The yield of **6** could be minimised to less than 10% by first treating **2** with phenylisothiocyanate then adding the metal hydride. Compound **6** could be also obtained following the procedure described for cyclisation of **3a**.

Compound **3a**, brown crystals; yield 60%, m.p. 95–97 °C. IR (KBr): 3400–2700  $cm^{-1}$  (NH); 1710–1620  $cm^{-1}$  (CO and C=C).  $^1H$ NMR: 2.1–3 (CH<sub>3</sub> and NH); 7.4–7.2 (aromatic protons).

$C_{19}H_{16}N_2O_3S$

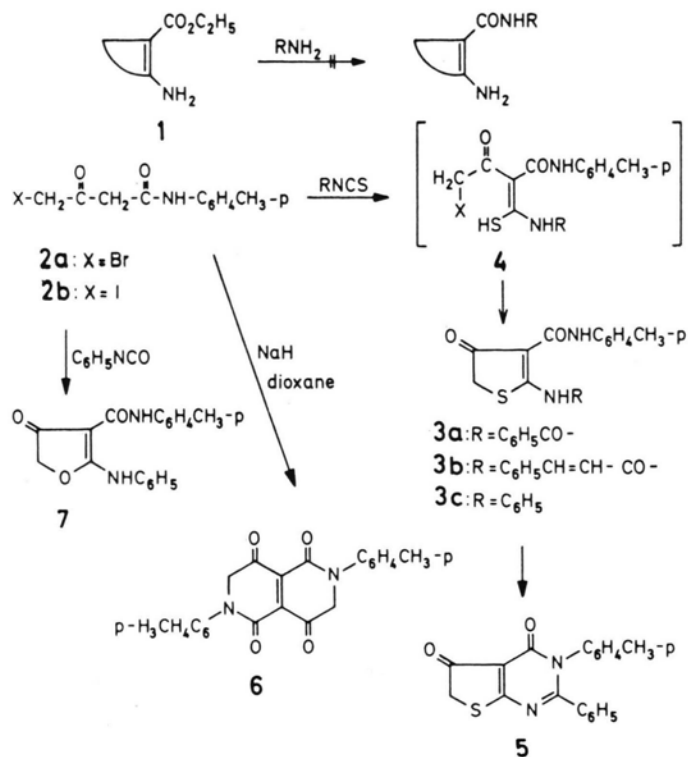
Calcd	C 64.7	H 4.5	N 7.9
Found	C 64.8	H 4.8	N 7.8

Heterocyclic enamines are versatile reagents and their synthetic application has received considerable attention [1, 2]. Although the chemistry of  $\beta$ -enaminoesters and  $\beta$ -enaminonitriles has been well explored [3–5]. Up to our knowledge, only few  $\beta$ -enaminoamides have been reported in literature. Attempted conversion of  $\beta$ -enaminoesters of type **1** into the corresponding amides has failed [6].

As a part of our program aiming to develop simple new procedures for the synthesis of azoles and fused azoles [7], we have recently reported on the utility of  $\beta$ -enaminoesters and nitriles for the synthesis of azoles and fused azoles [4, 7–9]. In conjunction to this work we report here a novel efficient synthesis of  $\beta$ -enaminoamides. Thus, it has been found that **2a**, **b** reacted with benzoylisothiocyanate to yield two products of molecular formulae  $C_{19}H_{16}N_2O_3S$  and  $C_{19}H_{14}N_2O_2S$  in 60% and 20% yields respectively. The IR spectrum of the first product revealed two broad bands extending from 3400–2700  $cm^{-1}$  (NH) and from 1710–1620  $cm^{-1}$  (CO and C=C). The  $^1H$ NMR shows two broad signals at  $\delta$  7.4–7.2 ppm for aromatic protons and at  $\delta$  2.1–3 ppm for CH<sub>3</sub> and NH. Based on these data structure **3a** was suggested for the reaction product. The formation of **3a** in this reaction was assumed to proceed *via* addition of **2** to benzoylisothiocyanate to yield the acyclic intermediate **4** which can then be cyclised into **3a** *via* elimination of HBr. The possibility that the reaction involved a mercapto pyrrole derivative was eliminated based on the stability of the reaction product on attempted alkylation with ethyl iodide or with 2,4-

\* Reprint requests to Dr. N. S. Ibrahim.  
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Compound **5**, yellow crystals; yield 20%, m.p. 277 °C. IR (KBr): 3360 (OH), 1660–1620  $\text{cm}^{-1}$  (CO and C=C).  $^1\text{HNMR}$ : Insoluble in commonly used  $^1\text{HNMR}$  solvents.

$\text{C}_{19}\text{H}_{14}\text{N}_2\text{O}_2\text{S}$

Calcd C 68.3 H 4.7 N 8.4 S 9.6,  
Found C 68.6 H 4.5 N 8.3 S 9.6.

Compound **3b**, brown crystals; yield 45%; m.p. 188–190 °C (ethanol). IR (KBr): 3400–2950 (NH); 1720–1630  $\text{cm}^{-1}$  (CO and C=C).

$\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}_3\text{S}$

Calcd C 66.6 H 4.7 N 7.4 S 8.5,  
Found C 66.4 H 4.7 N 7.3 S 8.4.

Compound **3c**, brown crystals from ethanol, yield 65%, m.p. 178 °C. IR (KBr): 3500–2400  $\text{cm}^{-1}$  (NH); 1700–1650  $\text{cm}^{-1}$  (CO and C=C).  $^1\text{HNMR}$ : 2.33 (CH<sub>3</sub> and NH), 6.8–7.6 (aromatic protons).

$\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_2\text{S}$

Calcd C 66.8 H 4.9 N 8.6 S 9.9,  
Found C 66.8 H 5.1 N 8.6 S 9.7.

Compound **6**, yellow crystals from DMF, yield 20%, m.p. 353 °C. IR (KBr): 3400, 3050  $\text{cm}^{-1}$  (OH); 2930  $\text{cm}^{-1}$  (CH<sub>2</sub>); 1680–1620  $\text{cm}^{-1}$  (CO and C=C).

$^1\text{HNMR}$ : Insoluble in commonly used  $^1\text{HNMR}$  solvents.

$\text{C}_{22}\text{H}_{18}\text{N}_2\text{O}_4$

Calcd C 70.5 H 4.8 N 7.4,  
Found C 70.4 H 5.0 N 7.6.

Compound **7**, colourless crystals from ethanol, yield 85%, m.p. 192 °C. IR (KBr): 3400–3300  $\text{cm}^{-1}$  (NH); 16800–1600  $\text{cm}^{-1}$  (CO and C=C).  $^1\text{HNMR}$ : 1.7 (NH); 2.33 (CH<sub>3</sub>); 4.7 (CH<sub>2</sub>); 7.2–7.66 (aromatic protons) and 10.8 (NH).

$\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_3$

Calcd C 70.1 H 5.1 N 9.0,  
Found C 70.0 H 5.2 N 9.2.

#### Cyclisation of **3a**

To a solution of **3a** (0.01 mol) in dry dioxane (30 ml), sodium hydride (0.02 mol) was added and the reaction mixture was heated to reflux for 5 h then poured onto water and neutralised with 2 ml concentrated hydrochloric acid (37.5%). The solid product, so formed, was collected by filtration and crystallised from dioxane.

The product obtained was found identical with an authentic specimen of compound **5**.

- [1] H. A. Elfahham, K. U. Sadek, G. E. H. Elgemeie, and M. H. Elnagdi, *J. Chem. Soc. Perkin Trans. I* **1983**, 2663.
- [2] M. R. H. Elmoghayar, M. A. E. Khalifa, M. K. A. Ibrahim, and M. H. Elnagdi, *Monatsh. Chem.* **113**, 53 (1982).
- [3] H. Wamhoff, in R. N. Castle and S. W. Schneller (eds): *Lectures in Heterocyclic Chemistry*, vol. V, Heterocorporation, Orem, Utah 1980, p.s. 61.
- [4] M. H. Elnagdi and H. Wamhoff, *Chem. Lett.* **1981**, 415.
- [5] M. H. Elnagdi and H. Wamhoff, *J. Heterocyclic Chem.* **18**, 1289 (1981).
- [6] M. H. Elnagdi and H. Wamhoff, unpublished data.
- [7] M. H. Elnagdi, H. A. Elfahham, M. R. H. Elmoghayar, K. U. Sadek, and G. E. H. Elgemeie, *J. Chem. Soc. Perkin Trans. I* **1982**, 989.
- [8] For a review see M. H. Elnagdi, H. A. Elfahham, and G. E. H. Elgemeie, *Heterocycles* **20**, 519 (1983).
- [9] M. H. Elnagdi, H. A. Elfahham, S. A. S. Ghozlan, and G. E. H. Elgemeie, *J. Chem. Soc. Perkin Trans. I* **1982**, 2667.