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IMINOFORMYLATION PRODUCTS OF THIOAMIDES, PART 17 (1): SYNTHESIS OF 5-COUMAROYLTHIOPHENES FROM 3-AMINOTHIOACRYLAMIDES AND THEIR DERIVATIVES

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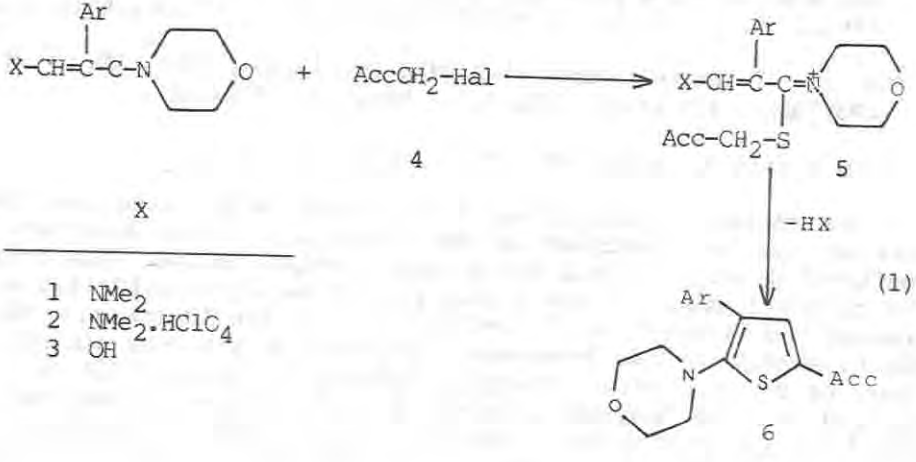
ABSTRACT: The reaction of 3-amino and 3-hydroxythioacrylamides with 3-bromoacetylcoumarin results in the formation of new 2-coumaroyl-5-morpholinothiophenes. Their structure is elucidated by spectroscopic methods and by microanalysis.

INTRODUCTION

Recently we found an efficient synthesis of N,N-disubstituted 2-aminothiophenes **6** (2-4) based on the reaction of acceptor substituted methyl halides **4**, such as α-halmoethylketones, α-haloacetates, bromonitromethane, or substituted benzyl halides, with 3-aminothioacrylamides **1**, their hydroperchlorates **2** or 3-hydroxythioacrylamides **3**. In some cases intermediate salts **5** could be isolated (2).



X

1 NMe_2
2 $NMe_2.HClO_4$
3 OH

4

5

(1)

6

The reactants 1(5,6), 2(5,6) and 3(5,7) can easily be prepared from substituted thioacetamides which are iminoformylated by formamide chlorides. In continuation of our investigations in the synthesis of N,N-disubstituted thiophenes **6** following reaction (1) as well as of coumaroylheterocycles (8) we have achieved the preparation of coumaroylthiophenes.

RESULTS AND DISCUSSION

When ethanolic solutions of 3-bromoacetylcoumarine **7**, 3-aminothioacrylamide hydroperchlorates 2 or 3-hydroxythioacrylamides 3 and triethyl amine are heated a smooth reaction (2) takes place. The crystalline products obtained are already the cyclized thiopenes 8. Intermediates, such as alkylation products 5 (Acc = 3-coumaroyl) were not isolated. High yields of the 2-coumaroylthiophenes **8** are achieved which can easily be purified by recrystallization.

Table: 2-Coumaroyl-5-morpholinothiophenes **8**

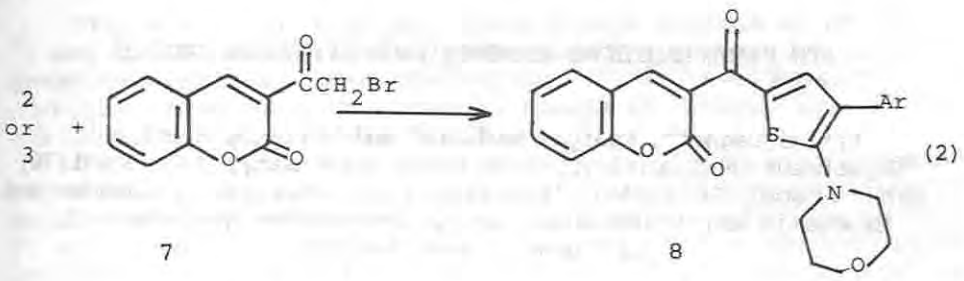
	Ar	Yield/reactant [%]	m.p. [°C]	^{1}H NMR ($CDCl_3$) [δ ppm]
8a[1]	C_6H_5	77/2	200-202 (Ethanol)	3.01(m;4H), 3.65(m;4H), 7.38(m;1H), 7.96(s;1H),
8b[2]	4-$CH_3C_6H_4$	79/2	199-200 (Acetonitrile)	2.55(s;3H), 2.99(m;4H), 3.63(m;4H), 7.29(m;9H), 7.93(s;1H).
8c	4-ClC_6H_4	94/2 94/3[3]	180-182 (Ethanol)	3.02(m;4H), 3.63(m;4H), 7.42(m;9H), 7.96(s;1H).
8d	4-$CH_3OC_6H_4$	92/2	158-161 (Ethanol)	2.98(m;4H), 3.64(m;4H), 3.70(s;3H), 6.78(d;2H), 7.38(m;7H), 7.91(s;1H).

[1] UV (Acetonitrile) λ_{max} nm (log ε): 224(4.26), 279(4.29), 387(4.23). MS: m/e (relative intensity) 418(29.1), 417(M^+, 100), 358(19.3), 186(33.7), 173(78.1), 115(28.5), 101(22.1), 89(27.4), 63(17.5).

[2] MS: m/e (relative intensity) 432(28.9), 431(M^+, 100), 200(29.3), 173(78.1), 129(14.6), 115(11.5), 89(13.0), 44(15.9).

[3] 1.01 g triethyl amine was used instead of 2.02 g.

The coumarylthienylketones 8 are stable yellow compounds that have not yet been described in the literature. Their structure is confirmed by microanalysis and by spectroscopic methods (see table). The carbonyl groups of the **8** give rise to peaks at 1610-1620 (C=O ketone) and 1720-1730 cm^{-1} (C=O lactone) in the IR-spectra (KBr). The UV-spectra of the 2-coumaroylthiophenes 8 are very similar to those of corresponding 5-aroylthiophenes **6** (Acc=arylCO) (2). A typical intense fragment peak of 173 (M^+ - thienyl fragment) is found in the MS-spectra. The biological test of compound **8a** revealed a significant inhibition of the angiotensin converting



(2)

enzyme (IC_{50}= 18.10^{-6}mol).

EXPERIMENTAL

The mixture of 3-aminothioacrylamide hydroperchlorate **2** (0.01 mol), or 0.01 mol 3-hydroxythioacrylamide **3**, 2.67 g (0.01 mol) 3-bromoacetylcoumarine **7**, 2.02 g (0.01 mol) triethyl amine and 15 ml ethanol is refluxed for 3 minutes. After cooling to room temperature the product precipitates. It is filtered by suction and recrystallised.

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