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SYNTHESIS OF THIAZOLE, BENZOTHIAZOLE, OXADIAZOLE, THIADIAZOLE, TRIAZOLE AND THIAZOLIDINONE INCORPORATED COUMARINS

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3-Bromoacetylcoumarin (**2**) obtained by bromination of 3-acetylcoumarin (**1**) was condensed with 2-amino-4-phenylthiazole, 2-aminothiazole, 2-aminobenzothiazole, 2-amino-4-phenyloxadiazole, 2-aminothiadiazole, 3-aminotriazole to form the corresponding heteroaryl aminoacetylcoumarins (**3a-f**). The reaction of **2** with thiourea furnished 2-amino-4-(coumarinyl-3) thiazole (**4**) which further reacted with phenylisothiocyanate forming the unsymmetrical thiourea (**5**). The thiourea on cyclocondensation with chloroacetic acid gave the thiazolidinone (**6**) which on further reaction with different aromatic aldehydes resulted in the formation of the corresponding arylidene compounds (**7**). The structures of the products were confirmed from their analytical and spectral data.

In view of reported application of thiazolo coumarins in medicine and dye industries[1] the synthesis of title compounds have been under taken.

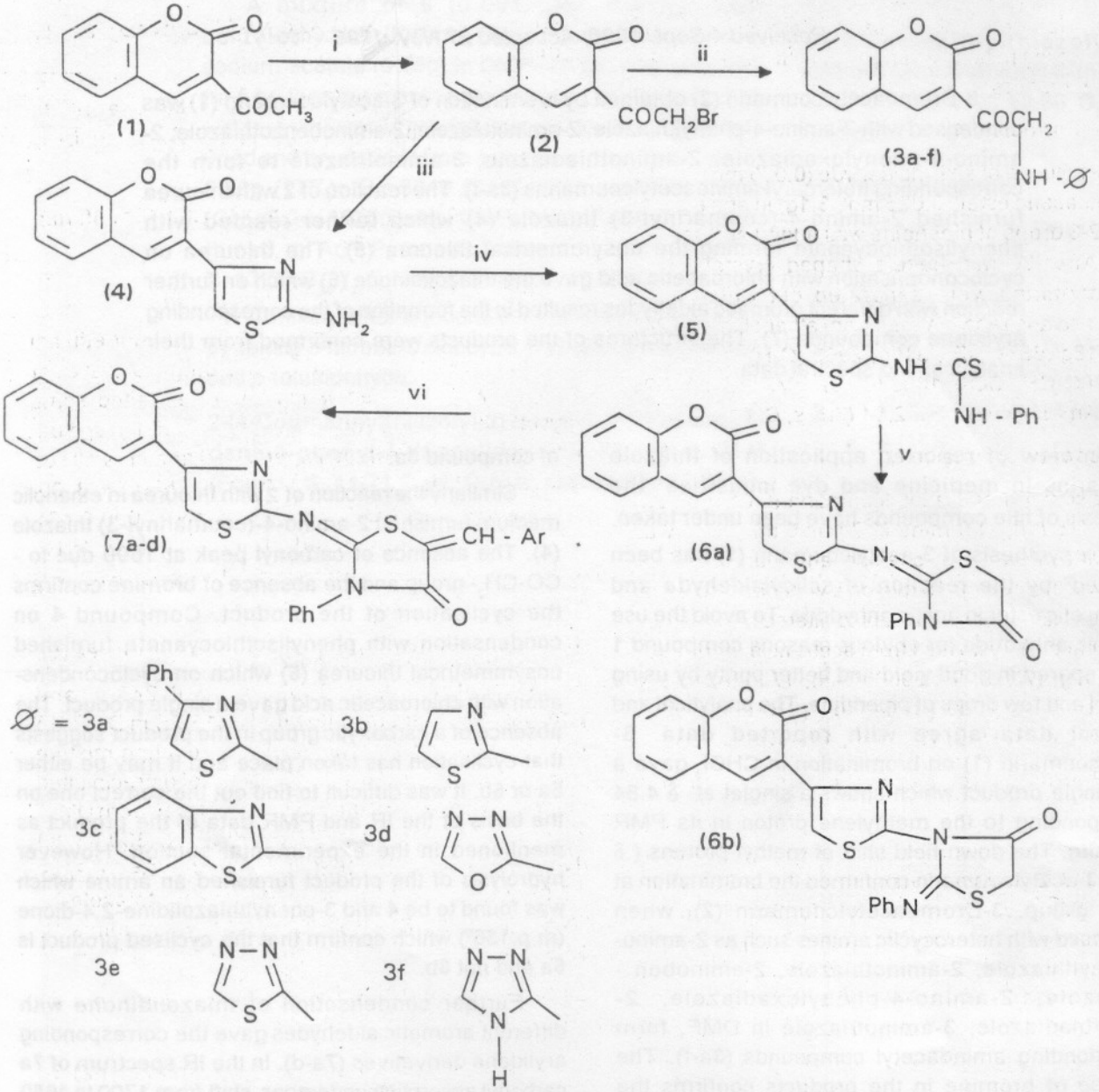
The synthesis of 3-acetylcoumarin (**1**) has been reported[2] by the reaction of salicylaldehyde and acetoacetic ester in acetic anhydride. To avoid the use of acetic anhydride for obvious reasons compound **1** was prepared in good yield and better purity by using ethanol and few drops of piperidine. The analytical and spectral data agree with reported data. 3-Acetylcoumarin (**1**) on bromination in $CHCl_3$ gave a TLC single product which shows a singlet at δ 4.84 corresponding to the methylene proton in its PMR spectrum. The down field shift of methyl protons (δ 2.3) in 3-acetylcoumarin confirmed the bromination at acetyl group. 3-Bromoacetylcoumarin (**2**), when condensed with heterocyclic amines such as 2-amino-4-phenylthiazole, 2-aminothiazole, 2-aminoben - zothiazole, 2-amino-4-phenyloxadiazole, 2-aminothiadiazole, 3-aminotriazole in DMF, form corresponding aminoacetyl compounds (**3a-f**). The absence of bromine in the products confirms the successful condensation of the amines. The appearance of a broad band at 3300 cm^{-1} corresponding to the N-H group along with other bands due to carbonyl groups, aliphatic and aromatic C-H bands in the IR spectrum of compound **3a** and a broad singlet at 5.02 for the N-H proton, a singlet at 3.04 corresponding to methyl proton and a multiplet at 7.22-8.14 (eleven aromatic protons) support the formation of compound **3a**.

Similarly the reaction of **2** with thiourea in ethanolic medium furnished 2-amino-4-(coumarinyl-3) thiazole (**4**). The absence of carbonyl peak at 1690 due to -$CO\text{-}CH_2$- group and the absence of bromine confirms the cyclisation of the product. Compound **4** on condensation with phenylisothiocyanate furnished unsymmetrical thiourea (**5**) which on cyclocondensation with chloroacetic acid gave a single product. The absence of a carboxylic group in the product suggests that cyclisation has taken place and it may be either **6a** or **6b**. It was difficult to find out the correct one on the basis of the IR and PMR data of the product as mentioned in the experimental section. However hydrolysis of the product furnished an amine which was found to be **4** and 3-phenylthiazolidine-2,4-dione (m.p.136°) which confirm that the cyclised product is **6a** and not **6b**.

Further condensation of thiazolidinone with different aromatic aldehydes gave the corresponding arylidene derivatives (**7a-d**). In the IR spectrum of **7a** carbonyl absorption undergoes shift from 1700 to 1680 due to conjugation of the carbonyl group with exocyclic double bond. The absence of the peak at 3.44 due to $CO\text{-}CH_2$ proton in its PMR spectrum confirmed the structure **7a**.

Experimental

Melting points were determined in a sulphuric acid bath and are uncorrected. IR spectra were recorded



Ar = 7a : C_6H_5 -, 7b : *p*-NO_2 - C_6H_4 - , 7c : *p*-Cl C_6H_4 - , 7d : *p*-Me-C_6H_4 - .

i : Br_2, ii: ∅ - NH_2, iii : NH_2 $CSNH_2$, iv : PhNCS, v : $ClCH_2$ COOH, NaOAc, vi : ArCHO.

SCHEME-1

in nujol mull on Perkin-Elmer IR 157 and PMR spectra in DMSO-d_6 on a Perkin-Elmer R-32 NMR instrument using TMS as internal standard (chemical shifts in δ ppm). Compounds were checked for their purity by TLC on silica gel G plates using Methanol-benzene (v/v) by varying polarity as irrigant and the spots located by iodine vapours.

3-Acetylcoumerin (1)

To a solution of salicylaldehyde (0.025 mol, 3.44g) and acetoacetic ester (0.025 mol, 3.1g) in abs ethanol (15 ml) 2-3 drops of piperidine was added and shaken gently. After 30 min needle shaped crystals of 3-acetylcoumarins were separated out which were filtered dried and recrystallised from ethanol, m.p. 124°, yield: 3.18g (68%); IR : 3100, 2900 (C-H), 1720 (-O-CO-), 1700 (CH_3-CO-), 1605 (C=C); PMR; δ 7.05-7.95 (5H, m, ArH & Pyrone-H), 2.54 (3H, s, CH_3).

3-Bromoacetylcoumarin (2)

To a solution of 3-acetylcoumarin (0.01 mol, 2g) in $CHCl_3$ (15 ml),, bromine (1.7g) in 6 ml $CHCl_3$ was added with intermittent shaking and warming. The mixture was heated for 15 min on a water bath to expel most of the HBr. It was then cooled filtered and washed with ether and recrystalised from acetic acid, m.p. 162°, yield : 1.97g, (70%); IR: 2960 (C-H), 1720 (-O-CO-), 1690 (-CH-CO-), 1600 (C=C), 760 (CH_2-Br); PMR : 7.1-8.0 (5H, m, ArH & pyrone-H), 4.84 (2H, s, CH_2).

3-[N-(4-Phenylthiazolyl-2) amino] acetylcoumarin (3a)

A mixture of 3-bromoacetylcoumarin (0.001 mol, 0.267g) and 2-amino-4-phenylthiazole (0.001 mol, 0.36g) in DMF (15 ml) was refluxed for 3 hr. Then the reaction mixture was poured into water. The precipitate so produced was filtered, dried and crystallised from ethanol, m.p. 115°, yield: 0.27g (75%); IR: 3300 (N-H), 2950 (C-N), 1715 (-O-CO-), 1700 (-CH_2-CO-), 1605 (C=C & C-N); NMR : 7.22-8.14 (11H, m, ArH, Pyrone-H, thiazole-H), 5.02 (1H, bs, NH), 3.04 (2H, s, CH_2).(Found: S, 8.93, $C_{20}H_{15}O_3N_2S$ requires S, 8.81%)

Similarly other heteroaryl aminoacetylcoumarins (3b-f) were synthesised and characterised by taking 2-aminothiazole, 2-aminobenzothiazole, 2-amino-4-phenyloxadiazole, 2-aminothiadiazole, and 3-aminotriazole.

3-[N-(Thiazolyl-2) amino] acetylcoumarin (3b) : m.p. 253°, (Found : S, 11.08, $C_{14}H_{11}O_3N_2S$ requires S, 11.15%).

3-[N-(Benzothiazolyl-2) amino] acetylcoumarin : 3c: m.p. >250° (Found : S, 10.12; $C_{17}H_{12}O_3N_2S$ requires S, 9.87%).

3-[N-(5-Phenyloxadiazolyl-2) amino] acetyl coumarin : (3d): m.p. 180°.

3-[N-(Thiadiazolyl-2) amino] acetylcoumarin : 3e: m.p. 170° (Found : S, 11.24, $C_{13}H_9O_3N_3S$ requirs S, 11.15%).

3-[N-(Triazolyl-2) amino] acetylcoumarin: 3f: m.p. 210°.

2-Amino-4-(coumarinyl-3) thiazole (4)

A solution of **2** (0.005 mol, 1.35g) in hot ethanol was treated with thiourea (0.01 mol, 0.8g) so that clear solution was obtained which soon deposited some crystals. It was then boiled in water containing sodium acetate, which was then filtered dried and crystallised from ethanol, m.p. 225°, yield : 0.792g (65%); IR: 3300-3210 (N-H), 1720 (-O-CO-), 1630 (C=N), 1600(C=C); PMR : 7.14-8.12 (6H, m, ArH, Pyrone-H, thiazole-H), 4.88 (2H, bs, NH_2).(Found : S, 12.89 $C_{12}H_8O_2N_2S$ requires S, 13.11%)

1-(4-Coumarynylthiazolyl-2)-3-phenylthiourea (5)

A solution of **4** (0.001 mol, 0.244g) and phenylisothiocyanate (0.001 mol, 0.135g) in DMF (15 ml) was refluxed for 5 hr. Then the reaction mixture was poured into cold water. A yellow solid precipitated out which was filtered, dried and crystallised from DMF-water, m.p. 177°, yield : 0.253g (66%); IR : 3300-3280 (N-H), 1720 (-O-CO-), 1620 (C=N), 1600 (C=C); PMR : 7.98-8.98 (broad, m, ArH, Pyrone-H, thiazole-H, 2NH). (Found : S, 16.76 $C_{19}H_{13}O_2N_3S_2$ requires S, 16.88%).

2-(4-Coumarinylthiazolyl-2) imino-3-phenyl-4-thiazolidinone (6)

A mixture of 1-(4-coumarinylnylthiazolyl-2)-3-phenyltiourea (0-001 mol, 0.379g) and chloroacetic acid (0.001 mol, 0.082g) in DMF (15 ml) was refluxed for 5 hr. Then the reaction mixture was poured into cold water. A reddish solid precipitated out which was filtered, dried and crystallised from acetic acid, m.p. 140°, yield : 0.315g (75%); IR : 3070 (C-H), 2930 (C-H), 1720 (-O-CO-), 1700 (-CH_2-CO), 1620 (C=N), 1600 (C=C); PMR : 7.12-8.05 (11H, m, ArH, Pyrone-H, thiazole-H), 3.44 (2H, s, CH_2).(Found : S, 15.11 $C_{11}H_{13}O_3N_3S_2$ requires S, 15.27%).

2-(4-Coumarinylthiazolyl-2) imino-5-benzylidene-3-phenyl-4-thiazolidenone (7a)

A mixture of **6** (0.001 mol, 0.419g) and benzaldehyde (0.001 mol, 0.1g) in presence of anhyd sodium acetate (0.05g) in DMF (20 ml) was refluxed for 5 hr. then the reaction mixture was poured into cold water. A white solid precipitated out which was filtered, dried and crystallised from acetic acid, m.p. 210°, yield: 0.39g (77%); IR : 3040 (C-H), 1720 (-O-CO-), 1680 (CH_2-CO-), 1620(C=N), 1605 (C=C); PMR : 7.02-8.08 (broad, m. ArH, Pyrone-H, Thiazole-H, =CH),(Found : S, 13.06 $C_{28}H_{17}O_3N_3S_2$ requires S, 12.87%).

Similarly other arylidene derivatives were prepared by taking *p*-nitrobenzaldehyde, *p*-chlorobenzaldehyde, and *p*-tolualdehyde.

2-(4-Coumarinylthiazoiyl-2) imino-5-*p*-nitrobenzylidene-3-phenyl-4-thiazolidenone :7b : m.p. 214° (Found : S, 11.71 $C_{28}H_{16}O_5N_4S_2$ requires S, 11.63%).

2-(4-Coumarinylthiazolyl-2) imino-5-*p*-chlorobenzylidene-3-phenyl-4-thiazolidenone : 7c: m.p. 195° (Found : S, 11.77 $C_{28}H_{16}ClO_3N_3S_2$ requires S, 11.82%).

2-(4-Coumarinylthiazolyl-2) imino-5-methyl benzylidene-3-phenyl-4-thiazolidenone :7d: m.p. 224° (Found : S, 12.36 $C_{29}H_{19}O_3N_3S_2$ requires S, 12.28%).

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References

1. V.K. Ahluwalia, N. Mallika, R.P. Singh and C. H. Khandur, *Indian J. Chem.*, 29B (1990), 667
2. P. Czerney and H. Hartmann, *J. Prakt. Chem.*, 4 (1983), 551.

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