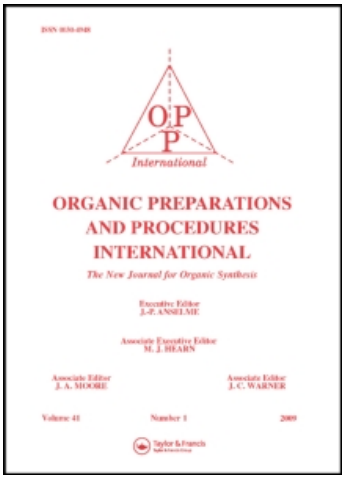

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SYNTHESIS OF THIADIAZINE AND ARYLMETHINEAZOTHIAZOLONE DERIVATIVES OF COUMARIN

R. Djudjic[a]; M. Trkovnik[a]; D. Kitan[a]
[a] Laboratory of Organic Chemistry and Biochemistry Technological Faculty, University "Djuro Pucar-Stari", Banja Luka, YUGOSLAVIA

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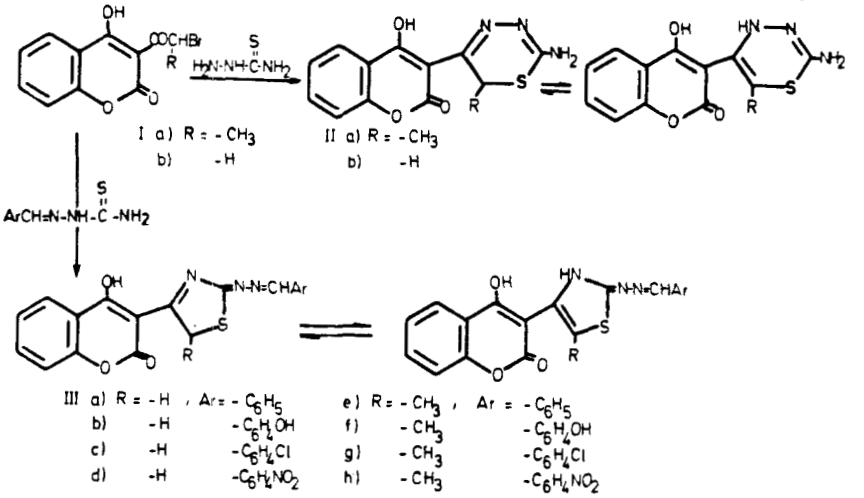
SYNTHESIS OF THIADIAZINE AND ARYLMETHINEAZOTHIAZOLONE DERIVATIVES OF COUMARIN

Submitted by R. Djudjic, M. Trkovnik* and D. Kitan
(09/19/84)

Laboratory of Organic Chemistry and Biochemistry
Technological Faculty, University "Djuro Pucar-Stari"
78000 Banja Luka, YUGOSLAVIA

Coumarin derivatives are reported[1] to possess antibacterial properies and can inhibit biological oxidations. We have tried to obtain agents of these types which could be of practical use. In a previous communication,[2] we described reactions of 3-(α-haloacyl)-4-hydroxycoumarins (I) with thiourea, which yielded the corresponding 3-aminothiazole derivatives. We now report the reactions of compounds I with thiosemicarbazide and with aryl thiosemicarbazones to yield 2-amino-5-(4'-hydroxycoumarin-3'-yl)-1-



thia-3,4-diazines (IIa,b) and the 2-arylmethineazo-4-(4'-hydroxycoumarin-3'-yl)-thiazol-2-ones (IIIa-h), respectively. The synthesis of substituted thiadiazines starting from phenacyl halides has previously been described by Postovskii et al.[3] and by Pfeiffer et al.[4]

The thiadiazine and thiazolone derivatives can assume two tautomeric forms. Nmr evidence shows that in solution, the former compounds exist predominantly in the form in which both ring-nitrogens are doubly bonded. The existence of this form is indicated by 6C-proton quartets at 5.6 ppm

and methyl hydrogen doublets at 1.5 ppm. In the solid state, the other tautomer seems to predominate as the crystalline compounds exhibit IR bands characteristic of the NH group. But, in contrast to the thiadiazine derivatives, the predominant tautomeric form of the thiazolone derivatives, both in solution and solid form, appears to be that with a doubly bonded ring-nitrogen, as shown by the absence of NH-bands in the IR and the presence of a 5C-proton singlet in the nmr spectra.

EXPERIMENTAL SECTION

All mps are uncorrected. The spectra were recorded on the following instruments: Perkin Elmer M-377 infrared spectrometer (KBr pellets); Perkin-Elmer B-12 nmr spectrometer (solvents DMSO d-6, $CDCl_3$) and mass spectra were obtained on a Hitachi-Perkin-Elmer RMU-6L spectrometer.

2-Amino-5-(4'-hydroxycoumarin-3'-yl)-6-methyl-1-thia-3,4-diazine (IIa).- One gram (3.36 mmol) of 3-α-bromopropionyl-4-hydroxycoumarin (Ia) was dissolved in 90 ml of ethanol by heating under reflux. The solution was allowed to cool to 60° then 0.31 g (3.36 mmol) of thiosemicarbazide was added. After 30 min. stirring at 60°, then 5 min. at reflux temperature, the volume was reduced to one-half and a few drops of conc. ammonia solution added. The product was induced to precipitate by the addition of 50 ml of water to yield 0.60 g (61%) of yellow crystals, mp. 220° (50% EtOH).

IR: 3295-3395 (NH_2, OH), 3190 (NH), 2990 (CH arom.), 1670 (CO), 1608 (C=C arom.) cm^{-1}; nmr: δ 7.1-8.03 (m, 4H arom. NH_2), 5.65 (q, CH), 1.5 (d, CH_3); MS: M^+ 289 (100).

Anal. Calcd for $C_{13}H_{11}N_3O_3S$: C, 53.96; H, 3.83; N, 14.52

Found: C, 53.46; H, 4.03; N, 13.95

2-Amino-5-(4'-hydroxycoumarin-3'-yl)-1-thia-3,4-diazine (IIb).- One gram (3.53 mmol) of 3-α-bromoacetyl-4-hydroxycoumarin (Ib) was dissolved in 70 ml of ethanol by gentle heating and the solution was allowed to cool to

room temperature. An equimolar amount of thiosemicarbazide, in 50 ml of ethanol was then added and the mixture stirred for 15 min. without heating. The solid product (0.52 g, 51%) was obtained by precipitaion with 60 ml of water as yellow crystals, mp. 246-248° (50% EtOH). IR: 3190-3300 (NH_2, OH), 3120 (NH), 3020 (CH arom.), 1650 (CO), 1600 (C=C arom.) cm^{-1}.

Anal. Calcd for $C_{12}H_9N_3O_3S$: C, 52.35; H, 3.29; N, 15.26

Found: C, 51.82; H, 3.61; N, 14.87

2-Benzalazo-4-(4'-hydroxycoumarin-3'-yl)-thiazol-2-one (IIIa).- To 1 g (3.53 mmol) of Ib in 50 ml of ethanol was added benzaldehyde thiosemicarbazone (0.61 g, 3.53 mmol). Crystals of the product started to separate at once. The reaction was completed by refluxing for 1 hr to yield 0.91 g (70%) of yellow crystals, mp. 284-286° (after digestion with hot 96% EtOH). IR: 3180 (OH) 3020, 2930 (CH arom.), 1750 (CO), 1615 (C=C arom.). nmr: δ 7.35-8.12 (m, 9H arom., CH, NH). MS: M^+ 363 (100).

Anal. Calcd for $C_{19}H_{13}N_3O_3S$: C, 62.79; H, 3.60; N, 11.56

Found: C, 62.31; H, 3.38; N, 11.09

Further compounds in the III series were prepared by the same procedure as that described for IIIa, using the appropriate starting compounds.

2-(o-Hydroxybenzalazo)-4-(4'-hydroxycoumarin-3'-yl)-thiazol-2-one (IIIb) in 71% yield as yellow crystals, mp. 313-314°. IR: 3400, 3280 (OH), 3080, 2980 (CH, arom.), 1680 (CO), 1600 (C=C arom.) cm^{-1}; nmr: δ 10.5 (OH), 8.4 (NH), 6.8-8.1 (CH, m, 8H arom.); MS: M^+ 379 (100).

Anal. Calcd for $C_{19}H_{13}N_3O_4S$: C, 60.16; H, 3.43; N, 11.08

Found: C, 59.41; H, 2.89; N, 10.64

2-(p-Chlorobenzalazo)-4-(4'-hydroxycoumarin-3'-yl)-thiazol-2-one (IIIc) in 74% yield as yellow crystals, mp. 307-309°. IR: 3200 (OH), 3000, 2900 (CH,arom.), 1670 (CO), 1605 (C=C arom.) cm^{-1}; nmr: δ 8.12 (NH), 7.35-8.05 (m, 8H arom. CH); MS: M^+ 398 (50).

Anal. Calcd for $C_{19}H_{12}ClN_3O_3S$: C, 57.21; H, 3.03; N, 10.53

Found: C, 57.69; H, 2.60; N, 10.18

2-(p-Nitrobenzalazo)-4-(4'-hydroxycoumarin-3'-yl)-thiazol-2-one (IIId) in 80% yield as yellow crystals, mp. 338-340°. IR: 3420 (OH), 2910 (CH, arom.), 1678 (CO), 1615 (C=C arom.), 1510 (NO_2) cm^{-1}; nmr: δ 8.5 (NH), 6.90-7.90 (m, 8H arom., CH).

Anal. Calcd for $C_{19}H_{12}N_4O_5S$: C, 55.88; H, 2.96; N, 13.72

Found: C, 56.45; H, 2.43, N, 13.18

2-Benzalazo-4-(4'-hydroxycoumarin-3'-yl)-5-methylthiazol-2-one (IIIe) in 74% yield as yellow crystals, mp. 252-254°. IR: 2900 (CH arom.), 1750 (CO), 1600 (C=C arom.) cm^{-1}; nmr: δ 7.25-8.12 (m, 9H arom., NH), 1.9 (s, CH_3); MS: M^+ 377 (15).

Anal. Calcd for $C_{20}H_{15}N_3O_3S$: C, 63.64; H, 4.01; N, 11.14

Found: C, 63.21; H, 3.72; N, 10.76

2-(o-Hydroxybenzalazo)-4-(4'-hydroxycoumarin-3'-yl)-5-methylthiazol-2-one (IIIf) in 78% yield as yellow crystals, mp. 237-239°. IR: 3400 (OH), 3050 (CH, arom.), 2750 (CH_3), 1675 (CO), 1600 (C=C arom.) cm^{-1}; nmr: δ 8.95 (OH), 8.4 (NH), 6.85-8.10 (m, 8H, arom., CH), 2.3 (s, CH_3); MS: M^+ 393 (100).

Anal. Calcd for $C_{20}H_{15}N_3O_4S$: C, 61.10; H, 3.84; N, 10.69

Found: C, 60.73; H, 3.48; N, 10.16

2-(p-Chlorobenzalazo)-4-(4'-hydroxycoumarin-3'-yl)-5-methylthiazol-2-one-(IIIg) in 79% yield as yellow crystals, mp. 236-238°. IR: 3410 (OH), 2810 (CH, arom.), 2710 (CH_3), 1665 (CO), 1600 (C=C arom.) cm^{-1}; nmr ($CDCl_3$): δ 8.18 (NH), 7.3-8.1 (m, 8H arom., CH), 2.45 (s, CH_3); MS: M^+ 412 (30).

Anal. Calcd for $C_{20}H_{14}ClN_3O_3S$: C, 58.18; H, 3.41; N, 10.18

Found: C, 57.74; H, 3.07; N, 10.50

2-(p-Nitrobenzalazo)-4-(4'-hydroxycoumarin-3'-yl)-5-methylthiazol-2-one (IIIh) in 85% yield as yellow crystals, mp. 305-308°. IR: 3420 (OH), 3000 (CH arom.), 2910 (CH_3), 1675 (CO), 1612 (C=C, arom.) cm^{-1}; nmr: δ 7.3-8.35 (m, 8H arom., NH, CH), 2.20 (s, CH_3); MS: M^+ 422 (100).

Anal. Calcd for $C_{20}H_{14}N_4O_5S$: C, 56.86; H, 3.34; N, 13.26

Found: C, 57.45; H, 3.51; N, 13.27

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AN EFFICIENT SYNTHESIS OF N-(2,4-DIFLUOROPHENYL)-N-METHYL-2,4-DINITRO-6-(TRIFLUOROMETHYL)ANILINE

Submitted by E. V. P. Tao* and H. A. Corbitt
(11/05/84)
The Lilly Research Laboratories
Eli Lilly and Company
Indianapolis, IN 46285

N-(2,4-difluorophenyl)-N-methyl-2,4-dinitro-6-(trifluoromethyl)aniline (2),[1] is a contact miticide which has demonstrated effective control of phytophagus mites on cotton and tree fruits and nuts. Methyl bromide has