

Short Communication

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STUDIES ON 3-CARBETHOXY-5,6-BENZO-COUMARIN

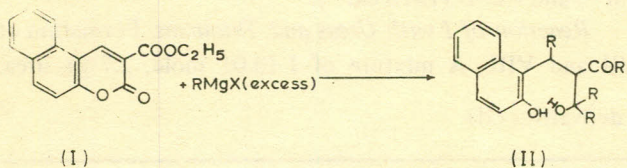
Part I. Action of Grignard reagents, Ureas, Thioureas and Thiophenols

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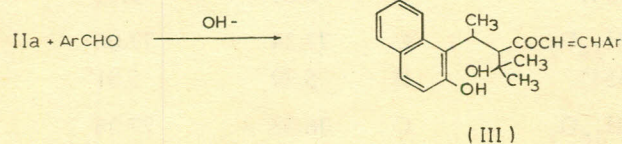
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In continuation of the previous studies [1-10], the present communications reports on reactivity of 3-carbethoxy-5,6-benzocoumarin (I) towards Grignard reagents, ureas thioureas and thiophenols. It has been reported that (I) reacts with Grignard reagents namely methylmagnesium iodide, ethylmagnesium iodide, n-butylmagnesium bromide, benzylmagnesium chloride, phenylmagnesium bromide, *o*, *p*-anisylmagnesium bromide to give the naphthol derivatives IIa-g respectively.



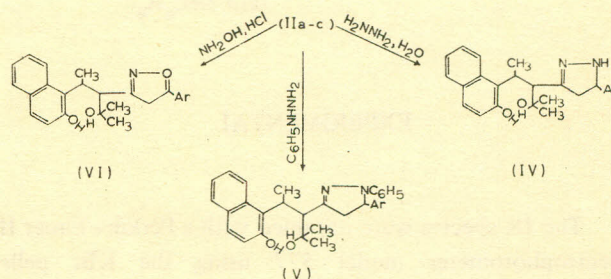
R, (a) CH₃; (b) C₂H₅;
(c) n-C₄H₉; (d) C₆H₅CH₂;
(e) C₆H₅; (f) *o*-MeOC₆H₄;
(g) *p*-MeOC₆H₄.

The structures of II were established from correct analytical data, colour reaction for naphthols with alcoholic ferric chloride and their IR spectra which showed bands attributed to ketonic (C=O) and OH groups [12] confirming the structure for II. Further evidence for structure of IIa is furnished by condensation with aldehyde to give the cinnamoyl derivatives IIIa-c. The IR spectra of III showed bands for α , β -unsaturated ketones and OH [12].



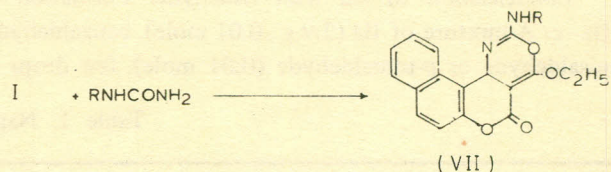
Ar, (a) C₆H₅; (b) *p*-MeOC₆H₄;
(c) *p*-MeC₆H₄.

The activity of the exocyclic C=C conjugated with the carbonyl group in III prompted us to investigate their behaviour towards the action of hydrazinehydrate, phenylhydrazine and hydroxylamine to give the corresponding pyrazoline (gave colour test of pyrazoline [11]) and oxazoline derivatives IV-VI respectively.



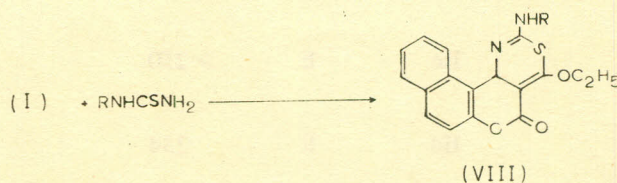
Ar, (a) C₆H₅; *p*-MeOC₆H₄
(c) *p*-MeC₆H₄

The olefinic double bond in I is activated to both the carbonyl and carboxy groups, thus the reaction of I with urea and methylurea gave oxazinobenzocoumarin derivatives VIIa and b:



R, (a) H; (b) CH₃.

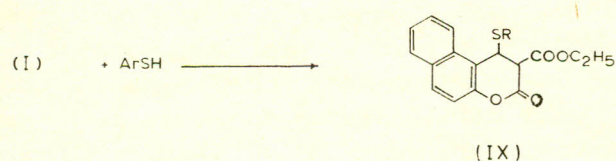
In a similar manner I reacts with thiourea, phenyl, benzyl and *o*-chlorophenyl thioureas to give thiazinobenzocoumarin derivatives VIIIa-d respectively.



R, (a) H; (b) C₆H₅;
(c) C₆H₅CH₂; (d) *o*-ClC₆H₄.

Compounds VIIa and VIIIa gave the acetoxy derivatives on boiling with acetic anhydride (IR spectra showed acetyl) (C=O at 1690 cm⁻¹)

With thiophenols, I furnishes benzocoumarin derivatives IX via addition on the olefinic double bond in I



Ar, (a) C_6H_5 ; (b) *o*- MeC_6H_4 ;
(c) *p*- MeC_6H_4 .

EXPERIMENTAL

The IR spectra were obtained with a Perkin-Elmer IR spectrophotometer model 577 using the KBr pellet technique. M.ps. are uncorrected.

Reaction of I with Grignard Reagents. A solution of Grignard reagent (0.08 mole) in dry ether was treated with a solution of I (0.01 mole; 2.7 g) in dry benzene (50 ml). The ether was evaporated and the reaction mixture was worked up as usual and crystallized from a proper solvent to give II (40–50%) as yellow crystals (cf. Table 1); IR spectra: ν OH (3450 cm^{-1}) and ν C=O ketonic (1690 cm^{-1}).

Condensation of IIa with Aldehyde. Formation of IIIa–c: A mixture of IIa (2.9 g, 0.01 mole), benzaldehyde, anisaldehyde or *p*-tolualdehyde (0.01 mole), few drops of

piperidine and ethanol (30 ml) was refluxed for 6 hr. The yellow products separated after cooling were recrystallised from benzene to give IIIa–c as pale yellow crystals (cf. Table 2); IR spectra: ν OH (3450 cm^{-1}), and ν C=O (1660 cm^{-1}).

Condensation of III with Hydrazinehydrate and Phenylhydrazine. Formation of Pyrazolines IV and V: A solution of IIIa–c (0.01 mole) in ethanol (20 ml) was treated with hydrazinehydrate or phenylhydrazine (0.015 mole) and the solution was refluxed for 3 hr. The solids that separated after cooling were crystallised from suitable solvents to give IV and Va–c respectively (50–60%). The results are listed in Table 3; IR spectral IV, OH ($3440, 3150\text{ cm}^{-1}$) and ν C=N (1618 cm^{-1}); for V, ν OH (3420 cm^{-1}) and ν C=N (1608 cm^{-1}) and NH.

Reaction of III with Hydroxylamine. Formation of Isooxazolines Derivative VI: Hydroxylamine hydrochloride (0.03 mole, 2.1g) and sodium acetate (0.03 mole, 2.5 g) were dissolved in the least amount of water and added to a solution of III (0.01 mole) in ethanol (50 ml). The reaction mixture was refluxed for 4 hr, concentrated and cooled, the solid product which separated was collected and recrystallised from acetic acid to give VIa–c respectively as pale yellow crystals (Table 4); IR spectra ν OH (3450 cm^{-1}) and ν C=N (1610 cm^{-1}).

Reaction of I with Ureas and Thioureas. Formation of VII and VIII: A mixture of I (0.01 mole, 2.7 g), urea,

Table 1. Naphthol derivatives (II).

Compound	Solvent of crystn	M.p. ($^{\circ}\text{C}$)	Formula (mol.wt.)	Analysis(%)		
				Found	Calcd	
IIa	E	248	$C_{18}H_{22}O_3$ (286)	C	75.39	75.52
				H	7.72	7.69
IIb	B	> 250	$C_{22}H_{30}O_3$ (342)	C	77.29	77.19
				H	8.73	8.77
IIc	E	> 250	$C_{30}H_{46}O_3$ (454)	C	79.10	79.29
				H	10.16	10.13
IId	E	234	$C_{42}H_{38}O_3$ (590)	C	85.01	85.42
				H	6.47	6.44
IIe	B	> 250	$C_{38}H_{30}O_3$ (534)	C	85.77	85.39
				H	5.61	5.62
IIf	B	> 250	$C_{42}H_{38}O_7$ (654)	C	77.24	77.06
				H	5.79	5.81
IIg	B	> 250	$C_{42}H_{38}O_7$ (654)	C	76.83	77.06
				H	5.84	5.81

E Ethanol, B benzene

Table 2. Cinnamoyl derivative of IIa.

Compound	M.p. (°C)	Formula (m.wt.)		Analysis(%)	
				Found	Calcd
IIIa	164	C ₂₅ H ₂₆ O ₃ (374)	C	80.67	80.21
			H	6.91	6.95
IIIb	182	C ₂₆ H ₂₈ O ₄ (404)	C	77.00	77.22
			H	6.95	6.93
IIIc	203	C ₂₆ H ₂₈ O ₃ (388)	C	80.01	80.41
			H	7.22	7.21

Table 3. Pyrazolines (IV and V).

Compound	Solvent of crystn	M.p. (°C)	Formula (m.wt)		Analysis(%)	
					Found	Calcd
IVa	E	186	C ₂₅ H ₂₈ N ₂ O ₂ (388)	C	77.60	77.31
				H	7.18	7.21
				N	7.29	7.21
IVb	E	210	C ₂₆ H ₃₀ N ₂ O ₃ (418)	C	74.35	74.64
				H	7.19	7.17
				N	6.73	6.69
IVc	E	233	C ₂₆ H ₃₀ N ₂ O ₂ (402)	C	77.91	77.61
				H	7.40	7.46
				N	7.05	6.96
Va	Ac	144	C ₃₁ H ₃₂ N ₂ O ₂ (464)	C	80.43	80.17
				H	6.85	6.89
				N	6.08	6.03
Vb	Ac	158	C ₃₂ H ₃₄ N ₂ O ₃ (494)	C	77.94	77.73
				H	68.86	6.88
				N	5.69	5.66
Vc	Ac	180	C ₃₂ H ₃₄ N ₂ O ₂ (478)	C	80.00	80.33
				H	7.17	7.11
				N	6.00	5.85

E ethanol, Ac acetic acid

methylurea, thiourea, phenylthiourea and benzyl-*o*-chlorophenyl thiourea (0.02 mole), (20 ml) was treated with ten drops of glacial acetic acid. The mixture was then refluxed for 6 hr. The solid, which separated after evaporation of most of solvent and cooling, was crystallised from the suitable solvents to give VII and VIII (60–70%). The results are listed in Table 5. IR spectra for VII and VIII; δ lacton C=O in the region (1640–1645 cm⁻¹),

NH (3200–3260 cm⁻¹) and cyclic C=N (1600–1610 cm⁻¹)

Acetylation of VIIa and VIIIa. A solution of VIIa and or VIIIa (2 g) in acetic anhydride (20 ml) was heated for 2 hr on the steam-bath. The cooled solution was poured into ice and the solid which separated was collected and recrystallised from ethanol. The acetyl derivative of VIIa (50%) hadan m.p. 182°. (Found: C, 64.79; H, 4.80; N, 7.96. C₁₉H₁₇N₂O₅ (353) requires: C, 64.58; H, 4.81;

Table 4. Isooxazolines (VI).

Compound	M.p. (°C)	Formula (mol.wt.)	Analysis(%)		
				Found	Calcd
VIa	198	C ₂₅ H ₂₇ NO ₃ (389)	C	77.40	77.12
			H	7.00	6.96
			N	3.68	3.59
VIb	> 250	C ₂₆ H ₂₉ NO ₄ (419)	C	74.60	74.46
			H	6.90	6.92
			N	3.33	3.34
VIc	> 250	C ₂₆ H ₂₉ NO ₃ (403)	C	77.55	77.41
			H	7.20	7.19
			N	3.46	3.47

Table 5. Oxazino and thiazinobenzocoumarins.

Compound	Solvent of crystn.	M.p. (°C)	Formula (mol.wt.)	Analysis(%)		
					Found	Calcd
VIIa	B	138	C ₁₇ H ₁₄ N ₂ O ₄ (310)	C	65.92	65.80
				H	4.49	4.51
				N	9.13	9.03
VIIb	B	122	C ₁₈ H ₁₆ N ₂ O ₄ (324)	C	66.87	66.66
				H	4.90	4.93
				N	8.68	8.64
VIIIa	T	212	C ₁₇ H ₁₄ N ₂ O ₃ S (326)	C	62.39	62.57
				H	4.30	4.29
				N	8.62	8.58
				S	9.84	9.81
VIIIb	T	224	C ₂₃ H ₁₈ N ₂ O ₃ S (402)	C	68.91	68.65
				H	4.46	4.47
				N	6.90	6.96
				S	7.99	7.96
VIIIc	X	> 250	C ₂₄ H ₂₀ N ₂ O ₃ S (416)	C	69.50	69.23
				H	4.80	4.80
				N	6.76	6.73
				S	7.73	7.69
VIIIId	X	> 250	C ₂₃ H ₁₇ ClN ₂ O ₃ S	C	63.37	63.23
				H	4.90	3.89
				N	6.44	6.41
				S	7.38	7.33

B benzene, T toluene, X xylene

Table 6. Substituted benzocoumarins (IX).

Compound	M.p. (°C)	Formula (mol.wt.)	Analysis (%)		
				Found	Calcd
IXa	146	C ₂₂ H ₁₈ O ₄ S (378)	C	69.70	69.84
			H	4.78	4.76
			S	8.51	8.46
IXb	131	C ₂₃ H ₂₀ O ₄ S (392)	C	70.29	70.40
			H	5.11	5.11
			S	8.25	8.16
IXc	152	C ₂₃ H ₂₀ O ₄ S (392)	C	70.30	70.40
			H	5.12	5.10
			S	8.06	8.16

N, 7.93%.) The acetyl derivative of VIIIa (44%, had an m.p. 163°) (Found: C, 61.90; H, 4.59; N, 7.61. C₁₉H₁₇N₂O₄S (369) requires: C, 61.78; H, 4.60; N, 7.58%).

Reaction of I with Thiophenols. To a mixture of I (0.01 mole, 2.7 g), thiophenol or thiocresol (0.01 mole) in dry benzene (40 ml), 0.5 ml of piperidine was added and the mixture was vigorously shaken. After standing for 36 hr, glacial acetic acid was added dropwise until the solution was acidic and the solvent was removed under reduced pressure to give a solid which was crystallised from benzene to give IX as colourless crystals (65–75%)(cf. Table 6).The IR spectra of IX showed bands at 1740 cm⁻¹ for ester (C=O) and at 1670 cm⁻¹ for ketonic (C=O).

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