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SYNTHESIS AND REACTION OF 2-BIS(METHYLTHIO)METHYLENE-COUMARAN-3-ONES

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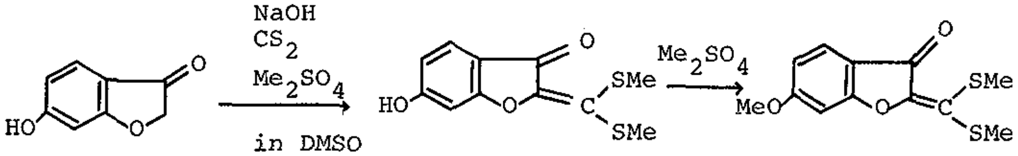
6-Methoxy-2-bis(methylthio)methylenecoumaran-3-one, which was prepared by the reaction of 6-hydroxycoumaran-3-one with carbon disulfide and subsequent alkylation with dimethyl sulfate in the presence of sodium hydroxide in dimethyl sulfoxide, reacted with nucleophiles to give the correspnding substitution products of one methylthio group in good yield.

Recently we have found a convenient and versatile procedure to prepare bis(methylthio)methylene derivatives of heterocyclic compounds by treating the parent compounds with carbon disulfide, followed by alkylation with dimethyl sulfate in the presence of sodium hydroxide in dimethylformamide or dimethyl sulfoxide.[1) These bis(methylthio)methylene compounds are very useful as a synthetic intermediate for heterocyclic compounds.

We synthesized *2-bis(methylthio)methylenecoumaran-3-one*, which are heterocyclic ketenethioacetals, in order to examine the reactivity of the methylthio group and to prepare coumarone derivatives.

Reaction of 6-hydroxycoumaran-3-one with carbon disulfide, followed by treatment of its reaction mixture with an excess amount of dimethyl sulfate in the presence of sodium hydroxide in dimethylformamide *gave a heterocyclic* ketenethioacetal, 6-methoxy-2-bis(methylthio)methylenecoumaran-3-one (III),[2,3] yellow needles, mp 123°, in good yield.

The use of 2 mol of dimethyl sulfate in the above reaction afforded 6-hydroxy-2-bis(methylthio)methylenecoumaran-3-one (II) as yellow needles, mp 211°. This compound (II) was soluble in 10% sodium hydroxide and was alkylated with dimethyl sulfate to *afford III in good yield.*



I II III

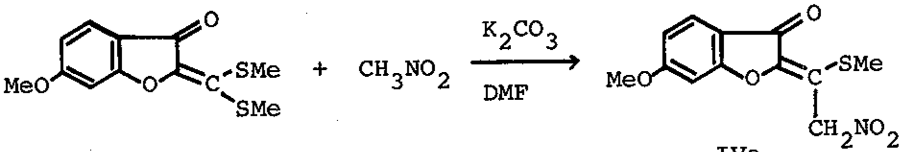
	IR(KBr) cm^{-1} ν(C=O)	UV λ_{max}^{EtOH} nm(logε)	NMR(in CF_3COOH) δ(ppm)
II:	3050-3100(OH)	226(4.00)	3.00(6H, s, SMe)
	1644	254(3.86)	6.88(1H, d, J=2 Hz, 7-H)
		364(4.29)	6.99(1H, dd, J=2, 10 Hz, 5-H)
			7.91(1H, d, J=10 Hz, 4-H)
III:	1660	225(3.99)	3.00(6H, s, SMe)
		256(3.94)	3.99(3H, s, OMe)
		352(4.30)	6.88(1H, d, J=2 Hz, 7-H)
			7.01(1H, dd, J=2, 10 Hz, 5-H)
			7.76(1H, d, J=10 Hz, 4-H)

The reaction of III with excess nitromethane in the presence of potassium carbonate in dimethylformamide, on a steam bath, gave the monosubstituted product, 6-methoxy-2-(1-methylthio-2-nitro)ethylidenecoumaran-3-one (IVa) as yellow needles, mp 139-140°, in 78% yield. In contrast, II did not react with nitromethane under the same conditions.

Compound III easily reacted with dimethyl malonate to give a monosubstituted product, 6-methoxy-2-[2-bis(methoxycarbonyl)]-ethylidenecoumaran-3-one (IVb), pale yellow prisms, mp 114°, in 67% yield. Similarly, III reacted with N-ylide, pyridinium ethoxycarbonylmethylide, to afford the stable pyridinium N-ylide (IVc), mp 117°, in 82% yield.

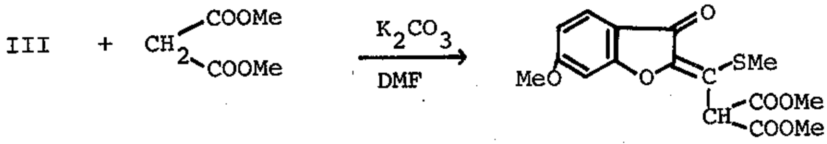
On the other hand, the reaction of III with methyl cyanoacetate or malononitrile also afforded replacement products, but these products could not be purified by recrystallization from methanol or ethanol. Because of its two strongly electron-withdrawing group (CN, COOMe) at the adjacent carbon, the methylthio group in IVd and IVe is considered to have a very high reactivity. In fact, IVd and IVe were easily converted into hydrolysis products (Va, mp 316° and Vb, mp 246°) when refluxed in methanol or ethanol.

	IR(KBr) νcm^{-1}	UVλ_{max}^{EtOH}nm(logε)	NMR(CF_3COOH) δ(ppm)
IVa:	1665(C=O)	275(3.86) 325(3.78)	2.70(SMe), 3.98(OMe) 6.03(CH_2-NO_2)
IVb:	1740(C=O) 1670(C=O)	256(4.01) 350(4.31)	2.86(SMe), 3.94(OMe) 3.97(OMe), 8.37(-CH-)
IVc:	1675(C=O) 1610(C=O)	274(4.49) 330(4.10)	———
Va:	2220(CN) 1635(C=O)	247 330 (insolubility)	———
Vb:	1665(C=O) 1645(C=O)	247 326 (insolubility)	4.00(OMe) 4.22(OMe)

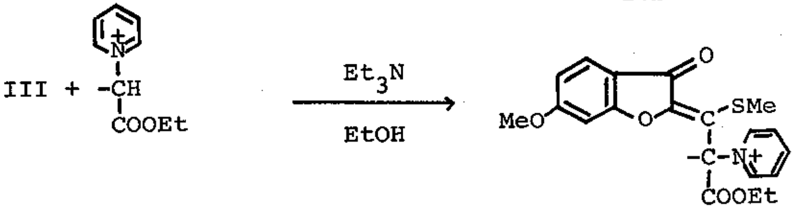


III

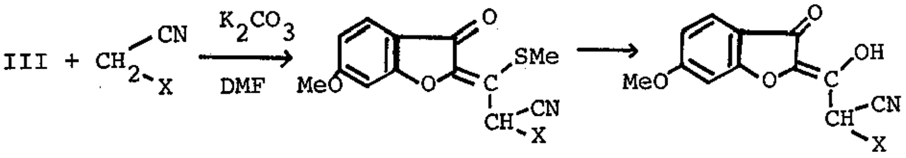
IVa



IVb



IVc

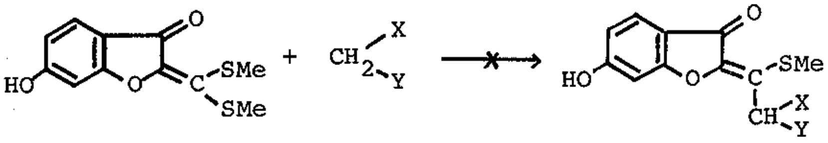


IVd, e

Va, b

a; X=CN

b; X=COOMe



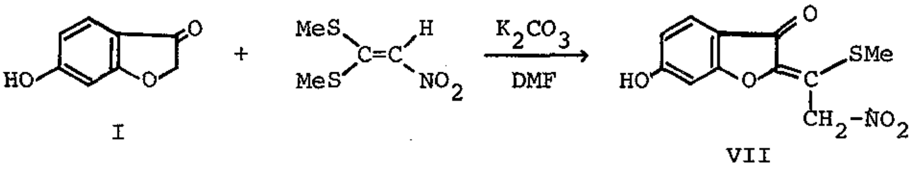
X; CN, NO_2

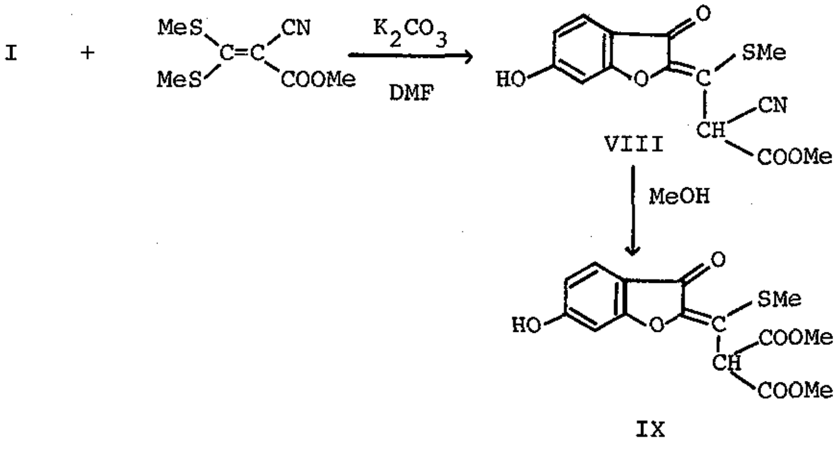
Y; CN, COOMe, H

VI

It is well known that the reaction of heterocyclic compounds, having an active methylene in their molecule, with ketenethioacetal derivatives results in the replacement of ketenethioacetals.[1)] Since a direct to the 2-ethylidene derivative via the reaction between II and active methylene compounds (methyl cyanoacetate, malononitrile, dimethyl malonate, nitromethane), the reaction of I with ketenethioacetals was examined as an alternative.

Reaction of I with 2,2-bis(methylthio)-1-nitroethylene gave the expected compound, 6-hydroxy-2-(1-methylthio-2-nitro)ethylidenecoumaran-3-one (VII), mp 221°, in 82% yield. Similarly, I reacted with methyl 2-cyano-3,3-bis(methylthio)acrylate to yield 2-(2-cyano-2-methoxycarbonyl-1-methylthio)ethylidene-6-hydroxycoumaran-3-one (VIII) which was easily converted into the bis(methoxycarbonyl)-ethylidenecoumaran-3-one derivatives (IX), mp 279°, when refluxed in methanol.





	IR(KBr) cm^{-1} ν (C=O)	UVλ_{max}^{EtOH}nm(logε)	NMR(VII:DMSO-D_6 / IX:CF_3COOH) δ(ppm)
VII:	1620	252(3.92) 362(4.37)	2.52(3H, s, SMe) 6.13(2H, s, $-CH_2-$)
IX:	1735, 1752 1630	257(3.91) 356(4.29)	2.88(3H, s, SMe) 4.00(6H, s, 2 OMe) 6.38(1H, sb, -CH-)

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2) Geometry of IV, V, VII, VIII, and IX was not elucidated.

3) Structures of all the new compounds were supported by elemental analysis and their spectral (UV, IR, NMR, and Mass) data.

4) This report is "Heterocyclic Ketenethioacetal Derivatives.X."

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