HETEROCYCLES, Vol 22, No 2, 1984

OXYGEN HETEROCYCLES BY SULPHUR YLIDE ANNULATION : SYNTHESIS OF 3,4-DIHYDRO-2H,5H-PYRANO[3,2-c][1]BENZOPYRAN-5-ONES BY DIMETHYLSULPHOXONIUM METHYLIDE

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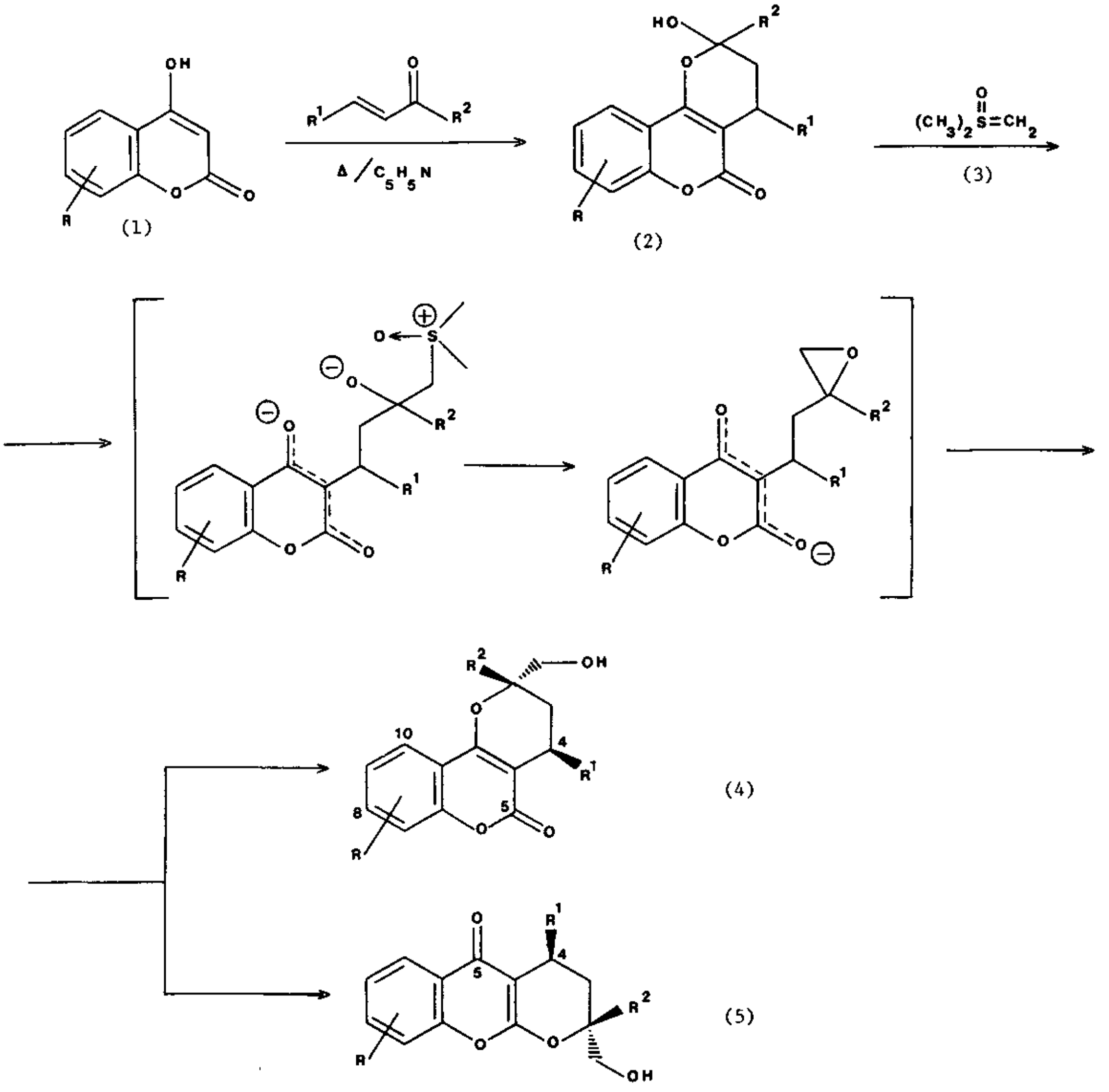
Abstract - 3,4-Dihydro-2-hydroxymethyl-2H,5H-pyrano[3,2-c][1]benzopyran-5-ones are the main products of the reaction of dimethylsulphoxonium methylide on Michael adducts of 4-hydroxycoumarins and α,β-unsaturated ketones. Minor quantities of 3,4-dihydro-2-hydroxymethyl-2H,5H-pyrano[2,3-b][1]benzopyran-5-ones are also sometimes obtained.

As a part of a larger on going research project in our laboratory on oxygen heterocycles obtained by sulphur ylide annulation[1] we tested the reaction between dimethylsulphoxonium methylide and some Michael adducts obtained by condensing 4-hydroxycoumarins with α,β-unsaturated ketones in a basic medium[2]. The aim of the reaction was to synthesize the title heterocyclic skeleton to which we were interested as it is present in numerous compounds isolated from various genera of Fam. Compositae[3].

When differently substituted coumarins (1) were reacted with α,β-unsaturated ketones the Michael adducts were isolated mainly as diastereoisomeric mixtures of cyclic hemiketals[4] (2). These compounds were treated with a two to three molar excess of dimethylsulphoxonium methylide (3) in dimethylsulphoxide or tetrahydrofurane for a period of time ranging from four to twenty hours. Crude reaction products were obtained quencing with ice-water and diluted hydrochloric acid and working up in the usual manner. Pure compounds were separated by chromatography on silica gel eluting with n-hexane/ethyl acetate. The reaction pathway bringing to the products isolated from some typical runs is outlined in the Scheme. Yields (see table) range from 45 to 75% and predominant reaction products are angular isomers, 3,4-dihydro-2H,5H-pyrano[3,2-c][1]benzopyran-5-ones (4). Linear isomers, 3,4-dihydro-2H,5H-pyrano[2,3-b][1]benzopyran-5-ones (5), could be isolated as pure compounds only in some cases, but their presence in trace amounts was always evidenciated by comparing ^1H NMR spectra of a pure sample[5] with that of the proper chromatographic fraction.

Structures of compounds (4) and (5) were mainly determined by ^1H and ^{13}C NMR data[6].

SCHEME



^{13}C NMR spectra allowed to distinguish with certainty angular compounds from linear isomers. The former show the 5-oxo-carbon signal at 160.0 - 162.5 ppm and the latter ones at 175.0 - 180.0. These values are in accordance with those reported for similarly substituted coumarins and chromones[7]. The proton signal of the methylene introduced by action of (3) appears as an AB system centered at about 3.6 - 3.8 ppm (further coupling with the hydroxyl hydrogen is often present) and is shifted about 0.6 ppm to lower fields upon acetylation. This indicates that no 3-hydroxyoxepin ring was formed implying that 6-<u>Exo</u> cyclization was favoured with respect to 7-<u>Endo</u> one[8]. The CH_2-CH group gives rise to an ABX system; H_A and H_B showing chemical shift differences of about 0.4 - 0.6 ppm in the most abundant diastereoisomers of both angular and linear compounds in which the subtituent in position 4 and the hydroxymethyl group are trans each other (see onwards). On the contrary H_A and H_B are almost coincident in the less abundant diastereoisomers and H_A shows long-range coupling with the methyl group in position 2 which is characteristic of a W-pattern (0.8 Hz in 4a,b and 5a,b) and another coupling with the vicinal X proton (10 Hz in previous substrates) typical for a trans diaxial position. These facts imply that the hydroxymethyl group and the substituent in position 4 are cis each other.

The E.I. mass spectra of (4) and (5) show a very similar fragmentation pattern, only small differences in relative abundances can be seen. On the contrary, mass analyzed ion kinetic energy spectra (MIKES) show peculiar loss of C_6H_4O for (4) and of C_6H_6 for (5). This different behaviour may be ascribed to the ester group in compounds (4) whose presence causes the specific fragmentation.

TABLE - Yields and physical data of compounds (4) and (5).

Run	Starting material[a]	R	R^1	R^2	Product	Yield[b] (%)	mp (°C) (solvent)[b,c]
1	2a	H	CH_3	CH_3	4a	40	133-134 (n-hexane/AcOEt)
					5a	35	136-137 (n-hexane/AcOEt)
2	2b	8,10-$(CH_3)_2$	CH_3	CH_3	4b	70	173-174 (AcOEt)
					5b	-	-
3	2c	H	C_6H_5	CH_3	4c	60	173-174 (benzene)
					5c	5	160-162 (benzene)
4	2d	8,10-$(CH_3)_2$	C_6H_5	CH_3	4d	50	175-176 (AcOEt)
					5d	-	-
5	2e	H	CH_3	C_6H_5	4e	45	162-163 (acetone)
					5e	-	-
6	2f	H	C_6H_5	C_6H_5	4f	63	231-232 (acetone)
					5f	10	209-210 (acetone)

(a) Diastereoisomeric mixtures of hemiketals and open tautomer were used as starting materials.
(b) Reported values are referred to the prevailing diastereoisomer; no attempts were made to maximize yields and selectivity. (c) Uncorrected values.

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5. The high yield synthesis of these compounds was made by reacting (2) with methylenetriphenylphosforane and oxydizing the so-obtained olefin with MCPBA in acid medium. This synthesis will be discussed in a future publication.
6. Detailed description of spectral data usefull for stereochemical assignment will be reported elsewhere.
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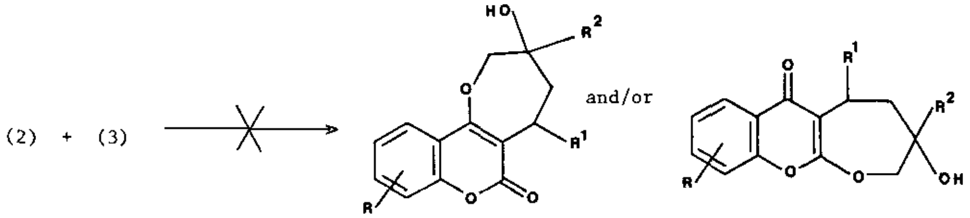
8. We could not exclude in principle the formation of the oxepin ring:



this was in fact the preferred product when similarly substituted phenolic ketones were used as substrates (see ref. 1).

Received, 16th September, 1983