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SPECIFIC REACTIONS OF 5-OXOTETRAHYDRO-4H-THIOCHROMENES WITH GRIGNARD REAGENTS

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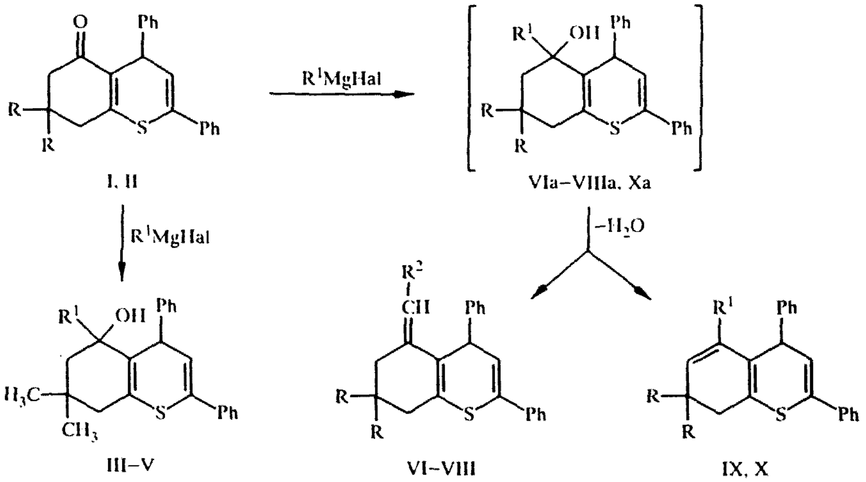
The reaction of 5-oxotetrahydro-4H-thiochromenes with Grignard reagents has been studied and it has been shown that the reagent adds to the 1,2-position of the conjugated system in the cyclic ketones. The structure of the products depends on that of the starting cyclic ketone.

The position of the carbonyl group in 5-oxo-5,6,7,8-tetrahydro-4H-thiochromenes is an important determinant in their properties when compared with 4-oxothiochromenes [1] and aliphatic α,β-unsaturated ketones. It was therefore of interest to study the particular effect of conjugation on the carbonyl group reactivity in the above series.

Hence we have studied the behavior of the cyclic ketones 2,4-diphenyl- (I) and 7,7-dimethyl-2,4-diphenyl-5-oxo-5,6,7,8-tetrahydro-4H-thiochromene (II) with the Grignard reagents methylmagnesium iodide, ethyl- and phenylmagnesium bromide, and benzylmagnesium chloride.

It is known that the Grignard reaction of α,β unsaturated carbonyl compounds is determined both by the particular structure and stereochemistry of the conjugated system itself and by the character of the reagent [2]. Studies of the structures of Grignard reaction products suggest that addition of the nucleophilic reagent occurs at the 1,2 position of the conjugated ketones I, II. Moreover, the presence of methyl groups at C-7 of II has a stabilizing effect on the initially formed tertiary alcohols. Thus the carbinols III-V proved to be quite stable and we were able to separate and characterize them.



The reaction of II with benzylmagnesium chloride is an exception. Reaction of I, not containing methyl groups at position 7, with Grignard reagents forms only the products of dehydration of the initially formed tertiary alcohols showing their lower stability when compared with the corresponding carbinols III-V. The nature of the dehydration products when reacting the 5-oxosulfides I,II with Grignard reagents (VIa-VIIIa, Xa) depends on the structure of the starting sulfide and on the entering substituent.

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TABLE 1. PMR Spectral Data for VI-IX in $CDCl_3$

Compound	δ, ppm					J, Hz
	H-3	H-4	R-7	H-11	R-11	$^3J_{3,4}$
VI	6,20	4,75	—	5,5	1,59	7,1
VII	6,26	4,88	—	4,45	7,02, 7,53	7,0
VIII	6,24	4,86	1,02, 0,89	6,55	7,25, 7,45	7,0
IX*	5,87	4,34	1,06, 1,01	3,3	7,50, 7,0	6,5

*Chemical shift of H−6 = 5.26 ppm.

TABLE 2. Data for Compounds III-X

Compound	Empirical formula	MP, °C (ethanol-dioxane)	IR Spectrum, cm^{-1}		Yield, %
			$\nu_{C=C}$	ν_{OH}	
III	$C_{24}H_{26}SO$	200...201	1620, 1650	3552, 3567	12
IV	$C_{25}H_{28}SO$	191...193*	1620, 1655	3550, 3570	55
V	$C_{29}H_{28}SO$	187...188	1618...1652	3550, 3572	22
VI	$C_{23}H_{22}S$	95...96*	1600, 1635	—	52
VII	$C_{28}H_{24}S$	173...175	1600, 1649	—	61
VIII, IX	$C_{30}H_{28}S$	161...162,5	1600, 1640	—	67
X	$C_{27}H_{22}S$	150...151	1600, 1645	—	55

*Ethanol.

Treatment of ketone I with phenylmagnesium bromide gives only the dihydrothiochromene X, the product of dehydration to the endo positioned double bond. Reaction of ketones I,II with benzylmagnesium chloride and also ketone I with ethylmagnesium bromide might be expected to involve dehydration of the intermediate carbinols VIa-VIIIa via two routes. Formation of an exocyclic double bond through loss of a proton from the methylene group in the entering substitutent or an endocyclic double bond through elimination of a proton in the alicycle at $C_{(6)}$. According to the PMR spectra of VI-IX in deuterochloroform (Table 1) the dehydration of intermediate alcohols VIa, VIIa gives the exocyclic double bond. Broad singlets at 5.5 and 4.5 ppm, in agreement with literature data [3], can be assigned to proton H-11 of the benzyl or ethylidene groups.

It was also found that the presence of methyl groups at C-7 has a marked effect on the nature of the dehydration product in the reaction of II with benzylmagnesium chloride. Dehydration of VIIIa occurs by two routes: via formation of sulfide VIII with the exocyclic double bond at C-5 and of sulfide IX with the endocyclic double bond as shown. Sulfide IX could not be separated in a pure state. Its presence in the reaction product was inferred using PMR.

Compound VIII shows the presence of a signal for 11-H at 6.55 ppm and IX a signal for 6-H at 5.26 ppm. The retention of the benzylic methylene in sulfide IX is shown by the signal at 3.3 ppm. The existence of the endocyclic double bond in the sulfide changes the geometry of the interaction between the alicyclic double bond and the heterocycle. This is reflected by a change in the spin-spin coupling constant for the 4H thiopyran part of the molecule to 6.5 Hz from 7.0-7.1 Hz in VI-VIII. There is also a significant high field shift of protons 3-H and 4-H. The retention of the 4H thiopyran molecular fragment is confirmed by the presence of proton signals for 3-H at 5.8-6.25 ppm and 4-H at 4.34-4.88 ppm in the PMR spectra of VI-IX.

Carbinols III-V show hydroxyl group absorption bands at 3550-3570 cm^{-1} in the IR and double bond absorption for the 4H-thiopyran ring at 1620-1650 cm^{-1} (Table 2). This hydroxyl absorption is absent in the dehydration products VI-X. 4-H thiopyran double bond absorption is seen at 1635-1649 cm^{-1}. Several strong bands are seen at 1500-1600 cm^{-1} which are assigned to double bond absorptions from the phenyl substituents and the alicyclic double bonds.

EXPERIMENTAL

IR Spectra were taken on a UR-20 instrument as a suspension in Vaseline oil and perchloro-1,3-butadiene. PMR spectra were recorded on an 80 MHz Varian instrument for 0.1 molar solutions in $CDCl_3$ at 30°C and with HMDS internal standard. Monitoring of the reaction was carried out by TLC on Silufol UV-254 plates in hexane–ether–chloroform (2:1:1) and visualized with iodine.

Elemental analytical data for C, H, and S agreed with that calculated.

Starting 2,4-diphenyl- (I) and 7,7-dimethyl-2,4-diphenyl-5-oxo-5,6,7,8-tetrahydro-4H-thiochromene (II) were obtained by [4].

2,4-Diphenyl-5-benzylidene-5,6,7,8-tetrahydro-4H-thio-chromene (VII). 5-Oxosulfide I (10 g, 0.03 mole) was added slowly at room temperature with continuous stirring to a Grignard solution prepared from magnesium turnings (8.7 g, 0.36 mole) and benzyl chloride (6.9 ml, 0.06 mole) in absolute ether (160 ml). The product was stirred for a further 2 h, the ether solution decanted onto ice, and the precipitate extracted several times with ether (4 × 100 ml). The ether extracts were also poured onto ice, filtered from the precipitate of magnesium hydroxide, and washed with water to neutral pH. The ether solution was dried with sodium sulfate, the ether evaporated, and the residue crystallized to give 5-benzylidenetetrahydro-4H-thiochromene VII (7.5 g, 61%). It was recrystallized from ethanol–dioxane (2:1).

Compounds III-VI and VIII-X were obtained similarly (Table 2).

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