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DUAL FRAGMENTATION OF THIACHROMANONES-4 UPON SULFUR-YLID TREATMENT. FORMATION OF THIANAPHTHENES.

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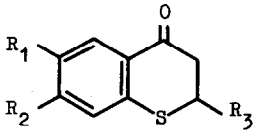
The observation of an unusual fragmentation of dihydroquinolones upon ylid treatment[2] stimulated a further investigation of this reaction with other heterocyclic ketones. The recent report of a similar reaction occurring in a chromanone-4 derivative[3] prompts us to communicate our results on the corresponding thiachromanones 1, which in some respects markedly differ from the previously observed reaction pattern.



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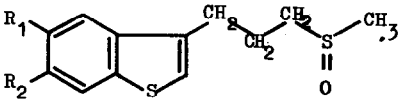

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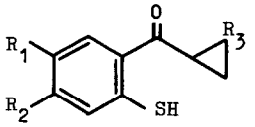

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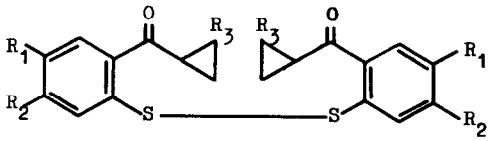

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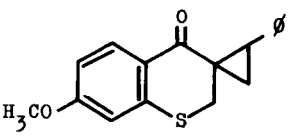

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a: R_1 = H, R_2 = OCH_3, R_3 = H

b: R_1 = OCH_3, R_2 = OCH_3, R_3 = H

c: R_1 = H, R_2 = OCH_3, R_3 = CH_3

d: R_1 = OCH_3, R_2 = OCH_3, R_3 = CH_3

Upon reaction of 1a with dimethylsulphoxonium methylide (2) (1.1 eq of 2, DMSO, 30 mn/20°, 1 hr/50°) a 1 : 1 mixture of thianaphthene 3a and cyclopropylketone 4a was

obtained, which was possible to separate via repeated base extraction and acidification procedures. The thianaphthene 3a*, m.p. 72-74°, UV, λ_{max}^{EtOH} 234 (32.700), 267 (7000), λ max 276 (6700); NMR 100 Mc ($CDCl_3$) 2.20 quintet ($-\underline{CH}_2-$), 2.51 s ($-SO\underline{CH}_3-$), 2.72 t ($Ar\underline{CH}_2$), 2.97 t ($S\underline{CH}_2$), 7.32 d ($=\underline{CH}-S$), constituted the exclusive reactionproduct when the addition was carried out at low temperature[4] or when an excess of ylid 2 was used[5]. (Yield 33%). The second product, the oily cyclopropyl ketone 4a could be characterized via its S-acetate, or preferably by its conversion into the corresponding crystalline disulfide[6] 5a, m.p. 142-145°. IR (KBr) 1640 cm^{-1} (C=O); NMR 100 Mc ($CDCl_3$) 0.8-1.4 m ($<\!\!\underline{\overset{CH_2}{\underset{CH_2}{|}}}$), 2.55 m ($\underline{CH}$-CO), 3.70 s ($O\underline{CH}_3$), 6.76, 7.49, 8.06 ($Ar\underline{H}$).

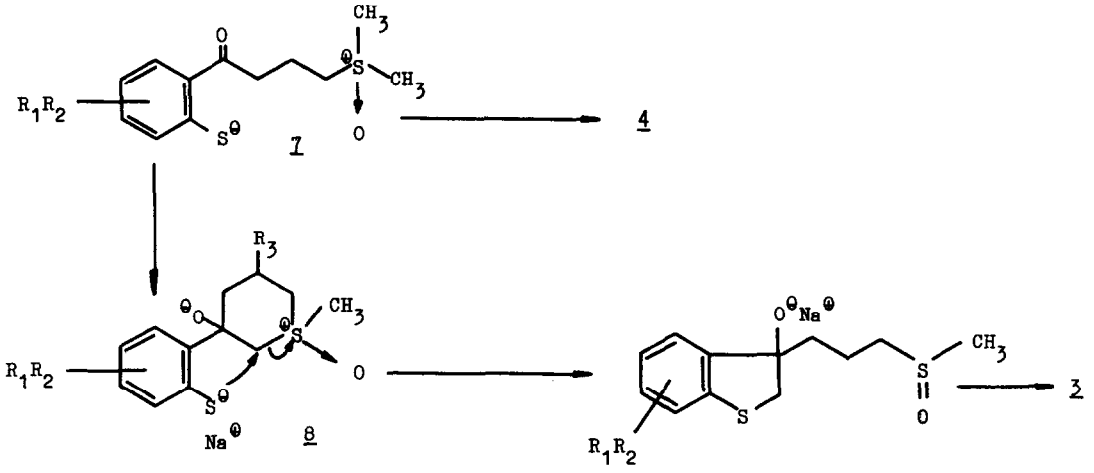
To account for the product formation reaction at the carbonyl as well as carbon-sulfur cleavage have to be involved. Additional information on the reaction course was obtained from experiments with a number of appropriately substituted thiachromanones.

Reaction of 1b at room temperature (1.1 eq 2, DMSO) gave the thianaphthene 3b as the major (>70%) product, at higher reaction temperatures, however, only very small quantities of ketone 4b were formed[7], 3b still being present in superior amounts.

On the other hand, quite different results were noted upon reaction of the ketones 1c and 1d [8]. When the reaction was carried out at 0-5° (3 hr, 1.1 eq 2), the ketones were hardly affected, while at 50-60° an almost quantitative conversion (>80%) into the cyclopropylderivatives 4c and 4d occurred, the latter compounds being characterized again as the crystalline disulfides 5c and 5d: 5c, m.p. 118-121°. IR (KBr) 1635 cm^{-1} (C=O); NMR 100 Mc ($CDCl_3$) 0.88 m ($\triangleright\!\!-\underline{H}$) 1.22 d ($\underline{CH}_3$), 1.55 m ($\triangleright\!\!-\underline{H}_2$), 2.29 quintet ($\underline{CH}CO$); 5d, m.p. 186,5-189°, IR (KBr) 1635 cm^{-1} (C=O); NMR 100 Mc ($CDCl_3$) 0.90 m ($\triangleright\!\!-\underline{H}$), 1.25 d ($\underline{CH}$)$_3$, 1.58 m ($\triangleright\!\!-\underline{H}_2$), 2.24 quintet (CO-$\underline{CH}$). The observed J values for the cyclopropylprotons ($J_1 = J_2 = 4$ c/s, $J_3 = 8$ c/s) indicate a trans relationship of the aroyl and methylsubstituent.[9]

Finally, to examine the influence of additional C_3 substitution, the benzylidene derivative of ketone 1a was reacted with 2 to produce the cyclopropylthiachromanone 6, which did not undergo further fragmentation upon treatment with an excess of ylid 2. Reaction of ketones 1 with other ylids, in particular dimethylsulphonium methylide, gave no synthetically useful results. Low temperature reaction did not affect the starting ketone, while at room temperature decomposition occurred.

The observed product formation can be conveniently accommodated via the postulation of the intermediacy of the ringopened zwitterion 7, the α-ketocarbanion of which may



displace the DMSO-moiety under formation of the cyclopropylketone 4 in a manner analogous as reported in the fragmentation of the dihydroquinolone system[2]. In the absence of steric and/or kinetic factors, 7 might undergo an internal cyclization to the thianaphthene precursor 8, which either by the way of a methylene transfer or via direct ringopening through attack of the sulfide anion[10] is leading to the thianaphthene derivatives. The origin of trans cyclopropylketones finds its parallel in similar reactions of S-ylids with cinnamic esters[11] where as a consequence of the energy differences between the possible conformers the formation of the trans product is highly favoured. Among the discriminating factors which determine the formation of thianaphthene vs cyclopropylderivatives, the necessity of a higher temperature to cleave the 2-methylsubstituted carbon-sulfur bond, as well as a sterical influence in the reaction at the carbonylgroup leading to the intermediate 8 might play important roles.

The present results are of synthetic significance in so far the preparation of 3-substituted thianaphthenes 3 is concerned. The latter class of compounds is currently under active interest[12] in view of their structural relationship to the tryptophane molecule. In order to evaluate the scope of this cyclization further work will be carried out.

Literature and Footnotes:

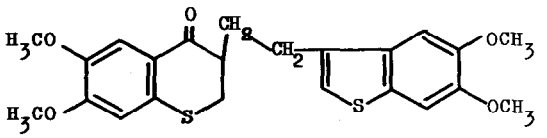
* Satisfactory analytical data have been obtained for all crystalline compounds. Unreported spectral data - UV and Mass - were also in accord with the proposed structures.

1. To whom all correspondence should be directed.

2. W.N. Speckamp, R. Neeter, P.D. Rademaker and H.O. Huisman,

Tetrahedron Letters, 3795 (1968).

3. P. Bennett and J.A. Donelly, Chem.Ind., 783 (1969).
4. Addition of a small amount of tetrahydrofuran was necessary to avoid solidification of the reaction mixture.
5. Extensive decomposition occurred at high concentrations of ylid 2. Tar formation was also observed when excess of base (NaH) was used.
6. Oxidation of the sulfide was carried out by passing a stream of air through a solution of 4 in ethanol or alternatively by means of iodine and NaOH.
7. In some cases a byproduct i was isolated from the reaction mixture. Its structure was proved via the following spectral data: m.p. 166-168°. IR (KBr) 1650 cm^{-1} (C=O); NMR 100 Mc ($CDCl_3$) 2.0-3.5 m (7 protons), 3.87 s (6 p OCH_3), 3.91 s (3 p OCH_3), 6.63, 7.23, 7.26 and 7.61 4 singlets (ArH) and 6.99 s (S-CH=). No attempts were carried out to improve the yield of this product.



i

8. Prepared by Mr W.M.B. Könst, of this laboratory.
9. In agreement with the well established magnitude of the J values in cyclopropyl-derivatives in which $J_{cis} > J_{trans}$, the observed J values are in accordance with a trans relationship of aroyl and methylsubstituent. No trace of an eventually formed cis product could be detected.
10. Compare for instance:
P. Bravo, G. Gaudiana and A. Umani-Ronchi, Tetrahedron Letters, 679 (1969).
11. C. Kaiser, B.M. Trost, J. Beeson and J. Weinstock, J.Org.Chem. 30, 3972 (1965).
12. cf. E. Campaigne, E.S. Neiss and T. Bosin. Quarterly Reports on Sulfur Chemistry, 4, no. 3, 229 (1969).