Anal. Calcd. for $C_{28}H_{20}O_2$: C, 86.57; H, 5.19. Found: C, 86.09; H, 5.43.

Similar oxidation of X (0.100 g.) gave 0.060 g. (65%) of product, m.p. 210.5–211.5°, undepressed by admixture with the product from IX and with identical spectral properties.

Attempted Conversion of Ia to IX and X.—Ia (0.50 g.) was dissolved in dioxane (25 ml.) and two drops of concentrated hydrochloric acid were added. The solution was heated on the steam-bath and samples were removed after 3, 9, 18 and 36 hours. Infrared spectroscopic examination of the material from these samples showed that although extensive changes were occurring no IX or X was formed. After 57 hours the solution was poured into excess water and the mixture extracted with ether. The extract was dried and freed of solvent yielding an oil which solidified on trituration with ethanol. Crystallization from ethanol gave very pale yellow plates, m.p. 166.5–167°; infrared spectrum band at 6.09 μ. This was shown to be 2-benzoyl-3,4,5-triphenylfuran by direct comparison with a sample obtained by heating Ia above its melting point for five minutes[2a] (Pütter and Dilthey[2a] give m.p. 166° for this compound). Attempts to obtain other crystalline products from the crude reaction mixture were unsuccessful.

Monoacetate of Ia (XIII).—Ia (1.5 g.) was dissolved in a mixture of pyridine (20 ml.) and acetic anhydride (10 ml.) and the solution was heated on the steam-bath for 3 hours. It was then poured into excess cold water when a sticky brown tar separated. This solidified on washing with water by trituration and decantation. The solid was taken up in methanol and was partially precipitated as a dark tar by addition of water. The solution was decanted and treated twice in the cold with Norit. By treating the hot solution with water and cooling very slowly, there was obtained 0.30 g. of pale yellow crystals, m.p. 137–142°. The dark tar which had separated from the original aqueous methanol solution was crystallized from aqueous methanol using the same technique with seeding. The further 0.10 g. of crystalline material thus obtained was combined with the 0.30 g. of crystals and the combined product was crystallized from ether–petroleum ether. There was thus obtained 0.31 g. of a crystalline powder, m.p. 142–144°; by working up all the mother liquors an additional 0.13 g. of product of similar m.p. was obtained; total yield 0.44 g. (27%). On recrystallization from aqueous methanol and from ether–petroleum ether, the acetate was obtained as microcrystals, m.p. 144.2–145.2° (Pütter and Dilthey[2a] give m.p. 145°). Zerewitinoff determination: Calcd. for 1 active H: 5.5 ml. CH_4. Found: 4.4 ml. CH_4. Infrared spectrum ($CHCl_3$), band at 5.83 μ; ultraviolet spectrum (95% EtOH) λ_{max} 308 mμ (log ε 4.06).

Anal. Calcd. for $C_{31}H_{24}O_4$: C, 80.85; H, 5.25. Found: C, 80.54; H, 5.51.

Boric Acid Acidity Measurements.—Solutions containing 0.1 millimole of Ia, IX and X in 5-ml. portions of a 0.500 *M* solution of boric acid in methanol were made up. To each of these solutions and to 5 ml. of the boric acid solution was added 1 ml. of water and the *p*H of the resulting solutions was measured with a glass electrode using a Coleman *p*H meter. The following data were obtained:

	*p*H	*p*H after standing overnight
Ia	3.01	3.01
IX	4.72	3.50
X	4.63	3.94
Blank	4.72	4.74

After standing overnight Ia, IX and X could not be recovered from their solutions: the infrared spectra of the recovered materials differed considerably from those of the starting materials.

Action of Nitric Acid on Other Unsaturated Compounds.—Benzalacetophenone, dibenzalacetone and stilbene were each treated with nitric acid in dioxane under identical conditions to those used for the nitric acid oxidation of tetracyclone. In every case the starting material was recovered quantitatively. When the reactions mixtures containing benzalacetophenone and dibenzalacetone were boiled under reflux for ten minutes, the starting materials were still recovered in 92–99% yield. On heating the stilbene solution to boiling for ten minutes, reaction did occur and on working up the mixture in the usual manner a crystalline, nitrogenous product was obtained, infrared spectrum bands at 6.05 and 6.40 μ.

Acknowledgment.—The authors are indebted to the Mallinckrodt Chemical Works for a grant defraying part of the expenses of this investigation.

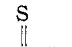
CAMBRIDGE, MASSACHUSETTS

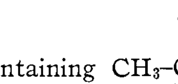
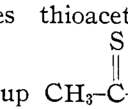
[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, FACULTY OF SCIENCE, CAIRO UNIVERSITY]

The Application of the Principle of Vinylogy to the Chemistry of γ-Pyrone Derivatives

BY ALEXANDER SCHÖNBERG, MAHMOUD MOHAMED SIDKY AND GAMIL AZIZ

RECEIVED MARCH 22, 1954

Whether aromatic thioketones containing the group  $-\overset{\overset{S}{\|}}{C}-CH_3$ will undergo condensations of the aldol type cannot be determined directly, because of the sensitivity of these compounds toward alkali and their tendency to polymerize: however, it was found that the methyl group in 2-methyl-4-thiochromones, which may be regarded as vinylogs of the above thioacetyl compounds condenses with aromatic aldehydes as well as with aromatic nitroso compounds in the presence of a base to form 2-styryl-4-thiochromones and nitrons, respectively. The thermoinstability of 2,6-diphenyl-4-thiopyrone and the easy hydrolysis of the methoxy group in visnagin are discussed in the light of the principle of vinylogy.

No condensation of the aldol type with thioketones containing  $CH_3-\overset{\overset{S}{\|}}{C}-$ have been reported, probably due to the instability of such substances, thus thioacetophenone readily forms a trimer as does thioacetone. To determine whether the group  $CH_3-\overset{\overset{S}{\|}}{C}-$ in thioketones is capable of condensing with aromatic aldehydes in the presence of a base, the vinylogs of these compounds were investigated. The principle of vinylogy[1] gives an explanation for the condensation of 2-methylchromone[2] and 2,3-dimethylchromone[3] with aromatic aldehydes, *e.g.*, benzaldehyde, since both chromones may be regarded as vinylogs of Ar–CO–CH_3.

We have found that 2-methyl-4-thiochromone (I), 2,3-dimethyl-4-thiochromone (II) and 2,3-

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[1] R. C. Fuson, *Chem. Revs.*, **16**, 1 (1935).

[2] U. Cheema, K. Gulati and K. Venkataraman, *J. Chem. Soc.*, **925** (1932).

[3] I. Heilbron, H. Barnes and R. Morton, *ibid.*, 123, 2559 (1923).

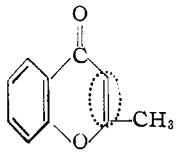
Table I

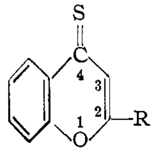
Molar Equivalents of the Thiochromone[a] and Appropriate Aldehyde Were Condensed; Yield 30–50%

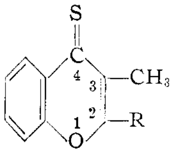
	Condensation product R	M.p., °C.	Color			Formula	Analyses, %					
			Solid	With concd. H_2SO_4	In benzene[b]		Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Sulfur Calcd.	Sulfur Found
Ia[c]	$CH{=}CHC_6H_5$	164	Brown	Orange	Orange	$C_{17}H_{12}OS$	77.3	77.7	4.5	4.7	..	..
Ib	$CH{=}CH{\cdot}C_6H_4{\cdot}OCH_3\text{-}p$	188	Violet	Red-orange	Yellow-brown	$C_{16}H_{14}O_2S$	73.5	73.4	4.7	4.8	10.9	10.9
Ic	$CH{=}CH{\cdot}CH{=}CHC_6H_5$	157	Purple	Red	Yellow-brown	$C_{19}H_{14}OS$	78.6	78.3	4.8	5.2	11.0	11.3
Id	$CH{=}CHC_6H_4N(CH_3)_2\text{-}p$	176	Purple	Yellow	Red	$C_{19}H_{17}OSN$[d]	..	..	..	..	10.4	11.0
Ie	$CH{=}CHC_6H_3{<}^{O}_{O}{>}CH_2(3',4')$	196	Red	Red	Yellow-brown	$C_{18}H_{12}O_3S$	70.1	70.0	3.9	4.3	10.4	9.9
IIa	$CH{=}CHC_6H_5$	148	Violet	Orange	Yellow-brown	$C_{18}H_{14}OS$	77.7	77.7	5.0	4.3	11.6	12.1
IIb[c]	$CH{=}CHC_6H_4OCH_3\text{-}p$	170	Violet	Orange	Yellow	$C_{19}H_{16}O_2S$	74.0	73.7	5.2	4.7	10.4	10.8
IIc	$CH{=}CHC_6H_3{<}^{O}_{O}{>}CH_2(3',4')$	204	Violet	Violet	Yellow	$C_{19}H_{14}O_3S$	70.8	70.6	4.3	4.5	..	..
IIIa	$CH{=}CHC_6H_4OCH_3\text{-}p$	143	Brown	Red-brown	....	$C_{19}H_{16}OS_2$	70.4	70.1	4.9	5.0	..	..

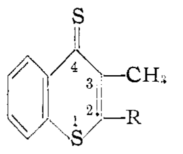
[a] 0.44 g. of thiochromone [I], 0.47 g. of thiochromone II, 0.51 g. of thiochromone III. [b] Compounds are soluble in benzene except for IIIa which is difficultly soluble in cold benzene. [c] Ia and IIb as difficultly soluble in dilute HCl. [d] % N calcd. 4.6; found 4.4.

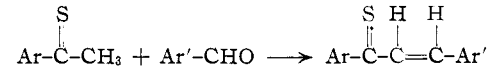
dimethyl-1,4-dithiochromone (III) condense readily with aromatic aldehydes in the presence of piperidine. As these thiochromones are vinylogs of $Ar{-}\overset{S}{\overset{\|}{C}}{-}CH_3$, the ability of the group $CH_3{-}\overset{S}{\overset{\|}{C}}{-}$ to condense with aromatic aldehydes seems to be proved in principle.


2-methylchromone


I, R = CH₃

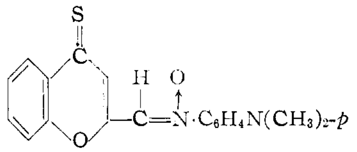

II. R = CH₃


III. R = CH₃

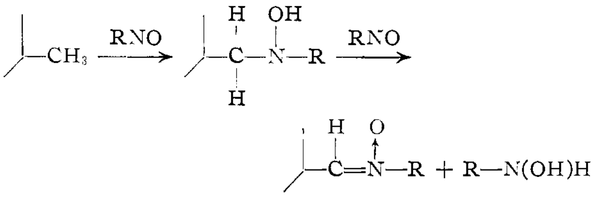


$$Ar{-}\overset{S}{\overset{\|}{C}}{-}CH_3 + Ar'{-}CHO \longrightarrow Ar{-}\overset{S}{\overset{\|}{C}}{-}\overset{H}{\overset{|}{C}}{=}\overset{H}{\overset{|}{C}}{-}Ar'$$

The aldehydes used were benzaldehyde, anisaldehyde, cinnamaldehyde, *p*-dimethylaminobenzaldehyde and piperonal.

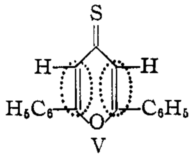

IV

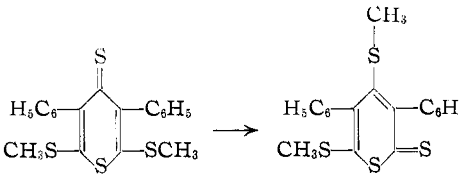
In contrast to the stability of 2-methylchromone to *p*-nitrosodimethylaniline in presence of piperidine even at high temperature,[4] it has been found that 2-methyl-4-thiochromone, reacts at room temperature forming the nitron IV. Thus the ability of the group $CH_3{-}\overset{S}{\overset{\|}{C}}{-}$ to react with *p*-nitrosodimethylaniline seems to be also proved in principle. The formation of IV can be explained in the light of the following scheme[5]



Application of the Theory Vinylogy to Thermal Reactions of 4-Thiopyrones.—In contrast to many thioketones, 2,6-diphenyl-4-thiopyrone[6] (V) like thiobenzophenone reacts on heating according to the following scheme $2{>}C{=}S \rightarrow {>}C{=}C{<} + 2S$.

It is evident that 2,6-diphenyl-4-thiopyrone (V) may be regarded as a vinylog of thiobenzophenone, which explains the similarity of their behavior, thiobenzophenone[7] decomposes at 170–180° forming tetraphenylethylene and sulfur. Special reference should be made to the 2,6-bismethylthio-4-thio-3,5-diphenyl-1-thiopyrone (VI) which on heating at 240–250° for ten minutes isomerizes to 4,6-bismethylthio-2-thio-3,5-diphenyl-1-thio-α- pyrone[8] (VII).


V


VI VII

Then according to the theory of vinylogy, dimethyltrithiocarbonate should rearrange on heating by migration of the methyl group as

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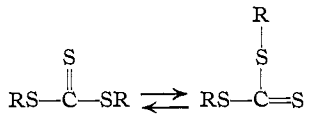
[4] J. Schmutz, R. Hirt and H. Lauener, *Helv. Chim. Acta*, **35**, 1171 (1952).

[5] A. Schönberg and R. Michaelis, *J. Chem. Soc.*, 627 (1937).

[6] F. Arndt, E. Scholz and P. Nachtwey, *Ber.*, **57**, 1903 (1924).

[7] H. Staudinger and H. Freudenberger, *ibid.*, **61**, 1580 (1928).

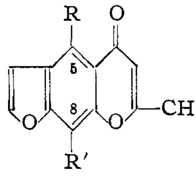
[8] A. Schönberg and W. Asker, *J. Chem. Soc.*, 604 (1946).


$$RS\overset{S}{\overset{\|}{C}}SR \rightleftarrows RS\overset{\overset{R}{|}\atop S}{\overset{|}{C}}{=}S$$

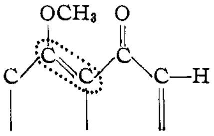
This hypothesis could be tested by the use of labeled sulfur.[9]

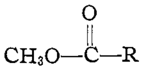
The Concept of Vinylogy and the Ease of Hydrolysis of 5-Methoxychromones.—The facile demethylation of visnagin[10] (VIII) ($R = OCH_3$, $R' = H$) has been reported; in the case of khellin[11] (VIII) ($R = R' = OCH_3$) facile demethylation takes place only in position 5. Ready demethylation of methoxy groups in position 5 of chromones also has been observed in other cases, *e.g.*, in the 5,3-methyl ether of chromone.[12]

Shady and Soine explain the facile hydrolysis of khellin and visnagin by regarding these substances as vinylogs of the ester[11b] (IX). They do not take into consideration the importance of the heterocyclic oxygen in the pyrone ring. If their theory were correct, visnaginone (X) which may be also regarded as a vinylog of the ester IX, should also be easily demethylated. However, it was found that in dilute hydrochloric acid and dioxane, visnagin was demethylated, whereas visnaginone (X) was not demethylated at all or only to a very minor extent.

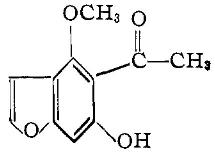


VIII




$$CH_3O\overset{O}{\overset{\|}{C}}R$$

IX



X

Experimental

2-Methyl-4-thiochromone.—2-Methylchromone (1 g.) was refluxed with 1 g. of phosphorus pentasulfide[13] in 30 ml. of benzene on a steam-bath for 2 hours. The hot deep red solution was filtered and the residue repeatedly extracted with boiling benzene. The combined extracts were evaporated to dryness.

2-Methyl-4-thiochromone was crystallized from alcohol as violet red needles, m.p. 95°, which dissolved in concentrated sulfuric acid giving a colorless solution; yield 70–80%. Baker[13] gave m.p. 96–97°.

Anal. Calcd. for $C_{10}H_8OS$: C, 68.1; H, 4.5; S, 18.2. Found: C, 68.3; H, 4.5; S, 18.2.

The same procedure was followed for 2,3-dimethylchromone and 2,3-dimethyl-1-thiochromone (yield 70–80%); it is superior to melting of the chromone with phosphorus pentasulfide.

Condensation of 2-Methyl-4-thiochromones with Aromatic Aldehydes.—Molar equivalents of the thiochromone and the aromatic aldehyde were dissolved in about 20 ml. of absolute ethyl alcohol; then a few drops of piperidine were added and the mixture left for 24 hours at 25°. The solid that separated was filtered off (in some cases concentration of the solution was necessary), washed with small amount of cold ethyl alcohol and crystallized from ethyl alcohol.

4-Thio-2-chromyl-N-(*p*-dimethylaminophenyl)-nitron (IV).—2-Methyl-4-thiochromone (0.44 g.) together with *p*-nitrosodiomethylaniline (0.37 g.) were dissolved in about 20 ml. of absolute ethyl alcohol, a few drops of piperidine added and the mixture left for 24 hours at 25°. The separating crystals were filtered off, washed with small amount of cold ethyl alcohol and crystallized from ethyl alcohol in deep green crystals, m.p. 236°, difficultly soluble in benzene, dissolving in concentrated sulfuric acid to violet-brown solution; yield *ca.* 20%.

Anal. Calcd. for $C_{18}H_{16}O_2N_2S$: C, 66.7; H, 4.9; N, 8.6; S, 9.9. Found: C, 67.1; H, 4.7; N, 8.4; S, 10.1.

However, it was found that in the case of 2-methylchromone, no reaction occurred.

Color Reactions of Condensation Products (I–III).—A few small crystals of mercuric chloride were added to the benzene solution of the condensation products; the surface of the colorless crystals acquired color almost immediately due to the formation of a mercuric chloride addition complex.[14] The reaction was positive in all cases, *e.g.*, the color acquired by the mercuric chloride crystals was orange in the case of 2-styryl-4-thiochromone (Ia).

Action of Hydrochloric Acid on Visnagin (a).—To 0.5 g. of visnagin in 20 ml. of dioxane was added 15 ml. of hydrochloric acid (7.5 ml. of concentrated hydrochloric acid, sp. gr. 1.18, mixed with 7.5 ml. of water) and the solution refluxed for one hour. The clear solution was allowed to cool and 0.32 g. of crystals, m.p. 155–156°, separated out; admixture with an authentic sample of demethylated visnagin gave no depression of m.p. The two samples showed the same color reaction with ferric chloride.

(b) **Visnaginone.**—To 0.5 g. of visnaginone in 20 ml. of dioxane was added 16.5 ml. of hydrochloric acid (8.25 ml. of hydrochloric acid, sp. gr. 1.18, and 8.25 ml. of water). The mixture was refluxed for one hour, the clear solution allowed to cool and water added until no more deposit formed. The deposit was filtered off and dissolved in 10% sodium hydroxide; the alkaline solution was then filtered and the filtrate acidified with dilute hydrochloric acid, whereupon a yellow deposit formed, m.p. 108°. On crystallization from alcohol, yellow crystals were obtained which were proved to be visnaginone by their m.p. and mixed m.p.; yield 0.21 g. An additional amount of visnaginone was obtained from the alcoholic mother liquor.

CAIRO, EGYPT

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[9] This department is, however, not equipped for isotopic investigations.

[10] A. Schönberg and N. Badran, THIS JOURNAL, **73**, 2960 (1951).

[11] (a) A. Schönberg and A. Sina, *ibid.*, **72**, 3396 (1950); (b) H. Abu Shady and Tatio O. Soine, *J. Am. Pharm. Assoc.*, **41**, 395 (1952); (c) A. Schönberg and G. Aziz, THIS JOURNAL, **75**, 3265 (1953).

[12] B. Krishnaswamy and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **15A**, 437 (1942); and K. V. Rao and T. R. Seshadri, *ibid.*, **22A**, 383 (1945).

[13] Phosphorus pentasulfide was purified according to W. Baker, J. Harborne and W. Ollis, *J. Chem. Soc.*, 1306 (1952).

[14] A. Schönberg, *Ber.*, **58**, 1793 (1925); A. Schönberg and Th. Stolpp, *ibid.*, **63**, 3102 (1930).