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SHORT COMMUNICATION

CASSIAXANTHONE, A HYDROXYXANTHONE DICARBOXYLIC ACID FROM *CASSIA* SPECIES

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Abstract—A pale yellow crystalline material isolated from a bicarbonate extract of leaves of *Cassia reticulata* has been identified as 1-hydroxyxanthone-6,8-dicarboxylic acid. The possibility that this compound is a natural product rather than an artefact, as suggested earlier, is discussed.

INTRODUCTION

ISOLATION of an unidentified pale-yellow crystalline compound from dried leaves of *Cassia reticulata* Willdenow (Leguminosae) was reported in 1949.[1] The same compound[2] was obtained also from the leaves of *C. alata*.[3] In both instances, the compound was suspected of being an artefact resulting from alkaline treatment of some anthraquinone present in *Cassia* species. On the basis of evidence presented in this paper, the structure I has been assigned to the compound, which we have named "Cassiaxanthone". The xanthone structure of I suggests the possibility that it may be not an artefact, but a true metabolite.

RESULTS

Analyses of the compound (I) agree with the formula $C_{15}H_8O_7$.[2,3] The u.v. absorption spectrum is suggestive of a xanthone nucleus.[4] The i.r. spectrum† shows broad bands at 2500–2700 cm^{-1} (carboxyl) and 1635 cm^{-1} (nuclear carbonyl of the xanthone[5]). Acetylation of I yields a colorless monoacetate (II) in which the carbonyl peak is shifted to 1667 cm^{-1}, behavior indicating the presence of a hydroxyl group in the 1 position. As expected for a 1-hydroxyxanthone, treatment with diazomethane does not affect the hydroxyl group: A dimethyl derivative (III) is obtained from which the parent compound can be regenerated by alkaline hydrolysis. The NMR spectrum of I, as well as that of III, shows a signal at $\tau - 2{\cdot}06$, as expected for the highly chelated hydroxyl at C_1. It also shows two doublets centered at τ 3·1 ($J = 9$ Hz), and 2·85 ($J = 8$ Hz), assigned to the protons on carbons 2 and 4. The signal for the C_2 proton in the acetate shows the expected downfield shift. The expanded spectrum of I shows fine splitting ($J = 1{\cdot}5$ Hz) due to *meta* coupling. The C_3 proton appears as a triplet around τ 2·2 ($J = 9$ Hz). These shifts are comparable to those of the corresponding protons

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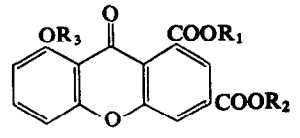
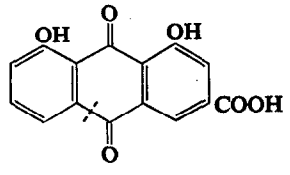
† All i.r. spectra were taken as KBr pellets.

[1] M. ANCHEL, *J. Biol. Chem.* **177**, 169 (1949).
[2] M. ANCHEL, *J. Am. Chem. Soc.* **72**, 1832 (1950).
[3] H. HAUPTMANN and L. L. NAZARIO, *J. Am. Chem. Soc.* **72**, 1492 (1950).
[4] B. JACKSON, H. D. LOCKSLEY and F. SCHEINMANN, *J. Chem. Soc.* (C) 871 (1967).
[5] E. D. BERGMANN and S. PINCHAS, *J. Chim. Phys.* **49**, 537 (1952).

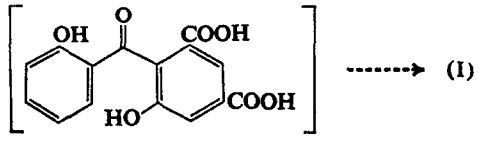
in 1-hydroxyxanthones.[4] The remaining two aromatic protons give doublets at τ 2·2 ($J = 2$ Hz) and 1·9 ($J = 2$ Hz) indicating the *meta* relationship of the carboxyl groups, which must therefore be either at C_5 and C_7, or at C_6 and C_8. The reported spectra of a number of xanthones show signals for the C_6 and C_8 protons at much lower field than those for the C_5 and C_7 protons.[4] The C_8 proton in 1-hydroxyxanthone* comes as a doublet around τ 1·85. A carboxyl group *ortho* to this proton would shift the signal by about 0·6 τ to lower field.[6] This would be further downfield than the observed value. The carboxyl groups are accordingly assigned to the C_6 and C_8 positions.



(I) R_1R_2 = H, R_3 = H
(II) R_1R_2 = H, R_3 = CH_3CO—
(III) R_1R_2 = CH_3, R_3 = H



(IV)



(V) ⟶ (I)

DISCUSSION

Because the "yellow crystalline substance" was obtained from *Cassia* leaves only after alkaline treatment, it was thought originally that it might not be a natural product, but rather an artefact formed from rhein, an anthraquinone found in both species of *Cassia* from which the compound was isolated. However, identification of the compound as a xanthone makes this less likely. We have been unable to find any example of *in vitro* conversion of an anthraquinone to a xanthone, nor have we been able to effect this conversion. Atkinson and Lewis[7] have demonstrated the oxidative coupling of benzophenones to xanthones under alkaline conditions, and it is conceivable that if the appropriate benzophenone were present in sufficient amount in *Cassia* leaves, that cassiaxanthone might have been formed by the alkaline treatment. But the presence of benzophenones in *Cassia reticulata* has not been reported. Money[8] has postulated that xanthones may be formed biogenetically not from the anthraquinone, but rather by oxidative cleavage of the precursor anthrone. We felt that this might have a chemical analogy, since Hauptmann and Nazario,[3] in discussing the basis for considering that the yellow substance was an artefact, stated: "We observed its formation when boiling a fraction of reduced anthraquinones with sodium carbonate solution." On the assumption that an anthrone component in the mixture of "reduced anthraquinones" was responsible

* This was prepared by the method of B. M. DESAI, P. P. DESAI and R. D. DESAI. *J. Ind. Chem. Soc.* 37, 53 (1960). It melted at 147–148°.

[6] L. M. JACKMAN, *Applications of NMR Spectroscopy in Organic Chemistry*, p. 63, Pergamon Press, New York (1959).

[7] J. E. ATKINSON and J. R. LEWIS, *J. Chem. Soc.* (c) 281 (1969).

[8] T. MONEY, *Nature* **199**, 592 (1963).

for this result, we tried to effect this conversion by treatment of a number of anthrones with alkali or alkaline peroxide. Instead of forming a xanthone, the anthrone under these conditions tended to revert to the anthraquinone.

The possibility that cassiaxanthone is a natural product, on the other hand, fits in well with the fact that xanthones accompany anthraquinones in a number of plant species. Gröger *et al.*[9] using a ^{14}C or ^{3}H label, have demonstrated the biological transformation of the anthraquinone, emodin, to the ergochromes, closely related xanthones. Hölker and Kagal[10] have pointed out that the co-occurrence of the anthraquinone versicolorin A and the xanthone sterigmatocystin, suggests a similar biological relationship. The postulated biological conversion of rhein to cassiaxanthone (IV → V → I) might involve either cleavage to a benzophenone followed by oxidative coupling, or oxidative cleavage to a benzophenone, followed by dehydration.

The question of whether cassiaxanthone is an artefact or a natural product still remains open.[11]

EXPERIMENTAL

Cassiaxanthone (I)

Dried leaves of *Cassia reticulata* Willd. (200 g) were boiled with *ca.* 1 per cent $NaHCO_3$ (5 l.) for about 30 min. The alkaline extract was acidified to pH 2 with HCl and the precipitate centrifuged off. The supernatant was extracted with methyl-isobutyl ketone (*ca.* 500 ml). The residue from this extract was taken up in Et_2O and extracted with dil. $NaHCO_3$. On acidification, *ca.* 900 mg of a light-brown precipitate was obtained which was suspended in H_2O and treated with benzylamine until a bright red color persisted. The solution was acidified, giving *ca.* 500 mg of a yellow precipitate, m.p. 220–230°. After recrystallization from acetic acid, it melted at 330–340° decomp. (Found: C, 60·16; H, 2·95. Calc. for $C_{15}H_8O_7$: C, 60·01; H, 2·69%). λ_{max}: (EtOH) 235, 262, 290, 300, 375 nm (ϵ 25,400, 23,200, 6900, 6900 (sh) 3900): 0·1 N NaOH 240, 270, 320, 400 nm (ϵ 32,100, 19,650, 9300, 5400). ν_{max} 2500–2700, 1635 cm^{-1}. NMR signal at τ 3·1 (doublet $J = 9$ Hz), 2·85 (doublet $J = 8$ Hz), 2·2 (triplet of doublets, $J = 9$ Hz, $J = 2$ Hz), 1·9 (doublet, $J = 2$ Hz) and −2·06 (singlet).

Cassiaxanthone Acetate (II)

Cassiaxanthone acetate (II) was prepared in the usual way (acetic anhydride and sodium acetate) and crystallized from aqueous EtOH. Colorless needles, m.p. 215–216°, λ_{max} EtOH 235, 250, 275 and 360 nm. ν_{max} 1738, 1710, 1660, 1615, and 1605 cm^{-1}. NMR signals at τ 7·65 (3H, singlet), 2·82 (1H, broad doublet $J = 8$ Hz), 2·40 (1H, broad doublet, $J = 8$ Hz), 2·25 (1H, doublet, $J = 2$ Hz), 2·20 (1H, broad triplet, $J = 8$ Hz), 1·9 (1H, doublet, $J = 2$ Hz). (Found: C, 60·10; H, 3·27; Calc. for $C_{17}H_{10}O_8$: C, 59·64; H, 2·95%.)

Dimethyl cassiaxanthone (III)

Dimethyl cassiaxanthone (III) was prepared with CH_2N_2 in Et_2O and crystallized from EtOH, m.p. 183–184°; (Found: C, 61·93; H, 3·94; OCH_3, 19·21. Calc. for $C_{17}H_{12}O_7$: C, 62·18; H 3·63; OCH_3, 18·91%). λ_{max}, EtOH, 231, 237, 263, 303, 315 and 375 nm. ν_{max} 1730, 1650, and 1610 cm^{-1}. NMR signals at τ 6·03 (6H, singlet), 3·1 (1H, broad doublet, 9 Hz), 2·87 (1H, broad doublet, 9 Hz), 2·17 (1H, broad triplet, 9 Hz), 2·1 (1H, doublet, 2 Hz), 1·87 (doublet, 2 Hz).

Acknowledgements—This work was supported by grants AI-00226 and GM 12150 from the National Institutes of Health. The NMR spectra were done on a Varian A60A nuclear magnetic resonance spectrometer, purchased on a General Research Support Grant, 5-S01-FRO-5621.

[9] D. Gröger, D. Erge, B. Franck, U. Ohnsorge, H. Flasch and F. Hüper, *Chem. Ber.* **101**, 1907 (1968).
[10] J. S. E. Hölker and S. A. Kagal, *Chem. Commun.* 1574 (1968).
[11] A recent review by Carpenter, Locksley and Scheinman [*Phytochem*, **8**, 2013 (1969)] on xanthones in higher plants lists the four families of angiosperms from which xanthones have been isolated. These do not include the Leguminosae, the family in which *Cassia* belongs. If Cassiaxanthone is a natural product, it is accordingly the first xanthone isolated from this family.