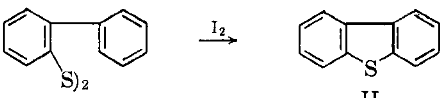
thiophene-2-carboxylic acids. More recently,[4] condensed 2,3-dihydrothiophenes have been obtained from bis(β-arylethyl) disulfides using iodine or aluminum bromide as the catalyst.

During the course of further work on the scope of the disulfide ring-closure reaction, we have found that bis(2-biphenylyl) disulfide (I) will cyclize in good yield in the presence of iodine to give dibenzothiophene (II).



I II

A combination of catalyst and conditions was sought which might be even more favorable for ring closure, and therefore the reaction was repeated, using catalysts other than iodine and varying the solvent and temperature. The results are summarized in Table I.

TABLE I

CYCLIZATION OF BIS(2-BIPHENYLYL) DISULFIDE

Catalyst	Moles catalyst/ mole disulfide	Conditions, °C.	Dibenzothiophene, % yield
I_2	1.1	198°, 1 hr.[a]	64
I_2	Excess	101°, 24 hr.[b]	0
I_2	2.0	Reflux, 12 hr.[c]	50
$I_2 + Me_2SO_4$	0.6, 1.2, resp.	Reflux, 5 hr.[b]	0
$I_2 + SnCl_4$	0.6, 2.1, resp.	Reflux, 2.5 hr.[d]	0
$AlBr_3$	1.0	80°, 3 hr.[d]	38
$AlCl_3$	2.0	65°, 3 hr.[d]	35
BF_3	Excess	Reflux, 3 hr.[d]	0
Br_2	1.0	78°, 37 hr.[e]	16
Poly-H_3PO_4	Excess	200°, 24 hr.	0
Conc. H_2SO_4	Excess	25°	0

Solvents: [a] Ethylene glycol. [b] Dioxane. [c] Toluene. [d] Benzene. [e] Carbon tetrachloride.

Iodine was found to be the most effective of the catalysts employed, as the reaction can be run at higher temperatures without significant desulfurization occurring, and it has a further advantage over reagents such as aluminum chloride in that it has the ability to oxidize the thiol[4] (formed as the by-product on cleavage of the disulfide) to starting material. However, even with iodine present, no dibenzothiophene could be isolated when stannic chloride was employed.

With bromine, ring closure was expected to proceed in good yield *via* the formation of the sulfenium bromide. In fact a surprisingly low yield of dibenzothiophene was obtained and 70% of the disulfide was recovered. In contrast, bis(2-biphenylyl) diselenide affords an essentially quantitative yield of dibenzoselenophene under the same conditions.[5]

In addition to dibenzothiophene, a very small amount of a compound, m.p. 163–165°, was isolated when iodine and ethylene glycol were employed as the catalyst and solvent respectively. Its analysis was consistent with $C_{14}H_{12}S$ and it seems probable that the two additional carbon atoms are acquired by reaction with either a solvent molecule or a product of the interaction of solvent and iodine. The infrared spectrum indicated the presence of both aromatic and aliphatic carbon–hydrogen bonds. Furthermore, absorption suggesting aromatic monosubstitution together with 1,2,3-trisubstitution and the absence of C-methyl absorption provide reason for the tentative formulation of the by-product, m.p. 163°, as 2,3-dihydro-7-phenylbenzo[*b*]thiophene, which to our knowledge has not yet been reported in the literature.

Experimental[6]

Bis(2-biphenylyl) Disulfide (I).—The disulfide I was prepared as previously reported by Campaigne and Osborn[7] from 2-aminobiphenyl and melted at 117–118°.

Dibenzothiophene (II).—The following details exemplify the general work-up procedure for the majority of experiments in Table I and also describe the isolation of the by-product, m.p. 163°.

A solution of I (3.70 g., 0.01 mole), and iodine (2.70 g., 0.011 mole) in freshly redistilled ethylene glycol (300 ml.) was heated under reflux for 1 hr., cooled, and poured slowly into water (1 l.). The small excess of iodine was bleached by the addition of dilute sodium bisulfite solution, and, after cooling overnight, the white solid was collected, washed well with water, and dried under reduced pressure. The solid (3.53 g., m.p. 92–96°) was dissolved in a large volume of boiling ethanol. On cooling the solution, plates (0.1 g.) were obtained which crystallized from benzene–ethanol as fine white needles, m.p. 163–165°. Infrared spectrum: ν_{max}^{KBr} 3049 cm.$^{-1}$ (aromatic C—H); 2920 and 2841 cm.$^{-1}$ (aliphatic C—H); 702(s) and 744 cm.$^{-1}$ (s) (aromatic monosubstitution); and 697(m) and 769 cm.$^{-1}$ (s) (aromatic 1,2,3-trisubstitution).

Anal. Calcd. for $C_{14}H_{12}S$: C, 79.19; H, 5.70; S, 15.10. Found: C, 78.42; H, 5.73; S, 15.35.

The filtrate was partially evaporated and on cooling gave needles, m.p. 97–99° (2.34 g., 64%). Recrystallization afforded white needles m.p. 97.5–99.5°.[8] No melting point depression was observed on admixture with dibenzothiophene prepared by an independent route.

Anal. Calcd. for $C_{12}H_8S$: C, 78.22; H, 4.38; S, 17.40. Found: C, 78.17; H, 4.45; S, 17.27.

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(5) J. D. McCullough, T. W. Campbell, and E. S. Gould, *J. Am. Chem. Soc.*, **72**, 5753 (1950).

(6) All melting points are corrected.

(7) E. Campaigne and S. W. Osborn, *J. Org. Chem.*, **22**, 561 (1957).

(8) H. Gilman and A. Jacoby, *ibid.*, **3**, 108 (1938), report the melting point of dibenzothiophene to be 99°.

On the Color Reaction of Khellin with Alkali

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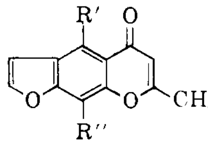
Khellin (Ia), the main active principle of the fruits of *Ammi visnaga* (L.), has attracted interest, being antispasmodic and a coronary vasodilator.[1] It is used in the treatment of angina pectoris and as a duiretic.

According to Abd-El-Rahman[2] and Fahmy, Badran, and Messeid[3] khellin gives an intense red-violet color with potassium or sodium hydroxide pellets. The method has been used for colorimetric estimations by Anrep.[4]

Schönberg and Sina[5] showed, however, that this color reaction is not specific for khellin, since visnagin (Ib) among other 2-methylchromones gives the same test.

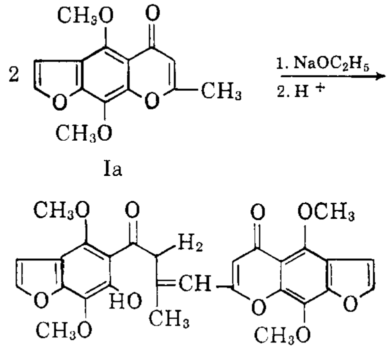


Ia. $R' = R'' = OCH_3$
Ib. $R' = OCH_3$, $R'' = H$

The nature of the violet substance obtained from the reaction of khellin with alkali remained, however, unsettled because of difficulty in its isolation.[5]

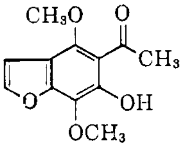
We have now found that khellin suspended in dry ether and shaken with dry freshly prepared sodium ethoxide produces a solid deep violet reaction product. Treatment of the violet product with acetic acid yields a yellow crystalline substance which proved to be the dimer of the starting material. The yellow substance when dissolved in ethanol (difficultly soluble) gives at once with 1% aqueous potassium hydroxide the red-violet color. Khellin, on the other hand, develops the color only when treated with moistened alkali pellets.[5] A certain time elapses before the color appears.

Nature of the Reaction Product of Khellin with Alkali.—Structure II is proposed for the reaction product of khellin with sodium ethoxide. This structure finds confirmation from the following: (a) The molecular weight of the product is double that of khellin. (b) The n.m.r. spectrum of compound II contains signals for an OH—, CH_2—, and CH_3— groups.[6] The resonance of the hydroxyl proton indicates an intramolecular hydrogen bonded OH group. (c) Infrared curves[7] are resolved very poorly around the 3-μ region, a case observed also with khellinone (III), which contains a chelated hydroxyl group. The CO band of compound II lies at 6.05 μ while that of khellin and khellinone lie at 6.00 μ and 6.10 μ, respectively.[7] (d) Pyrolysis of II results in the formation of two molecules of khellin. (e) The similarity of the formation of compound II and that of the dimeric product of 2-methylchromone[8] as well as their thermochromic behavior in piperidine solutions suggests that both compounds are of analogous constitution.

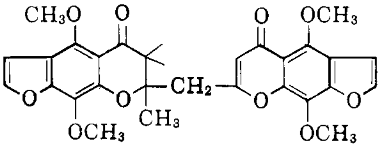


Ia

II



III



IV

Compound II could be formed by 1:4 addition of the carbanion to the $\alpha{:}\beta$-unsaturated system of another molecule, followed by ring opening of the intermediate adduct IV.[8] This mechanism of a Michael condensation reaction is supported by the fact that the methyl group in khellin is strongly activated in alkaline media and undergoes condensation reactions,[9] as do other 2-methylchromones.[10]

Experimental[11]

Action of Sodium Ethoxide on Khellin.—Two grams of khellin was added to ethanol-free dry powdered sodium ethoxide suspended in about 50 ml. of dry ether (E. Merck, peroxide-free). The sodium ethoxide was prepared by dissolving 1 g. of sodium metal in absolute ethyl alcohol, and the excess alcohol was removed under vacuum at 160–170° (bath temperature). The mixture was shaken in a tightly closed vessel for about 1 hr., then kept at room temperature for 48 hr. The deep violet-colored deposit was quickly filtered, washed with ether, then decomposed with ice cold 10% aqueous acetic acid. The reddish yellow substance, which separated, was treated with ethyl alcohol, filtered, washed several times with hot ethyl alcohol, and crystallized from *n*-butyl alcohol to give compound II as pale yellow crystals, m.p. 170–172° (uncorrected); yield, *ca.* 0.2 g.

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(1) G. V. Anrep, G. S. Barsoum, M. R. Kenawy, and G. Misrahy, *Brit. Heart J.*, **8**, 171 (1946); *Lancet*, **I**, 557 (1947).

(2) Abd-El-Rahman, Master's thesis, Fouad I University, Cairo, 1943.

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(5) A. Schönberg and A. Sina, *J. Chem. Soc.*, 3344 (1950).

(6) We wish to acknowledge our thanks to Dr. N. S. Bhacca, NMR Applications Laboratory Instrument Division, Varian associates, Palo Alto, Calif., for carrying out the n.m.r. and for helpful discussion.

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(8) A. Schönberg, E. Singer, and M. M. Sidky, *Ber.*, **94**, 660 (1961).

(9) A. Schönberg and A. Sina, *J. Am. Chem. Soc.*, **72**, 1611 (1950).

(10) I. M. Heilbron, H. Barnes, and R. A. Morton, *J. Chem. Soc.*, 2559 (1923); J. Schmutz, R. Hirt, and L. Lauener, *Helv. Chim. Acta.*, **35**, 1171 (1952).

(11) The khellin used was provided by the Memphis Chemical Co., Cairo.

Anal. Calcd. for $C_{14}H_{12}O_5$: C, 64.6; H, 4.6; mol. wt., 520.5. Found: C, 64.9; H, 4.8; mol. wt., 509.0 (in camphor).

Pyrolysis of Compound II.—One-half gram of compound II was heated in a distilling apparatus at 270–280° (bath temperature) under normal pressure. The reaction vessel was left to cool and the substance collected was crystallized from ethyl alcohol and proved to be khellin (m.p. and m.m.p.). Yield, *ca.* 70%.

Thermochromic Behavior in Piperidine.—Compound II dissolved in piperidine (E. Merck), produces a red-violet color at room temperature. The color discharges almost completely on heating. On cooling the red color is regenerated. The phenomenon is reversible for several times, but on standing for a long time at room temperature, the color of the solution fades considerably.

Action of Alumina on II.—When compound II in benzene (thiophene-free and dried over sodium) is treated with a small amount of alumina (Aluminiumoxyd Woelm, alkalifrei, annährend neutral, Akt. Stufe 1, M. Woelm-Eschwege), a red-violet color appears instantaneously on the surface of the inorganic material and the benzene solution remains practically colorless.

The Configurations of Flavan-3,4-diols

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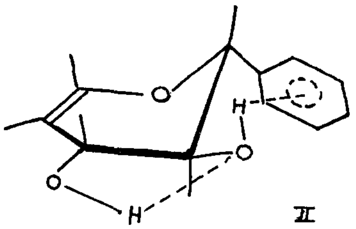
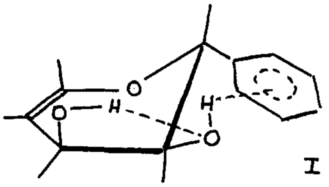
Corey, Philbin, and Wheeler[2] have recently reported proton magnetic resonance studies on the carbonates and benzoates of two flavan-3,4-diols, the results of which allow an unambiguous assignment of configuration to these two materials. The diol, m.p. 145°, prepared by direct reduction of the 4-ketone has the *trans* relationship of the alcohol functions. The diol, m.p. 160°, which was prepared *via* the oxime followed by reduction to the amine and deamination by nitrous acid possesses a *cis* relationship of the alcohol functions. We now report confirmation of these assignments on the basis of infrared study of the intramolecular hydrogen bonding (H-bonding) in the parent diols.[3]

Infrared spectra of the flavandiols were measured in a saturated solution in carbon tetrachloride (about 0.005 *M*) in a pair of matched, one-cm. silica cells and employing a Beckman DK-1 recording spectrophotometer. The material, m.p. 145°, showed a sharp band at 3608 cm.$^{-1}$. The diol, m.p. 160°, showed a pair of maxima of equal intensity at 3606 cm.$^{-1}$ and 3578 cm.$^{-1}$.



II



I

Consideration of the stretching frequencies to be expected for the several OH...O and OH...π H-bonded species as well as for the free hydroxyl functions permits discussion of the stereo arrangement of the two flavandiols. Benzyl alcohol[4] shows a peak associated with the free alcohol at 3632 cm.$^{-1}$ and a H-bonded (OH...π) peak at 3615 cm.$^{-1}$. Similarly, β-phenylethanols have a free peak near 3630 cm.$^{-1}$ and a bonded peak about 25 cm.$^{-1}$ lower in frequency.[5] The shifts ($\Delta\nu = \nu_{free} - \nu_{bonded}$) in cyclic glycols range from about 30 cm.$^{-1}$ to 103 cm.$^{-1}$ as the projection angle (θ) between the C—O bonds is reduced from near 60° to 0°. Thus the cyclohexane diols with θ near 60° for both the *cis*- and *trans*-diols show similar shifts. The tetrahydronaphthalene-1,2-diols reveal a greater strength of the H-bond in the *cis*- than the *trans*-diol. In the less puckered cyclopentane diols the *cis*-diol shows a strong H-bond, but the *trans*-material shows none. In the bicycloheptanediols[6] with $\theta = 0°$ the shift $\Delta\nu$ is 102–103 cm.$^{-1}$.

The presence of a strong intramolecular OH....O bond at 3578 cm.$^{-1}$ in the isomer with m.p. 160° allows an assignment of a *cis*-configuration to the hydroxyl functions. Chemical evidence[7] which has been confirmed by n.m.r studies[1] shows that the 2-phenyl and 3-hydroxyl groups in the flavandiols are equatorial and *trans*. The diol, m.p. 160°, is therefore represented as at I. The isomer m.p. 145° which must be the *trans*-diol is shown at II.

The sharp band 3608 cm.$^{-1}$ in this latter compound must result from two different O—H stretching frequencies. One involves the π-bonding of the hydrogen atom of the 3-hydroxyl group to the phenyl ring; the other relates to the hydrogen

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[1] Harrison Fellow at the University of Pennsylvania, 1961–1962.

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[3] For development of the method see (a) A. R. H. Cole and P. Jefferies, *J. Chem. Soc.*, 4391 (1956); (b) L. P. Kuhn, *J. Am. Chem. Soc.*, **74**, 2492 (1952); **76**, 4323 (1954); **80**, 5950 (1958).

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