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ORGANIC PHOTOCHEMISTRY—II

PHOTOCHEMICAL REACTION OF 5-PHENYLTROPOLONE AND ITS METHYL ETHER[1]

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Abstract—Photochemistry of 5-phenyltropolone methyl ether (I) has been compared with that of colchicine and isocolchicine. Irradiation of I in methanol using high pressure mercury lamp afforded 3-methoxy-6-phenyl-$\Delta^{3,6}$-bicyclo[3.2.0]heptadiene-2-one (II). This is the first example giving type C photo-valence isomerization in the photo-reaction of a simple troponoid system. Photochemistry of 5-phenyltropolone (IX) was also studied, where both type B and C valence isomerization were observed and the reaction pathway is discussed.

PHOTOCHEMISTRY of troponoid compounds has been studied independently and revealed various types of interesting reactions such as valence isomerization,[3-8] rearrangement,[9-11] dimerization,[1,12-14] and addition.[7] In most cases, however, the irradiation induces the valence isomerization to afford bicycloheptadienones as a primary reaction. In regard to this photo-isomerization, there are three different modes, conveniently termed type A, B and C cyclization.[3b] Type A cyclization represents a mode of valence isomerization giving norcaradienones (A), which then lead to benzene derivatives (B), as illustrated in Eq. (1). The examples were provided in the photolysis of tropone[15] and 2-phenyltropone,[16] but the yields were extremely poor.

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[1] Preceding paper in this series, T. Mukai, T. Tezuka, Y. Akasaki, *J. Amer. Chem. Soc.* **88**, in press (1966). Support for this work by the Ministry of Education of Japan and by Sankyo Co., Tokyo, is gratefully acknowledged.

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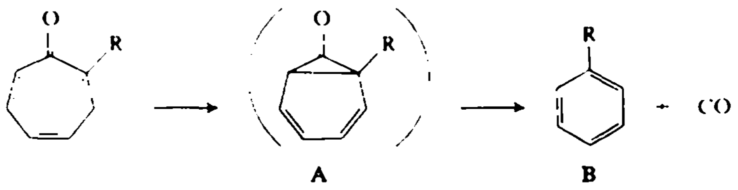
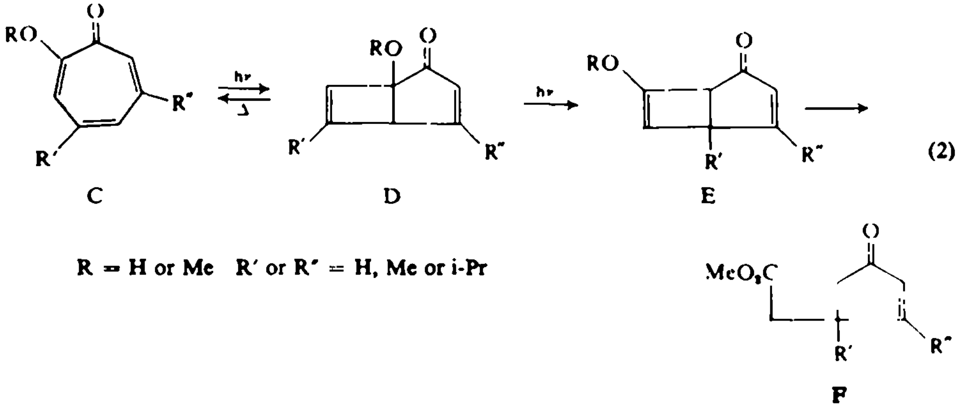


(1)

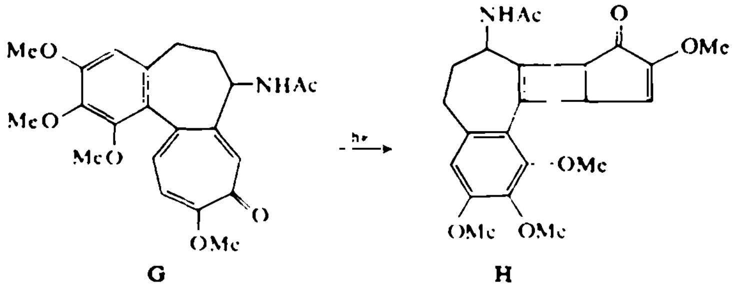
The irradiation of simple monocyclic tropolones[9,10] and their methyl ethers[3,4] results in type B cyclization giving bicyclo[3.2.0]heptadiene-2-ones, in which formation of the new bond occurs at the carbon atom bearing the OH or OMe groups (C → D), and this is occasionally accompanied by deep-seated rearrangements (D → E → F) as shown in Eq. (2).[4,9]



R = H or Me R′ or R″ = H, Me or i-Pr

(2)

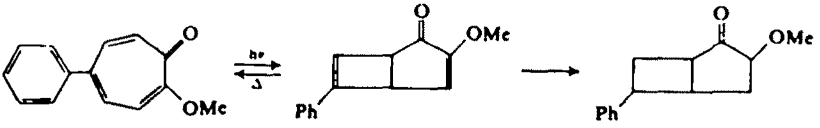
On the other hand, complicated polycyclic troponoids such as colchicine (G)[5,6] and isocolchicine[7,8] undergo type C cyclization at a carbon atom not bearing the OMe group (G → H) as illustrated in Eq. (3). Upon irradiation of colchicine, a photodimer, α-lumicolchicine also was obtained together with β- and γ-lumicolchicine, the valence isomerization products.[12] It should be noted that type C cyclization has never been observed in the photochemistry of simple monocyclic troponoids.



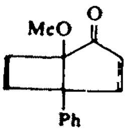
(3)

In order to elucidate the differences in the modes of photoinduced valence isomerization between simple and complicated troponoids, the photochemistry of 5-phenyltropolone and its methyl ether was studied. 5-phenyltropolone and its methyl ether are simple troponoids which can be regarded as model compounds of colchiceine, colchicine and isocolchicine.

5-Phenyltropolone methyl ether (I) was irradiated in 1% methanol solution, in Pyrex vessel, using a 400 Watt high pressure mercury lamp. The photo-reaction was rather slow and after 70 hr of irradiation, a crystalline photo-product (II) was obtained in 30% yield with recovery of 60% of the starting material. The product II, with formula $C_{14}H_{12}O_2$, was isomeric to the starting material, and its UV spectrum showed absorption maxima at 255 and 330 mμ (log ε, 4·52 and 3·40), and the IR spectrum exhibited a CO band (1701 cm^{-1}) characteristic of cyclopentenones, but not of tropones. Pyrolysis of II at 450° afforded 5-phenyltropolone methyl ether (I) in 65% yield. On catalytic reduction using Pd–C, II consumed 2 moles of hydrogen to give a tetrahydro compound (III), which showed a CO band of a cyclopentanone (1730 cm^{-1}). From these facts, the structure IV as well as II would be suggested for the photo-product, but IV was rejected on the basis of the following NMR spectral evidence. There are two doublets due to C_7 and C_4 olefinic protons at 3·37 and 3·58 τ (J_{17} = 3·6, J_{45} = 2·4 c/s), a triplet due to C_1 methine proton at 5·96 τ ($J_{15} = J_{17}$ = 3·6 c/s) and a quartet due to C_5 methine proton at 6·52 τ (J_{15} = 3·6, J_{45} = 2·4 c/s), besides a singlet due to the OMe group at 6·36 τ and the phenyl proton signal at 2·65 τ. When II was heated with 1 N HCl, it was almost completely unchanged. Reduction of II with $NaBH_4$ in methanol afforded a vinyl ether (V), which, without isolation, was treated with diluted acid to give an α-ketol (VI). The structural proof of VI was based in its



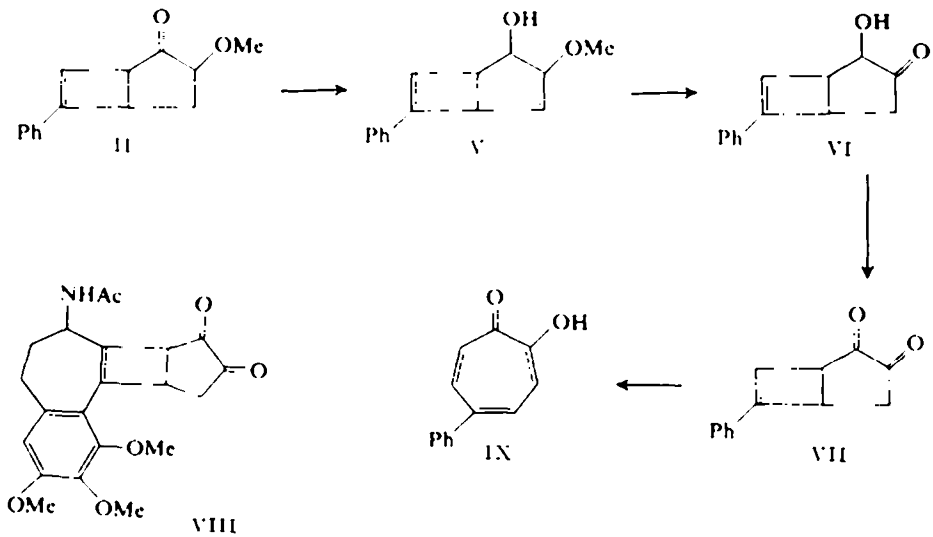
I II III



IV

IR and NMR spectra, which indicated the presence of a OH group (3348 cm^{-1}), a five-membered cyclic ketone (1739 cm^{-1}) and one olefinic proton at C_7 position (a triplet at 3·63 τ with $J_{17} = J_{67}$ = 2·4 c/s. Upon oxidation with cupric acetate, VI afforded a diketon (VII), whose structure was assigned as 6-phenyl-Δ^6-bicyclo[3.2.0]-heptene-2,3-dione on the basis of the following data. In the IR spectrum, two CO bands appeared at 1750 and 1700 cm^{-1} in excellent agreement with the CO bands of the five membered α-diketone (VIII) derived from lumiisocolchicine.[7] Pyrolysis of VII afforded 5-phenyltropolone (IX). From the above series of experiments, it became clear that the irradiation of 5-phenyltropolone methyl ether (I) underwent only type C cyclization like that of colchicine[5,6] and isocolchicine.[7,8] This is the first example giving type C cyclization in the photo-reaction of simple tropolone methyl ethers. Since Dauben observed that irradiation of 5-isopropyltropolone methyl ether resulted in the type B cyclization,[4b] the phenyl group seems to have an effect different from the isopropyl group on the photolysis of troponoids.

The photochemistry of 5-phenyltropolone (IX) was studied to compare with that of the methyl ether (I). After irradiation of 0·3% methanolic solution of IX for 30 hr in the same manner as mentioned above, a crystalline photo-product (X) was isolated in 15% yield accompanied by resinous products and recovery of 50% of the starting material (IX). The elemental analysis, $C_{14}H_{14}O_3$, shows that the product X was not photoisomer of IX. The UV spectrum of X exhibited a strong end absorption around



II V VI VII IX VIII

220 mμ and the IR spectrum showed the absorption bands of ester (1724 cm^{-1}) and cyclopentenone groups (1709 cm^{-1}). On the basis of the analogy to the photochemistry of tropolone itself,[9,10] X would be assigned as methyl 4-oxo-2-cyclopentenylphenylacetate. Additional support for the structure X could be obtained from the NMR spectrum, which showed two quartets due to C_2 and C_3 olefinic protons at 2·29 and 3·78 τ (J_{23} = 5·4, J_{12} = J_{13} = 2·4 c/s), two other quartets due to C_5 methylene protons (designated as A and B) at 7·66 and 8·12 τ (J_{AB} = 19·2, J_{1A} = 2·4 and J_{1B} = 5·4 c/s), and multiplets due to C_1 and C_6 protons at 6·20 to 6·70 τ.

Since the photo-product (X) is assumed to arise from 1,3-diketone (XII), through the formation of type B cyclization product (XI) followed by rearrangement,[4b] X belongs to the category of type B cyclization product. The intermediates XI and XII could not be isolated, presumably because XI reverts readily to IX[17] or the 1,3-diketone (XII) is converted easily to the product X by the action of light or during the isolation of the product by alumina column chromatography.

Furthermore, it was found by inspection of the IR spectrum that the resinous photo-products from IX contain some amount of α-diketone (VII), type C cyclization product, but it was difficult to isolate VII directly from the resinous products. Isolation of VII as its dimethyl ketal (XIII) was attempted, because it has found that XIII forms when VII is allowed to stand in methanol containing a trace of hydrogen chloride at room temperature.[18]

When the irradiation of IX was carried out in the same solvent containing a trace of acid, the expected product XIII could be obtained although in rather poor yield (8%). The structure of XIII was confirmed by the following spectral data. The UV spectrum showed an absorption max at 250 mμ (log ε, 4·48) due to styrene chromophore and the IR spectrum, a strong CO band (1754 cm^{-1}) ascribed to 5-membered ketone. The NMR spectrum exhibited two singlets due to two OMe groups at 6·80

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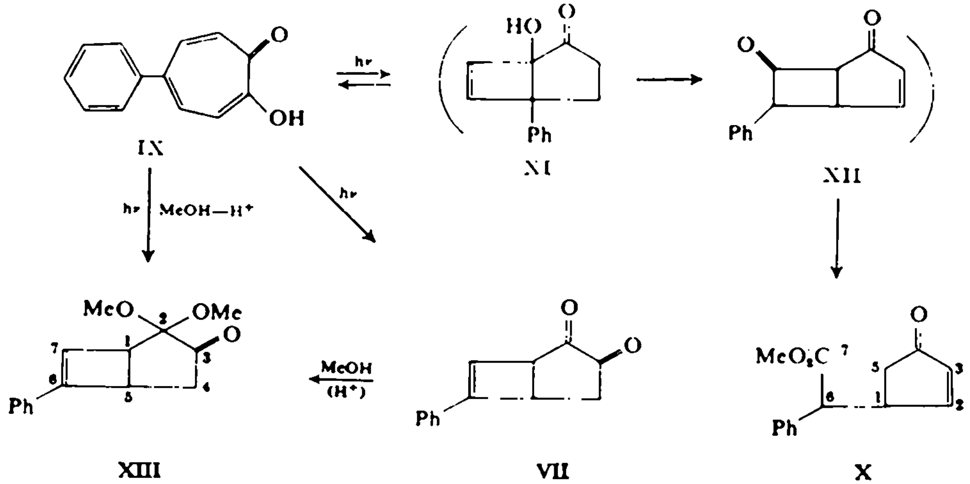
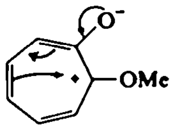
[17] It has been established by S. Ogata that the irradiation of 1-methoxy-3-chloro-$\Delta^{3,6}$-bicyclo[3.2.0]-heptadiene-2-one resulted in return back to 2-chloro-7-methoxytropone.

[18] T. Mukai and T. Shishido, *J. Org. Chem.* in press.

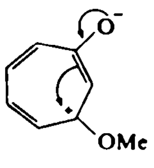
and 6·50 τ in addition to the phenyl proton signal at 2·70 τ. The C_7 olefinic proton appeared as a triplet at 3·91 τ ($J_{17} = J_{67} = 1{\cdot}5$ c/s); C_4 methylene protons (designated as A and B), as two quartets at 7·64 and 7·22 τ ($J_{AB} = 17{\cdot}0$, $J_{A6} = 2{\cdot}0$ and $J_{B6} = 8{\cdot}0$ c/s) and C_1 and C_6 methine protons, as complex signals at 6·28 to 6·66 τ. Because the irradiation of 5-phenyltropolone (IX) gave a complex mixture of products, it is difficult to discuss its photo-behavior in detail. However, it may be concluded that the irradiation of IX results in both type B and C cyclization.



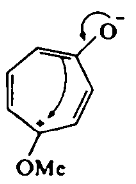
Concerning the photo-induced valence isomerization of troponoids, Chapman had pointed out that 2-, 3- and 4-methoxytropones showed different photochemical behavior.[15] A possible function for the OMe group may be visualized as shown in the excited molecules (I), (J) and (K). In I and K from 2- or 4-methoxytropone, smooth electron redistributions are available for collapse to the type B cyclization products. On the other hand, the corresponding intermediate (J) from 3-methoxytropone can only return to the starting material by electron redistribution without giving the bicyclic products.



I



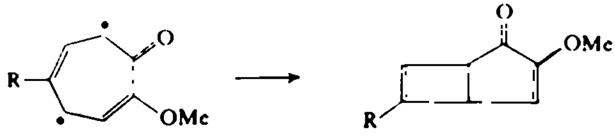
J



K

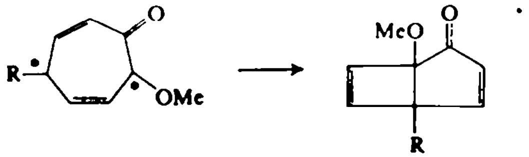
However, this generalization did not hold for the photochemistry of colchicine and isocolchicine. Chapman and Dauben have explained that both steric and styrene chromophore effects force the cyclization to occur only type C cyclization,[6,7] but they have not clarified which effect is more influential for determining the course of the induced valence isomerization. As pointed out previously, the irradiation of 5-isopropyltropolone methyl ether gave only type B cyclization product,[4] although there is appreciable steric interference between the isopropyl and OMe groups. Therefore it might be concluded with safety that the steric effect between Ph and OMe groups in the excited state of the methyl ether (I) is not so serious that the styrene chromophore effect plays the more important role in determination of the direction of the valence isomerization.

Thus, for mechanistic interpretation for the photo-induced valence isomerization of tropolone methyl ethers, it will be assumed that two species XIV and XV are formed by photo-excitation. If the species XIV is stabilized by substituents in the tropone ring, the cyclization will occur to give product XVI, but if XV is more stable, product XVII would be favored. In our case, the species XIV may be stabilized more by styrene chromophore than XV (R = Ph), giving rise to type C cyclization product II. Since we are interested in this substituent effect on photo-excitation of troponoid system, further studies are in progress in accordance with this idea.



XIV
R = Ph

XVI



XV
R = i-Pr
• = –, +, ·

XVII

EXPERIMENTAL

Irradiation of 5-phenyltropolone methyl ether (I)

A soln of 2·8 g (13 mmole) of I in 300 ml MeOH was externally irradiated with Toshiba H-400 P (400 Watt high press Hg lamp) placed 5 cm distance from a vessel. The vessel was Pyrex cylindrical tube (diam 45 mm) equipped with a glass spiral tube for cooling water and another tube for N gas stream. The soln was flushed with pure N for 30 min prior to irradiation. During the irradiation the soln was agitated with magnetic stirring and a slow stream of N. The temp of the reaction soln did not rise above 35°. The reaction was followed by periodic withdrawal of the soln and the UV spectrum was measured. As the reaction proceeded, the absorption max of I at 240 and 340 mμ diminished gradually and a new max of the product at 255 mμ appeared. After 70 hr of the irradiation, the solvent was evaporated under reduced press. The residual oil (3·1 g) was dissolved in benzene, and the soln was passed through an alumina column (activity II, 100 g). Evaporation of the eluted benzene–cyclohexane (1:1) fraction gave 875 mg of colorless crystals, m.p. 141–143°, which, on recrystallization from EtOH, afforded 820 mg (29%) of II as colorless plates, m.p. 151°. (Found: C, 78·77; H, 5·72. $C_{14}H_{12}O_2$ requires: C, 79·22; H, 5·70%.)

Subsequent elution with both benzene and ether afforded 1·7 g (61%) of recovered starting material (I), m.p. 140°.

Pyrolysis of 3-methoxy-6-phenyl-$\Delta^{3,6}$-bicyclo[3.2.0]heptadiene-2-one (II)

A soln of 300 mg of II in 4 ml benzene was dropped (12 drops/min) into a neutral Pyrex-helix packed vertical column 0·8 cm in diam and 10 cm in length preheated to 450°. During the pyrolysis, a stream of N was passed through the column (60 bubbles/min) to sweep the product out. The pyrolysate was collected into a flask immersed in an ince-salt bath. After the column has been cooled to room temp, it was washed with Chf. The combined soln of the pyrolysate and Chf washing was evaporated to give 300 mg of an oil, which was chromatographed on alumina (activity II, 10 g). Elution with benzene–cyclohexane (1:1) gave 40 mg of II, as colorless crystals, m.p. 150°. Elution with benzene afforded 190 mg (63%) of I as pale yellow crystals, m.p. 139°, which were identified by mixed m.p. determination and IR spectrum inspection.

Hydrogenation of 3-*methoxy*-6-*phenyl*-$\Delta^{3,6}$-*bicyclo*[3.2.0]*heptadiene*-2-*one* (II)

A soln of 100 mg (0·5 mmole) of II in 5 ml MeOH was hydrogenated over 30 mg of 5% Pd–C, and 24 ml (1·1 mmoles) of H was absorbed. After the catalyst was removed by filtration, evaporation of the filtrate gave 95 mg of a colorless oil (III), which distilled at 1 mm, by heating in an oil bath at 125°. (Found: C, 77·77; H, 7·30. $C_{14}H_{16}O_2$ requires: C, 77·75; H, 7·46%.)

Treatment of 3-*methoxy*-6-*phenyl*-$\Delta^{3,6}$-*bicyclo*[3.2.0]*heptadiene*-2-*one* (II) *with acid*

A soln of 70 mg of II in 2 ml MeOH and 1 ml 1N HCl was heated under reflux on a water bath for 15 min. Evaporation of the methanolic soln under reduced press afforded 50 mg colorless crystals, m.p. 151°, which were found to be identical with the starting material (II) by mixed m.p. determination.

2-*Hydroxy*-6-*phenyl*-Δ^{6}-*bicyclo*[3.2.0]*heptene*-3-*one* (VI)

To a soln of 500 mg (2·3 mmoles) of II in 40 ml MeOH, 90 mg (2·4 mmoles) $NaBH_4$ was added. After it had been stirred at room temp for 24 hr, the reaction mixture was acidified with dil HCl, followed by concentration under reduced press. The residue was diluted with water, and extracted with Chf. The extract was washed with water, dried over Na_2SO_4 and evaporated to give 0·51 g of colorless crystals, m.p. 144°, which on recrystallization from EtOH afforded 390 mg (83%) of VI as colorless needles, m.p. 144·5°. λ_{max}^{MeOH} 262 mμ (log ε = 4·42). (Found: C, 77·63; H, 5·84. $C_{13}H_{12}O_2$ requires: C 77·98; H, 6·04%.)

6-*Phenyl*-Δ^{6}-*bicyclo*[3.2.0]*heptene*-2,3-*dione* (VII)

To a soln of 100 mg (0·5 mmole) of VI in 6 ml MeOH, a soln of 200 mg (1 mmole) cupric acetate monohydrate dissolved in 1 ml water and 4 ml MeOH was added, and the resulting soln was heated under reflux on a water bath for 30 min and concentrated under reduced press. The residue was poured into water and extracted with Chf. The extract was washed with water, dried over Na_2SO_4, and evaporated to give 100 mg yellowish brown viscous oil, which was dissolved in ether and passed through a short silica gel column. Evaporation of eluted ether soln afforded 50 mg (50%) pale yellow viscous oil (VII). ν_{max}^{Chf} 1750 and 1700 cm^{-1}. (Found: C, 79·05; H, 4·97. $C_{13}H_{10}O_2$ requires: C, 78·77; H, 5·09%.)

Pyrolysis of 6-*phenyl*-Δ^{6}-*bicyclo*[3.2.0]*heptene*-2,3-*dione* (VII)

A soln of 140 mg (0·7 mmole) of VII in 2 ml benzene was pyrolysed at 480° in the same manner as described in the pyrolysis of II. Evaporation of solvents from the combined mixture of pyrolysate and washing afforded crystals, which on, recrystallization from EtOH gave 77 mg (55%) yellow needles, m.p. 124°. These were found to be identical with IX by the mixed m.p. determination and by the comparison of its IR spectrum with an authentic sample.

Irradiation of 5-*phenyltropolone* (IX)

(a) *In methanol.* A soln of 1·0 g (5 mmoles) of IX dissolved in 300 ml MeOH was irradiated with Toshiba H-400P lamp for 30 hr as described in the irradiation of I. The methanolic soln was concentrated and Chf was poured into the residue. The extract was washed with 0·5N KOH to remove acidic materials, and then with water and dried over Na_2SO_4. Evaporation of Chf soln afforded 480 mg of a neutral oil, which was dissolved in benzene and the soln was passed through a column containing 20 g of alumina (activity II). Evaporation of the eluted benzene fraction gave 140 mg pale yellow oil, which crystallized on standing. Recrystallization from pet. ether (b.p. 50–60°) afforded 130 mg (15%) of X as colorless needles, m.p. 67–68°. (Found: C, 72·38; H, 6·33. $C_{14}H_{14}O_3$ requires: C, 73·02; H, 6·13%.)

Elutions with ether and ether–MeOH (10:1) gave only 50 mg of resinous material.

After the alkaline extract had been acidified with 6N HCl, it was extracted with Chf. The Chf extract was washed with water, dried over Na_2SO_4, and evaporated to give 580 mg of an oil, which crystallized on standing. Recrystallization from EtOH gave 500 mg (50%) of IX, as yellow needles, m.p. 123°.

(b) *In methanol containing a trace of hydrogen chloride.* A soln of 1·0 g (5 mmoles) of IX in 300 ml MeOH was placed in the vessel and flushed with 5 bubbles of HCl gas prior to the irradiation. The irradiation was carried out for 13 hr as described for the irradiation of I. After it had been concentrated, the reaction mixture was added to water and extracted with benzene. The benzene-extract was washed with 0·5N KOH and water, dried over Na_2SO_4 and evaporated to give 920 mg of a reddish brown viscous oil, which was dissolved in benzene and chromatographed on alumina (activity II, 28 g). Evaporation of the eluted benzene–cyclohexane (1:1) soln gave 80 mg (8%) of colorless crystals, m.p. 120–122°, which, on recrystallization from EtOH, afforded 66 mg of XIII, m.p. 122°. (Found: C, 73·57; H, 6·63. $C_{15}H_{16}O_3$ requires: C, 73·75; H, 6·60%.)

The next fraction eluted by the same solvent gave 810 mg of yellow resinous products, which was difficult to separate even by use of the TLC or VPC.

After the alkaline washing had been neutralized with 2N HCl, it was extracted with Chf. The Chf extract was washed with water, dried over Na_2SO_4 and evaporated to give 72 mg viscous oil, which on sublimation at 150–170° and 1 mm afforded 15 mg of the starting material (IX), m.p. 139°.

Preparation of the ketal XIII *from the dione* VII

Five bubbles of HCl gas were flushed through a soln of 160 mg (0·8 mmole) of VII dissolved in 50 ml MeOH. After the resulting soln had been allowed to stand in dark for 6 hr at room temp, it was concentrated under reduced press and extracted with Chf. The Chf-extract was washed with water, dried over Na_2SO_4 and evaporated. The residue obtained was dissolved in benzene and the soln was chromatographed on alumina (activity II, 5 g). Elution with benzene–pet. ether (1:1) afforded 70 mg (36%) of colorless crystals, m.p. 119°. Recrystallization from EtOH gave 58 mg of colorless needles, m.p. 122°, which were proved identical with XIII by the mixed m.p. determination and by the comparison of its IR spectrum with that of XIII.

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