Tetrahedron. Vol. 26, pp. 5255–5263. Pergamon Press 1970. Printed in Great Britain

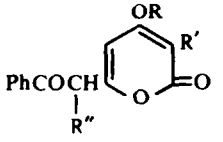
AROMATIZATION REACTIONS OF 4-HYDROXY-6-PHENACYL-2-PYRONE AND RELATED COMPOUNDS*

T. M. HARRIS† and M. P. WACHTER‡
Department of Chemistry, Vanderbilt University, Nashville, Tennessee 37203

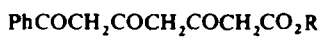
(*Received in the UK* 8 *June* 1970; *Accepted for publication* 27 *July* 1970)

Abstract—Treatment of the title compound with various acidic and basic reagents brought about cleavage of the lactone ring to form unstable intermediates which recyclized in several manners. With strong acids the compound was transformed to γ-pyrones, with nucleophilic bases to resorcinols, and with non-nucleophilic bases to benzoylphloroglucinol. In the first two reactions the corresponding 3,5,7-triketo acid or ester is an intermediate. The use of a large excess of a chelating metal ion (Ca^{++}) caused an isolable amount of the ester to accumulate. A ketene derivative is proposed as the intermediate in the formation of benzoylphloroglucinol. The reactions of four derivatives of the title pyrone have been explored.

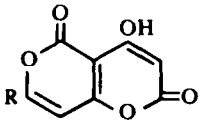
WE HAVE recently described several methods for synthesis of 4-hydroxy-6-phenacyl-2-pyrone (**1a**).[1,2] The chemistry of **1a** is of interest in relation to the reactions of 3,5,7-triketo acids (e.g. **2a**) and pyranopyrones **3**, which have been studied as models of phenol biosynthesis.[1,3–8] Compounds **2a** and **3** (R = Ph) are related to each other structurally; however, certain aspects of their chemical behavior are different. Thus a study of the reactions of α-pyrone **1a**, which is the lactone of **2a**, provides opportunities for comparison with both systems.



1a; R = R′ = R″ = H
b; R = Me, R′ = R″ = H
c; R = H, R′ = Me, R″ = H
d; R = R′ = H, R″ = Me
e; R = H, R′ = COMe, R″ = H



2a; R = H
b; R = Me



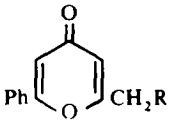
3

* Supported by grants from the Alfred P. Sloan Foundation and the National Institutes of Health, U.S. Public Health Service (Research Grant GM-12848).

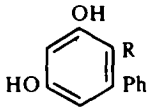
† Research Career Development Awardee, K3-GM-27013, of the National Institutes of Health, U.S. Public Health Service.

‡ National Science Foundation Trainee.

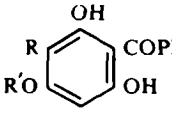
Triketo acid **2a** undergoes cyclization in liquid hydrogen fluoride to form γ-pyrone **4a**.[9] Weakly acidic buffers and most bases efficiently catalyze aldol-type cyclizations of **2a–b** to give resorcinol derivatives **5a–c**.[3,4] With aqueous but not with methanolic potassium hydroxide, the reaction of **2b** takes another course to give the Claisen-type cyclization product, benzoylphloroglucinol (**6a**).[3]



4a; R = CO_2H
b; R = CO_2Me
c; R = H



5a; R = CO_2H
b; R = CO_2Me
c; R = H



6a; R = R′ = H
b; R = CO_2Me, R′ = H
c; R = H; R′ = Me
d; R = Me; R′ = H
e; R = COMe, R′ = H

Pyranopyrones **3** react with aqueous and methanolic potassium hydroxide to form resorcinol derivatives; i.e. **3** (R = Ph) gave **5b–c**.[6–8] The corresponding triketodicarboxylic acid (or ester) has been suggested as an intermediate in these reactions. With magnesium methoxide the course of reaction is altered to give a Claisen-type product. For example, phloroglucinol **6b** is obtained from **3** (R = C_6H_5).[8] A comparable metallic cation effect is not observed with **2b**; magnesium ion merely decreases the rate of aldol cyclization (Experimental).

The effect of strongly acidic conditions on **1a** was investigated first. Treatment of **1a** with a mixture of conc hydrochloric acid and acetic acid gave two isolable products. The major one (33%) was identified as γ-pyrone **4a**; the minor as **4c**. Treatment of **1a** with refluxing methanolic sulfuric acid for 56 hr gave α-pyrone **1b** and γ-pyrones **4b–c** in the ratio of 3:3:2; 26% of **4b** was isolated. Both reactions require opening of the α-pyrone ring and subsequent reclosure to the γ-pyrone. Equilibria between α- and γ-pyrones have been shown to favor α-pyrones.[10] However, γ-pyrones are more basic and are protonated in strongly acidic solutions to give pyrylium ions.[10] The formation of γ-pyrones **4a** and **4b** can be ascribed to accumulation of the corresponding pyrylium ions during the course of the reactions. With methanolic sulfuric acid, the failure of the α-pyrones **1a** and **1b** to be converted completely to γ-pyrones **4b** and **4c** probably results from insufficient acidity of the medium rather than too short a reaction period.

Weakly acidic buffers attacked **1a**, but only very slowly. Treatment of **1a** with sodium acetate, pH 5·0, for 1 month at 50° gave only a low conversion to **5a** and **5c**. Much of **1a** still remained; the reaction is too slow to be of any practical value.

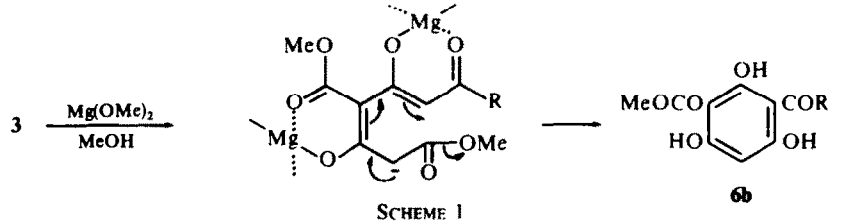
Reactions under basic conditions were more useful and interesting.* Aqueous potassium hydroxide converted **1a** into a mixture of **5a** and **5c** but methanolic potassium hydroxide gave a good yield of resorcylic ester **5b**. In the latter reaction

* We have described certain of these results.[11] Scott *et al.* have also investigated the reactions of **1a** with nucleophilic bases.[12]

a trace (<5%) of phloroglucinol **6a** was detected by NMR but was not isolated. These reactions are similar to the aldol-type cyclizations of **2a** and **2b**.[3]* It is not possible to duplicate with **1a** the circumstances under which **6a** was the major cyclization product of **2b**, since cleavage of the lactone ring of **1a** by aqueous base leads to the triketo acid not the ester.

The observation[8] that magnesium ion affected the course of the reaction of **3** with methoxide ion prompted a search for similar metallic cation effects on the reactions of **1a**. The use of magnesium methoxide did indeed cause a partial change in the course of aromatization. A 2:1 ratio (NMR) of **6a** and **5b** was obtained when magnesium methoxide (1·1 equivs) was employed; 44% of **6a** was isolated. The NMR spectrum of unfractionated product mixture showed the presence of triketo ester **2b** in addition to the two cyclization products.

The formation of phloroglucinol **6a** under these conditions was surprising. The reaction is formally similar to the magnesium methoxide catalyzed conversion of pyranopyrone **3** (R = Ph) to phloroglucinol **6b**. Crombie and James have suggested the following explanation for the effect of magnesium ion on the reaction of **3**.[13] Cleavage of the two lactone rings of **3** by nucleophilic attack of methoxide ion gives a triketo diester (Scheme 1). Chelation of magnesium ions with the two keto ester groups holds the molecule in a conformation conducive to Claisen-type cyclization. This proposal, although satisfactorily accounting for formation of phloroglucinol derivatives from **3**, fails with **1a** because it would afford monoester **2b**, which does not contain the requisite second site of chelation. This conclusion is reinforced by the observation that methanolic magnesium methoxide does not catalyze the conversion of **2b** to **6a**.



SCHEME 1

At this point[11] a working hypothesis was formulated to explain the formation of **6a**. Treatment of **1a** with magnesium methoxide was postulated to involve nucleophilic attack on the lactone carbonyl group by methoxide ion to give a magnesium chelate of triketo-ester **2b**. This chelate must be a different one from that formed by direct reaction of **2b** with magnesium methoxide, since in the latter reaction mixture **2b** is quite stable and cyclization, to the extent that it occurs, gives **5b** not **6a**. Further work was undertaken in an attempt to substantiate this proposal.

The use of large excesses of magnesium methoxide with **1a** enhanced the accumulation of **2b**. When 20 equivs of magnesium methoxide was employed, NMR spectra of neutralized aliquots showed that **1a** was depleted within 2·5 hr and that significant quantities of **2b** were present. Within this period little or no cyclization occurred to form either **5b** or **6a**. Isolation of pure **2b** was difficult because of its reactivity and because of the presence of minor impurities which were not removed

* A trace of **6a** can similarly be detected (TLC and NMR) in the crude product of the reaction of **2b** with methanolic potassium hydroxide.

readily. Calcium methoxide gave better results and **2b** was obtained from **1a** in 58% yield.

Confirmation of the proposed mechanism was sought by periodically assaying by NMR the relative amounts of **2b** and **6a**. Although the ratio of **1a** and **6a** is readily measured, quantitative determination of **2b** is hindered by its existence as a mixture of tautomers. However, estimation of the relative amounts of **2b** and **6a** suggested parallel formation of the two compounds instead of sequential formation.

The yield of **6a** was improved through the use of dimethylformamide as the reaction solvent; an 87% yield was obtained employing 0·27 equiv of magnesium methoxide. The use of other base-solvent systems provided results which were incompatible with the mechanistic proposal.

Aqueous magnesium hydroxide was found to effect the conversion of **1a** to **6a**. The reaction was slow but no resorcinol derivatives were produced. If this reagent had acted as a nucleophile in the reaction, the magnesium salt of acid **2a** would have resulted. It seems improbable that the magnesium salt of **2a** would undergo Claisen-type cyclization.

Lithium hydride in tetrahydrofuran gave rapid and efficient conversion of **1a** into **6a**. Hydride ion must act as a base rather than as a nucleophile, since nucleophilic attack would lead to products of a lower oxidation state. Similar results were obtained with sodium hydride and also when dimethylformamide and dioxane were substituted as solvents.* The stoichiometry of the lithium hydride reaction was found to be significant; the reaction was faster with one equivalent of this base than with excess.

Finally, lithium diisopropylamide, which is a very strong base but a poor nucleophile, converted **1a** into **6a**. With 1 equiv of base the reaction was rapid but with 2 equivs no reaction was observed.

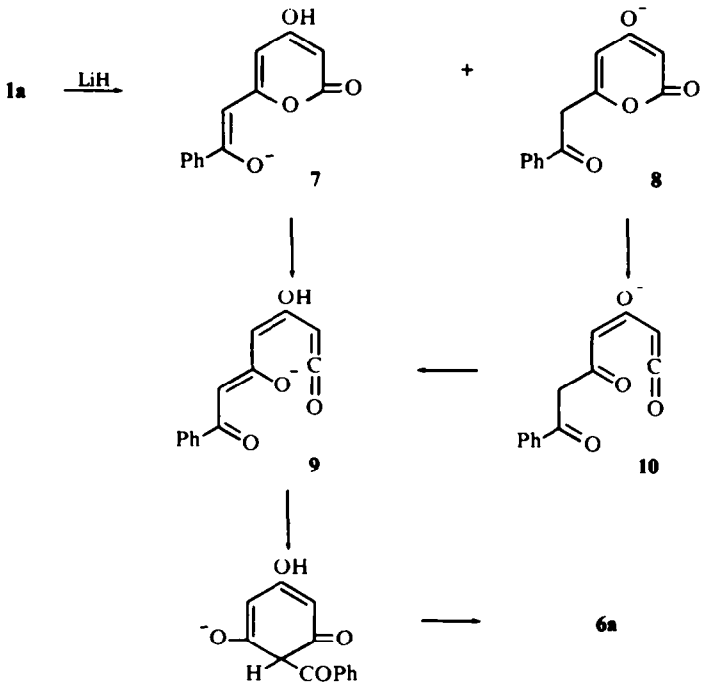
In conclusion we are forced to abandon our original mechanistic proposal. An alternate one, which is consistent with these observations, is that non-nucleophilic basic reagents, such as lithium hydride, convert **1a** into anions **7** and/or **8**. These undergo spontaneous cleavage to form ketene **9**, which cyclizes to give an anion of **6a** (Scheme 2). With **8** ketene **10** is formed initially; proton transfer is required for formation of **9**.

Treatment of **1a** with nucleophilic bases, such as soluble hydroxides and methoxides, may also result in the formation of ketenes **9** and **10**. In these cases subsequent reaction would occur with the external nucleophiles in preference to the internal one (Scheme 3). Methanolic magnesium methoxide represents an intermediate situation in which the internal and external nucleophiles are competitive. Another explanation for the formation of **2a** and aldol products **5a–c** is that the nucleophile attacks **1a** directly to give **2a–b**. These alternatives cannot be distinguished on the basis of the present results.

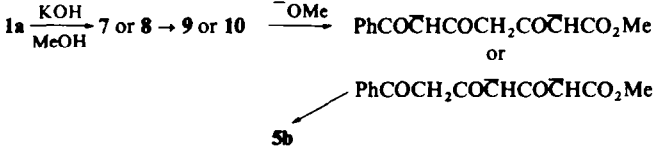
In view of the inhibition caused by excess lithium hydride and lithium diisopropylamide, dianion **11** must not be a significant contributor to the aromatization reactions of **1a**.† Explanations for this include the possibilities that **11** is thermo-

* The possibility cannot be excluded that a trace of some nucleophile, such as methoxide ion, was present in the reaction mixtures employing hydride ion and that this nucleophile catalyzed the conversion of **1a** into **6a** via **2b** or a similar species. However, reasonable precautions were taken to avoid this.

† Pyrone **1d** has been synthesized by methylation of **11**.[2] The dianion was prepared in liquid ammonia by treatment with sodium amide.

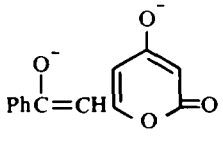


SCHEME 2



SCHEME 3

dynamically more stable than the ketene dianion and that the ketene dianion is not susceptible to nucleophilic attack. Inhibition does not occur with excess hydroxide and methoxide, undoubtedly because they are not strong enough bases to form **11**.



11

The stability of **1a** in pH 5 buffer indicates that the neutral species is also not a major participant in the aromatization reactions. Here again two explanations are possible. Either cleavage to the neutral ketene is not occurring or the ketene, in the absence of reactive nucleophiles, recyclizes to form **1a**.

Certain precedents are known for the proposed ketene intermediate in the reactions of **1a**. Recent kinetic studies have implicated ketenes in the alkaline hydrolysis of malonic esters and of 5-nitrocoumaranone.[14,15] The uncatalyzed reaction of

4-hydroxy-6-methyl-2-pyrone with ethanol to give ethyl 3,5-dioxohexanoate may be another example of this type reaction.[16] It should be noted in passing that the reaction required a relatively high temperature (110°) and was only about one half complete at equilibrium. Ketene intermediates have been proposed for the corresponding photochemical reaction of this and related pyrones.[17]

It is difficult to determine whether the conversion of **1a** to **6a** proceeds only from **8**, only from **9**, or from both. The initial product of the reaction of **1a** with aqueous base is **8**. The UV spectrum of **1a** in aqueous base corresponds well to a composite of the spectrum of acetophenone and the anion of 4-hydroxy-6-methyl-2-pyrone. Nevertheless, the undetectable amount of **9** in equilibrium with **8** may be the reactive species.

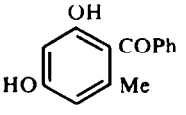
This question was investigated further by treatment of pyrone **1b** with lithium hydride. Pyrone **1b** is the 4-O-methyl derivative of **1a** and, as such, can only undergo ionization at the 6α-position. The aromatization reaction gave an excellent yield of Claisen product **6c** suggesting that anion **8** can undergo this reaction. Needless to say, the result does not exclude rearrangement of **9**. The reaction of **1b** was slower than the reaction of **1a** with one equivalent of lithium hydride but the significance of this is questionable because of the heterogeneity of the reaction mixtures.

Two C-methyl derivatives of **1a**, pyrones **1c** and **1d**, were studied because the first was prohibited by its structure from being converted to a resorcylic ester and the second from being converted to an acylphloroglucinol. Pyrone **1c** did not react with methanolic potassium hydroxide at room temperature but apparently underwent Claisen-type aromatization at reflux to form **6d**. However, alkaline cleavage of **6d** gave methylphloroglucinol and benzoic acid as the only isolable products. Similar results were obtained with magnesium methoxide. However, lithium hydride transformed the pyrone to **6d** without subsequent cleavage.

Treatment of **1d** with basic reagents did not lead to the corresponding resorcylic ester or other isolable products. Reagents that were investigated included methanolic potassium hydroxide, magnesium methoxide and calcium methoxide.

The 3-acetyl derivative (**1e**) of **1a** was converted to resorcylic ester **5b** by methanolic potassium hydroxide and to phloroglucinol **6a** by methanolic magnesium methoxide. These are the expected products if removal of the acetyl group preceeds ring opening. However, the sequence of these events is not known. Deacetylation was avoided through the use of lithium hydride which gave efficient but slow conversion of **1e** into phloroglucinol **6e**. As with **1a**, the use of excess lithium hydride decreased the reaction rate.

The treatment of **1e** with a mixture of hydrochloric and acetic acids has been described previously.[18] This reagent gives resorcinol **12** apparently by hydrolytic cleavage of the pyrone ring, decarboxylation to give a 1,3,5,7-tetraketone, and subsequent recyclization.



12

The results obtained with pyrones **1a–e** suggest the need for further study of the reaction of both triketo esters and pyranopyrones in order to discern whether ketene intermediates are involved in their aromatization reactions.

EXPERIMENTAL*

Reactions of pyrone **1a**

With hydrochloric and acetic acids. A soln of **1a**[2] (1·0 g) in HCl (10 ml) and AcOH (30 ml) was heated at 75° for 34 hr. The soln was cooled; water and ether were added. γ-Pyrone **4a** (335 mg, 33%) was separated by filtration, m.p. 104–105° and 115–115·5° dec after reprecipitation from 2% $NaHCO_3$ aq (Lit.[9] m.p. 115–115·5°); IR 1720, 1650 cm^{-1}; NMR (DMSO-d_6) 3·82 (s, 2, $C\underline{H}_2$), 6·36 (d, 1, J = 2 Hz, vinyl $\underline{H}$), 6·88 (d, 1, J = 2 Hz, vinyl $\underline{H}$), and 7·4–8·0 (m, 5, Ph). Pyrone **4a** was identified by comparison (IR and TLC) with an authentic sample. The ethereal soln from above was concentrated to afford **4c** (61 mg, 8%), which was identified by comparison with an authentic sample.

With methanolic sulfuric acid. A soln of **1a** (500 mg) and H_2SO_4 (500 mg) in anhyd MeOH (50 ml) was refluxed for 56 hr. Work up gave 352 mg of a mixture of **1b**, **4b**, and **4c** in an approximate ratio of 3:3:2. Chromatography gave pyrone **4b** (138 mg, 26%), m.p. 88–91° and 90–92° after recrystallization from hexane (Lit.[19] m.p. 92–94°), and an unresolved mixture (166 mg) of **1b** and **4c**.

With potassium hydroxide. A soln of **1a** (500 mg) in 1M methanolic KOH (250 ml) was stored at room temp for 17 hr. The MeOH was evaporated and dil HCl was added. Cooling to 0° afforded 384 mg of a crystalline mixture of **5b**, **1a** and a trace of **6a**. The ratio of **5b** and **6a** was 13:1 (NMR). Chromatography gave 291 mg (55%) of **5b**, m.p. 120–122° (Lit.[3] m.p. 120–121°), which was identical (TLC and NMR) with authentic material.

Treatment of **1a** (500 mg) with 0·5 M KOH aq for 6 hr at 80–85° gave a mixture of **5a** and **5c** (TLC). Recrystallization from chloroform-hexane gave 104 mg (21%) of **5c**, m.p. 151–155° and 154–157° after a second recrystallization (Lit.[20] m.p. 157–158°). The material was identical (TLC and NMR) with an authentic sample[21] of **5c**.

With methanolic magnesium methoxide. A mixture of **1a** (500 mg), magnesium methoxide (200 mg, 1·1 equivs), and MeOH (100 ml) was refluxed for 70 hr. After work up, NMR indicated the presence of **6a**, **5b**, and **1a** in the ratio 6:3:1. A significant amount of triketo ester **2b** was present also. Chromatography gave 15% of **5b**, m.p. 119–121° after recrystallization from chloroform–hexane, and 44% of **6a**, m.p. 164–166° (Lit.[22] m.p. 165°) after recrystallization from chloroform–hexane.

With methanolic calcium methoxide. A mixture of **1a** (500 mg), calcium methoxide (4·4 g, 20 equiv), and MeOH (200 ml) was refluxed for 2·5 hr.† The usual work up gave 471 mg of crude product, chromatography of which gave 287 mg (58%) of **2b**, m.p. 58–65° and 70–74° (Lit.[3] m.p. 73–76°) after recrystallization from hexane. The recrystallized material was identical (NMR) with authentic **2b**.

Unrecrystallized **2b** was treated with methanolic NaOAc for 1·5 hr at room temp to give after work up and recrystallization from chloroform–hexane 68% of **5b**. This represents a 39% overall yield based on **1a**.

With magnesium methoxide in dimethylformamide. A mixture of **1a** (500 mg), magnesium methoxide (50 mg, 0·27 equiv), and DMF (100 ml) was heated at 130° for 45 min. The usual work up was followed by chromatography to give 438 mg (87%) of **6a**, m.p. 158–163° and 164–167° after recrystallization from chloroform. An NMR spectrum of unfractionated product showed no trace of **5b** or other resorcinol derivatives.

With lithium hydride. A mixture of **1a** (500 mg), LiH (17 mg, 1 equiv), and THF (125 ml) was refluxed with vigorous stirring for 2 hr, after which time TLC of an acidified aliquot indicated that the reaction was complete. Work up gave an oil from which 430 mg (86%) of **6a**, m.p. 164–165°, was obtained by trituration with hexane.

With 2·7 equiv of LiH a comparable yield of **6a** was obtained but the reaction took approximately 5 hr for completion. No significant change was detected when sodium hydride was employed as the base or dioxan or DMF as the solvent.

* All m.ps were taken with a Thomas–Hoover apparatus in unsealed capillaries and are corrected. The elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. IR spectra were obtained with a Beckman IR-10 spectrophotometer by the KBr pellet method. NMR spectra were determined with a Varian A-60 spectrometer and are reported in δ units. TMS was employed as an internal standard. All alkaline reactions were carried out under N_2. Unless otherwise noted, reaction mixtures were worked up by evaporation of the solvent *in vacuo*, addition of cold, dilute HCl, and extraction with ether. The ethereal soln was dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product mixture. Preparative chromatography was on silica gel columns; elution was monitored by TLC.

† Preliminary experiments had indicated that this reaction period gave maximum conversion to **2b**.

With lithium diisopropylamide. Lithium diisopropylamide (2·17 mmoles) was prepared by addition of commercial n-BuLi to a stoichiometric quantity of diisopropylamine in THF (75 ml) at 0°. Pyrone **1a** (500 mg, 2·17 mmole) was added in 50 ml of THF and the mixture was refluxed for 6 hr. Work up followed by trituration with chloroform gave 373 mg (76%) of **6a**, m.p. 164–165°.

The procedure was repeated with 2·5 equivs lithium diisopropylamide. After 24 hr at reflux, the usual work up gave unaltered pyrone **1a**. No detectable amount of **6a** or other aromatization product was formed.

Treatment of **2b** *with magnesium methoxide*

A mixture of **2b** (200 mg), magnesium methoxide (16 mg, 0·25 equiv) and MeOH (40 ml) was refluxed for 40 hr. Work up gave 187 mg (88%) of **5b**, m.p. 115–120° and 119–121° after recrystallization from chloroform–hexane. Phloroglucinol **6a** could not be detected by NMR or TLC.

A similar reaction employing 4·6 equivs magnesium methoxide gave only **5b**, but was largely incomplete after 48 hr at reflux. When 10 equivs of the base was employed little or no reaction occurred within this period.

Treatment of **1b** *with lithium hydride*

A mixture of **1b** (400 mg), LiH (50 mg, 3·8 equivs) and dioxan (100 ml) was refluxed for 56 hr, after which time TLC of an acidified sample indicated that the reaction was complete. Work up followed by chromatography gave 356 mg (89%) of **6c**, m.p. 128–131° (Lit.[23] m.p. 131–132°); IR 1635 cm^{-1}; NMR ($CDCl_3$ and DMSO-d_6) 3·73 (s, 3, OCH_3), 5·98 (s, 2, 3- and 5-H), 7·2–7·7 (m, 5, C_6H_5). The IR spectrum was identical with a spectrum of authentic cotoin.

Reactions of pyrone **1c**

With methanolic magnesium methoxide. A mixture of **1c** (500 mg), magnesium methoxide (47 mg, 0·25 equiv) and MeOH (100 ml) was refluxed for 54 hr. The solvent was evaporated; ether and dil HCl were added. Crystalline material (240 mg) sparingly soluble in both ether and water was isolated. TLC and NMR showed it to be unaltered pyrone **1c**. The ether phase contained **6d**, additional **1c** and lesser amounts of unidentified products. Chromatography gave 20% of **6d**, m.p. 135–142° and 138–142° (Lit.[24] m.p. 139–140°) after recrystallization from chloroform–hexane; NMR ($CDCl_3$-DMSO-d_6) 2·00 (s, 3, CH_3), 6·00 (s, 1, 5-H), 7·2–7·7 (m, 5, Ph), 9·47 (broad s, 1 OH), 9·57 (broad s, 1, OH), and 12·07 (broad s, 1, OH). The reaction was repeated with 3·5 equivs magnesium methoxide which gave 18% of **6d** and 43% of methylphloroglucinol.

With lithium hydride. A mixture of **1c** (80 mg), LiH (2·3 mg, 1 equiv) and THF (25 ml) was refluxed with vigorous stirring for 5 hr. The usual work up followed by crystallization from chloroform–hexane gave 42 mg (54%) of **6d**, m.p. 129–135°, 141–143° after recrystallization.

Treatment of pyrone **1d** *with bases*

Several sets of conditions were tried with **1d**. Calcium methoxide (30 equivs) in refluxing MeOH and 1M methanolic KOMe caused extensive decomposition; no aromatization products could be detected. Pyrone **1d** did not react with magnesium methoxide (3·5 equivs) in refluxing MeOH during 48 hr.

Treatment of pyrone **1e** *with lithium hydride*

A mixture of **1e** (500 mg), LiH (15 mg, 1 equiv), and THF (125 ml) was refluxed. Aliquots removed after 48 and 72 hr indicated that the reaction was 58 and 72% complete, respectively. After 168 hr the usual work up followed by recrystallization from chloroform–hexane gave 72% of **6e**, m.p. 155–157° and 156–158° after further recrystallization; IR 1620 cm^{-1}; NMR ($CDCl_3$) 2·68 (s, 3, $COCH_3$), 5·98 (s, 1, 5-H), 7·3–7·7 (m, 5, C_6H_5). (Found: C, 66·27; H, 4·50. Calc. for $C_{15}H_{12}O_5$: C, 66·17; H, 4·44%).

A similar reaction mixture containing 3·3 equivs of LiH gave 42% of **6e** after a reflux period of 120 hr. In addition 40% of unaltered **1e** was recovered.

REFERENCES

[1] T. M. Harris and C. M. Harris, *Tetrahedron* **25**, 2687 (1969)
[2] M. P. Wachter and T. M. Harris, *Ibid.* **26**, 1685 (1970)
[3] T. M. Harris and R. L. Carney, *J. Am. Chem. Soc.* **89**, 6734 (1967)
[4] T. M. Harris and T. T. Howarth, *Chem. Commun.* 1253 (1968)

[5] T. T. Howarth, G. P. Murphy and T. M. Harris, *J. Am. Chem. Soc.* **91**, 517 (1969)
[6] T. Money, F. W. Comer, G. R. B. Webster, I. G. Wright and A. I. Scott, *Tetrahedron* **23**, 3435 (1967)
[7] J. L. Douglas and T. Money, *Ibid.* **23**, 3545 (1967)
[8] J. L. Douglas and T. Money, *Canad. J. Chem.* **45**, 1990 (1967)
[9] K. G. Hampton, T. M. Harris, C. M. Harris and C. R. Hauser, *J. Org. Chem.* **30**, 4263 (1965)
[10] P. Beak, *Tetrahedron* **20**, 831 (1964)
[11] T. M. Harris, M. P. Wachter and G. A. Wiseman, *Chem. Commun.* 177 (1969)
[12] H. Guilford, A. I. Scott, D. Skingle and M. Yalpani, *Ibid.* 1127 (1968)
[13] L. Crombie and A. W. G. James, *Ibid.* 357 (1966)
[14] T. C. Bruice and B. Holmquist, *J. Am. Chem. Soc.* **90**, 7136 (1968)
[15] P. S. Tobias and F. J. Kezdy, *Ibid.* **91**, 5171 (1969)
[16] R. F. Witter and E. Stotz, *J. Biol. Chem.* **176**, 485 (1948)
[17] P. de Mayo, *Advan. Org. Chem.* **2**, 394 (1960); C. T. Bedford and T. Money, *Chem. Commun.* 685 (1969); W. H. Pirkle and L. H. McKendry, *J. Am. Chem. Soc.* **91**, 1179 (1969); R. Srinivasan, *J. Org. Chem.* **35**, 786 (1970)
[18] T. M. Harris, C. M. Harris and M. P. Wachter, *Tetrahedron* **24**, 6897 (1968)
[19] T. M. Harris and T. T. Howarth, unpublished observations
[20] C. M. Suter and P. G. Smith, *J. Am. Chem. Soc.* **61**, 166 (1939)
[21] T. T. Howarth and T. M. Harris, *Canad. J. Chem.* **46**, 3439 (1968)
[22] K. W. Rosenmund and M. Rosenmund, *Ber. Dtsch. Chem. Ges.* **61**, 2608 (1928)
[23] O. R. Gottlieb and W. B. Mors, *J. Am. Chem. Soc.* **80**, 2263 (1958)
[24] A. Robertson and T. H. Simpson, *J. Chem. Soc.* 2021 (1951)