Tetrahedron. Vol. 26, pp. 1685 to 1694. Pergamon Press 1970. Printed in Great Britain

# CONDENSATIONS AT THE 6α-POSITION OF TRIACETIC LACTONE VIA THE DIANION*

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

(*Received in USA* 17 *October* 1969; *Received in the UK for publication* 20 *November* 1969)

**Abstract**—Triacetic lactone (**1**) on treatment with two or more equivs of alkali amides in liquid ammonia was converted into dianion **8**. Treatment of **8** with benzyl chloride and other alkyl halides gave mixtures of 6α- and 5-alkylation products **9** and **10**. Benzophenone condensed with **8** to give 6α-aldol product **14**, which was readily dehydrated to form unsaturated pyrone **15**. 6α-Carboxylation of dilithio **8**, which had been formed in THF by treatment of **1** with lithium diisopropylamide, was also effected. Aroylation of **8** with methyl benzoate gave 6-phenacyl pyrone **17**, but acetylation of **8** was not successful. Two monomethylation (**18** and **24**) and three dimethylation (**19–21**) products of **17** were prepared and identified. Condensation of **17** with malonyl chloride gave pyranopyran **25**.

TRIACETIC lactone (4-hydroxy-6-methyl-2*H*-pyran-2-one, **1**) was first prepared by Collie in 1891 by treatment of dehydroacetic acid with 90% sulfuric acid.[1] We were prompted to investigate the chemistry of triacetic lactone because certain of its derivatives, in particular 6α-acylation products, can potentially serve as precursors for biogenetic-type syntheses of naturally occurring phenols. In this paper§‖ a method is presented by which C—C condensations can be brought about at the 6α-position of **1** to form the benzoyl derivative and other useful compounds.

Activation of the Me group of **1**, either by ionization or enolization, would provide a convenient route to 6α-derivatives. However, acid-catalyzed enolization of **1** is precluded by the stability of the readily formed pyrylium ion. Moreover, ionization of the 6-methyl group is not readily achieved by basic reagents because the 4-OH group is far more acidic ($pK_a$ 5·00).[4] Anion **3**, formed by ionization of the OH group, should not be particularly prone to undergo further ionization.

A few years ago Vul'fson *et al.* reported that the condensation of **1** with benzaldehyde in the presence of piperidine acetate catalyst gave the 6α-benzylidene adduct **4**.[5] However, Douglas and Money reinvestigated this reaction and showed the product to be benzylidene-bis-pyrone **5** resulting from the condensation of two molecules of **1** at the 3-position with one molecule of benzaldehyde.[6] The 3-position of **1** is the usual site of attack by electrophilic reagents.[7]

* Supported by research grant GM-12848 from the National Institutes of Health, U.S. Public Health Service, Bethesda, Maryland.

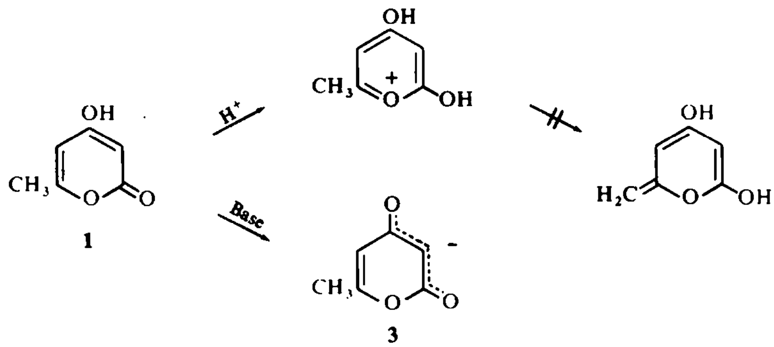
† National Science Foundation Trainee.

‡ Alfred P. Sloan Fellow and Research Career Development Awardee (K3-GM-27013) of the National Institutes of Health, U.S. Public Health Service, Bethesda, Maryland.

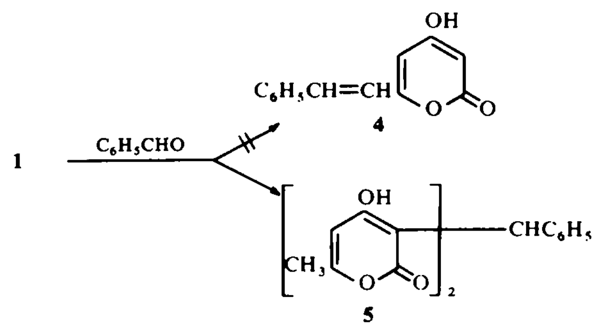
§ Certain of the results described herein have been reported in a preliminary communcation.[2]

‖ Scott and coworkers have also effected benzoylation of the dianion of triacetic lactone; this result has been described in a preliminary communication.[3] We are grateful to Professor Scott for providing us with a copy of his manuscript prior to publication.

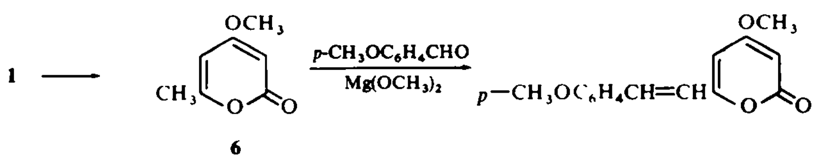
Bu'Lock and Smith have devised one solution to the problem of relative reactivities of the 3- and 6α-positions.[8] Conversion of **1** into its methyl ether (**6**) reduces the reactivity of the 3-position to electrophilic attack; enolate anion **3** can no longer




participate in the condensations. On the other hand, reactivity of the 6-Me group of **6** with bases is enhanced because the base is not required to attack a negative species (i.e., **3**). These investigators effected the condensation of anisaldehyde with **6** at the 6α-position using magnesium methoxide as the condensing agent.[8] Douglas and

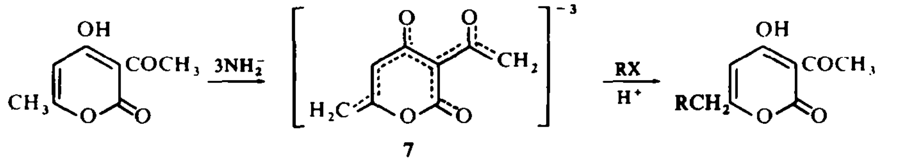



Money subsequently carried out the analogous reaction with benzaldehyde[6] and have extended the method to a Claisen-type condensation with ethyl oxalate using sodium as the condensing agent.[9]




Recently we observed that condensations could be effected at the 6α-position of dehydroacetic acid through the use of three equivalents of alkali amides in liquid ammonia.[10] Alkali amides are sufficiently basic to remove two or three protons from dehydroacetic acid; the anion intermediate in these condensations is believed to be trianion **7**. Reactivity of **7** was observed almost exclusively at the 6α-position.[10]

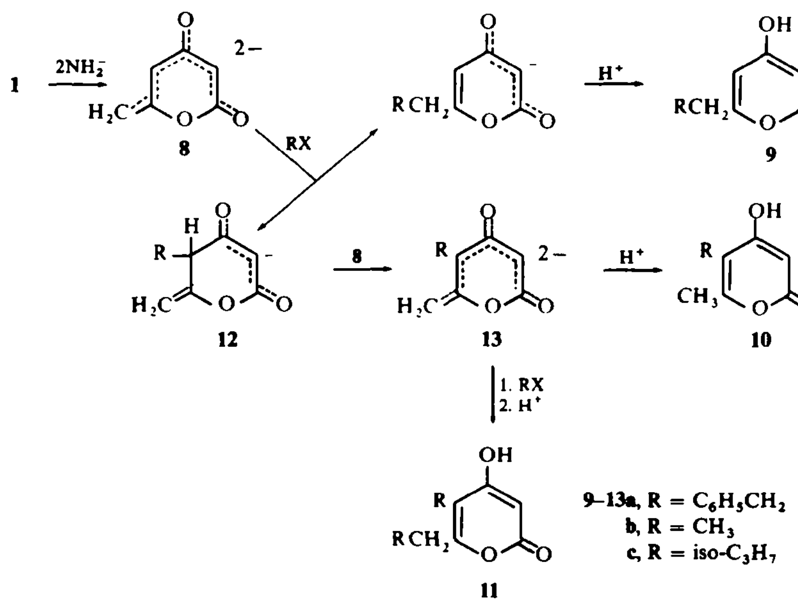
In the present investigation this method has been applied to condensations of triacetic lactone (1). The dianion of 1 has been found to undergo condensations predominantly, although not entirely, at the 6α-position.




## RESULTS AND DISCUSSION

Addition of pyrone 1 to two equivs of alkali amides in liquid ammonia produced yellow-green suspensions presumably of dianion 8. Treatment of the disodio or dilithio 8 with benzyl chloride gave a mixture of 6-phenethyl pyrone 9a and 5-benzyl-6-methyl pyrone 10a in an approximate ratio of 7:3. Employment of dipotassio 8 led to 9a, 10a, and a small amount of yet another alkylation product, 5-benzyl-6-phenethyl pyrone 11a. In the product mixtures the anticipated 6α-alkylation product 9a was identified by NMR comparison with an authentic sample.[11] Although 9a was the major product, its purification was exceptionally difficult on account of its low melting point and chromatographic similarity to higher melting pyrone 10a.

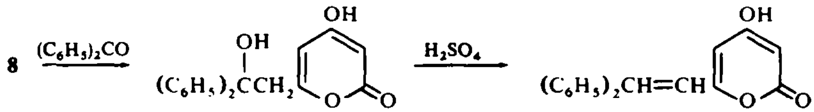
The formation of the three alkylation products can be explained as follows. Delocalized dianion 8 is capable of undergoing benzylation either at position 6α or position 5. Neutralization of the 6α-benzylation product gives 9a. Benzylation of 8 at position 5 gives monoanion 12a; tautomerization, which is required for formation of 10a, might occur after acidification of the reaction mixture. Alternatively, attack of a base (i.e., 8) on 12a could give rearrangement to 10a via a new dianion (13a). Furthermore, benzylation of 13a would give pyrone 11a.



The situation is similar to alkylation of the dianion of acetylacetone.[12] During alkylation of dipotassio acetylacetone, the terminal alkylation product undergoes reionization at the remaining Me group to give a new dianion which also undergoes alkylation. The proton transfer reaction, although facile with the dipotassio salt, is not observed with the disodio or dilithio salt.[12]

Treatment of the disodio **8** with methyl iodide and isopropyl bromide gave similar mixtures of 6α- and 5-alkylation products **9b–c** and **10b–c**, respectively. It can be concluded that dianion **8** is not a particularly useful reagent for the preparation of 6α-derivatives of **1**. The preferred method for synthesis of pyrones of structure **9** is probably from the corresponding 3,5-diketo acid.[11]

An aldol-type condensation of **8** with benzophenone was effected in liquid ammonia. The 6α-adduct (**14**) was isolated in 55% yield. NMR unambiguously established the site of substitution; the 6-Me signal of **1** had been replaced by a methylene singlet at lower field. Neither the 5- nor the 3-adduct of **8** was formed in detectable quantity in the condensation. Treatment of **14** with cold, concentrated sulfuric acid gave unsaturated pyrone **15**, which was identical with material prepared independently.[11]

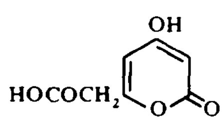



**14** **15**

Carboxylation of the disodio and dipotassio **8** was attempted in ether. The dianion was prepared in liquid ammonia, then the solvent was replaced by ether before introduction of carbon dioxide. This procedure was chosen to avoid the reaction between carbon dioxide and ammonia. However, no carboxylic acids could be detected and large quantities of **1** were recovered from the reactions. It appears likely that the equilibrium between monoanion **3** and dianion **8** is driven toward the monoanion by solubility factors that are operative during evaporation of the ammonia and addition of ether.*

$$\mathbf{8} + NH_3 \rightleftarrows \mathbf{3} + NH_2^-$$

This problem was avoided by use of another base system. Pyrone **1** was treated with 2 equivalents of lithium diisopropylamide in THF giving a deep red suspension of the sparingly soluble dilithio salt. After addition of carbon dioxide, carboxylic acid **16** was isolated in 26% yield; no other acid was detected.



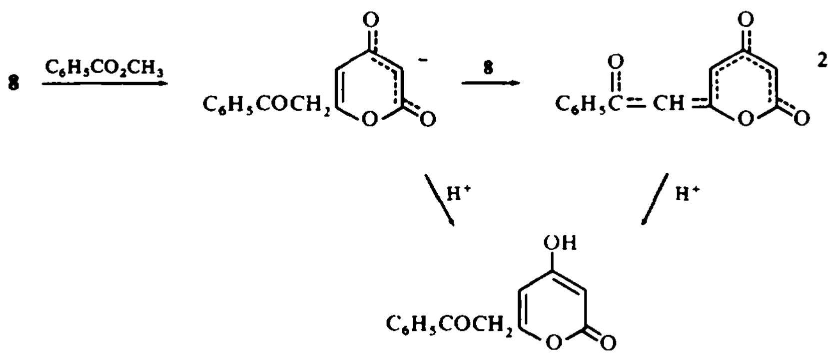

**16**

* Several other anions, formed in liquid ammonia, undergo protonation by ammonia during transfer into ether.[13]

The yield obtained in the present procedure compares favorably with an 11% overall yield of the methyl ester of **16** obtained by Douglas and Money in a 5 step sequence starting with methyl ether **6**.[9]*

Yamamura *et al.* have treated the 4-methyl ether of **16** with acetic anhydride to form tetraacetic lactone,[15] which is a polyketide-type fungal metabolite.[16] Pike *et al.* have converted the same ether to a bis-pyrone by treatment with acetic anhydride, apparently employing slightly different conditions.[17] A xanthone has been prepared from the bis-pyrone by a cleavage-recyclization pathway.[7]

Acylation of triacetic lactone was achieved by treatment of the disodio **8** with methyl benzoate. The reaction was carried out in liquid ammonia. The 6α-benzoylation product (**17**) was isolated in 44% yield. This may be very nearly the theoretical yield for the reaction since proton abstraction from the acylation product by dianion **8** probably occurs quite rapidly. Depending upon the rate of proton transfer, up to one half the initial quantity of dianion **8** could be consumed in this manner.




17

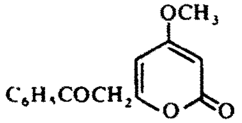
Acetylation of **8** was not achieved. Attempts to use ethyl acetate, phenyl acetate, isopropenyl acetate, acetonitrile, and acetic anhydride were unsuccessful. In most of these cases the dilithio salt of **8** was used.

It should be mentioned that an alternate method for the synthesis of **17** has been developed in this laboratory. The procedure involves lactonization of a 3,5,7-triketo acid.[18] Although acylation of **8** is probably more convenient for the synthesis of **17** and other aromatic homologs, the lactonization reaction appears to have greater generality, and is of particular utility for the synthesis of lactones of aliphatic triketo acids (for example, tetraacetic lactone[19]). Other procedures for the preparation of tetraacetic lactone, which may be applicable to other homologs, have been reported by Yamamura *et al.*,[15] as mentioned above, and by Guilford *et al.*[3]

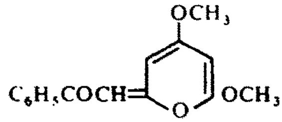
O-Methylation of **17** was achieved with diazomethane. Approximately 2 equivs of the reagent were employed, and the reaction gave at least four methylation products. One of them (**18**) crystallized directly from the reaction mixture. A second (**19**) crystallized after the mixture was concentrated; it was purified by chromatography on silica gel. Ethers **20** and **21** were isolated by chromatography of the residual material.

* Money *et al.* have also obtained acid **16** from reactions of the ester and a related compound.[14] However, no spectral details or other physical characterization have been reported.

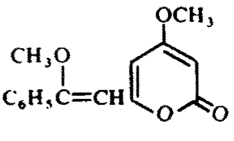
The structure of **18** was assigned on the basis of the elemental analysis and the NMR and UV spectra. The elemental analysis indicated that one Me group had been introduced. The NMR spectrum showed that the Me group was located on



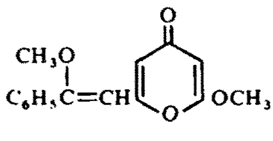
**18**



**19**



**20**



**21**

oxygen and that the 6-methylene group was unaltered. The UV spectrum was very similar to that of **17**. In addition it corresponded well to a composite of the spectra of acetophenone and 4-methoxy-6-methyl-2-pyrone (**6**) but not to a composite of the spectra of acetophenone and 2-methoxy-6-methyl-4-pyrone (See Table 1).[20, 21]

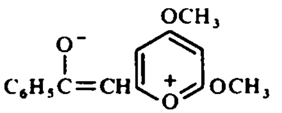
TABLE 1. UV SPECTRA[a]

| Compound | $\lambda_{max}$, nm (log $\varepsilon$) |
|---|---|
| **17**[18] | 284 (3·96), 245 (4·16) |
| **18** | 280 (3·96), 245 (4·17) |
| **19** | 430 (4·55), 415 (4·55), 304 (3·50), 249 (4·05), 226 (3·97) |
| **20** | 339 (4·35), 256 (4·04), 220 sh (4·06) |
| **21** | 312 (4·32), 224 sh (4·14) |
| **23**[22] | 474 (4·23), 366 sh (3·97), 3·50 (4·04), 291 (4·42), 236 (4·31) |
| Acetophenone[20] | 310 sh (1·82), 279·5 (3·02), 242·5 (4·10) |
| 4-Methoxy-6-methyl-2-pyrone (**6**)[21] | 280 (3·80) |
| 2-Methoxy-6-methyl-4-pyrone[21] | 240 (4·13) |
| 4-Methoxy-6-styryl-2-pyrone[23] | 345 (4·32) |
| 2-Methoxy-6-styryl-4-pyrone[23] | 330 (3·80) |

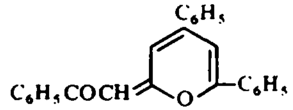
[a] Solutions in 95% ethanol.

Elemental analyses indicated that the remaining compounds (**19**–**21**) were dimethylation products. Structure assignments were made primarily on the basis of UV-VIS spectra. Pyrylium ion **22** can be expected to make a substantial contribution to the resonance structure of **19**; a similar compound, **23**, has a maximum at 474 nm (see Table 1).[22] Only one of the methylation products had maxima in the visible region; it was assigned structure **19**. Methyl ethers **20** and **21**, which are isomeric 2- and 4-pyrones, were assigned by analogy with 4-methoxy-6-styryl-2-pyrone and 2-methoxy-6-styryl-4-pyrone (see Table 1).[23]

The structures of **18–21** were supported by IR spectra. The CO stretching frequency of 2-pyrones is characteristically ~ 1710 $cm^{-1}$ whereas for 4-pyrones it is ~ 1670 $cm^{-1}$.[21,23] The CO stretching frequency of 2-pyrone **20** was 1720 $cm^{-1}$; the frequencies of **19** and **21** were 1660 and 1670 $cm^{-1}$, respectively. Pyrone **18** contains two CO groups and produced partially resolved stretching bands at 1695 and 1710 $cm^{-1}$.

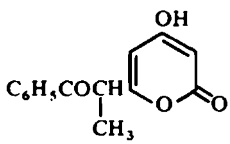


**22**



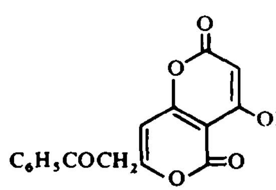
**23**

Treatment of **17** with two equivs of sodium amide in liquid ammonia converted it to a dianion which underwent alkylation with methyl iodide to give the 6α-methylation product **24**. The structure of **24** was established by NMR; the Me signal appeared as a doublet at 1·5 ppm.



**24**

Acylation of **17** with malonyl chloride in trifluoroacetic acid gave pyranopyran **25**. The reaction is analogous to the acylation of triacetic lactone with malonyl chloride which was reported by Money and Scott.[24]



**25**

In conclusion, although alkylation of the dianion of triacetic lactone gave mixtures of products, condensations with CO compounds, i.e., benzophenone, carbon dioxide and methyl benzoate, occurred entirely at the 6α-position. The 6α-benzoylation product (**17**) is of particular interest because the pyrone, its methylation products, and other derivatives can be converted to oligo-β-carbonyl compounds, which can then undergo internal aldol and Claisen condensations to form aromatic compounds.[2] Reactions such as these appear to be similar to the pathways by which phenolic natural products are biosynthesized.[24,25] We will describe ring cleavage-aromatic recyclization reactions of **17** and its derivatives in a subsequent communication.

## EXPERIMENTAL*

*Alkylation of dianion* **8**. Triacetic lactone (**1**; 4·0 g; 0·0318 mole) was added to 0·07 mole $NaNH_2$ (prepared from 1·6 g Na) in liquid ammonia. After 30 min, benzyl chloride (4·1 g; 0·032 mole) was added to the resulting green suspension of **8**. The ammonia was evaporated; ether and cold, dil HCl were added. Insoluble material (1·0 g) was isolated by filtration; NMR and TLC showed it to be mainly **10a**, although chromatography and several recrystallizations from EtOH-water were required for complete purification, m.p. 195–197°; IR (KBr) 1740, 1660, 1510, 1340, 1320, 1270, 745 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 2·25 (s, 3, 6-C$\underline{H}_3$), 3·75 (s, 2, 5-C$\underline{H}_2$), 5·53 (s, 1, 3-$\underline{H}$), 7·2 (m, 5, $C_6\underline{H}_5$). (Found: C, 72·27; H, 5·63. Calc. for $C_{13}H_{12}O_3$: C, 72·21; H, 5·60%). Evaporation of the ether extract gave 5·4 g of material which was shown by NMR to be **9a** and small quantities of **10a** and starting lactone **1**. Pyrone **9a** was identified by NMR comparison with authentic material:[11] NMR ($CDCl_3$) $\delta$ 2·75–3·0 (m, 4, 6-C$\underline{H}_2$C$\underline{H}_2$), 5·62 (d, 1, $J$ = 2·5 Hz, 3-$\underline{H}$), 5·97 (d, 1, $J$ = 2·5 Hz, 5-$\underline{H}$), 7·2 (m, 5, $C_6\underline{H}_5$). TLC comparison confirmed this assignment. Integration of the NMR spectra of the two fractions indicated that approx 90% alkylation had occurred and that **9a** and **10a** had been formed in a ratio of 2·5:1.

The alkylation reaction was repeated with $LiNH_2$ employed as the base. A similar result was obtained; the NMR spectrum of crude product indicated that the ratio of **9a** to **10a** was 2·2:1. Benzylation employing $KNH_2$ as the base gave a slightly different result. In the work-up **10a** was removed by filtration of the ether–water mixture. The ethereal soln was concentrated to ca. 100 ml, at which point additional material (0·7 g; m.p. 215–225°) was isolated by filtration. NMR showed the latter to be mainly **11a**, m.p. 226–230° after recrystallization from EtOH-water; IR (KBr) 1700, 1650, 1575, 1300, 1260, 700 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 2·81 (m, 4, 6-C$\underline{H}_2$C$\underline{H}_2$), 3·61 (s, 2, 5-C$\underline{H}_2$), 5·54 (s, 1, 3-$\underline{H}$), 7·0–7·35 (m, 10, $C_6\underline{H}_5$). (Found: C, 78·36; H, 5·81. Calc. for $C_{20}H_{18}O_3$: C, 78·41; H, 5·92%). Integration of NMR spectra indicated that the molar ratios of **9a**, **10a** and **11a** were 4:2:1, and that the alkylation yield was approx 80%.

Alkylations with MeI and i-PrBr gave similar mixtures of **9b–c** and **10b–c**, respectively. Methylation product **10b** was identified in the product mixture by NMR comparison with an authentic sample that had been prepared in a manner described previously.[10] Compound **10c** was separated by chromatography and recrystallized from EtOH, m.p. 200–202·5°; IR (KBr) 1675, 1600, 1485, 1330, 1260 $cm^{-1}$; NMR ($CDCl_3$ and DMSO-$d_6$) $\delta$ 1·26 (d, 6, $J$ = 12 Hz, 5-CH(C$\underline{H}_3$)$_2$), 2·25 (s, 3, 6-C$\underline{H}_3$), 2·97 (m, 1, 5-C$\underline{H}$(CH$_3$)$_2$), 5·47 (s, 1, 3-$\underline{H}$). (Found: C, 64·51; H, 7·11. Calc. for $C_9H_{12}O_3$: C, 64·27; H, 7·19%).

*Condensation of dianion* **8** *with benzophenone*. Dianion **8** was prepared by addition of 4·0 g (0·032 mole) of **1** to 0·70 mole of $NaNH_2$ (prepared from 1·6 g Na) in liquid ammonia. Benzophenone (5·8 g; 0·03 mole) was added in a small volume of ether. The ammonia was evaporated and ether was added. The resulting slurry was poured into cold, dil HCl. Insoluble material (3·5 g) was isolated by filtration. The ether layer was separated, dried, and evaporated to leave a solid residue (3·7 g). The two solids were combined and recrystallized from EtOH-water to give 5·4 g (55%) of **14**, m.p. 183–186° and 184–186° after further recrystallization from EtOH-water; IR (KBr) 1640, 1560, 1455, 1240, 710 $cm^{-1}$; NMR (DMSO-$d_6$) $\delta$ 3·58 (s, 2, 6-C$\underline{H}_2$), 5·25 (d, 1, $J$ = 2·5 Hz, 3-$\underline{H}$), 5·88 (d, 1, $J$ = 2·5 Hz, 5-$\underline{H}$), 7·1–7·75 (m, 10, $C_6\underline{H}_5$). (Found: C, 74·12; H, 5·09 Calc. for $C_{19}H_{16}O_4$: C, 74·01; H, 5·23%).

Pyrone **14** (0·85 g) was treated with cold, conc $H_2SO_4$ (10 ml) for 15 min. The mixture was poured onto ice. The ppt was separated by filtration and recrystallized from EtOH-water to give 0·50 g (63%) of **15**, m.p. 227–233° and 231–233° after further recrystallization from EtOH-water (Lit[11] m.p. 234–236°); IR (KBr) 1695, 1640, 1570, 1305, 1275 $cm^{-1}$; NMR (DMSO-$d_6$) $\delta$ 5·25 (d, 1, $J$ = 2 Hz, 3-$\underline{H}$), 5·67 (d, 1, $J$ = 2 Hz, 5-$\underline{H}$), 6·67 (s, 1, 6-C$\underline{H}$), 6·9–7·5 (m, 10, $C_6\underline{H}_5$).

*Carboxylation of dianion* **8**. Initial attempts to carboxylate **1** at the 6α-position involved preparation of dianion **8** in liquid ammonia, evaporation of the ammonia with simultaneous addition of ether and finally treatment with carbon dioxide. Only pyrone **1** was obtained from this procedure. A satisfactory method involved the use of lithium diisopropylamide as the ionizing base. Commerical n-BuLi (0·029 mole) in

* All m.ps were taken with a Thomas-Hoover apparatus in unsealed capillaries and are corrected. Preparative chromatography was on silica gel columns using mixtures of ether and hexane for elution. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. IR spectra were obtained with a Beckman IR-10 spectrophotometer. UV-VIS spectra were recorded with a Beckman DB spectophotometer. NMR spectra were determined with a Varian A-60 spectrometer. TMS was employed as an internal standard. The NMR spectrometer was purchased with funds obtained from the National Science Foundation.

hexane soln was added to diisopropylamine (3·05 g; 0·03 mole) in THF (50 ml) at 0° under $N_2$. The soln was warmed to room temp. Pyrone 1 (1·26 g; 0·01 mole) in THF was added, forming dianion 8 as a deep red suspension. After 1 hr, gaseous $CO_2$ was added. During the addition the mixture initially turned yellow, but gradually became deep orange. The solvent was evaporated, the resulting solid was treated with cold, dil $H_2SO_4$, and the soln was extracted with EtOAc. The organic soln was dried ($MgSO_4$) and evaporated. Crystallization of the residue from EtOAc gave 0·44 g (26%) of 16, m.p. 151–154° and 161–162° after two recrystallizations from EtOAc-$CHCl_3$; IR (KBr) 1730, 1660, 1560, 1490, 1310, 1265, 1190 $cm^{-1}$, NMR ($CDCl_3$ and DMSO-$d_6$) δ 3·48 (s, 2, 6-C$\underline{H}_2$), 5·34 (d, 1, J = 2 Hz, 3-$\underline{H}$), 6·07 (d, 1, J = 2 Hz, 5-$\underline{H}$). (Found: C, 49·15; H, 3·75. Calc. for $C_7H_6O_5$: C, 49·42; H, 3·55%). Chromatography of the mother liquors from the initial crystallization provided a small additional amount of acid 16.

*Aroylation of dianion 8 with methyl benzoate.* Pyrone 1 (4·0 g, 0·032 mole) was added to 0·70 mole $NaNH_2$ (prepared from 1·6 g Na) followed by 4·4 g (0·032 mole) methyl benzoate. The ammonia was evaporated. Ether and cold water were added; the aqueous layer was separated and acidified with dil HCl to precipitate 4·5 g crude 17, m.p. 170–180°. Recrystallization from water gave 3·2 g (44%) of purified pyrone 17, m.p. 183–186° (Lit[18] m.p. 185·5–186·5°). The structure was confirmed by NMR comparison with authentic 17.[18]

*Methylation of 17 with diazomethane.* Pyrone 17 (3·0 g; 0·013 mole) was added to an ethereal soln (100 ml) of diazomethane (0·025 mole) After 5 hr, a ppt (1·13 g) was collected by filtration. The material was mainly 18. Three recrystallizations from MeOH gave pure 18, m.p. 135·5–137·5°; IR (KBr) 1710, 1695, 1580, 1335, 1260 $cm^{-1}$; UV, see Table 1; NMR ($CDCl_3$) δ 3·8 (s, 3, 4-OC$\underline{H}_3$), 4·12 (s, 2, 6-C$\underline{H}_2$), 5·43 (d, 1, J = 2·5 Hz, 3-$\underline{H}$), 5·99 (d, 1, J = 2·5 Hz, 5-$\underline{H}$), 7·2–8·1 (m, 5, $C_6\underline{H}_5$). (Found: C, 68·61; H, 5·06. Calc. for $C_{14}H_{12}O_4$: C, 68·85; H, 4·95%).

The filtrate was concentrated to ca. 15 ml and a second ppt (0·75 g) was removed by filtration. The major component of this fraction, 19, was isolated by chromatography. Recrystallization from $CHCl_3$-ether gave 19, m.p. 142–142·5°; IR (KBr) 1660, 1490, 1325, 1210 $cm^{-1}$; UV, see Table 1; NMR ($CDCl_3$) δ 3·8 (s, 3, OC$\underline{H}_3$), 3·88 (s, 3, OC$\underline{H}_3$), 5·03 (d, 1, J = 3 Hz), 6·15 (s, 1), 7·62 (d, 1, J = 3 Hz), 7·25–7·55 and 7·8–8·0 (m, 5, $C_6\underline{H}_5$). The probable assignments of the signals at 5·03, 6·15, and 7·62 ppm are the vinyl protons at positions 3, 6α, and 5, respectively. (Found: C, 69·97; H, 5·58. Calc. for $C_{15}H_{14}O_4$: C, 69·76; H, 5·46%).

The filtrate from the second precipitation was evaporated leaving a 1·43 g residue of which 0·90 g was chromatographed. One fraction (0·25 g) contained 20, m.p. 93–94° after recrystallization from ether-hexane; IR (KBr) 1720, 1620, 1560, 1420, 1080 $cm^{-1}$; UV, see Table 1; NMR ($CDCl_3$) δ 3·68 (s, 3, 6β-OC$\underline{H}_3$), 3·83 (s, 3, 4-OC$\underline{H}_3$) 5·44 (d, 1, J = 4 Hz, 3-$\underline{H}$), 5·66 (s, 1, 6-C$\underline{H}$), 6·7 (d, 1, J = 4 Hz, 5-$\underline{H}$), 7·42 (m, 5, $C_6\underline{H}_5$). (Found: C, 69·60; H, 5·40, Calc. for $C_{15}H_{14}O_4$: C, 69·76; H, 5·46%). Another fraction (0·081 g) contained 21, m.p. 114–116° after recrystallization from ether-hexane; IR (KBr) 1670, 1620, 1570, 1410, 1250, 1060 $cm^{-1}$, UV, see Table 1, NMR ($CDCl_3$) δ 3·67 (s, 3, 6β-OC$\underline{H}_3$), 3·87 (s, 3, 2-OC$\underline{H}_3$), 5·45–5·55 (m, 2), 6·8 (d, 1), 7·45 (m, 5, $C_6\underline{H}_5$). The vinyl signals have not been assigned; two of them coincide at 5·45–5·55 ppm. (Found: C, 69·56; H, 5·58; Calc. for $C_{15}H_{14}O_4$: C, 69·76; H, 5·46%).

*Methylation of 17 with methyl iodide.* Pyrone 17 (8·0 g; 0·035 mole) was added to 0·078 mole of $NaNH_2$ (prepared from 1·8 g Na) in liquid ammonia. After 1 hr, MeI (4·8 g; 0·034 mole) was added. The ammonia was evaporated after 0·5 hr and cold, dil HCl was added. Filtration afforded a mixture (7·4 g) of 24 and starting pyrone 17 in a 60:40 ratio (NMR). Chromatography gave 1·3 g (16%) of 24, m.p. 145–147° after recrystallization from EtOH-water; IR (KBr) 1680, 1610, 1550, 1430, 1240, 970, 810 $cm^{-1}$; NMR ($CDCl_3$) δ 1·5 (d, 3, J = 7 Hz, 6-CHC$\underline{H}_3$), 4·6 (q, 1, J = 7 Hz, 6-C$\underline{H}$), 5·4 (d, 1, J = 2·5 Hz, 3-$\underline{H}$), 5·98 (d, 1, J = 2·5 Hz, 5-$\underline{H}$), 7·3–8·1 (m, 5, $C_6\underline{H}_5$). (Found: C, 68·86; H, 5·09. Calc. for $C_{14}H_{12}O_4$: C, 68·85; H, 4·95%).

*Acylation of 17 with malonyl chloride.* A mixture of 17 (5·0 g; 0·022 mole), malonyl chloride (6·03 g; 0·043 mole) and trifluoroacetic acid (5 ml) was refluxed for 3 hr. The mixture was cooled to 0°, EtOAc was added and precipitated material was collected by filtration. Chromatography and crystallization from $CHCl_3$ gave 1·2 g (18%) of 25, m.p. 223–229° and 224–227° after recrystallization from $CHCl_3$; IR (KBr) 3200, 1715, 1690, 1565, 1190, 1000 $cm^{-1}$; NMR ($CF_3CO_2H$) δ 4·62 (s, 2, 6-C$\underline{H}_2$), 5·99 (s, 1, vinyl), 6·90 (s, 1, vinyl), 7·4–8·2 (m, 5, $C_6\underline{H}_5$). (Found: C, 64·25; H, 3·36. Calc. for $C_{16}H_{10}O_6$: C, 64·43; H, 3·38%).

## REFERENCES


1 J. N. Collie, *J. Chem. Soc.* **59**, 179 (1891).
2 T. M. Harris, M. P. Wachter, and G. A. Wiseman, *Chem. Commun.* 177 (1969).
3 H. Guilford, A. I. Scott, D. Skingle, and M. Yalpani, *Ibid.* 1127 (1968).
4 J. A. Berson, *J. Am. Chem. Soc.* **74**, 5172 (1952).

[5] N. S. Vul'fson, E. B. Savenkova, and L. B. Senyavina, *J. Gen. Chem. U.S.S.R.* (Engl. trans.) **34**, 2766 (1964).
[6] J. L. Douglas and T. Money, *Tetrahedron* **23**, 3545 (1967).
[7] F. Arndt and S. Avan, *Chem. Ber.* **84**, 343 (1951).
[8] J. D. Bu'Lock and H. G. Smith, *J. Chem. Soc.* 502 (1960).
[9] J. L. Douglas and T. Money, *Canad. J. Chem.* **46**, 695 (1968).
[10] T. M. Harris and C. M. Harris, *Chem. Commun.* 699 (1966); T. M. Harris, C. M. Harris, and M. P. Wachter, *Tetrahedron* **24**, 6897 (1968).
[11] T. M. Harris and C. M. Harris, *J. Org. Chem.* **31**, 1032 (1966).
[12] K. G. Hampton, T. M. Harris, and C. R. Hauser, *Ibid.* **30**, 61 (1965).
[13] C. R. Hauser, D. S. Hoffenberg, W. H. Puterbaugh, and F. C. Frostick, *Ibid.* **20**, 1531 (1955); W. S. Murphy and C. R. Hauser, *Chem. & Ind.* 832 (1969).
[14] C. T. Bedford, J. L. Douglas, B. E. McCarry, and T. Money, *Chem. Commun.* 1091 (1968).
[15] S. Yamamura, K. Kato, and Y. Hirata, *Ibid.* 1580 (1968).
[16] R. Bentley and P. M. Zwitkowits, *J. Am. Chem. Soc.* **89**, 676 (1967).
[17] D. G. Pike, J. J. Ryan, and A. I. Scott, *Chem. Commun.* 629 (1968).
[18] T. M. Harris and C. M. Harris, *Tetrahedron* **25**, 2687 (1969).
[19] Unpublished results, G. P. Murphy and T. T. Howarth.
[20] G. H. Beaven and E. A. Johnson, *J. Chem. Soc.* 651 (1957).
[21] D. Herbst, W. B. Mors, O. R. Gottlieb, and C. Djerassi, *J. Am. Chem. Soc.* **81**, 2427 (1959).
[22] T. M. Harris and C. M. Harris, *J. Org. Chem.* **32**, 970 (1967).
[23] I. Chmielewska, J. Cieslak, K. Gorczynska, B. Kontnik, and K. Pitakowska, *Tetrahedron* **4**, 36 (1958).
[24] T. Money and A. I. Scott, *Ibid.* **23**, 3435 (1967).
[25] T. M. Harris and R. L. Carney, *J. Am. Chem. Soc.* **89**, 6734 (1967).