lized from acetone–hexane as needles: double mp 174–175, 182–184°; $[\alpha]D$ +85°; $\lambda_{max}$ 241 mμ (log ε 4.21); $\nu_{max}$ 3370, 1680, 1615, and 1060 cm$^{-1}$; nmr, 62 ($J$ = 6 cps) (18-methyl H), 71 (19-H), 129.5 (O$H$), 225 (broad multiplet for 17-H), and 344 cps (multiplet for 4-H).

*Anal.* Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00; O, 10.58. Found: C, 79.50; H, 10.16; O, 10.63.

**17α-Ethynyl-18-methylandrost-4-ene-3β,17β-diol** (**9d**).—A solution of 3β-hydroxy-18-methylandrost-4-en-17-one (**9b**, 980 mg) in dichloromethane (5 ml) and ether (20 ml) was added to a solution of potassium acetylide (from 390 mg of potassium) in liquid ammonia (100 ml). The mixture was stirred for 6 hr, ammonium chloride (800 mg) was added, and the ammonia was allowed to evaporate overnight. The residue was extracted with dichloromethane and water and the organic layer was washed with water, dried ($Na_2SO_4$), and evaporated to give a pale yellow solid which contained *ca.* 30% of starting material by tlc. The crude product was adsorbed on alumina (100 g), and elution with benzene–ether (4:1 and 1:1) afforded a mixture of the ethynyldiol **9d** and the unchanged hydroxy ketone **9b** (*ca.* 2.5:1, 900 mg) from which the ethynyldiol **9d** was isolated by crystallization from acetone–hexane as prisms: mp 190–191°; $[\alpha]D$ −4°; $\nu_{max}$ 3540, 3460, 3270, and 1055 cm$^{-1}$; nmr (in pyridine-$d_5$), 62 (19-H), 197 (ethynyl H), 280 (broad multiplet for 3-H), and 341 cps (multiplet for 4-H).

*Anal.* Calcd for $C_{22}H_{32}O_2$: C, 80.44; H, 9.83; O, 9.74. Found: C, 80.75; H, 9.96; O, 9.65.

**17α-Ethynyl-17β-hydroxy-18-methylandrost-4-en-3-one** (**10b**).—A mixture (800 mg) containing the crude ethynyldiol **9d** (70%) and the hydroxy ketone **9b** in dioxane (25 ml) was oxidized by DDQ (1.0 g) with stirring at 25° for 5.5 hr. The reaction mixture was worked up through dichloromethane to give a crude product (810 mg), which was subjected to preparative tlc on GF silica gel in chloroform–methanol (100:1). 17α-Ethynyl-17β-hydroxy-18-methylandrost-4-en-3-one (**10b**, 420 mg) was thereby obtained and crystallized from acetone–hexane as prisms: mp 242–244°; $[\alpha]D$ +27°; $\lambda_{max}$ 243 mμ (log ε 4.20); $\nu_{max}$ 3370, 3290, 1655, 1610, and 1065 cm$^{-1}$; nmr (in DMSO-$d_6$), 56.5 ($J$ = 6 cps) (18-methyl H), 68 (19-H), 194.5 (ethynyl H), 313 (O$H$), and 338 cps (multiplet for 4-H).

*Anal.* Calcd for $C_{22}H_{30}O_2$: C, 80.93; H, 9.26; O, 9.80. Found: C, 80.84; H, 9.17; O, 9.66.

The ORD of 3β-hydroxypregn-5-en-20-one acetate was $[\phi]_{600}$ ±0°, $[\phi]_{400}$ +350°, $[\phi]_{330}$ +3400°, $[\phi]_{316}$ +6200°, $[\phi]_{311}$ +6100°, $[\phi]_{309}$ +6150°, $[\phi]_{296}$ ±0°, $[\phi]_{269}$ −10,200°, $[\phi]_{237}$ −8400°, and $[\phi]_{215}$ −10,800° (*c* 0.1, dioxane).

The ORD of 17α-hydroxyprogesterone was $[\phi]_{589}$ +440°, $[\phi]_{378}$ +1020°, $[\phi]_{365}$ +530°, $[\phi]_{358}$ +1020°, $[\phi]_{352}$ +960°, $[\phi]_{316}$ +10,800°, and $[\phi]_{285}$ +1420° (*c* 0.1, dioxane).

**Acknowledgment.**—We wish to thank Dr. A. D. Cross for helpful discussions on the nmr aspects of this work.

# Carboxylation of β-Dicarbonyl Compounds through Dicarbanions. Cyclizations to 4-Hydroxy-2-pyrones[1]

THOMAS M. HARRIS AND CONSTANCE M. HARRIS

*Department of Chemistry, Vanderbilt University, Nashville, Tennessee*

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Six β-diketones and 2-acetyl-1-napthol were converted to disodio salts by treatment with excess sodium amide. Suspensions of the disodio salts in ether were treated with carbon dioxide to afford the corresponding terminal carboxylic acids in yields of 31–74%. The acids were cyclized by means of liquid hydrogen fluoride to the corresponding 4-hydroxy-2-pyrones in excellent yields. Carboxylation of ethyl dipotassioacetoacetate afforded acetonedicarboxylic acid monoethyl ester. Diketo acids have previously been postulated to be precursors of certain aromatic natural products; the efficient syntheses of these acids and the related 4-hydroxy-2-pyrones provide a basis for future investigation of the metabolism of these compounds.

Treatment of β-dicarbonyl compounds with 2 equiv of an alkali amide affords the corresponding dicarbanions, which undergo condensations selectively at the γ position. By this method many β-diketones, β-keto esters, and β-ketoaldehydes have been condensed with alkyl halides, aldehydes, ketones, and esters.[2] However, no systematic study has been made of the reaction of dicarbanions of dicarbonyl compounds with carbon dioxide to form the corresponding carboxylic acids; only two examples have been reported.[2a,3] The carboxylation of benzoylacetone (**1a**) is one of these (see Scheme I).

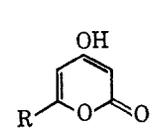
This paper reports more thorough studies that have been made of the carboxylation reaction to form these acids and of the cyclization of the diketo acids **2a–f** to 4-hydroxy-2-pyrones (**3a–f**). Certain of these dicarbonyl acids are of interest in investigations of the biosynthesis of phenolic compounds.

SCHEME I

$$RCOCH_2COCH_3 \xrightarrow[\text{liq } NH_3]{NH_2^-} RCO\bar{C}HCO\bar{C}H_2 \xrightarrow[2.\ H^+]{1.\ CO_2,\ \text{ether}} RCOCH_2COCH_2CO_2H$$

| | |
|---|---|
| **1a**, R = $C_6H_5$ | **2a**, R = $C_6H_5$ |
| **b**, R = $CH_3$ | **b**, R = $CH_3$ |
| **c**, R = $C_6H_5CH_2CH_2$ | **c**, R = $C_6H_5CH_2CH_2$ |
| **d**, R = $(CH_3)_2CHCH_2$ | **d**, R = $(CH_3)_2CHCH_2$ |
| **e**, R = $C_6H_5CH{=}CH$ | **e**, R = $C_6H_5CH{=}CH$ |
| **f**, R = $(C_6H_5)_2C{=}CH$ | **f**, R = $(C_6H_5)_2C{=}CH$ |
| **g**, R = H | **g**, R = H |
| **h**, R = $C_2H_5O$ | **h**, R = $C_2H_5O$ |

Initially a short search was made with diketone **1a** for preferred conditions to effect the carboxylation reaction (Table I). Sodium amide afforded a significantly better yield of keto acid **2a** than had potassium



**3a**, R = $C_6H_5$
**b**, R = $CH_3$
**c**, R = $C_6H_5CH_2CH_2$
**d**, R = $(CH_3)_2CHCH_3$
**e**, R = $C_6H_5CH{=}CH$
**f**, R = $(C_6H_5)_2C{=}CH$
**g**, R = H

(1) Supported by grants from the Institute of General Medical Sciences of the U. S. Public Health Service (GM-12848), the Research Corp., and the American Cancer Society.

(2) For examples see (a) C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **80**, 6360 (1958); (b) J. F. Wolfe, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **29**, 3249 (1964); (c) T. M. Harris and C. R. Hauser, *J. Am. Chem. Soc.*, **84**, 1750 (1962).

(3) W. I. O'Sullivan and C. R. Hauser, *J. Org. Chem.*, **25**, 1110 (1960).

TABLE I

CARBOXYLATION OF 1a EFFECTED BY VARIOUS BASES

| Base | Solvent | Yield, % | Mp, °C |
|---|---|---|---|
| $NaNH_2$[a] | Ether | 74 | 93–94.5 |
| $KNH_2$[a] | Ether | 58[b] | 94–97[b] |
| $NaCH_2SOCH_3$ | Dimethyl sulfoxide | 44 | 91–92 |
| NaH | Tetrahydrofuran | 0 | ... |
| $Mg(OCO_2CH_3)_2$ | Toluene | 0 | ... |

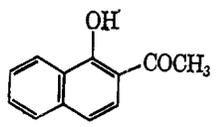
[a] The dicarbanion was formed in liquid ammonia; the ammonia was replaced by ether. [b] Previously reported result; ref 2a.

amide in the earlier work[1,2a] and it is concluded that sodium amide is probably the reagent of choice in most cases. Somewhat lower yields were obtained with sodium methylsulfinyl carbanion in dimethyl sulfoxide and difficulty was experienced in purifying the resulting keto acid **2a**. In addition, the use of sodium hydride in tetrahydrofuran and of methyl magnesium carbonate was tried but neither reagent afforded isolable amounts of keto acid **2a**.

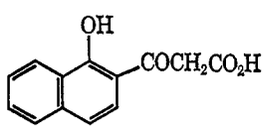
On the basis of the results in Table I, the general procedure used in most of the subsequent carboxylations involved addition of the dicarbonyl compound to 2.5–3.5 equiv of sodium amide in liquid ammonia. The liquid ammonia was evaporated with simultaneous replacement by ether. Carboxylation was effected by rapid addition of a large excess of Dry Ice to the ethereal suspension.

Excess sodium amide provided a safeguard against neutralization of the dicarbanion by adventitious moisture and apparently interfered in no way with the subsequent carboxylation reaction. Carbamate ion, which resulted from reaction of carbon dioxide with sodium amide, decomposed to carbon dioxide and ammonia during the isolation procedure.

The carboxylation of eight additional dicarbonyl compounds, **1b–h** and **4**, to form the corresponding carboxylic acids, **2b–h** and **5**, was investigated. Compound **4** is considered to be homologous to compounds **1** because the phenolic hydroxyl group represents a fully enolized carbonyl group.




**4**




**5**

As can be seen in Table II, seven of the eight dicarbonyl compounds were successfully carboxylated at terminal methyl positions. The yields, although not so high as had been obtained with benzoylacetone (**1a**), ranged from 31–61%.

Diketo acid **2b** had previously been prepared by a complex route involving ring opening of 4-hydroxy-2-pyrone **3b**, which in turn had been prepared from dehydracetic acid.[4]

Diketones **1c** and **1d** could possibly have formed either of two isomeric carboxylation products depending on whether the second ionization was effected by amide ion at the 1 or the 5 position. On the basis of a previous study of structural effects on dianion formation carboxylation of **1c–d** at the methyl positions was strongly indicated.[5] Moreover, the nmr spectrum of carboxylic acid **2c** showed the complete absence of the methyl group that had been present in diketone **1c**; thus, this had been the site of carboxylation.

Particularly noteworthy among these results are the carboxylations of **1e–f** to form the corresponding carboxylic acids **2e–f**. The formation of the dicarbanions of these unsaturated β-diketones, for example, dianion **6** from **1e**, represents an important extension of the use of dianions of β-dicarbonyl compounds. Although it was conceivable that the second equivalent of amide ion might have added across the conjugate double bond of **1e** to form dianion **7** instead of **6**, the nmr spectrum of the carboxylation product clearly showed retention of the -CH=CH- group and loss of the methyl group. This excluded the isomeric carboxylic acid **8**, that would haver esulted from carboxylation of **7**, if subsequent loss of ammonia had occurred.

$C_6H_5CH{=}CHCO\bar{C}HCO\bar{C}H_2$

**6**

$C_6H_5CH\bar{C}HCO\bar{C}HCOCH_3$
|
$NH_2$

**7**

$C_6H_5CH{=}\bar{C}COCH_2COCH_3$
|
$CO_2H$

**8**

The failure of formylacetone (**1g**) to undergo carboxylation may possibly be accounted for by lack of suitable conditions for isolation of the product (**2g**). Similar acylacetaldehyde compounds are extremely sensitive to acid and base catalysis and readily undergo self-condensation reactions.[6] Formylacetone itself is commonly handled as its sodium salt and can be isolated as the free compound only under carefully controlled conditions.[7] Among the methods that were investigated for isolation and purification of the carboxylation product **2g** was treatment of the crude reaction mixture with anhydrous hydrogen fluoride in an attempt to directly cyclize **2g** to 4-hydroxy-2-pyrone **3g**; this was unsuccessful.

Hydrogen fluoride was successfully employed to cyclize the diketo acids to the 4-hydroxy-2-pyrones. This reagent previously has been employed for other types of cyclizations and has the advantage over many other cyclizing agents that its volatility permits facile recovery of the pyrones. The general procedure involved addition of anhydrous, liquid hydrogen fluoride to the diketo acid in a polyethylene flask. The reactions were allowed to stand at room temperature for 24–48 hr, during which period the hydrogen fluoride evaporated. The results obtained by this method with seven diketo acids (**2a–f** and **5**) are shown in Table III.

From Table III it can be seen that the yields of 4-hydroxy-2-pyrones **3a–f** and **9** were very good (72–95%). Four of the seven compounds were new, and in addition the melting point of **9** was about 25° higher than previously reported.

(4) R. F. Witter and E. Stotz, *J. Biol. Chem.*, **176**, 485 (1948).

(5) K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **31**, 663 (1966).

(6) See T. M. Harris, S. Boatman, and C. R. Hauser, *J. Am. Chem. Soc.*, **85**, 3273 (1963).

(7) D. Dahm, R. Johnson, and F. H. Rathmann, *Proc. N. Dakota Acad. Sci.*, **12**, 19 (1958); *Chem. Abstr.*, **53**, 2084 (1959). See also R. L. Frank and R. H. Varland, *Org. Syn.*, **3**, 829 (1955).

TABLE II

CARBOXYLATION OF β-DICARBONYL COMPOUNDS BY MEANS OF THEIR DISODIO SALTS TO FORM TERMINAL CARBOXYLIC ACIDS

| Dicarbonyl compound | Carboxylic acid | Yield,[a] % | Mp, °C | Infrared, cm$^{-1}$ | Formula | Calcd C, % | Calcd H, % | Found C, % | Found H, % |
|---|---|---|---|---|---|---|---|---|---|
| 1b | 3,5-Hexanedionoic acid (2b) | 44 | 37.5–39[b] | 1730, 1620 | $C_6H_8O_4$ | 50.00 | 5.59 | 49.77 | 5.80 |
| 1c | 7-Phenyl-3,5-heptanedionoic acid (2c) | 48 | 70–73 | 1725, 1600 | $C_{13}H_{14}O_4$ | 66.66 | 6.02 | 66.74 | 6.11 |
| 1d | 7-Methyl 3,5-octanedionoic acid (2d) | 31[c] | ... | 1720, 1605 | $C_9H_{14}O_4$ | ... | ... | ... | ... |
| 1e | 7-Phenyl-6-heptene-3,5-dionoic acid (2e) | 52 | 107–108 | 1738, 1638, 1560 | $C_{13}H_{12}O_4$ | 67.23 | 5.21 | 67.46 | 5.25 |
| 1f | 7,7-Diphenyl-6-heptene-3,5-dionoic (2f) | 41 | 89–90 | 1740, 1715, 1625, 1560 | $C_{19}H_{16}O_4$ | 74.01 | 5.23 | 74.21 | 5.29 |
| 1g | 3,5-Pentanedionic acid (2g) | *d* | ... | ... | ... | ... | ... | ... | ... |
| 1h | Acetonedicarboxylic acid, monoethyl ester (2h) | 55[e] | 29.5–30.5[f] | 1750 (br) | $C_7H_{10}O_5$ | 48.27 | 5.74 | 48.37 | 5.90 |
| 4 | 2′-(1′-Naphthol)-3-oxopropionic acid (5) | 61 | 142–143 | 1710, 1620, 1570 | $C_{13}H_{10}O_4$ | 67.82 | 4.38 | 67.93 | 4.45 |

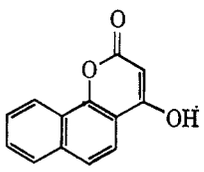
[a] The yield was determined in some cases with material melting slightly lower than the reported value. [b] Reported mp 29–31°, ref 4. [c] The product was an oil; it was cyclized satisfactorily to the 2-pyrone (Table III). [d] A small amount of dark oil was obtained; it could not be purified. [e] Prepared from ethyl dipotassioacetoacetate. [f] Neutralization equivalent: calcd, 174; found, 178. The compound was previously prepared but not crystallized, see R. Willstatter and A. Pfannenstiel, *Ann. Chem.*, **422**, 1 (1921).

TABLE III

CYCLIZATION OF DIKETO ACIDS TO 4-HYDROXY-2-PYRONES BY MEANS OF LIQUID HYDROGEN FLUORIDE

| Diketo acid | 4-Hydroxy-2-pyrone | Yield,[a] % | Mp, °C | Formula | Calcd C, % | Calcd H, % | Found C, % | Found H, % |
|---|---|---|---|---|---|---|---|---|
| 2a | 4-Hydroxy-6-phenyl-(2H)-pyran-2-one (3a) | 89 | 254–256[b] | $C_{11}H_8O_3$ | ... | ... | ... | ... |
| 2b | 4-Hydroxy-6-methyl-(2H)-pyran-2-one (3b) | 90 | 186–187[c] | $C_6H_6O_3$ | ... | ... | ... | ... |
| 2c | 4-Hydroxy-6-phenethyl-(2H)-pyran-2-one (3c) | 95 | 137.5–138.5 | $C_{13}H_{12}O_3$ | 72.21 | 5.59 | 72.29 | 5.70 |
| 2d | 4-Hydroxy-6-isobutyl-(2H)-pyran-2-one (3d) | 72 | 107–108 | $C_9H_{12}O_3$ | 64.27 | 7.19 | 64.47 | 7.14 |
| 2e | 4-Hydroxy-6-styryl-(2H)-pyran-2-one (3e) | 86 | 242–245 | $C_{13}H_{10}O_3$ | 72.89 | 4.71 | 73.25 | 4.92 |
| 2f | 4-Hydroxy-6-(2,2-diphenylvinyl)-(2H)-pyran-2-one (3f) | 91 | 234–236 | $C_{19}H_{14}O_3$ | 78.61 | 4.86 | 78.78 | 4.89 |
| 5 | 4-Hydroxy-(2H)-naphtho[1,2-b]-pyran-2-one (9) | 81 | 279–284[d] | $C_{13}H_8O_3$ | 73.58 | 3.80 | 73.65 | 3.88 |

[a] In certain cases yields were determined with material melting slightly lower than the reported value. [b] Reported mp 258–259°, ref 2b. [c] Reported mp 186–187°, ref 4. [d] Reported mp 256–258°, R. Anschütz and K. Runkel, *Ann. Chem.*, **368**, 43 (1909).




9

## Discussion

The preparation of diketo acids 2 has previously been by careful hydrolysis of 4-hydroxy-2-pyrones **3**, which were derived from natural sources or obtained by multistep condensation procedures.[8] These diketo acids have been reconverted to 4-hydroxy-2-pyrones by treatment with warm polyphosphoric acid or refluxing acetic anhydride.[2a,3,9] With polyphosphoric acid the isolation procedure involves dilution of the acid with water in order to precipitate the 4-hydroxy-2-pyrone. This procedure is not convenient for preparation of **3b** because of its water solubility. Decarboxylation of the diketo acids may be a problem with both methods.

Diketo acids and their derivatives have been postulated to be precursors of many natural products.[10] For example, **2b** has been suggested as an intermediate in the formation of orsellinic acid[11] and 6-methylsalicylic acid.[12] This diketo acid was identified as a product of acetate metabolism in avian liver.[13]

The related pyrone **3b** has been reported to stimulate formation of gentisyl alcohol by *Penicillium urticae;* the mechanism of this stimulation remains unknown.[14] Pyrone **3b** has recently been isolated from cultures of *P. patulum.*[15]

The dicarbanion method for direct synthesis of diketo acids and the hydrogen fluoride catalyzed cyclization to 4-hydroxy-2-pyrones should provide convenient methods for the preparation of other naturally

(8) See F. M. Dean, "Naturally Occurring Oxygen Ring Compounds," Butterworths and Co. (Publishers) Ltd., London, 1963, Chapter 4.

(9) W. Borsche and C. K. Bodenstein, *Ber.*, **62**, 2515 (1929).

(10) A. J. Birch and F. W. Donovan, *Australian J. Chem.*, **6**, 360 (1953); see also J. H. Richards and J. B. Hendrickson, "The Biosynthesis of Steroids, Terpenes and Acetogenins," W. A. Benjamin, Inc., New York, N. Y., 1964.

(11) S. Gatenbeck and K. Mosbach, *Acta Chem. Scand.*, **13**, 1561 (1959).

(12) A. J. Birch, R. A. Massy-Westropp, and C. J. Moye, *Australian J. Chem.*, **8**, 539 (1955).

(13) J. D. Brodie, G. Wasson, and J. W. Porter, *J. Biol. Chem.*, **239**, 1346 (1964).

(14) G. Ehrensvärd, *Exptl. Cell Res., Suppl.*, 3, 102 (1955).

(15) T. M. Harris, C. M. Harris, and R. J. Light, unpublished observation.

occurring 2-pyrones including yangonin, 4-methoxy-paracotoin, and anibine.[8] These synthetic methods will provide a basis for study of the biosynthesis and metabolism of such compounds, since diketo acids, the 2-pyrones and other derivatives, labeled with $C^{14}$ at the carboxyl position, can be readily and inexpensively prepared from carbon-14 labeled carbon dioxide.

## Experimental Section[16]

**Starting β-Diketones.**—Benzoylacetone (**1a**), 2,4-pentanedione (**1b**), and ethyl acetoacetate (**1h**) were obtained from commercial sources. 6,6-Diphenyl-5-hexene-2,4-dione (**1f**) was prepared by the condensation of benzophenone and dipotassio-2,4-pentanedione.[17] Sodioacetoacetaldehyde was prepared by a published procedure.[6] 7-Methyl-2,4-heptanedione (**1d**) and 2-acetyl-1-naphthol (**4**) were gifts of Professor D. E. Pearson. 6-Phenyl-5-hexene-2,4-dione (**1e**) was prepared in low yield by acylation of acetone with cinnamoyl chloride as described by Linn and Hauser.[18]

**Preparation of 5-Phenyl-3,5-pentanedionoic Acid (2a) (Table I).**—Several methods were investigated for preparation of **2a**. The preferred procedure involved preparation of a suspension of 0.087 mole of sodium amide[19] (from 2.0 g of sodium) in 300 ml of commercial anhydrous liquid ammonia in a 1-l., three-neck flask equipped with a condenser and glass stirrer. Benzoylacetone (4.05 g, 0.025 mole) was added through a powder funnel and the reaction mixture was stirred 30 min. The ammonia was rapidly evaporated on a steam bath as an equal volume of anhydrous ether was added. The ether was allowed to reflux for several minutes to ensure removal of most of the ammonia. Lumps of Dry Ice (about 200 g) were added and the reaction mixture stirred for 45 min. The ethereal suspension was poured into a mixture of ice and 40 ml of 12 *N* hydrochloric acid. The layers were separated and the ether layer was extracted several times with a cold, 5% solution of sodium bicarbonate. The alkaline extract was immediately acidified with hydrochloric acid. The white precipitate was collected and air dried at room temperature to yield 3.6 g (74%) of diketo acid **2a**, mp 93–94.5° (lit[20] mp 94°).

In order to obtain good yields of pure product, it was essential that the bicarbonate solution of diketo acid be rapidly acidified so as to minimize spontaneous decarboxylation. Diketo acid **2a** and the other acids prepared in this study (with the exception of **5**, which was quite stable) were handled and stored at room temperature or below to avoid decarboxylation.

No carboxylation was obtained with sodium hydride in tetrahydrofuran as the base or with methyl magnesium carbonate[21] in toluene as the combined base and carboxylating agent.

**Preparation of Dicarbonyl Acids 2b–h and 5 (Table II).**—Dicarbonyl acids **2b–h** and **5** were prepared by procedures similar to the above preparation of **2a** employing sodium amide, except for the variations noted below. Acid **1f** was prepared from ethyl dipotassioacetoacetate.

In the case of diketo acid **2b**, the bicarbonate extraction was omitted. The initial ether extract was dried over magnesium sulfate and the solvent was evaporated. Unreacted 2,4-pentanedione was removed under reduced pressure (0.02 mm) at room temperature.

All products were essentially pure as obtained by the above procedures. Acids **2b, e,** and **h** were recrystallized from ether–hexane, **2c** from ether–benzene–hexane, and **2f** from benzene–hexane. The compounds were placed in the solvent at room temperature and cooled to −20° to effect crystallization. Suitable conditions could not be found for crystallization of **2d**. The naphthol derivative **5** was somewhat more stable and was recrystallized from hot ethanol.

**Preparation of 4-Hydroxy-2-pyrones 3a–f and 9.**—Approximately 20 ml of commercial anhydrous liquid hydrogen fluoride was placed in a 50-ml polyethylene bottle containing 1.0 g of diketo acid. The mixture was allowed to stand in the hood for 24–48 hr until the hydrogen fluoride had evaporated. To ensure that all traces of hydrogen fluoride had been removed, the flask was allowed to stand in an evacuated desiccator over sodium hydroxide pellets for several hours. In some cases the residue was also washed with a dilute solution of sodium bicarbonate. The residues of 2-pyrones were usually essentially pure as indicated by melting point and infrared spectra. Analytical samples of **2c** and **2d** were prepared by recrystallization from ether. Ethanol was employed for **2f** and ether–acetic acid for **9**. 2-Pyrone **2e** was analyzed without recrystallization.

(16) Melting points were determined in open capillaries using a silicone oil bath and are corrected. Infrared spectra were determined with a Beckman IR-10 spectrometer using the potassium bromide pellet method for solids, and the neat liquid between sodium chloride plates for liquids. Nmr spectra were determined with a Varian A-60 spectrometer employing approximately 10% solutions in deuteriochloroform. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

(17) R. J. Light and C. R. Hauser, *J. Org. Chem.*, **26**, 1716 (1961).

(18) B. O. Linn and C. R. Hauser, *J. Am. Chem. Soc.*, **78**, 6066 (1956).

(19) J. T. Adams and C. R. Hauser, *ibid.*, **66**, 1220 (1944); R. Levine, J. A. Conroy, J. T. Adams, and C. R. Hauser, *ibid.*, **67**, 1510 (1945).

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# Relative Reactivities of Certain Disodio-β-diketones toward Alkyl Halides in Liquid Ammonia[1]

K. GERALD HAMPTON, THOMAS M. HARRIS, AND CHARLES R. HAUSER

*Department of Chemistry, Duke University, Durham, North Carolina*

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A study was made of the relative reactivities of disodio salts of β-diketones towards alkyl halides in liquid ammonia. The procedure involved treatment of an equal amount of two different disodio-β-diketones with a limited amount of an alkyl halide. The order of relative reactivities observed was isobutyryl, propionyl > acetyl > phenylacetyl. The relationship of these reactivities to basicity is discussed.

It has previously been observed that not only the mode of alkylation of acetylacetone or benzoylacetone is changed, but also the rate of the reaction is greatly increased on converting the common intermediate monocarbanion **1′** to the dicarbanion **1″** before adding the alkyl halide.[2,3] Thus, alkylation of **1′** to form the 3 derivative is too slow to be practical in liquid ammonia (at −33°), whereas that of **1″** to give the 1-derivative is sufficiently rapid in this medium to furnish a useful method of synthesis.[2,4]

$$\underset{\mathbf{1'}}{RCO\bar{C}HCOCH_3} \qquad \underset{\mathbf{1''}}{RCO\bar{C}HCO\bar{C}H_2}$$

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(2) C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **80**, 6360 (1958).

(3) For convenience mono- and dicarbanions are designated prime and double prime, respectively, and only carbanion resonance forms are represented even though other resonance forms may make more important contributions to the structures of the anions.

(4) See (a) K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **30**, 61 (1965); (b) K. G. Hampton, T. M. Harris, and C. R. Hauser, *ibid.*, **31**, 663 (1966).