hydrogen bromide began after reaching a temperature of 50°. The reaction product after cooling to room temperature, was poured onto 150 g. of wet ice containing 10 ml. of conc. hydrochloric acid. The organic layer was separated and the aqueous layer extracted twice with 50 ml. of benzene. The combined benzene solutions were dried over sodium sulfate, filtered, and concentrated to a volume of 60 ml. The crystals which precipitated from the concentrated benzene solution were recrystallized from benzene, yield 2.5 g. (51%), m.p. 270–271°.

Anal. Calcd. for $C_{32}H_{38}$: C, 90.93; H, 9.06. Found: C, 90.95; H, 8.94.

3,3′-Bisaminomethyl-1,1′-biadamantane (XII).—Powdered lithium aluminum hydride (0.6 g.) was charged into a three-neck flask (fitted with a thermometer, nitrogen inlet, addition funnel, and reflux condenser) together with 15 ml. of anhydrous tetrahydrofuran. A solution of 2.5 g. of 3,3′-dicyano-1,1′-diadamantane in 20 ml. of anhydrous tetrahydrofuran was added over a period of 15 min. The reaction product, after cooling to room temperature, was poured onto wet ice containing dilute hydrochloric acid. Recrystallization from dilute hydrochloric acid gave about 2 g. (64%) of the dihydrochloride of 3,3′-diaminomethyl-1,1′-biadamantane (XI) in the form of fine white needles. The compound does not melt at temperatures up to 320°.

Anal. Calcd. for $C_{22}H_{38}Cl_2N_2$: C, 65.81; H, 9.54; Cl, 17.66. Found: C, 65.32; H, 9.63; Cl, 17.32.

The free diamine was obtained from the dihydrochloride by reaction with ammonia. It is a white solid melting below 50°.

3,3′-Dihydroxy-1,1′-biadamantane (XIII).—Eleven and five-tenths grams of II, 20 g. of silver nitrate, 120 ml. of dioxane, and 40 ml. of water were charged into a three-neck flask fitted with thermometer, stirrer, and reflux condenser. The mixture was heated to gentle reflux for 3.5 hr. with stirring. The reaction product was then cooled to room temperature and filtered. The solids were extracted with refluxing dioxane and, on cooling to room temperature, 3.5 g. (93%) of 3,3′-dihydroxy-1,1′-biadamantane crystallized as transparent needles, m.p. 271–272° (sealed tube).

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 9.99. Found: C, 79.53; H, 9.98.

Physical and Chemical Properties of Hydroxyflavones. II. 3-Aroyl-5-hydroxyflavones. Synthetic and Infrared Spectral Studies[1,2]

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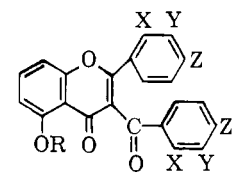
The Baker-Venkataraman rearrangement with the dibenzoate and bis(methoxybenzoates) of 2,6-dihydroxyacetophenone at the reflux temperature of pyridine or 2,6-lutidine, with subsequent ring-closure, resulted in the 3-aroyl-5-hydroxyflavones as principal product. The carbonyl region of the infrared spectra of 3-aroyl-5-hydroxyflavones contains two absorption bands, of which the high frequency one is assigned to the carbonyl function of the 3-aroyl group.

In the synthesis of flavones by the Kostanecki-Robinson, (Allan-Robinson) reaction, the 3-aroylflavone often is obtained as a by-product.[4] In many instances, the 3-aroyl group is removed readily by subsequent treatment with alcoholic alkali. The present paper reports an investigation of the Baker-Venkataraman rearrangement,[5] with subsequent ring-closure, as a synthetic route to 5-hydroxy-*n*-methoxyflavone (n = 2′, 3′, or 4′), and infrared spectral data which in virtually all instances afford a method for distinguishing between the 5-hydroxyflavone and its 3-aroyl derivative. The spectral method is of added significance since combustion analyses will not always distinguish between these two classes.[6]

The dibenzoate or bis(methoxybenzoate) was



I. X = Y = Z = R = H
II. X = Y = Z = H; R = $COCH_3$
III. Y = Z = R = H; X = CH_3O
IV. Y = Z = H; R = CH_3CO; X = CH_3O
V. X = Z = R = H; Y = CH_3O
VI. X = Z = H; R = CH_3CO; Y = CH_3O
VII. X = Y = R = H; Z = CH_3O
VIII. X = Y = H; R = CH_3CO; Z = CH_3O

prepared from 2,6-dihydroxyacetophenone and excess acid chloride (benzoyl, *o*-methoxybenzoyl, *m*-methoxybenzoyl, or anisoyl chloride) in pyridine solution. The Baker-Venkataraman rearrangement was carried out with potassium carbonate in 2,6-lutidine or pyridine at reflux temperature, and the products (presumably a mixture of diaroylmethane, triaroylmethane, and possibly some flavone and 3-aroylflavone from thermal ring-closure) were isolated but not purified. Cyclization to the mixture of flavone and its 3-aroyl derivative was effected with sulfuric acid–acetic acid. The 3-aroylflavone was obtained as the major product by crystallization from ethyl acetate.

(1) From a portion of the Ph.D. thesis of Walter William Hanneman, The University of Nebraska, 1958.

(2) This investigation was supported in part by a research grant (E-1703) from the National Institute of Allergic and Infectious Diseases, Public Health Service, and in part by a grant from the University of Nebraska Research Council.

(3) Dow Chemical Fellow, 1956–57; Public Health Service Research Fellow of the National Institute of Dental Research, 1957–58.

(4) W. Baker, G. Flemans, and R. Winter, *J. Chem. Soc.*, 1560 (1949).

(5) W. Baker, *ibid.*, 1381 (1933); H. S. Mahal and K. Venkataraman, *Current Sci.*, **2**, 214 (1933).

(6) K. M. Gallagher, A. C. Hughes, M. O'Donnell, E. M. Philbin, and T. S. Wheeler, *J. Chem. Soc.*, 3777 (1953).

TABLE I

PRODUCTS FROM BAKER-VENKATARAMAN REARRANGEMENT[a] OF 2,6-$(ArCOO)_2C_6H_3$—$COCH_3$ AND SUBSEQUENT RING-CLOSURE

	n-CH_3O-5-OH-3-ArCO-Flavone				*n*-Methoxy-5-hydroxy-Flavone			
Ar	*n*	Yield, %	M.p., °C.	Lit. m.p., °C.	*n*	Yield %	M.p., °C.	Lit. m.p., °C.
C_6H_5	..	63	177–178	173–174[b]	..	5	158–159	156–157[b]
o-(CH_3O)—C_6H_4	2′	67	189–190	180–182[c]	2′	6	139–140	140[d]
m-(CH_3O)—C_6H_4	3′	69	129–130[e]	...	3′	8	147–148	145–148[f]
p-(CH_3O)—C_6H_4	4′	54	177.5–178, 160	174,[g] 160–161,[g] 142[g]	4′	6	154–156	155–156[h]

[a] Ref. 5. [b] Ref. 10. [c] Ref. 9. [d] Ref. 6. [e] *Anal.* Calcd. for $C_{24}H_{18}O_6$: C, 71.63; H, 4.51. Found: C, 71.74; H, 4.65. [f] B. L. Shaw and T. H. Simpson, *J. Chem. Soc.*, 655 (1955). [g] Trimorphous; ref. 4. [h] T. S. Wheeler and I. F. Syed, *J. Chem. Soc.*, 1714 (1936).

The 5-hydroxyflavone, unsubstituted at the 3-position, was obtained from the mother liquors in low yield, and purified by fractional crystallization from ethanol. Yield and melting point data are presented in Table I.

Infrared spectral data for the 3-aroylflavones of the present study are listed in Table II. It is evident that, with one exception, two carbonyl bands are present in all spectra.[7] In the solution spectra, the band at 1650 ± 5 cm.$^{-1}$ is assigned to the flavone carbonyl group, in accordance with our previous study of flavone, monohydroxyflavones, and derivatives.[8] The band at relatively higher frequency is assigned to the carbonyl group in the 3-aroyl substituent.

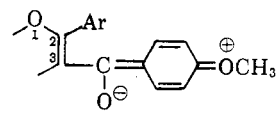
Although the spectra of all 3-aroylflavones (except IV) show the high frequency carbonyl band, there is considerable variation in the actual frequency value among the various 3-aroyl derivatives (Table II). The substances I, II, V, and VI possess nearly identical solution carbonyl frequencies near 1680 cm.$^{-1}$. In contrast, spectra of III, VII, and VIII have solution carbonyl frequencies appreciably lower than those of I, II, V, and VI. The greater single bond character thus indicated in the carbonyl groups of III, VII, and VIII very probably originates from well known resonance interactions between methoxyl and carbonyl groups; *e.g.*, as in VIIa. The *m*-methoxyl group in V and VI obviously is not in a position suitable for such resonance interaction. The relatively constant values for flavone carbonyl frequencies are in accord with our previous study,[8] and indicate again that the polarity of the flavone carbonyl group is not affected appreciably by methoxyl substituents on the side phenyl.

TABLE II

INFRARED CARBONYL BANDS[a] OF 3-AROYL-5-HYDROXY- AND 3-AROYL-5-ACETOXYFLAVONES

3-Aroyl-flavone	Aroyl-CO			Flavone-CO		
	KBr	Nujol	Soln.[b]	KBr	Nujol	Soln.[b]
I	...	1674	1680[c]	...	1649	1650[c]
II	...	1672	1680	...	1630	1647
III	1675	1673	1664	1646	1645	1649
IV	?	?	?	1633	1632	1649
V	1669	...	1678	1638	...	1650
VI	1665	...	1678	1629	...	1645
VII	...	1667	1673	...	1652	1650
VIII	...	1655	1669[c]	...	1631	1654[c]

[a] Absorption maxima expressed in cm.$^{-1}$, as determined with a Perkin-Elmer Model 21 recording spectrophotometer. [b] In carbon tetrachloride unless otherwise noted. [c] In dioxane solution.



VIIa

During this investigation, markedly different values of 140°[6] and 190–191°[9] were encountered for the melting point of 5-hydroxy-2′-methoxyflavone. It is apparent that the value of 190–191° is remarkably close to our melting point for the 3-aroyl derivative III (Table I, second entry). The data of Table II clearly indicate two carbonyl peaks for III, and in addition Rast molecular weight determination gave a value of 418 (theory 402) for III. We conclude that the substance m.p. 190–191° very probably is the 3-aroyl derivative (III), recovered and purified after attempted cleavage with carbonate, and that the actual melting point of 5-hydroxy-2′-methoxyflavone is 140°[6] (Table I).

Experimental

Dibenzoate and Bis(methoxybenzoates) of 2,6-Dihydroxyacetophenone.—In a flask fitted with drying tube, 15.2 g. (0.1 mole) of 2,6-dihydroxyacetophenone, 0.22 mole of the appropriate aroyl chloride, and 50 ml. of pyridine were placed and allowed to stand overnight. The reaction mixture was poured into excess 6 *N* hydrochloric acid, and the solid obtained by vigorous stirring collected by filtration. The benzene solution (*ca.* 500 ml.) of the solid was extracted with 3% hydrochloric acid, three times with 3% sodium hydroxide, again with 3% hydrochloric acid, twice with water, and then was dried over calcium chloride. Solvent removal *in vacuo* gave a residual solid, which was recrystallized from methanol. This product was used directly in the Baker-Venkataraman rearrangement.

Baker-Venkataraman Rearrangement of Dibenzoate and Bis(methoxybenzoates) of 2,6-Dihydroxyacetophenone.—

(7) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," J. Wiley and Sons, Inc., New York, 1958.

(8) J. H. Looker and W. W. Hanneman, *J. Org. Chem.*, **27**, 381 (1962).

(9) N. Narasimhachari, D. Rajagopalan, and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **37A**, 620 (1953).

In a three-necked flask fitted with stirrer and condenser, 10 g. of the appropriate 2,6-diaroyloxyacetophenone, 12 g. of anhydrous potassium carbonate, and 100 ml. of 2,6-lutidine (or pyridine) were placed, and the resulting mixture heated under reflux for 2 hr. The resulting yellow precipitate and 2,6-lutidine (or pyridine) were dissolved in water and poured cautiously into an excess of ice-cold 6 *N* hydrochloric acid. The resulting pale yellow to bright orange precipitate was collected by filtration and dried. Presumably this product consisted of a mixture of di- and triaroylmethanes, as well as some of the corresponding flavones. It was used in the cyclization step without further purification.

Cyclization of Rearrangement Products to Flavones.—A 2-g. quantity of the mixture of aroylmethanes (prepared as in section immediately preceding), 50 ml. of glacial acetic acid, and 2 ml. of concentrated sulfuric acid were heated at 95° for 1 hr. The resulting solution was poured into ice water, and the precipitate collected by filtration. The crude product, consisting chiefly of 3-benzoyl-5-hydroxyflavone with a small amount of 5-hydroxyflavone, or of the 3-aroyl-5-hydroxy-*n*-methoxyflavone (*n* = 2′, 3′, or 4′) with a small amount of 5-hydroxy-*n*-methoxyflavone, was separated into the components by fractional crystallization. The more insoluble 3-aroylflavone was separated fairly readily by crystallization from ethyl acetate. Concentration of the ethyl acetate mother liquors produced a small amount of 5-hydroxyflavone unsubstituted at the 3-position. The latter was collected by filtration, and purified by repeated recrystallization from ethanol.

5-Acetoxy-3-(*m*-methoxybenzoyl)-3′-methoxyflavone.—In a small flask were placed 200 mg. of 5-hydroxy-3-(*m*-methoxybenzoyl)-3′-methoxyflavone and 5 ml. of acetic anhydride. The mixture was warmed to about 120°, 3–4 drops of pyridine were added, and the resulting solution was heated an additional 3 hr. Then 15 ml. of water was added to the cooled solution. The precipitate resulting was collected by filtration, dissolved in hot dilute alcohol, the solution treated with charcoal, and the mixture filtered. The filtrate was cooled to precipitate the product, which was collected and recrystallized from dilute ethanol to give the colorless, analytically pure acetate; m.p. 145–146°.

Anal. Calcd. for $C_{26}H_{20}O_7$: C, 70.26; H, 4.54. Found: C, 70.03; H, 4.61.

Markedly similar acetylation procedures with the appropriate 3-aroyl-5-hydroxyflavone gave the following: 3-benzoyl-5-acetoxyflavone, m.p. 193–194°, lit.,[10] m.p. 189–190°; 3-anisoyl-5-acetoxy-4′-methoxyflavone, m.p. 222–223°, lit.,[4] m.p. 220°; 3-(*o*-methoxybenzoyl)-5-acetoxy-2′-methoxyflavone, m.p. 184.5–186°, lit.,[9] m.p. 180–181°.

(10) S. Sugasawa, *J. Chem. Soc.*, 1483 (1934).

Synthesis and Interconversion of 1-Acetyl-$\Delta^{1,8}$-hydrindene and 1-Acetyl-$\Delta^{8,9}$-hydrindene

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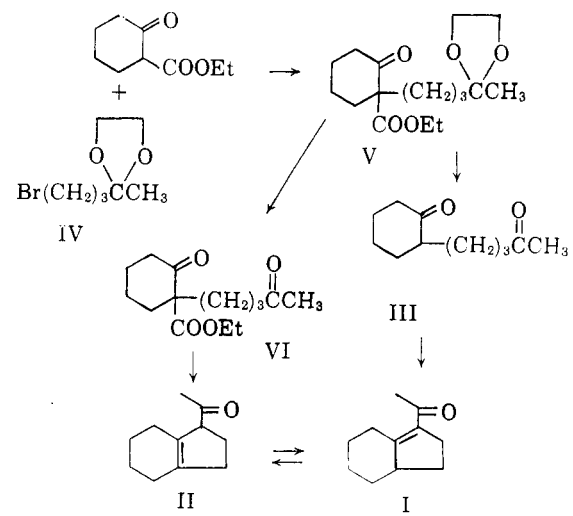
A new synthesis of 1-acetyl-$\Delta^{1,8}$-hydrindene (I) utilizing base-catalyzed cyclization of 2-(3′-acetylpropyl)cyclohexanone is reported. Treatment of I with acids or bases produces a 1:4 equilibrium mixture of I and its $\Delta^{8,9}$ isomer.

In connection with our study of the stereochemistry of conjugate addition at bridgehead positions of polycyclic unsaturated carbonyl compounds,[2] we desired to examine 1-acetyl-$\Delta^{1,8}$-hydrindene (I).[3] This ketone provides a model of potentially useful intermediates for syntheses of 18-functional steroids, and we thus desired a synthesis of I which could be readily adapted to the construction of tetracyclic homologs.[4] Such a synthesis of I and a study of its isomerization to the β,γ-unsaturated isomer II are the subjects of the present paper.

The synthetic approach involved 2-(3′-acetylpropyl)cyclohexanone (III) as the key intermediate which on aldol cyclization was expected to afford I. Early attempts to prepare diketone III by ozonolysis of 1-methyl-$\Delta^{1,9}$-octalin were discarded when we failed to find conditions for selective dehydration of 1-methyl-*trans*-1-decalol to



(1) United States Public Health Service Predoctoral Fellow 1960–1962.

(2) W. L. Meyer and N. G. Schnautz, *J. Org. Chem.*, **27**, 2011 (1962).

(3) L. E. Coles, W. H. Linnell, D. W. Mathieson, and A. S. Shoukri, *J. Chem. Soc.*, 2617 (1954).

(4) Such an approach to 18-norsteroids has been reported by (a) R. Anliker, M. Müller, M. Perelman, J. Wohlfahrt, and H. Heusser, *Helv. Chim. Acta*, **42**, 1071 (1959). Very recently intermediates of this type together with the conjugate addition reaction for introduction of C-18 functionality have been utilized in total syntheses by (b) W. Nagata, I. Kikkawa, and K. Takeda, *Chem. Pharm. Bull.* (Tokyo), **9**, 79 (1961), and (c) J. A. Marshall and W. S. Johnson *J. Am. Chem. Soc.*, **84**, 1485 (1962).