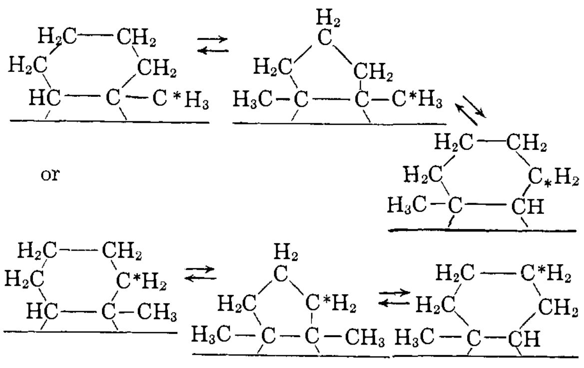
labeled toluene. They used the mechanism to explain the shift in label in methyl-C^{14}-cyclohexane over activated aluminum bromide at low temperature. To extend their mechanism to the dehydrocyclization conditions one assumes that rapid ring contraction and expansion occurs at 490° and that only the adsorbed methylcyclohexene species can desorb and dehydrogenate to toluene. Thus, for 2-heptene, one can write



depending on whether 2-heptene-C^{14}-1 or 2-heptene-C^{14}-7 is adsorbed. The assumption of the equal concentration and equal desorption probability of these four varieties of methyl cyclohexene leads to a prediction of 25% methyl-labeled toluene, 25% *o*-labelled, 25% *m*-labeled and 25% *p*-labeled.

One could argue that the 1-heptene is converted to toluene by simple ring closure but at a slower rate so as to contribute enough methyl-labeled toluene to raise the 25% to about 30%.

On the other hand, one could equally well reverse the role of the two olefins by arguing that adsorbed methylcyclohexene underwent a ring expansion to adsorbed cycloheptene. Then 1-heptene would yield equal proportions of methyl-, *o*-, *m*- and *p*-labeled toluene, and 2-heptene might be expected to give equal proportions of methyl-*o*-labeled toluene.

These speculations remain just that unless one can distinguish which mechanism is operating. It is interesting to note that schemes[12,13] now exist for assay of the radioactivity of the ring carbons in toluene. An assay of the C^{14} content of the *m*-position by one of these methods would allow one to distinguish between the transannular bridge and ring expansion and contraction mechanisms because the first predicts no *m*-labeled toluene and the second 25% *m*-labeled toluene.

Acknowledgment.—The author wishes to thank Dr. R. P. Eischens for suggesting this problem and Messrs. A. K. Blom and E. G. Northrop for their aid with the experimental work.

[12] A. E. H. Kilner, H. S. Turner and R. J. Warne, "Radioisotopes Conference, 1954. Vol. II. Physical Sciences and Industrial Applications," Academic Press, Inc., New York, N. Y., 1954, pp. 29–31.

[13] J. D. Roberts, D. A. Semenow, H. E. Simmons, Jr., and L. A. Carlsmith, THIS JOURNAL, **78**, 601 (1956).

BEACON, N. Y.

[CONTRIBUTION FROM THE COLLEGE OF CHEMISTRY AND PHYSICS, THE PENNSYLVANIA STATE UNIVERSITY]

Bis-(β-diketones). II. The Synthesis and Spectra of Compounds of the Type $[(RCO)R'COCH]_2CHR''$[1,2]

BY DEAN F. MARTIN, MAURICE SHAMMA AND W. CONARD FERNELIUS

RECEIVED JUNE 6, 1958

A number of new bis-(β-diketones) of the type $[(RCO)(R'CO)CH]_2CHR''$ have been prepared: $R = R' = CH_3$, $R'' = (CH_2)_5CH_3$, 2-ClC_6H_4, 2-$CH_3OC_6H_4$, 4-$CH_3OC_6H_4$, 4-$(CH_3)_2NC_6H_4$, 3,4-$CH_2O_2C_6H_3$, 2-C_5H_4N, 3-C_5H_4N, 4-C_5H_4N-; $R = CH_3$, $R' = CH_3OCH_2$, $R'' = C_6H_5$, 4-$CH_3OC_6H_4$, 4-HOC_6H_4, 3,4-$CH_2O_2C_6H_3$, 4-$(CH_3)_2NC_6H_4$, 2-C_5H_4N, 4-C_6H_4N. These bis-(β-diketones) were prepared by the condensation of a β-diketone, $RCOCH_2COR'$, with an appropriate aldehyde in a 2:1 molar ratio. The condensation was not successful for β-diketones containing a trifluoroacetyl group. The infrared and ultraviolet absorption spectra of the bis-(β-diketones) are recorded.

Introduction

In continuation of an investigation into the chelation behavior of bis-(β-diketones),[3,4] several new compounds of the type $[(RCO)(R'CO)CH]_2CHR''$ have been prepared by the interaction of a β-diketone of the type $RCOCH_2COR'$, and an aldehyde, $R''CHO$, in the presence of a suitable catalyst. Previous investigators have reported the synthesis of the compounds where $R = R' = CH_3$, $R'' = H$,[5] $R'' = CH_3$,[5] $R'' = 3\text{-}CH_3O\text{–}4\text{-}OH\text{–}C_6H_3$,[6] and $R'' = C_6H_5$[7,8]; $R = CH_3$, $R' = C_6H_5$, $R'' = H$,[9] $R'' = CH_3$,[10] $R'' = C_6H_5$,[11] and $R'' = 3\text{-}O_2NC_6H_3$[12]; $R = R' = C_6H_5$, $R'' = H$,[13,14] and $R'' = C_6H_5$.[15]

There are reported here the syntheses and proper-

---

[1] This research was supported in whole by the United States Air Force under Contact AF 33(616)-2742, monitored by the Materials Laboratory, Wright Air Development Center, Wright–Patterson Air Force Base, Ohio.

[2] Based upon a portion of the doctoral dissertation of Dean F. Martin, The Pennsylvania State University, 1958.

[3] E. H. Holst, Doctoral Dissertation, The Pennsylvania State University, August, 1955.

[4] D. F. Martin, M. Shamma and W. C. Fernelius, THIS JOURNAL, **80**, 4891 (1958).

[5] E. Knoevenagel, *et al.*, *Ber.*, **36**, 2136 (1903).

[6] E. Knoevenagel and F. Albert, *ibid.*, **37**, 4476 (1904).

[7] E. Knoevenagel and R. Werner, *Ann.*, **281**, 79 (1894).

[8] R. Schiff, *ibid.*, **309**, 206 (1899).

[9] K. Bodendorf and G. Koralowski. *Arch. Pharm.*, **271**, 101 (1903).

[10] G. Issoglio, *Atti accad. sci. Torino*, **41**, 1755 (1906); *Chem. Zentr.*, **78**, I, 409 (1907).

[11] E. Knoevenagel and A. Erler, *Ber.*, **36**, 2131 (1903).

[12] S. Ruheman, *J. Chem. Soc.*, **83**, 1376 (1903).

[13] Wesenberg, Dissertation, University of Leipzig, 1898, p. 39; *Beilstein*, Vol. 10, 1927, p. 1124.

[14] S. V. Lieberman and E. C. Wagner, *J. Org. Chem.*, **14**, 1001 (1949).

[15] W. Dieckmann and K. von Fischer. *Ber.*, **44**. 974 (1911).

TABLE I

COMPOUNDS PREPARED OF THE TYPE $[(RCO)(R'CO)CH]_2CHR''$[a,b]

R	R'	R''	M.p., °C.	Recrystn. solvent[c]	Yield, %	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
CH_3	CH_3	H	87.5–88.7[d]	A	10	....	...	...	..	..
CH_3	CH_3	$(CH_2)_5CH_3$	87–87.5	B + A	54	$C_{17}H_{28}O_4$	68.89	68.87	9.52	9.59
CH_3	CH_3	C_6H_5	165–167[e]	C	49	$C_{17}H_{20}O_4$	70.81	71.12	6.99	7.18
CH_3	C_6H_5	C_6H_5	202–202.5[f]	D	46	$C_{27}H_{24}O_4$	78.62	78.86	5.86	5.83
C_6H_5	C_6H_5	H	176–177[g]	D	67	....	...	...	..	..
CH_3	CH_3	$4\text{-}(CH_3)_2NC_6H_4$	187–189	C	45	$C_{19}H_{25}O_4N$	68.86	69.00	7.60	7.76
CH_3	CH_3	$2\text{-}CH_3OC_6H_4$	89–90	E	54	$C_{18}H_{22}O_5$	67.90	67.75	6.97	7.08
CH_3	CH_3	$4\text{-}CH_3OC_6H_4$	163–165	C	77	$C_{18}H_{22}O_5$	67.90	67.78	6.97	7.03
CH_3	CH_3	$2\text{-}ClC_6H_4$	97.5–98	E	57	$C_{17}H_{19}O_4Cl$	63.25	63.12	5.93	6.02
CH_3	CH_3	$3,4\text{-}CH_2O_2C_6H_3$	163.5–164	B	52	$C_{18}H_{20}O_6$	65.05	65.06	6.07	6.27
CH_3	CH_3	$2\text{-}C_5H_4N$[h]	153–154	C	28	$C_{16}H_{19}O_4N$	66.42	66.40	6.62	6.60
CH_3	CH_3	$3\text{-}C_5H_4N$	164–165	A + D	94	$C_{16}H_{19}O_4N$	66.42	66.30	6.62	6.79
CH_3	CH_3	$4\text{-}C_5H_4N$	187.5–187.8	F	47	$C_{16}H_{19}O_4N$	66.42	66.25	6.62	6.49
CH_3	CH_3OCH_2	C_6H_5	166–167	C	9	$C_{19}H_{24}O_6$	65.50	65.35	6.94	7.02
CH_3	CH_3OCH_2	$4\text{-}CH_3OC_6H_4$	165–167	C	4	$C_{20}H_{26}O_7$	63.47	63.36	6.93	7.03
CH_3	CH_3OCH_2	$4\text{-}HOC_6H_4$	199–200	A + D	17	$C_{19}H_{24}O_7$	62.62	62.79	6.64	6.88
CH_3	CH_3OCH_2	$3,4\text{-}CH_2O_2C_6H_3$	183–183.7	A + B	6	$C_{20}H_{24}O_8$	61.21	61.08	6.17	6.22
CH_3	CH_3OCH_2	$4\text{-}(CH_3)_2NC_6H_4$	200–202[d]	C	35	$C_{21}H_{29}O_6N$	64.43	64.37	7.47	7.33
CH_3	CH_3OCH_2	$2\text{-}C_5H_4N$	148–148.3	C + E	26	$C_{18}H_{23}O_6N$	61.88	61.79	6.63	6.56
CH_3	CH_3OCH_2	$4\text{-}C_5H_4N$	148–148.5	F	58	$C_{18}H_{23}O_6N$	61.88	62.05	6.63	6.52
$CH_2C(CH_3)_2CH_2$	H		190–191[i]	B	62	$C_{17}H_{24}O_4$	69.84	69.87	8.27	8.38

[a] All analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn. [b] All compounds except methylene-bis-(dimedone) gave a wine color with methanolic $FeCl_3$. [c] A, water; B, methanol; C, benzene; D, 95% ethanol; E, petroleum ether (67–92°); F, chlorobenzene. [d] Reported m.p. 87–88°; ref. 5. [e] Reported m.p. 166–167°; ref. 8. [f] Reported m.p. 195°; ref. 11. [g] Reported m.p. 175.5–176°; ref. 14 (prepared by B. B. Martin). [h] C_5H_4N = pyridyl. [i] Reported m.p. 191–191.5° [E. C. Horning and M. G. Horning, *J. Org. Chem.*, 11, 95 (1946)].

ties of the compounds where R = R' = CH_3, R'' = $(CH_2)_5CH_3$, $2\text{-}ClC_6H_4$, $2\text{-}CH_3OC_6H_4$, $4\text{-}CH_3OC_6H_4$, $4\text{-}(CH_3)_2NC_6H_4$, $3,4\text{-}CH_2O_2H_3$, $2\text{-}C_6H_4N$, $3\text{-}C_5H_4N$ and $4\text{-}C_5H_4N$; R = CH_3, R' = CH_3OCH_2, R'' = C_6H_5, $4\text{-}CH_3OC_6H_4$, $4\text{-}HOC_6H_4$, $3,4\text{-}CH_2O_2C_6H_3$, $4\text{-}(CH_3)_2NC_6H_4$, $2\text{-}C_5H_4N$, $4\text{-}C_5H_4N$.

Experimental

Materials. β-Diketones.—Benzoylacetone and dibenzoylmethane, "white label grade," were purchased from Distillation Products Industries and used without further treatment. Trifluoroacetylacetone, purchased from Peninsular Chemresearch, Inc., Gainesville, Fla., was redistilled prior to use; b.p. 107° (730 mm.), reported[16] b.p. 107°. Also redistilled before use were methoxyacetylacetone (b.p. 67–69° (10 mm.), reported[17] b.p. 68° (12 mm.)) and acetylacetone (b.p. 129–130° (730 mm.), reported[18] b.p. 139–141° (758 mm.)). Dr. Robert Levine of the University of Pittsburgh supplied the 2-naphthoyltrifluoroacetylmethane.

Aldehydes.—Most of the aldehydes were purchased from Distillation Products Industries and used without further purification. Pyridine-2-, 3- and 4-aldehydes were obtained from Aldrich Chemical Co.

Synthesis of Bis-(β-diketones) (Table I). General Procedure.—The appropriate β-diketone (0.1 mole) and aldehyde (0.05 mole) were dissolved in 70–95% ethanol. About 10 drops of piperidine was added. The mixture was allowed to stand at room temperature until the bis-(β-diketone) crystallized. The product was filtered and recrystallized. The time which elapsed between the addition of piperidine and the crystallization of the bis-(β-diketone) varied. Generally the product crystallized within a few days, but the derivatives of methoxyacetylacetone required several weeks.

The condensation of acetylacetone and 4-N,N-dimethylaminobenzaldehyde represents a typical synthesis. The condensation of acetylacetone and benzaldehyde resulted in the formation of the bis-(β-diketone) even though 100% excess of benzaldehyde was used.

$4\text{-}(CH_3)_2NC_6H_4CH[CH(COCH_3)_2]_2$.—Acetylacetone (10 g., 0.1 mole) and a solution of 4-N,N-dimethylaminobenzaldehyde (7.5 g., 0.05 mole) in 60 g. of 95% ethanol were mixed at room temperature. About ten drops of piperidine was added and the mixture allowed to stand. The product (7.5 g.), which crystallized within about three days, was filtered and recrystallized from benzene.

$[(CH_3CO)_2CH]_2CHC_6H_5$.[3,4]—Acetylacetone (50.0 g., 0.5 mole) and benzaldehyde (53.2 g., 0.5 mole) were dissolved in 50 g. of 70% ethanol. About 20 drops of piperidine was added and the mixture allowed to stand. After a week the reaction mixture solidified. The product (35.4 g.) was filtered, washed with 50% ethanol and recrystallized from benzene.

Attempted Preparation of 2-Phenyl-1,3-diacetyl-1,3-bis-(trifluoroacetyl)-propane, $[(CH_3CO)(CF_3CO)CH]_2CHC_6H_5$.—Trifluoroacetylacetone (7.70 g., 0.05 mole), benzaldehyde (2.65 g., 0.025 mole) and 10 drops of piperidine were mixed and heated at 55–60° for 47 hr. The resulting solid was filtered and dried to constant weight (5.4 g.). Upon recrystallization from petroleum ether, white crystals were obtained which softened at 140° and melted at 150–152°. *Anal.* Calcd. for $C_{17}H_{14}O_4F_6$: C, 51.52; H, 3.56; F, 28.77. Found: C, 49.29; H, 3.75; F, 24.00. Other attempts gave even less promising results.

Attempted Preparation of 2-Phenyl-1,3-bis-(trifluoroacetyl)-1,3-bis-(2-naphthoylpropane, $[(CF_3CO)(2\text{-}C_{10}H_7\text{-}CO)\text{-}CH]_2CHC_6H_5$.—Benzaldehyde (1.06 g., 0.01 mole) was added to a solution of 2-naphthoyltrifluoroacetylmethane (5.32 g., 0.02 mole) in 100 ml. of 95% ethanol, also ten drops of piperidine and the mixture allowed to stand. After two weeks, an additional 30 drops of piperidine was put in and one week later a further 10 drops of piperidine. After a total of nine weeks had elapsed, no crystallization had taken place. Ten drops of piperidine then was added and the reaction mixture heated at reflux temperature for about 5 min. The product crystallized upon standing at room temperature overnight and was filtered and dried *in vacuo*. The product (*ca.* 1 g.) was recrystallized from dilute methanol; yellow crystals, m.p. 104.3–105°. *Anal.* Calcd. for $C_{35}H_{22}O_4F_6$: C, 67.74; H, 3.57. Found: C, 87.42, 87.26; H, 5.12, 5.24. Calcd. for the structure $(2\text{-}C_{10}H_7COCH_2)_2\text{-}CHC_6H_4$: C, 86.89; H, 5.56.

---

(16) A. L. Henne, M. S. Newman, L. L. Quill and R. A. Staniforth, THIS JOURNAL, **69**, 1819 (1947).

(17) W. Renard and A. Maquinay, *Bull. soc. chim. Belg.*, **55**, 98 (1946).

(18) J. T. Adams and C. R. Hauser, THIS JOURNAL, **66**, 1220 (1944).

TABLE II

INFRARED ABSORPTION OF BIS-(β-DIKETONES) OF THE TYPE $[(RCO)(R'CO)CH]_2CHR''$

R	R'	R''	Hydroxyl, μ	Carbonyl, μ	Enol-chelate, μ
CH_3	CH_3	H	3.04	5.88	6.20 6.30
CH_3	CH_3	C_6H_5	2.92	5.80sh[a] 5.86	6.21
CH_3	CH_3	3-ClC_6H_4	2.88	5.87	6.25–6.28
CH_3	CH_3	2-$CH_3OC_6H_4$	2.93	5.88	6.25 6.30sh
CH_3	CH_3	4-$CH_3OC_6H_4$	2.93	5.78 5.82	6.17 6.28
CH_3	CH_3	2-C_5H_4N		5.84	6.25 6.34
CH_3	CH_3OCH_2	C_6H_5	2.95	5.77 5.83	6.24 6.31
CH_3	CH_3OCH_2	4-$CH_3OC_6H_4$		5.77 5.83	6.19 6.31
CH_3	C_6H_5	C_6H_5		5.83 5.94	6.26 6.33
C_6H_5	C_6H_5	H	2.96	5.91 5.97sh	6.25 6.32
$CH_2C(CH_3)_2CH_2$		H		5.90	6.19 6.30
Dimedone				5.78 5.90	6.17 6.32

[a] sh = shoulder.

The 2,4-dinitrophenylhydrazone of the product was prepared by a conventional procedure[19]; red crystals, m.p. 213–215° dec. (from 95% ethanol-ethyl acetate). *Anal.* Calcd. for the bis-(2,4-dinitrophenylhydrazone) of $(2\text{-}C_{10}H_7COCH_2)_2CHC_6H_5$: C, 65.47; H, 4.09. Found: C, 65.46; H, 3.99.

Infrared Absorption Spectra.—All spectra were obtained with a Perkin-Elmer model 21 recording infrared spectrophotometer using a sodium chloride prism. The spectra in the solid phase were made by incorporating the materials in potassium bromide pellets.[20] Tentative assignments from the spectra of typical bis-(β-diketones) of the type $[(RCO)(R'CO)CH]_2CHR''$ are summarized in Table II.

Ultraviolet Absorption Spectra.—All spectra were obtained with a Warren Spectracord with a hydrogen lamp light source using a 2-cm. quartz cell. Samples were obtained by dilution of stock solutions containing 10 mg. of bis-(β-diketone) per 100 ml. of 95% ethanol. The ultraviolet absorption maxima and extinction coefficients of representative bis-(β-diketones) of the type $[(RCO)(R'CO)CH]_2CHR''$ in 95% ethanol are listed in Table III.

Discussion

Syntheses of Bis-(β-diketones).—The properties of bis-(β-diketones) of the type $[(RCO)(R'CO)CH]_2CHR''$ prepared in this investigation are listed in Table I. These bis-(β-diketones) were prepared by the interaction of a β-diketone, $RCOCH_2COR'$, and an aldehyde, $R''CHO$, in the presence of a basic catalyst.

Previous investigators[5–15] have prepared aldehyde derivatives of acetylacetone, benzoylacetone and dibenzoylmethane. Only four aldehydes (formaldehyde, acetaldehyde, benzaldehyde, *m*-nitrobenzaldehyde and 3-methoxy-4-hydroxybenzaldehyde) seem to have been studied. In the present investigation the aldehyde condensation products of acetylacetone and of methoxyacetylacetone have been prepared using a wide variety of aldehydes. The bis-(β-diketones) derived from methoxyacetylacetone were found to be somewhat more soluble in the common organic solvents than the corresponding acetylacetone derivatives.

Most of the bis-(β-diketones) listed in Table I were prepared by the interaction of a β-diketone and aldehyde in a 2:1 molar ratio. A notable exception is the preparation of 2-phenyl-1,1,3,3-tetraacetylpropane from equimolar amounts of acetylacetone and benzaldehyde in the presence of piperidine. The yields obtained by this procedure were 42 and 49% (based on acetylacetone) as opposed to 77% yield obtained by Schiff[8] using the conventional ratio of reactants.

The preparation of a bis-(β-diketone) of the type $[(RCO)(R'CO)CH]_2CHR''$ probably involves an intermediate of the type $(RCO)(R'CO)CH{=}CHR''$, which readily undergoes the Michael addition reaction with a second molecule of β-diketone. The formation of 2-phenyl-1,1,3,3-tetraacetylpropane from equimolar amounts of benzaldehyde and acetylacetone reflects the great ease with which the unsaturated β-diketone undergoes the Michael condensation with unreacted β-diketone. On the other hand, it is known that the reaction of acetylacetone with cinnamaldehyde[17] or 2-hydroxynaphthaldehyde[21] does not proceed beyond formation of the unsaturated β-diketone, $(CH_3CO)_2C{=}CHR''$, thus precluding formation of the bis-(β-diketone). A similar difficulty is encountered in the reaction of acetylacetone and salicylaldehyde.[22]

It was not possible to isolate bis-(β-diketones) of the type $[(CF_3CO)(R'CO)CH]_2CHR''$. There is reason to believe that in this instance the bis-(β-diketone) has undergone hydrolytic cleavage. This is a well-known reaction of simple β-diketones[23]

---

[19] R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 171.

[20] M. M. Stimson and J. J. O'Donnell, THIS JOURNAL, **74**, 1805 (1952); U. Scheidt and H. Reinwein, *Z. Naturforschung*, **7B**, 270 (1952).

[21] E. Knoevenagel and F. Schröter, *Ber.*, **37**, 4484 (1904).

[22] E. Knoevenagel and R. Arnot, *ibid.*, **37**, 4496 (1904).

[23] R. G. Pearson and E. A. Mayerle, THIS JOURNAL, **73**, 926 (1951); R. G. Pearson and A. C. Sandy, *ibid.*, **73**, 931 (1951).

TABLE III

ULTRAVIOLET ABSORPTION SPECTRA OF BIS-(β-DIKETONES) OF THE TYPE $[(RCO)(R'CO)CH]_2CHR''$ IN 95% ETHANOL

R	R'	R''	Molarity × 10^5	λ, mμ	1	$\log \epsilon_{\max}$
CH_3	CH_3	2-ClC_6H_4	4.04	291	0.323	3.60
			5.38	290	0.412	3.58
CH_3	CH_3	3,4-$CH_2O_2C_6H_3$	1.51	257	.12	3.6
				288	.225	3.87
			2.41	257sh	.243	3.70
				287	.433	3.95
			3.01	257	.455	3.88
				287	.65	4.03
CH_3	CH_3	2-C_5H_4N	3.46	264	.418	3.78
				269	.420	3.78
				288	.422	3.78
			6.92	263.5sh	.720	3.72
				269	.758	3.74
				289	.800	3.75
CH_3	CH_3	3-C_5H_4N	3.46	263.5	0.425	3.79
				288	.385	3.75
			6.92	263.5	.650	3.67
				269	.650	3.67
				289	.580	3.62
CH_3	CH_3	4-C_5H_4N	3.46	259	0.370	3.73
				265	.375	3.73
				287	.420	3.78
			6.92	259	.520	3.57
				265	.558	3.61
				287	.693	3.70
CH_3	CH_3OCH_2	3,4-$CH_2O_2C_6H_3$	2.55	287	0.067	3.12
			3.82	285	.430	3.75
				288	.440	3.76
			5.10	273	1.20	4.07
				290	1.15	4.05
CH_3	CH_3OCH_2	4-$(CH_3)_2NC_6H_4$	2.55	266	0.550	4.03
			3.83	266	0.815	4.03
CH_3	C_6H_5	C_6H_5	1.94	248.5	0.760	4.29
			3.64	248.5	1.47	4.31
C_6H_5	C_6H_5	H	1.09	249	0.910	4.62
				340	0.055	3.40
			2.17	249	1.685	4.59
				340	0.040	2.96
$CH_2C(CH_3)_2CH_2$		H	1.71	257	0.890	4.42
			3.42	257	1.685	4.39

and occurs with great ease when the β-diketone contains a trifluoroacetyl group.[24]

It was of interest to determine whether the condensation of a β-diketone with an aldehyde having a basic group to act as a catalyst would occur in the absence of piperidine. Accordingly, the condensation of acetylacetone and methoxyacetylacetone with each of the three pyridine-aldehydes was attempted. The condensation product of acetylacetone with pyridine-4-aldehyde and the methoxyacetylacetone derivatives of pyridine-2- and pyridine-4-aldehydes precipitated without the addition of piperidine, but the acetylacetone derivatives of pyridine-2- and pyridine-3-aldehydes precipitated only after the addition of piperidine.

Infrared Absorption Spectra.—In the solid state, some bis-(β-diketones) of the type $[(RCO)(R'CO)CH]_2CHR''$ (Table II) may exist to an appreciable extent in the keto form. This is evidenced by the high intensity carbonyl absorption in the 5.77–5.85 μ region and the relatively low intensity enol-chelate absorption near 6.25 μ. Most of these bis-(β-diketones) have hydroxyl stretching bands near 2.95 μ. In nine cases, it appears that the hydroxyl bands may have been shifted to, and obscured by, the C–H stretching vibration bands; a similar shift has been observed in the spectra of acetylacetone and other enolic β-diketones and is regarded as evidence of strong intramolecular hydrogen-bonding.[25,26]

The position of the normal carbonyl band of these bis-(β-diketones) is influenced by the structure of the terminal groups, R and R'. Of the eleven compounds for which R = R' = CH_3, five have two carbonyl peaks of high intensity centered at 5.78 and 5.85 μ; six compounds have only the high intensity peak near 5.85 μ. The compounds for which R = CH_3, R' = CH_3OCH_2 also have two high intensity carbonyl bands; these are centered at 5.77 and 5.83 μ. The compounds $[(CH_3CO)(C_6H_5CO)CH]_2CHC_6H_5$ and $[(C_6H_5CO)_2CH]_2CH_2$ each have two carbonyl bands at 5.83, 5.94 μ and

---

[24] E. H. Cook and R. W. Taft, Jr., THIS JOURNAL, **74**, 6103 (1952).

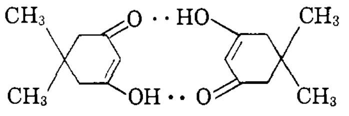
[25] R. S. Rasmussen, D. D. Tunnicliff and R. R. Brattain, *ibid.*, **71**, 1068 (1949).

[26] R. Mecke and E. Funck, *Z. Elektrochem.*, **60**, 1124 (1956).

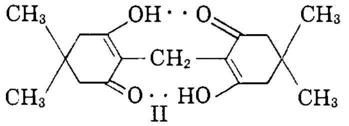
5.91, 5.97 μ, respectively. This change in the position of the carbonyl bands is attributed to increased carbonyl conjugation.

The enol-chelate absorption of the compounds listed in Table II generally appears as a low to moderate intensity band near 6.25 μ. In thirteen spectra a second band of comparable intensity appears near 6.35 μ. Only three compounds, $[(CH_3CO)_2CH]_2CHR''$ ($R'' = 2\text{-}ClC_6H_4$, $2\text{-}CH_3OC_6H_4$ and $2\text{-}C_5H_4N$), have enol-chelate intensities comparable to the carbonyl intensities. The reason for these exceptions is not definitely known. The fact that the R'' group of all three compounds contains a hetero atom or substitutent group in the *o*-position suggests the existence of steric and/or polar effects which favor the formation of the enol chelate structure.

The solid phase spectrum of methylene-bis-(dimedone) has a low intensity conjugated carbonyl at 5.90 μ and high intesity enol-chelate bands at 6.19 and 6.30 μ; this is similar to the spectrum of dimedone. Because of the ring in the dimedone molecule, it is sterically impossible for the hydroxyl of the enolized form to approach the carbonyl oxygen to form an enol-chelate structure. Rasmussen and co-workers[25] suggest that the 6.23 μ band appearing in the chloroform solution of dimedone is due to an enol-chelate structure formed by dimerization (I). A similar argument can, therefore, be put forward to explain the spectrum of methylene-bis-(dimedone) (II)



I



II

Interestingly enough, methylene-bis-(dimedone) did not produce a color with methanolic ferric chloride.

Ultraviolet Absorption Spectra.—One of the features of the ultraviolet absorption of bis-(β-diketones) of the type $[(RCO)(R'CO)CH]_2CHR''$ in 95% ethanol is the variation of extinction coefficient with concentration. The extinction coefficient of $3,4\text{-}CH_2O_2C_6H_3CH[CH(COCH_3)_2]_2$ at either 257 or 287 mμ increases almost linearly with increasing concentration. On the other hand, the extinction coefficient of the three isomers $[(CH_3CO)_2CH]_2CHC_5H_4N$ decreases at a higher concentration but the extinction coefficients of $2\text{-}ClC_6H_4CH[CH(COCH_3)_2]_2$, $4\text{-}(CH_3)_2NC_6H_4CH[CH(COCH_3)(COCH_2OCH_3)]_2$, tetrabenzoylpropane and methylene-bis-(dimedone) are about the same at two different concentrations.

Blout and co-workers[27] report that the ultraviolet absorption maxima of cyclohexane-1,3-dione derivatives appear at progressively higher wave lengths with increasing dilution although the extinction coefficients remain fairly constant. The shift in wave length is attributed to an increase in the degree of ionization with dilution. The fact that an acyclic β-diketone, such as acetylacetone, does not exhibit this phenomenon is ascribed to the lower acidity of the acyclic series and the ability of the acyclic compounds to form an enol-chelate structure.

The explanation of Blout, *et al.*,[24] should not apply to the variations observed in the spectra of the bis-(β-diketones). These compounds are capable of forming an enol-chelate structure and, in general, the wave length of these bis-(β-diketones) does not vary with concentration. It should be noted that the absorption maximum of methylene-bis-(dimedone) is the same at two concentrations suggesting the formation of a stable enol-chelate structure.

The variation in extinction coefficient can be explained in terms of change in enol content with concentration. On the basis of what is known about the ultraviolet absorption characteristics of acetylacetone,[28] the enolic and ketonic forms of tetraacetylpropane derivatives would be expected to absorb in the same region. The same would probably be true of bis-(β-diketones) of the type $[(CH_3CO)(CH_3OCH_2CO)CH]_2CHR''$. The extinction coefficient of the enolic form would be much greater than that of the ketonic. Therefore, an increase in the extinction coefficient of tetraacetylpropane derivatives and bis-(β-diketones) of the type $[(CH_3CO)(CH_3OCH_2CO)CH]_2CHR''$ is attributed to an increased enol content. It is conceivable that a change from a mono-enolic to a di-enolic form is involved. The variation of extinction coefficient with concentration should not be the same for all such bis-(β-diketones) since the nature of the R'' group seems to have some influence on the extent of enolization.

It is interesting to compare the absorption maxima of $[(CH_3CO)(C_6H_5CO)CH]_2CHC_6H_5$ with those of benzoylacetone. In ethanol, benzoylacetone has an absorption band at 245.5 mμ (log ϵ_{max} 3.78), a combination of keto- and enol-form absorption, and one at 310 mμ (log ϵ_{max} 4.14) almost entirely due to enol-form absorption.[29] By way of contrast, $[(CH_3CO)(C_6H_5CO)CH]_2CHC_6H_5$ lacks an absorption band near 310 mμ, but has a high intensity band at 248.5 mμ (log ϵ_{max} *ca.* 4.30). Thus, this bis-(β-diketone) does not exist in the enolic form in 95% ethanol to any appreciable extent.

A similar comparison can be made between dibenzoylmethane and tetrabenzoylpropane. Dibenzoylmethane, which exists almost entirely in the enolic form in ethanol,[30] has a high intensity band (log ε 4.36) near 345 mμ and a band near 250 mμ of lower intensity (log ε 3.92). The situation is reversed with tetrabenzoylpropane which has a high intensity band at 249 mμ (log ε *ca.* 4.6) and a band of lower intensity (log ε 3–3.4) at 340 mμ. This reversal is ascribed to the much lower ten-

---

(27) E. R. Blout, V. W. Eager and D. C. Silverman, THIS JOURNAL, **68**, 566 (1946).

(28) A. E. Gillam and E. S. Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Edward Arnold (Publishers) Ltd., London, 1954, pp. 223–229.

(29) R. A. Morton, A. Hassan and T. C. Calloway, *J. Chem. Soc.*, 883 (1934).

(30) K. H. Meyer, *Ber.*, **45**, 2849 (1912).

dency for tetrabenzoylpropane to exist in the enolic form.

Acknowledgments.—The authors gratefully acknowledge the help of Mr. Richard E. Dagle who made the infrared absorption spectral measurements and of Mrs. Barbara B. Martin who made the ultraviolet absorption spectral measurements. The authors are indebted to Merck and Co. for supplying the methoxyacetylacetone and to the Union Carbide Chemicals Co. for supplying the acetylacetone.

University Park, Penna.

[Contribution from the Department of Chemistry, Duquesne University]

Synthetic Evidence for the Stereochemistry of Isocitric Acid and Alloisocitric Acid Mechanism of *cis*-Aconitase Action

By Oscar Gawron, Andrew J. Glaid, III, Anthony LoMonte and Senophia Gary[1]

Received June 23, 1958

The configuration of the asymmetric carbon atoms of isocitric acid and alloisocitric acid has been elucidated by stereospecific synthesis of the two acids. Synthesis of DL-isocitric acid and DL-alloisocitric acid was achieved by malonate anion attack on the oxide rings of DL-*trans*-dicarboxyethylene oxide dimethyl ester and *cis*-dicarboxy-ethylene oxide dimethyl ester, respectively, followed by acid saponification, decarboxylation and chromatographic isolation of the acids as their respective lactones. The synthetic evidence plus the known *trans* opening of oxide rings by malonate anion leads to the conclusion that *d*-isocitric acid, the naturally occurring isomer, has the configuration α_{Ls}-β_{Ds}. This configuration, α_{Ls}-β_{Ds}, for *d*-isocitric acid indicates a *trans* mechanism to be operative in the *cis*-aconitase system.

In continuation of work on the stereochemistry of isocitric acid and alloisocitric acid,[2] we wish to report in this paper a sterospecific synthesis of DL-isocitric acid and DL-alloisocitric acid. The synthesis (Figs. 1 and 2) proceeds *via* malonate opening of the oxide ring of the dimethyl ester of dicarboxyethylene oxide, followed by acid saponification, decarboxylation and lactonization. Utilizing DL-*trans*-dicarbomethoxy-ethylene oxide dimethyl ester (I), DL-isocitric acid (IV), as the DL-lactone III, is obtained as the initial product of the synthesis and utilizing *cis*-dicarbomethoxy-ethylene oxide dimethyl ester (V), DL-alloisocitric acid (VIII), as the DL-lactone VII, is obtained.

Since malonate opening of oxide rings occurs by a *trans* mechanism,[3] assignment of relative configuration to the two asymmetric carbon atoms of DL-isocitric lactone (III) may be made on the basis of the configuration of the *trans*-oxide I and the relative configuration of the asymmetric carbons of DL-alloisocitric lactone (VII) may be deduced from the configuration of the *cis*-oxide V. Accordingly, the relative configurations of the two asymmetric carbons of DL-isocitric lactone (III) and of DL-alloisocitric lactone (VII) are such that the two free carboxyl groups are *cis* and *trans* in the respective lactones. This assignment of relative configuration is in agreement with that we have previously proposed[4] on the basis of pK_A values for the free carboxyl groups of the two lactones.

Experimental

DL-*trans*-Dicarboxy-ethylene Oxide.—The acid, isolated as the barium salt, was synthesized according to the procedure of Kuhn and Ebel.[5] The free acid was obtained from the barium salt by ion exchange with a sulfonic acid resin[6] in the (H^+) form, as follows. To a well-stirred suspension of 20.0 g. of the barium salt in 100 ml. of water, 80.0 g. of moist resin was added slowly and stirring was continued until the barium salt had gone into solution. The slightly cloudy supernatant liquid then was decanted and the resin was washed two times with 35-ml. portions of water. The combined supernatants were filtered rapidly and vacuum concentrated at 35°, and the residue from the vacuum concentration was dried *in vacuo* over sodium hydroxide and phosphorus pentoxide to yield 8.0 g. (70%) of crude DL-*trans*-dicarboxy-ethylene oxide. The product was purified by extraction in a Soxhlet apparatus with anhydrous ether, the pure acid, m.p. 212–213°,[7] crystallizing in the boiler during the extraction.

***cis*-Dicarboxy-ethylene Oxide.**—The acid, isolated as the barium salt, was prepared by hydrogen peroxide oxidation of hydroquinone,[8] using the procedure of Weitz, *et al.* In a one-l. beaker, 11.0 g. (0.01 mole) of hydroquinone and 90 ml. of 30% hydrogen peroxide[9] were stirred and heated to 80°. The heat source was then removed and with continued stirring 135–140 ml. of 2 *N* potassium hydroxide was dropped in over a period of 15–20 minutes. The alkali was added at a rate that maintained the reaction temperature at 80–85° (initially the temperature may rise to 100°) and that does not permit the reaction *p*H to become too alkaline. After addition of alkali, the reaction mixture was stirred for an additional 5–10 minutes, cooled at the tap, and the *p*H was adjusted to 6 with acetic acid. After the addition of 30 g. of barium chloride dihydrate and stirring for 30 minutes, the mixture was cooled to 5° and the dihydrate of the barium salt of the acid crystallized from solution, yield 16–20 g. (53–66%). The free acid was obtained by treating a suspension of the barium salt in moist ether with the calculated quantity of concentrated sulfuric acid.[5,8] The acid after recrystallization from anhydrous ether melted at 145–146°, literature value[5] 149°.

Dimethyl Ester of DL-*trans*-Dicarboxy-ethylene Oxide (I).—To 8.0 g. (0.066 mole) of DL-*trans*-dicarboxy-ethylene oxide suspended in 50 ml. of anhydrous ether, a cold ether solution of diazomethane was added dropwise. The addition of diazomethane was continued until all the acid went into solution and a faint yellow color persisted in the solution. The solution was then concentrated, the dimethyl ester crystallizing as the volume of solution was reduced. After filtering, the ester was recrystallized from ether, yield 9.6 g. (91%), m.p. 75–76°.

Anal.[10] Calcd. for $C_6H_8O_5$: C, 45.0; H, 5.00; sapon. equiv., 80.0. Found: C, 45.1; H, 4.91; sapon. equiv., 80.5.

---

(1) Abstracted in part from the Masters' Thesis of Senophia Gary.

(2) O. Gawron and A. J. Glaid, III, This Journal, **77**, 6638 (1955).

(3) S. Winstein and R. B. Henderson in R. C. Elderfield's "Heterocyclic Compounds," John Wiley and Sons, Inc., Vol. I, New York, N. Y., 1950, p. 31.

(4) Ref. 2. A preliminary account of the synthetic approach is also given in this reference.

(5) R. Kuhn and F. Ebel, *Ber.*, **58**, 919 (1925).

(6) Amberlite IR-120 (H^+), reagent grade. Prior to use 100 grams of resin was treated four times with 300-ml. portions of 6 *N* hydrochloric acid followed by thorough water washing to neutrality.

(7) Literature m.p. 209°, ref. 5.

(8) E. Weitz, H. Schobbert and H. Seibert, *Ber.*, **68B**, 1163 (1935).

(9) Stabilized with sodium stannate.

(10) Analyses by Drs. G. Weiler and F. B. Strauss.