[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, TOKYO UNIVERSITY OF EDUCATION]

Bicyclo[3.3.0]octane Derivatives

BY SANAE TANAKA

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Ethyl trichloroethylidenemalonate upon condensation with ethyl malonate in the presence of sodium ethoxide at low temperatures gives II, while at higher temperatures the product is Ia. The free compound I and dihydro-(I) have been prepared and the chemical and physical properties of these compounds are reported.

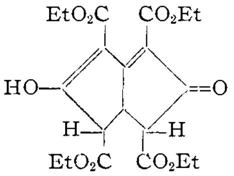
Schroeter and Vossen[1,2] have shown that methyl trichloroethylidenemalonate and methyl malonate in the presence of sodium methoxide condense to give in a good yield a red crystalline salt, $C_{16}H_{15}O_{10}Na$, whose structure they assumed to be that of the sodium salt of methyl bicyclo[3.3.0]octene-2,5-dione-1,3,4,6-tetracarboxylate (Ia, methyl ester instead of ethyl ester). The structure Ia was strongly supported by Wanzlick,[3] Yates and Bhat,[4] and Paul and Wendel[5] by work on the conversion of Ia to bicyclo[3.3.0]octane and its derivatives.

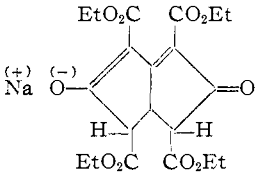
This reaction is of considerable interest since it can easily give bicyclo[3.3.0]octane, and furthermore it may provide an intermediate for the synthesis of pentalene or its derivatives. However, the course of this interesting reaction has been discussed only briefly in the above literature. This paper describes some new facts about this cyclization and new knowledge about the properties of its products.

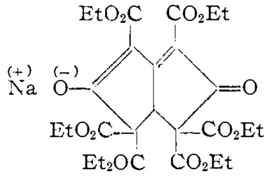
In the case of the condensation of ethyl trichloroethylidenemalonate and ethyl malonate (4–6 moles) in the presence of sodium ethoxide (4–6 moles), the products varied with reaction temperature as follows: in a slow addition of ethyl trichloroethylidenemalonate to ethyl sodiomalonate, where the reaction temperature reached the boiling point of ethanol only temporarily, the monosodium compound Ia was formed as reddish-orange crystals in about 65% yield; when the reaction temperature was kept below 40° throughout, a different monosodium compound (II), not previously found, was obtained as slightly pink crystals in 45% yield without formation of the monosodium compound Ia. The sodium compound II gave Ia in a good yield when subjected to refluxing on a steam-bath with sodium ethoxide. The sodium compounds Ia and II were stable, had definite melting points and their separation and purification were easy, differing from that of the methyl esters.

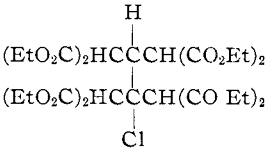
The formation of different sodium compounds (Ia and II) under slightly different reaction conditions and the easy conversion of II into Ia permit certain deductions about the possible course of this cyclization.

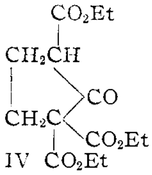
Ethyl trichloroethylidenemalonate on reaction with three moles of ethyl malonate probably would give the intermediate III. At low temperatures III would give II by elimination of the elements of ethanol through a double Dieckmann cyclization and one mole of hydrogen chloride. At higher temperatures III would give Ia by elimination of the elements of ethyl carbonate and hydrogen chloride.

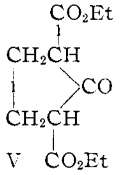

I

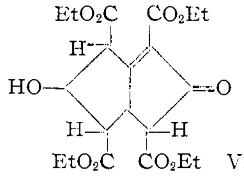

Ia


II


$$\begin{array}{c}(EtO_2C)_2HC\overset{H}{\underset{|}{\overset{|}{C}}}CH(CO_2Et)_2\\(EtO_2C)_2HC\underset{Cl}{\underset{|}{C}}CH(CO\ Et)_2\end{array}$$
III


IV


V


VI

The fact that two different cyclization products (Ia and II) were formed under different reaction temperature is comparable to the following example[6]; treatment of ethyl ethylenedimalonate with sodium ethoxide gave IV (cyclized product with the elimination of elements of ethanol) at low temperatures, while V (cyclized product with the elimination of elements of ethyl carbonate) was formed at high temperatures.

The sodium compounds Ia and II are stable, but the free compounds are unstable. Nevertheless it was possible to prepare I by gentle treatment of its sodium compound Ia with dilute mineral acid and to obtain it in a crystalline form. The free compound I in the solid state decomposed gradually when left in the air, and gave rapidly and quantitatively sodium, potassium and copper derivatives on treatment with aqueous sodium, potassium and copper salts, respectively. The separation of the free compound II in the pure state was unsuccessful, but its formation was indicated by reconversion to the sodium compound.

Both Ia and I did not give recognizable substances by treatment with carbonyl reagents. Attempted alkylation and acylation by treatment of the sodium compound Ia with methyl iodide, *n*-butyl bromide, ethyl bromoacetate, ethyl bromomalonate and acetyl chloride were all unsuccessful.

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(1) G. Vossen, Dissertation, Bonn, 1910.

(2) G. Schroeter, *Ann.*, **426**, 1 (1922).

(3) H.-W. Wanzlick, *Chem. Ber.*, **86**, 269 (1953).

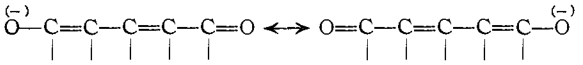
(4) P. Yates and G. Bhat, *Chemistry & Industry*, 1237 (1954).

(5) H. Paul and I. Wendel, *Chem. Tech.*, **8**, 189 (1956); *C. A.*, **51**, 5713 (1957).

(6) E. R. Meincke, R. F. B. Cox and S. M. McElvain, THIS JOURNAL, **57**, 1133 (1935).

This is quite contrary to the case with simple cyclopentan-1-one-2-carboxylate derivatives.[7,8b]

The infrared spectra of I, its derivatives and II were complicated; for instance, the sodium compound Ia absorbed at 1746 (free ester), 1715 (ketone), 1683 (chelated conjugated C=O) and 1623 cm.$^{-1}$ (conjugated C=C), all of which correspond to cyclopentan-1-one-2-carboxylate derivatives.[8] The infrared band at 1543 cm.$^{-1}$, however, is characteristic and corresponds to a vinylogous carboxylate resonance system.[9]



$$\overset{(-)}{O}-C=C-C=C-C=O \longleftrightarrow O=C-C=C-C=C-\overset{(-)}{O}$$

The sodium compound Ia and the free compound I have characteristic properties indicative of a vinylogous carboxylate system[9]: absorption at long wave range (λ_{max} 342 and 258 mμ); the free compound I is unstable and easily forms alkali metal compounds, but no carbonyl derivatives. In the free compound I, since the existence of two carbethoxy groups on the resonance system also contribute to its stability, its acidity becomes higher (pK_{a_1} 2.13 (25°)) than that of simple glutaconaldehyde type. From the above facts formula Ia which was proposed by Yates and Bhat is acceptable; hence the formula I for the free compound is reasonable. Since the sodium compound II has similar ultraviolet and infrared spectra to those of I and Ia (see Experimental), it must have the formula II.

The sodium compound Ia absorbed 1 mole of hydrogen on catalytic reduction at atmospheric pressure with platinum black as catalyst, yielding the dihydro compound. Dihydro-(I) has maximum absorption at 247 mμ, due to destruction of the vinylogous carboxylate resonance system and has a strong free OH-band at 3313 cm.$^{-1}$, hence formula VI is most probable.

Acknowledgments.—The author wishes to thank Dr. H.-W. Wanzlick for important advice, Dr. S. Yoshida and Mr. S. Baba for measurement of infrared spectra, Mr. Y. Oyagi for measurement of ultraviolet spectra and Mr. E. Ideno for measurement of dissociation constants.

Experimental[10]

Sodium Salt of Ethyl Bicyclo[3.3.0]octene-2,5-dione-1,3,4,6-tetracarboxylate (Ia).—To ethyl sodiomalonate prepared from ethyl malonate (96 g., 6 moles), sodium (13.8 g., 6 g. atoms) and absolute ethanol (400 cc.), was added dropwise ethyl trichloroethylidenemalonate (29 g., 1 mole) in 15 min. with stirring and cooling at 5–6°. The reaction mixture became turbid with a color change from yellow to red, and finally an orange-red precipitate was formed. The reaction temperature increased rapidly to 78° and the mixture boiled during the initial stages, but later remained at 30–40°. After the addition was finished, the stirring was continued for 30 min. with cooling, for 1 hr. at room temperature and then the mixture was allowed to stand overnight. Acidification (*p*H 6.0) with 5% ethanolic hydrogen chloride (140 cc.) gave 56 g. of a grayish-orange precipitate. Continuous extraction with absolute ethanol using a modified Soxhlet extractor gave the sodium salt Ia as reddish-orange crystals, m.p. 220–221° dec. The ethanol-insoluble residue (sodium chloride) weighed 28.5 g. (29 g. by theory). The former reaction filtrate was concentrated to about half-volume under reduced pressure by an aspirator, yielding an additional 6 g. of Ia. The total yield was 28 g. (65%). Two recrystallizations from ethanol gave reddish-orange, lustrous crystals, m.p. 225–226° dec.; ferric chloride test in ethanol blood-red; λ_{max} 342 (ϵ 52,500), 258 (ϵ 12,200) mμ; infrared bands at 1746, 1715, 1683, 1623 and 1543 cm.$^{-1}$.

Anal. Calcd. for $C_{20}H_{23}O_{10}Na$: C, 53.79; H, 5.19. Found: C, 53.65; H, 5.18.

In the above procedure when 4–6 moles of ethyl malonate and sodium were used per mole of ethyl trichloroethylidenemalonate, sodium compound Ia was likewise obtained in the same yield, but when 3 moles were used the yield decreased to 20–30%.

Sodium Salt of Ethyl Bicyclo[3.3.0]octene-2,5-dione-hexacarboxylate (II).—To ethyl sodiomalonate prepared from ethyl malonate (96 g., 6 moles), sodium (13.8 g., 6 atoms) and absolute ethanol (400 cc.), was added dropwise ethyl trichloroethylidenemalonate (29 g., 1 mole) in 30 min. with cooling and stirring as above. In this procedure in order to keep the reaction temperature under 40° (usually 10–25°) the initial rate of addition was controlled carefully. A yellow precipitate was formed at first and then gradually turned to reddish-orange. The whole was allowed to stand overnight and acidified (*p*H 6.0) with ethanolic hydrogen chloride. The precipitate (42 g.) was collected on a filter. Continuous extraction with absolute ethanol gave 14 g. of sodium salt II as pale pink crystals, m.p. 245–246° dec. The ethanol-insoluble residue (sodium chloride) weighed 27 g. (29 g. by theory). When the above filtrate was concentrated to about half-volume under reduced pressure by an aspirator, an additional 6.2 g. of II was obtained. The total yield was 20.2 g. (45%). Three recrystallizations from ethanol gave almost colorless (slightly pink) square plates, m.p. 255–256° dec.; ferric chloride test in ethanol, orange-red; λ_{max} 344.5 (ϵ 53,800), 265 (ϵ 10,600) mμ; infrared bands at 1754, 1730, 1710, 1636 and 1555 cm.$^{-1}$.

Anal. Calcd. for $C_{26}H_{31}O_{14}Na$: C, 52.88; H, 5.25. Found: C, 52.82; H, 5.40.

Conversion of II to Ia.—Finely powdered sodium salt II (10 g.) was added to a solution of sodium ethoxide (1 g. of sodium in 100 cc. of absolute ethanol), yielding a yellow precipitate. The whole was refluxed for 4 hr. on a steam-bath. After cooling, acidification (*p*H 6.0) with ethanolic hydrogen chloride gave a reddish-orange precipitate. The whole was allowed to stand overnight, and the precipitate collected on a filter weighed 9.2 g. Continuous extraction with absolute ethanol furnished 6.2 g. (82%) of sodium salt Ia, m.p. 220–222° dec.

Ethyl Bicyclo[3.3.0]octene-2,5-dione-1,3,4,6-tetracarboxylate (I).—To finely powdered sodium salt Ia (3 g.) suspended in ether (about 100 cc.) in a separatory funnel, 1 *N* hydrochloric acid (50 cc.) was added, and the whole was vigorously shaken. This procedure was repeated three times, and the ether solution was washed with a small quantity of water. The ether was evaporated in a water-bath below 60°, yielding 1.7 g. of pale pink crystals. Repeated recrystallizations from ether–petroleum ether (b.p. 30–40°) gave I as pale pink square plates, m.p. 75° dec., ferric chloride test in ethanol, blood red to purple. Since this material was unstable and slowly changed in appearance when placed in an ampoule, its analytical value did not coincide with theoretical value, but its structure is thought to be unambiguous because of the similarity of its ultraviolet and infrared spectra with those of Ia and its formation of sodium, potassium and copper derivatives as described later; λ_{max} 342 (ϵ 47,300), 258 (9,200), 222 (ϵ 3,900) mμ; λ_{max} 300 mμ (ϵ

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[7] N. N. Chatterjee, B. K. Das and G. N. Barpujari, *J. Indian Chem. Soc.*, **17**, 161 (1940); E. R. Goss and C. K. Ingold, *J. Chem. Soc.*, 1268 (1928); R. N. Adhya, A. C. Ghosh and J. C. Bardhan, *ibid.*, 358 (1956); W. Treibs, R. Mayer and M. Madejski, *Chem. Ber.*, **87**, 356 (1954).

[8] (a) N. J. Leonard, H. S. Gutowsky, W. J. Middleton and E. M. Petersen, THIS JOURNAL, **74**, 4070 (1952); (b) W. Herz, *ibid.*, **78**, 1485 (1956).

[9] For example, glutaconaldehyde enolate sodium-salt has a characteristic absorption at 1546 cm.$^{-1}$, λ_{max} 362 mμ; its free compound is unstable and it forms no carbonyl derivatives (H. J. Dauben, Jr., and G. Feniak, unpublished observations); the acidity of glutaconaldehyde is pK_a (25°) = 5.75 (G. Schwarzenbach and K. Lutz, *Helv. Chim. Acta*, **23**, 1147 (1940)). The author greatly appreciates the kindness of the referee who indicated these points.

[10] Melting points are uncorrected. Ultraviolet spectra were run in 95% ethanol solution. Infrared spectra were determined using a salt prism and Nujol mull unless otherwise specified.

4,500) (one month later); infrared bands (in chloroform) at 1745, 1660 and 1573 cm.$^{-1}$.

Anal. Calcd. for $C_{20}H_{24}O_{10}$: C, 56.59; H, 5.70. Found: C, 51.94, 52.45, 52.61; H, 6.24, 6.18, 6.31.

Potentiometric titration of 20 cc. of a $1.17 \times 10^{-2}M$ aqueous solution of I (0.493 g. of I in 100 cc. of water) with 0.0262 *N* aqueous sodium hydroxide free from carbonate (quinhydrone electrode-saturated calomel electrode, 25 ± 0.1°) gave a potentiometric titration curve, from which the ionization constant of I was obtained; pK_{a_1} 2.13 (25 ± 0.1°).

Sodium salt Ia was formed when an ether solution of I was shaken vigorously with aqueous sodium sulfate or aqueous sodium chloride, or when compound I was added to sodium ethoxide solution.

Potassium Salt of I.—(i) When to an ether solution of free compound I, prepared from sodium salt Ia (5 g.), anhydrous potassium carbonate (about 10 g.) was added for drying purposes, the granular potassium carbonate was transformed into a fine orange powder with vigorous emission of gas. When the ether solution was evaporated 0.7 g. of I was recovered. The solid was collected on a filter, and washed with water to remove potassium carbonate, yielding 2.5 g. of potassium salt of a reddish-orange solid. Recrystallization from ethanol gave reddish-orange long plates, m.p. 246–249° dec., ferric chloride test in ethanol blood-red; λ_{max} 342 (ϵ 50,700), 258 (ϵ 10,200) mμ; infrared bands at 1745, 1720, 1690 and 1544 cm.$^{-1}$.

Anal. Calcd. for $C_{20}H_{23}O_{10}K$: C, 51.92; H, 5.01. Found: C, 51.58; H, 5.08.

(ii) An ether solution of I prepared from Ia (2 g.) was vigorously shaken with aqueous potassium iodide, yielding a reddish-brown solid. Recrystallization from ethanol gave a pure compound which was identical with the potassium salt of I, m.p. 246–249° dec., prepared above; yield 1.8 g.

Copper Derivative of I (With Miss A. Yoshizawa).—(i) An ether solution of I prepared from Ia (3 g.) was vigorously shaken with aq. copper acetate (1.4 g.) in a separatory funnel, yielding a dark gray solid. Recrystallization from acetone, then from aq. methanol, gave the copper derivative of I as pale greenish-yellow square plates, m.p. 231–233° dec., yield 1.6 g. (52%), ferric chloride test in ethanol, dark red, λ_{max} 332 mμ (ϵ 273,000).

Anal. Calcd. for $C_{20}H_{23}O_{10}\cdot{}^1/_2Cu$: C, 52.77; H, 5.09. Found: C, 51.99; H, 5.07.

(ii) To an ether solution of I (0.2 g.) was added satd. aq. copper acetate (0.1 g.), and the whole was shaken vigorously and slightly warmed in a water-bath, yielding the copper derivative almost quantitatively; yield 0.21 g. (95%).

Ethyl Bicyclo[3.3.0]octene-2-one-5-ol-1,3,4,6-tetracarboxylate (VI).—When catalytic reduction of 0.5 g. of the sodium salt Ia in 30 cc. of acetic acid containing 10% water (catalyst was 0.2 g. of platinum black) was carried out, 25.1 cc. (0.92 mole) of hydrogen was absorbed in 30 min. at which time hydrogen uptake ceased. The catalyst was filtered off, and the filtrate was evaporated under reduced pressure below 40°. Ether was added to the residue, which then was washed with water, dried, and the ether evaporated, leaving 0.4 g. of crystals. Recrystallization from aq. methanol gave almost colorless (slightly pink) square plates, m.p. 106.5–108°, ferric chloride test in ethanol reddish purple, λ_{max} 247 mμ (ϵ 13,000), infrared bands at 3312, 1742, 1692, 1672 and 1647 cm.$^{-1}$.

Anal. Calcd. for $C_{20}H_{26}O_{10}$: C, 56.33; H, 6.15. Found: C, 56.58; H, 6.15.

BUNKYO-KU, TOKYO, JAPAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY]

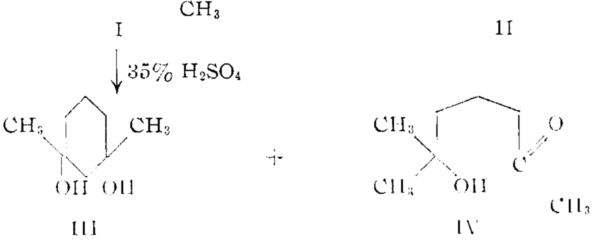
The Synthesis and Acid-catalyzed Cyclization of α-Methylheptenone

BY JERROLD MEINWALD AND JOHN A. YANKEELOV, JR.

RECEIVED APRIL 12, 1958

α-Methylheptenone (V) has been prepared from β-methylheptenone (I) by a reaction sequence consisting of hydration, acetylation and pyrolysis. Compound V cyclizes in 10% sulfuric acid to give a mixture of the *cis* and *trans* forms of 1,3-dimethylcyclohexan-1,3-diol; in 20% sulfuric acid only the *cis*-diol (IIIb) is formed. Compound I yields no carbocyclic products under comparable conditions. The mechanistic implications of these results are discussed, and the relationship to some other cyclization reactions noted.

Introduction.—The early claim that β-methylheptenone (I) gives rise to a dihydro-*m*-xylene (II) on vigorous acid treatment[1] recently has been shown to be substantially correct.[2a] It also has been found that a 1,3-dimethylcyclohexan-1,3-diol (III) is formed in small amounts, along with the ketol 6-methylheptan-6-ol-2-one (IV) when I is subjected to less strongly acidic conditions. These cyclizations of I to II and III are of interest since they seem at first sight to represent a novel type of reaction leading to carbocyclic systems.



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[1] A. Varley, *Bull. soc. chim. Paris*, [3] **17**, 175 (1897); *cf.* O. Wallach, *Ann.*, **395**, 74 (1913); **396**, 264 (1913).

[2] (a) J. Meinwald and R. F. Grossman, THIS JOURNAL, **78**, 992 (1956). (b) α-Methylheptenone has been the subject of a fair amount of controversy in the earlier chemical literature. Thus, Grignard and Verley debated about the content of α-methylheptenone in various samples of natural and synthetic "methylheptenone," but were unable to reach any agreement (see, for example, V. Grignard, J. Doeuvre and R. Escourou, *Compt. rend.*, **117**, 669 (1923); A. Verley, *Bull. soc. chim.*, **35**, 1653 (1924)). A considerable clarification of the situation was brought about by the infrared spectral studies of D. Barnard, L. Bateman, A. J. Harding, H. P. Koch, N. Sheppard and G. B. B. M. Sutherland, *J. Chem. Soc.*, 915 (1950). These authors studied methylheptenone from a variety of sources and found *no detectable amounts of the α-isomer*. These observations have been confirmed by infrared examination of the β-methylheptenone used in the present work.

One synthesis of α-methylheptenone has been reported recently (C. J. Albisetti, Jr., U. S. Patent 2,628,252 (1953); *C. A.*, **48**, 1423 (1954)), using a high-temperature, high-pressure reaction between isobutylene and methyl vinyl ketone. The properties of the product were not given in sufficient detail to allow a good comparison with the product obtained in the present investigation.

The first well-documented synthesis of α-methylheptenone (V) was carried out by H. Kappeler, D. Stauffacher, A. Eschenmoser and H. Schinz, *Helv. Chim. Acta*, **37**, 957 (1954). These authors prepared V by the action of methyllithium on the appropriate unsaturated acid. The properties of the product prepared by the new route described in the present work are in good agreement with those reported by the Swiss workers.