higher boiling fraction, b.p. 125–131° at 7 mm., indicated that this material was *syn*-7-iodo-exo-2-norbornyl acetate which was contaminated with a small amount of a diacetoxy derivative. Further purification could not be effected by fractional distillation, but a fair separation was obtained by chromatography through a 2 × 20 cm. neutral alumina column using petroleum ether–benzene for elution.

Anal. Calcd. for $C_9H_{13}O_2I$: C, 38.6; H, 4.7; I, 45.3. Found: C, 39.3; H, 4.6; I, 44.5.

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[CONTRIBUTION NO. 421 FROM THE CENTRAL RESEARCH DEPARTMENT, EXPERIMENTAL STATION, E. I. DU PONT DE NEMOURS AND CO.]

Dehydrohalogenation Products of Hexahydroterephthaloyl Chloride. A Bifunctional Ketene and a Bicyclo[2.2.1]-heptan-7-one Derivative

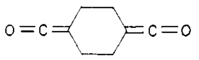
BY W. R. HATCHARD AND A. K. SCHNEIDER

RECEIVED MAY 27, 1957

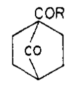
Two compounds of novel structure have been prepared by the dehydrohalogenation of hexahydroterephthaloyl chloride with triethylamine. With excess amine, the major product was 1,4-cyclohexanedimethenone, a crystalline reactive bisketene. Isolated in low yield by sublimation, the bisketene readily polymerized on slight warming. It reacted with moist air to form a mixture of *cis*- and *trans*-hexahydroterephthalic acids. Equimolar ratios of acid chloride and amine yielded 7-oxobicyclo[2.2.1]heptan-1-carbonyl chloride. Several derivatives retaining this structure were prepared by reaction of the keto-acid chloride with amines and alcohols.

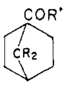
Efforts of several investigators to apply the trialkylamine–acid halide synthesis of ketenes to adipoyl chloride and sebacoyl chloride,[1] to suberoyl chloride and longer chain diacid chlorides,[2] and to hexahydroterephthaloyl chloride[3] have resulted in the formation of polymeric resins and reactive intermediates which polymerized on attempted isolation. Recently, while the present paper was in preparation, Blomquist and Meinwald[4] described the reaction of 9,10-dihydroanthracene-9,10-dicarbonyl chloride with triethylamine to yield anthraquinoketene, the first reported bisketene, with the unique exception of carbon suboxide.

We have found that reaction of hexahydroterephthaloyl chloride with triethylamine can lead to two monomeric products: a bisketene, 1,4-cyclohexanedimethenone (I), and 7-oxobicyclo[2.2.1]heptan-1-carbonyl chloride (II).

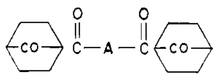


I





II, R = Cl V, R = R' = OCH_3
IV, R = OH VI, R = OCH_3,
VII, R = $N(C_2H_5)_2$ R' = OH



VIII, A = $-NHCH_2CH_2NH-$
IX, A = $-NH(CH_2)_4NH-$
X, A = $-OCH_2CH_2O-$

The bisketone I was prepared by the addition of the acid chloride to a fivefold excess of triethylamine in ethyl ether at 15–20°. Isolated in 8% yield by sublimation from the reaction mixture, it was a yellow, crystalline solid which spontaneously polymerized on slight warming. It reacted with moist air to form a mixture of *cis*- and *trans*-hexahydroterephthalic acids. It was identified by elemental analysis, by its infrared spectrum which exhibited a strong absorption band at 4.75 μ, and by its reaction with water. With 2,5-dimethylpiperazine in methylene chloride, the bisketene reacted to form a polyamide.

The bisketene also has been obtained in very low yield by the pyrolysis of hexahydroterephthaloyl chloride and of 7-oxo-bicyclo[2.2.1]heptan-1-carbonyl chloride at 575–625°.

The monodehydrohalogenation product II was formed concomitantly with the bisketene but was prepared in highest yield by the reverse addition of an equimolar quantity of triethylamine to a refluxing ether solution of the acid chloride. It was apparently not an intermediate in the formation of the bisketene since it was not further dehydrohalogenated under the conditions of the ketene preparation. Assignment of the bicyclic ketone structure II[5] rather than the isomeric ketene–acid chloride structure III was based on infrared spectra and failure of the product to undergo dimerization, halogen addition or dehydrohalogenation reactions. This compound exhibited a strong absorption band at 5.6 μ, similar to the spectra of previously described, more highly substituted bicyclo[2.2.1]heptan-7-one derivatives.[6,7] No bicyclo[2.2.1]-heptan-7-one derivatives having substitution only in the 1-position have been described previously.

III

Hydrolysis of II in water, dilute base or concentrated hydrochloric acid yielded a mixture of *cis*- and *trans*-hexahydroterephthalic acids. Attempts to prepare the keto-acid IV by stepwise hydrolysis of II failed, but this compound was obtained indirectly by reaction of the keto-acid chloride with acetic acid. The keto-acid readily hydrolyzed to the mixed hexahydroterephthalic acids. An attempt

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[1] J. C. Sauer, THIS JOURNAL, **69**, 2444 (1947).

[2] A. T. Blomquist and R. R. Spencer, *ibid.*, **70**, 30 (1948).

[3] J. M. Witzel, Doctoral Thesis, Cornell University, Ithaca, N. Y.

[4] A. T. Blomquist and Y. C. Meinwald, THIS JOURNAL, **79**, 2021 (1957).

[5] The structure was first suggested by Professor W. S. Johnson of the University of Wisconsin.

[6] C. F. H. Allen and J. A. Van Allan, *J. Org. Chem.*, **20**, 323 (1955).

[7] P. Wilder, Jr., and A. Winston, THIS JOURNAL, **78**, 868 (1956).

to thermally decarboxylate the keto acid IV was not successful, but this is not surprising in view of the reported resistance of bridgehead carboxyl compounds to decarboxylation.[8]

Alcoholysis of II did not rupture the ketone linkage but gave instead a ketal-ester V which could be hydrolyzed stepwise to a ketal-acid VI and thence to a mixture of *cis*- and *trans*-hexahydroterephthalic acids.

The keto-acid chloride II reacted with molar equivalents of amines or alcohols to form keto-amides or keto-esters. Thus, reaction with diethylamine yielded N,N-diethyl-7-oxo-bicyclo[2.2.1]heptan-1-carboamide (VII). Diamides VIII and IX were formed when the keto-acid chloride reacted with ethylenediamine and with hexamethylenediamine. In similar fashion, reaction with ethylene glycol gave a diester X which retained the bicyclic ketone structure.

Experimental

Hexahydroterephthaloyl Chloride.—Hexahydroterephthaloyl chloride was prepared by the method of Malachowski, *et al.*[9] No difference in reaction with triethylamine was noted between the pure *trans*-acid chloride and a 70/30 mixture of the *cis*/*trans*-acid chlorides.

1,4-Cyclohexanedimethenone (I).—A solution of 25 g. (0.12 mole) of hexahydroterephthaloyl chloride in 100 ml. of anhydrous ether was added dropwise over 30 minutes to a stirred mixture of 125 g. (1.25 moles) of anhydrous triethylamine in 500 ml. of ether while the temperature was maintained at 15–20° by cooling. After being stirred for an additional two hours and standing overnight at room temperature, the reaction mixture was filtered through a sintered glass funnel under nitrogen pressure. Mineral oil (50 ml.) was added to the yellow filtrate and then the mixture was concentrated by distillation at 0–20° under reduced pressure maintained by an oil-pump. The residual, yellow oil began to polymerize exothermically, raising the internal temperature to 40–60°. During the heat evolution, yellow crystals formed in the still-head. The yield of bisketene was 1.3 g. (8%). The infrared spectrum showed a strong band at 4.75 μ. Other ketone bands were absent. *Anal.* Calcd. for $C_8H_8O_2$: C, 70.5; H, 5.9. Found: C, 69.9; H, 5.9.

The ether-insoluble material filtered from the reaction weighed 29 g. (88% for triethylamine hydrochloride) and was completely soluble in water.

Mixing of a methylene chloride solution of the bisketene with a solution of 2,5-dimethylpiperazine caused immediate loss of color and the formation of a polymeric precipitate tentatively identified by analysis as a polyamide. The polymer could be pressed to a brittle film. *Anal.* Calcd. for $(C_{14}H_{22}O_2N_2)_x$: N, 11.2. Found: N, 10.5.

7-Oxo-bicyclo[2.2.1]heptan-1-carbonyl Chloride (II).—A solution of 29 g. (0.29 mole) of triethylamine in 100 ml. of anhydrous ether was added dropwise over 30 minutes to a stirred mixture of 50 g. (0.24 mole) of hexahydroterephthaloyl chloride in 550 ml. of ether maintained at reflux temperature. After being stirred for an additional 1.5 hours, the mixture was filtered under nitrogen pressure. The triethylamine hydrochloride, after drying in air, weighed 32 g. (95%) and was completely soluble in water. Distillation of the filtrate at reduced pressure gave a colorless fraction boiling at 66.5–68° (1 mm.), yield 25 g. (60%), $n^{25}D$ 1.5003. The solidified distillate melted at 29–30°. The infrared absorption spectrum showed bands at 5.5 and 5.6 μ. *Anal.* Calcd. for $C_8H_9O_2Cl$: C, 55.6; H, 5.2; Cl, 20.5. Found: C, 55.8; H, 5.5; Cl, 20.3.

7-Oxo-bicyclo[2.2.1]heptan-1-carboxylic Acid (IV).—A mixture of 5.0 g. of the keto-chloride II and 25 ml. of glacial acetic acid was warmed on the steam-bath for one hour after which the volatile products were removed by distillation at reduced pressure. The slightly pasty residue, after trituration in ether and filtration, yielded 1.8 g. of a white solid, m.p. 155–159°. Recrystallization from ether gave a product which melted at 158–160°. *Anal.* Calcd. for $C_8H_{10}O_3$: C, 62.3; H, 6.5; neut. equiv., 154. Found: C, 62.4; H, 6.5; neut. equiv., 150.

A solution of the keto-acid in dilute alkali was converted to a mixture of *cis*- and *trans*-hexahydroterephthalic acids identified by melting points and neutral equivalents.

Methyl 7,7-Dimethoxybicyclo[2.2.1]heptane-1-carboxylate (V).—A mixture of 150 ml. of methanol and 10 g. of II was heated under reflux for 30 minutes, diluted with 300 ml. of water and extracted with three 100-ml. portions of ether. After being washed several times with water, the extract was dried over calcium chloride and distilled. The portion which distilled at 88–90° (4 mm.) weighed 8.7 g. (90%) and was partially solid at room temperature. Recrystallization from petroleum ether yielded a product which melted at 39–40°. The infrared spectrum had a band at 5.75 μ (for ester carbonyl) and no band at 4.6 μ (expected for a ketone carbonyl). *Anal.* Calcd. for $C_{11}H_{18}O_4$: C, 61.7; H, 8.5; mol. wt., 214. Found: C, 61.7, 61.7; H, 8.7, 8.5; mol. wt., 204.

7,7-Dimethoxybicyclo[2.2.1]heptane-1-carboxylic Acid (VI).—A mixture of 3.0 g. of V, 3 g. of sodium hydroxide and 20 ml. of water was heated under reflux for 3 hours, then cooled and neutralized with hydrochloric acid. The solid acid which formed was collected on a filter and triturated in ethyl ether. Only 0.1 g. (m.p. 300–301°, *trans*-hexahydroterephthalic acid) was insoluble. Evaporation of the ether solution gave 1.1 g. of a crude mixture which had a neutral equivalent of 174. Recrystallization from water gave a product which melted at 111–112°. *Anal.* Calcd. for $C_{10}H_{16}O$: C, 59.9, H, 8.0, neut. equiv., 200. Found: C, 59.9; H, 7.8; neut. equiv., 219.

Overnight refluxing of the ketal-ester with aqueous alkali or concentrated hydrochloric acid yielded a mixture of *cis*- and *trans*-hexahydroterephthalic acids.

N,N-Diethyl-7-oxo-bicyclo[2.2.1]heptan-1-carboamide (VII).—A solution of 8.6 g. (0.05 mole) of II in 50 ml. of methylene chloride was added quickly to a mixture of 4.0 g. (0.055 mole) of diethylamine, 2.65 g. (0.025 mole) of sodium carbonate, 100 ml. of ice-water and 50 ml. of methylene chloride at 5° while the mixture was stirred in a Waring blendor. Stirring was continued for 10 minutes, and the reaction mixture was allowed to stand for an additional 10 minutes. The aqueous layer was separated, extracted several times with methylene chloride, and the extracts were added to the original methylene chloride layer. After being dried, the methylene chloride solution was evaporated and the residue distilled at reduced pressure. The product which distilled at 94–97° (0.25 mm.) (6.0 g., 58%) had $n^{25}D$ of 1.4978 and infrared absorption bands at 5.65 and 6.15 μ. *Anal.* Calcd. for $C_{12}H_{19}O_2N$: C, 69.2; H, 9.1; N, 6.7. Found: C, 68.8; H, 9.1; N, 6.9.

N,N′-Ethylenebis-(7-oxo-bicyclo[2.2.1]heptan-1-carboamide) (VIII).—A solution of 8.6 g. (0.05 mole) of II in 50 ml. of methylene chloride was caused to react with a mixture of 2.65 g. (0.025 mole) of sodium carbonate, 1.62 g. (0.027 mole) of ethylenediamine, 200 ml. of ice-water and 50 ml. of methylene chloride as described in the preparation of VII. From the methylene chloride layer there was obtained 3.8 g. of white solid residue. Two recrystallizations from a mixture of benzene and methylene chloride gave 1.5 g. (18%) of product which melted at 215–215.5°. *Anal.* Calcd. for $C_{18}H_{24}O_4N_2$: C, 65.2; H, 7.2; N, 8.4. Found: C, 65.1; H, 7.4; N, 8.4.

N,N′-Hexamethylenebis-(7-oxo-bicyclo[2.2.1]heptan-1-carboamide) (IX).—By the method described above, 3.10 g. (0.027 mole) of hexamethylenediamine yielded 7.5 g. of white, crystalline solid (74%). After recrystallization from benzene, the product melted at 149.5–150.5°. *Anal.* Calcd. for $C_{22}H_{32}N_2O_4$: C, 68.1; H, 8.3; N, 7.2. Found: C, 67.7; H, 8.4; N, 7.1.

Ethylenebis-(7-oxo-bicyclo[2.2.1]heptan-1-carboxylate) (X).—A mixture of 2.6 g. (0.042 mole) of ethylene glycol and 25 ml. of methylene chloride was added slowly to a solution of 15 g. (0.085 mole) of II in 25 ml. of methylene chloride. The mixture was heated under reflux for 30 minutes and then mixed with a solution of 9 g. of sodium carbonate in 100 ml. of water and allowed to stand 15 minutes. About 20 ml. of chloroform was added and the organic layer was separated, washed several times with water, dried over magnesium sulfate, and evaporated to a pot temperature of 130° at 2 mm. pressure. The sirupy residue weighed 9.4 g.

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[8] F. S. Fawcett, *Chem. Revs.*, **47**, 245 (1950).

[9] R. Malachowski, J. J. Wasawska, S. Jozkiewicz, J. Adamiczka and G. Zimmerman-Pasternak, *Ber.*, **71B**, 759 (1938).

(65%). *Anal.* Calcd. for $C_{18}H_{22}O_6$: C, 61.5; H, 6.5; mol. wt., 334. Found: C, 61.5; H, 6.5; mol wt., 333.

The sirup dissolved in hot water to form a solution from which a mixture of *cis*- and *trans*-hexahydroterephthalic acids was isolated.

WILMINGTON, DELAWARE

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE, THE WEIZMANN INSTITUTE OF SCIENCE]

Unsaturated Macrocyclic Compounds. IV. The Oxidation of Terminal Diacetylenes to Macrocyclic Tetraacetylenes

BY F. SONDHEIMER, Y. AMIEL AND R. WOLOVSKY

RECEIVED JULY 1, 1957

The scope of the cyclization reaction of terminal diacetylenes, previously carried out with octa-1,7-diyne (Ia), has been investigated. Nona-1,8-diyne (Ib) and hepta-1,6-diyne (Id) give the corresponding cyclic tetraacetylenes IIb and IId, respectively, the yields becoming better as the ring size decreases. In addition compounds derived by linear coupling result. These linear types of substances are the sole identified products when the reaction is performed with deca-1,9-diyne (Ic) and hexa-1,5-diyne (Ie). The parallel α-diacetylene rods in cyclotetradeca-1,3,8,10-tetrayne (IId) are very close to each other. The substance consequently exhibits unusual physical properties, which are discussed.

The coupling of two molecules of octa-1,7-diyne (Ia) through oxidation with oxygen in the presence of cuprous chloride and ammonium chloride to yield cyclohexadeca-1,3,9,11-tetrayne (IIa) besides linear products was described in the previous paper of this series.[1] This appears to be one of the few reactions in which two molecules of a symmetrical difunctional compound condense at both ends to give a carbocyclic large ring. Other examples of this type of reaction are the pyrolysis of heavy metal salts of aliphatic terminal dicarboxylic acids,[2a] treatment of the corresponding dinitriles with a sodium alkyl-anilide[2b] or of the diketenes with tertiary amines,[2c] all of which lead eventually to macrocyclic diketones derived from two molecules of the starting material in addition to the cyclic monomeric monoketones. Into this category also fall the acyloin condensation of diethyl hexahydrophthalate to produce what is probably an eight-membered di-acyloin[2d] and the reaction of certain terminal dibromoalkylbenzenes with sodium or lithium phenyl to give large ring hydrocarbons incorporating phenyl groups.[2e–h] It was of interest to investigate the generality of the cyclization reaction of terminal diacetylenes, especially in order to find out if cyclic tetraacetylenes of type II could be obtained in which the two α-diacetylene chains are sufficiently close for electronic interaction to occur. In the present paper we describe the results obtained by submitting the four aliphatic diacetylenes Ib, Ic, Id and Ie to the coupling reaction.[3]

All the reactions were carried out by bubbling oxygen through a mixture of the diacetylene, cuprous chloride and ammonium chloride in aqueous ethanol acidified with hydrochloric acid, at 55°. The products were best purified by chromatography on alumina. The next higher homolog to the previously studied Ia was nona-1,8-diyne (Ib) (readily prepared from 1,5-dibromopentane and sodium acetylide in liquid ammonia)[4] and was found to give three products. The least polar was a crystalline chlorine containing substance $C_{18}H_{22}Cl_4$, obtained in 5% yield, which was apparently not acetylenic (infrared) but showed high intensity absorption maxima at 228 and 235 mμ in the ultraviolet; its structure is now under investigation. Next in order of polarity was a hydrocarbon (2% yield), $C_{18}H_{20}$, m.p. 212°, the infrared spectrum of which showed bands at 2239 and 2138 cm.$^{-1}$ (disubstituted diacetylene) but not at *ca.* 3300 or 2100 cm.$^{-1}$ (lack of terminal acetylene).[1] It thus seems to be cyclic, and it was shown to be the cyclic dimer, cycloöctadeca-1,3,10,12-tetrayne (IIb), through full hydrogenation to cycloöctadecane (IIIb). Lastly, the linear dimer, octadeca-1,8,10,17-tetrayne (IVb), m. p. 22°, was obtained in *ca.* 60% yield; its structure was confirmed by the infrared spectrum (presence of terminal acetylene as well as disubstituted α-diacetylene) and by hydrogenation to *n*-octadecane (Vb). No linear tetramer VIb could be isolated and it must have been present in only small amounts if at all.

The next higher homolog, deca-1,9-diyne (Ic),[5] on being coupled under the usual conditions no longer yielded the cyclic dimer in appreciable amounts. Besides *ca.* 30% of a chlorine-containing substance, the linear dimer, eicosa-1,9,11,19-tetrayne (IVc), converted to *n*-eicosane (Vc) by full hydrogenation, was formed in 60% yield. In addition the linear tetramer, tetraconta-1,9,11,19,21,29,31,39-octayne (VIc) could be isolated in quite small yield (3%); its structure was established through hydrogenation to *n*-tetracontane (VIIc). The fact that in the case of Ib and Ic very little or none of the linear tetramers is obtained is doubtlessly due to the increasing insolubility of the dimers (type IV) in the aqueous ethanol employed as the carbon chain is increased.

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[1] For Part III, see F. Sondheimer and Y. Amiel, THIS JOURNAL, **79**, 5817 (1957).

[2] (a) L. Ruzicka, *et al.*, *Helv. Chim. Acta*, **11**, 496, 670 (1928); **13**, 1152 (1930); **17**, 78 (1934); (b) K. Ziegler and A. Lüttringhaus, *Ann.*, **511**, 1 (1934); (c) A. T. Blomquist and R. D. Spencer, THIS JOURNAL, **70**, 30 (1948); (d) A. C. Cope and E. C. Herrick, *ibid.*, **72**, 983 (1950); (e) W. Baker, *et al.*, *J. Chem. Soc.*, 27 (1945); 200, 1114, 1118 (1951); (f) H. Steinberg and D. J. Cram, THIS JOURNAL, **74**, 5388 (1952); (g) E. D. Bergmann and Z. Pelchowicz, *ibid.*, **75**, 4281 (1953); (h) see also C. J. Brown and A. C. Farthing, *Nature*, **164**, 915 (1949); *J. Chem. Soc.*, 3261, 3265 (1953).

[3] For a preliminary communication, see Y. Amiel, F. Sondheimer and R. Wolovsky, *Proc. Chem. Soc.*, 22 (1957). See also G. Eglinton and A. R. Galbraith (*Chemistry & Industry*, 737 (1956)) for an independent investigation into the coupling of higher terminal diacetylenes to give cyclic poly-acetylenes.

[4] A. L. Henne and K. W. Greenlee, THIS JOURNAL, **67**, 484 (1945).

[5] W. M. Lauer and W. J. Gensler, *ibid.*, **67**, 1171 (1945).