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Synthesis of Octene-4-dione-2,7 from 1,8-Bis(diazo)-octene-4-dione-2,7*

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The compound méntioned in the title has been prepared from 1,8-bis(diazo)-octene-4-dione-2,7 by reduction of the intermediate 1,8-dichloro-octene-4-dione-2,7 with zinc in acetic acid. The overall yield was 68%.

Several papers describing the synthesis of octene-4-dione-2,7 (I) appeared in the recent literature. The diketone I was extensively used for building of the central part of β-carotene and other carotenoids. [1, 2, 3] Octene-4-dione-2,7 was prepared by several routes. Karrer and Eugster[4] condensed anhydrous glyoxale with acetoacetic acid, and reduced the obtained octadiene-3,5-dione-2,7 (II) to the diketone I with zinc and glacial acetic acid in pyridine. The total yield of diketone I was less that 3%. Sondheimer and Weedon[5] gave in 1950 a preliminary account on the preparation of diketone I from dihydromuconic acid by the action of dimethyl cadmium, in a yield of 15%. Similar method was also used by Milas and collaborators[3,6] for the preparation of octene-4-dione-2,7. In 1951 Inhoffen and colaborators[7] prepared the diketone I from the readily available octadiyne-3,5-diol-2,7 (III)[8] which was hydrogenated by a poisoned palladium catalyst, the reduced product was then oxidized with *tert.*-butyl chromate to give diketone II, which was then reduced to octene-4-dione-2,7 following the method of Karrer an Eugster. The overall yield was about 3%.

$$\mathrm{MeCO{-}CH_2{-}CH{=}CH{-}CH_2{-}COMe} \qquad \mathrm{I}$$
$$\mathrm{MeCO{-}CH{=}CH{-}CH{=}CH{-}COMe} \qquad \mathrm{II}$$
$$\mathrm{MeCH(OH){-}C{\equiv}C{-}C{\equiv}C{-}CH(OH)Me} \qquad \mathrm{III}$$

Attempts to convert 1,3,5,7-octatetraene-diol-2,7-tetracarboxylic ethyl ester-1,1,8,8 (IV)[9,10] and 1,3,5,7-octatetraene-diol-2,7-dicarboxylic ethyl ester-1,8 (V)[10] to diketone I proved unsuccessful.

$$\mathrm{(EtO_2C)_2C{=}C(OH){-}CH{=}CH{-}CH{=}CH{-}C(OH){=}C(CO_2Et)_2} \qquad \mathrm{IV}$$
$$\mathrm{EtO_2C{-}CH{=}C(OH)\,CH{=}CH{-}CH{=}CH{-}C(OH){=}CH{-}CO_2Et} \qquad \mathrm{V}$$

A very elegant method for the preparation of the diketone I from the diacetylenic glycol III was published in 1952 by Ahmad, Sondheimer, Weedon and Woods[9]. The glycol III was first reduced with lithium aluminum hydride to the corresponding diene carbinol, which was then oxidized with manganese

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dioxide in acetone, and the obtained diketone II was converted to octene-4-dione-2,7 following the method of Karrer and Eugster. The overall yield based on diyne glycol III was 40%.

In the present paper we wish to report our own method for the preparation of octene-4-dione-2,7 from dihydromuconic acid. Dihydromuconic acid can be conveniently prepared from 1,4-dibromo- and 1,4-dicyano-butene-2[10] or by reduction of muconic acid with sodium amalgam[11]. Dihydromuconic acid was converted to dihydromuconyl dichloride and to 1,8-bis(diazo)-octene-4-dione-2-7 (IV) following the method of Grundmann[12]. When diazoketone IV was treated with dry hydrochloric acid in ether solution according to the method of Bacchetti[13], the trichloro derivative VI was obtained. But no addition of hydrochloric acid to the double bond occured when aqueous hydrochloric acid was used, and almost quantitative yield of 1,8-dichloro-octene-4-dione-2,7 (V) was obtained.

$N_2CHCO—CH_2—CH{=}CH—CH_2—COCHN_2$ IV

$ClCH_2CO—CH_2—CH{=}CH—CH_2—COCH_2Cl$ V

$ClCH_2CO—CH_2—CHCl—CH_2—CH_2—COCH_2Cl$ VI

The, dichloro diketone V was reduced with zinc in acetic acid to the desired octene-4-dione-2,7. The overall yield calculated on the bases of diazoketone IV was 68%.

We consider that the method described in this paper represents a very cheap and simple method for the preparation of octene-4-dione-2,7.

EXPERIMENTAL

1,8-Dichloro-octene-4-dione-2,7 (V)

1,8-Bis(diazo)-octene-4-dione-2,7 (3.5 g., 0.0182 mole) was dissolved in 60 ml. of ethyl acetate and treated with 30 ml. of 10% hydrochloric acid, under cooling with tap water, until the evolution of nitrogen ceased. The aqueous layer was separated, extracted with two 10-ml. portions of ethyl acetate, the combined organic layer washed with a saturated sodium bicarbonate solution, dried over magnesium sulfate, and the solvent evaporated under reduced pressure. 3.7 g. (97.4%) of slightly yellow needles melting at 92—93° were obtained. An analytical sample was crystallized twice from ethanol to a melting point of 95—97°.

Anal. 16.54 mg. subst. 28.00 mg. CO_2, 7.11 mg. H_2O
11.36 mg. subst. 5.41 ml. 0.02*N* $AgNO_3$
$C_8H_{10}Cl_2O_2$ (209.074) calc'd: C 45.96; H 4.82; Cl 33.92%
found: C 46.19; H 4.81; Cl 33.77%

1,3,8-Trichloro-octanedione-2,7 (VI)

1,8-Bis(diazo)-octene-4-dione-2,7 (2 g., 0.0095 mole) was suspended in 100 ml. of ether and under cooling with ice, the ether was saturated with dry hydrochloric acid. The solution was neutralized with sodium carbonate, ether layer dried over potassium carbonate, and solvent evaporated under reduced pressure. A crop of 1.2 g. of a dark colored semicrystalline product was obtained. The crude diketone was crystallized from 7 ml. of ethanol to give 0.6 g. of white needles melting at 60—65°. The product was dissolved in 4 ml. of a mixture of benzene-petroleum ether (1 : 1), treated with charcoal, and the semicrystalline product which separated upon the addition of 1 ml. of petroleum ether was discarded. The benzene-petroleum ether solution was cooled to —5° and the crystalline precipitate (150 mg.) was collected by filtration; m. p. 64—65°. A sample for analysis was recrystallized from a mixture of benzene-petroleum ether (1 : 1) to a melting point of 67—68°.

Anal. 17.73 mg. subst.: 25.37 mg. CO_2, 6.89 mg. H_2O
11.41 mg. subst.: 6.98 ml. 0.02*N* $AgNO_3$
$C_8H_{11}Cl_3O_2$ (245.539) calc'd.: C 39.13; H 4.51; Cl 43.33%
found: C 39.04; H 4.34; Cl 43.38%

Octene-4-dione-2,7 (I)

1,8-Dichloro-octene-4-dione-2,7 (1 g., 0.0048 mole) and 2.5 g. powdered zinc were suspended in 50 ml. of 80% acetic acid and heated for half an hour at a temperature of 60—70°. The reaction mixture was then diluted with 40 ml. of water, neutralized with solid sodium carbonate, extracted with six 20-ml. portions of ether and organic layer was dried over magnesium sulfate. Evaporation of ether gave 580 mg. of a crystaline product which was purified for analysis by distillation at a temperature of 65—75° (bath temperature) and a pressure of 0.05 mm., as colorless oil which solidified soon to a crystalline mass melting at 34—36°.* Yield of the pure diketone I was 490 mg. (70%) .

Anal. 17.21 mg. subst.: 43.25 mg. CO_2, 13.20 mg. H_2O
$C_8H_{12}O_2$ (140.18) calc'd.: C 68.54; H 8.63%
found: C 68.58; H 8.58%

2,4-*Dinitrophenylhydrazone* was prepared from 100 mg. of diketone I and 10 ml. of an alcoholic solution containing 250 mg. of 2,4-dinitrophenylhydrazine. The crude hydrazone (260 mg.) was recrystallized twice from a mixture of nitrobenzene-ethanol (1 : 2) to a melting point of 207—209° (corr.)*

Anal. 13.28 mg. subst.: 23.46 mg. CO_2, 5.14 mg. H_2O
1.06 mg. subst.: 0.206 ml. N_2 (23°, 760 mm.)
$C_{20}H_{20}N_8O_8$ (500.42) calc'd.: C 48.01; H 4.02; N 22.39%
found: C 48.21; H 4.33; N 22.41%

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* Reported m. p. 35—36°.

* Reported m. p. 208—209°.

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IZVOD

Priprava okten-4-diona-2,7 iz 1,8-bis(diazo)-okten-4-diona-2,7

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Okten-4-dion-2,7 (I) intermedijer u sintezi karotena i karotenoida priređen je, u iskorišćenju od 68%, iz 1,8-bis(diazo)-okten-4-diona-2,7 (IV). Diazo-keton IV preveden je djelovanjem solne kiseline u 1,8-diklor-okten-4-dion-2,7 (V), koji redukcijom s cinkom u 80%-tnoj octenoj kiselini daje diketon I. Djelovanjem suhe solne kiseline na diazo-keton IV dobiven je 1,3,8-triklor-okten-4-dion-2,7 (VI).

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