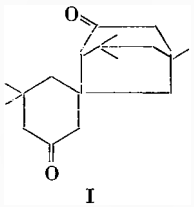
KURZE MITTEILUNGEN

Bis am 20. des Monats bei der Redaktion eingehende Kurze Mitteilungen werden in der Regel am 15. des folgenden Monats veröffentlicht
Es werden auch Manuskripte aus dem Ausland angenommen

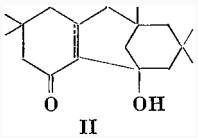
The Alkali-Catalyzed Self-Condensation of Isophorone, Part II[1]

The self-condensation of isophorone in the presence of solid potassium hydroxide in non polar solvents (ether or benzene) was found to yield the diketone dimer I togheter with the hydroxyketone II. The influence of several parameters on the ratio of I to II was investigated.

The base-catalyzed dimerization of 3-substituted 2-cyclohexen-1-ones and of isophorone in particular is recorded in the literature.[1,2] The isophorone diketone dimer[2] and hydroxyketone dimer[1] have been assigned structures I and II respectively.



I



II

[1] Part I: G. KABAS and H. C. RUTZ, *Tetrahedron 22* (1966) 1219.
[2] G. BUECHI, J. H. HANSEN, D. KNUTSON and E. KOLLER, *J. Amer. Chem. Soc. 80* (1958) 5517.

We were particularly interested in getting large quantities of the diketone I but the reported procedure[2] was found not to be easily applicable to large scale preparation. Thus, with the object of avoiding the use of sodium amide, several other bases were tried at different reaction conditions and it was found that by stirring a solution of isophorone in benzene or in ether in the presence of powdered potassium hydroxide a mixture of the two isophorone dimers (I and II) was obtained. Sodium hydroxide, sodium methoxide and ethoxide, calcium oxide and hydroxide, and benzyl trimethylammonium hydroxide were tried as catalysts, but they failed to show any efficiency. The separation of the two dimers could easily be effected by taking advantage of the greater tendency of the diketone dimer I to crystallize, and its greater insolubility in petroleum ether (b. p. 40 to 70°). In order to obtain high yields of I and to avoid the formation of II the influence of several reaction parameters, i. e. catalyst concentration, temperature, and reaction time on the isophorone self condensation

was investigated. Table I summarizes the influence of different potassium hydroxide-isophorone molar ratios on the isophorone conversion and on the dimer distribution. With a molar ratio of 3 : 1, the highest yield of compound I was obtained, whereas the highest conversion of isophorone could be reached already with a molar ratio of 1.5 : 1.

Table I. Influence of Potassium Hydroxide-Isophorone Molar Ratios on the Dimerization of Isophorone[a]

Molar ratio[b]	Isophorone Conversion, %	Dimer I yield ratio, %	Dimer II yield ratio, %
0.2	25	45	55
0.5	42	40	60
1.0	54	44	56
1.5	61	53	47
2.0	61	59	41
3.0	60	71	29
4.0	61	71	29

[a] In these experiments, 0.4 mole of isophorone in 400 ml of refluxing ether was stirred for 5 hours in the presence of the given amount of powdered potassium hydroxide.
[b] Molar ratios of potassium hydroxide to isophorone.

The influence of temperature and reaction time on the alkali-catalyzed dimerization of isophorone was investigated in two more experimental series not reported here in detail. It was found that an increase in reaction time and/or reaction temperature results in the disappearance of dimer I in favour of the formation of dimer II. With a two hour reaction time and a reaction temperature of 38–40° the highest proportion of diketone dimer I was obtained.

The last reaction parameter investigated was the effect of potassium hydroxide purity[3] on isophorone conversion and dimer distribution. It was found that by adding water to the powdered potassium hydroxide suspension in benzene or ether, the conversions are reduced considerably, the dimer ratio, however, remaining almost constant at the given alkali-isophorone molar ratio. Already with a 60–75% potassium hydroxide purity, the conversion was reduced to almost a negligible value.

From these results it may be seen that favourable conditions for the preparation of dimer I exist, when a molar ratio of 3 of potassium hydroxide to isophorone and a two hours reaction time in refluxing ether are used. Thus, with a 56% conversion of isophorone, dimer I is obtained in 85% yield.

Although a large excess of potassium hydroxide has to be used to obtain dimer I, this process is easily adaptable to large scale preparations—, the reaction mixture is filtered and the potassium hydroxide can be used for a second preparation. Moreover, also other 3-substituted 2-cyclohexen-1-ones, such as 3-methyl- and 3,5-dimethyl-2-cyclohexen-1-one could be dimerized to the corresponding diketone dimers with potassium hydroxide in ether.

[3] Since commercial potassium hydroxide pellets are 85% of KOH and, presumably, 15% of water, the term purity refers to potassium hydroxide concentration.

Experimental[4]

Commercial potassium hydroxide pellets (85–86% purity) were powdered in a ball-mill and sieved through a 8-DIN sieve. Ether and benzene were purified in the conventional method and dried over sodium wire.

Dimerization of isophorone. To a stirred suspension of 785 g (12 moles of 85.7% purity) of powdered potassium hydroxide in 2 liters of dry ether, a solution of 552 g (4 moles) of freshly distilled isophorone in 2 liters of dry ether was added. While stirring, the reaction mixture was refluxed for two hours. The color changed from yellow to brown-red. After cooling, the solution was filtered and the alkali washed with fresh ether. The combined ether extracts were washed in succession with diluted hydrochloric acid, sodium bicarbonate and water. Ether was removed from the dried solution and the residue distilled. After a forerun of unreacted isophorone (226.1 g), the mixture of dimers I and II (308.2 g, 56% based on the isophorone charged) was collected with b.p. 135–150° (0.1 mm). The dimers were dissolved in the minimum amount of refluxing ether and petrol ether (b.p. 40–70°) was added until incipient crystallization. After standing overnight in the freezer, 240 g of dimer I, m.p. 120–122°, was obtained. From the mother liquors an additional 21.5 g of dimer I could be obtained. The combined crystalline products (261.5 g, 85%) were again crystallized from the same solvents mixture and melted at 121–122° (lit. m.p. 121–122°)[2]. From the mother liquors, 40 g of pure dimer II, m.p. 86–88° (lit. m.p. 86–88°)[1] was obtained.

2,4-Dinitrophenylhydrazone of the diketone I. The diketone I in 82% yield gave only a mono 2,4-dinitrophenylhydrazone in the form of yellow-orange needles, m. p. 181–182°.

Anal. Calcd. for $C_{24}H_{32}N_4O_5$: C, 63.14; H, 7.07; N, 12.27. Found: C, 63.23; H, 7.06; N, 12.25.

Semicarbazone of the diketone I. The monosemicarbazone was obtained in 65% yield using the conventional method, m. p. 225–226° (dec.).

Anal. Calcd. for $C_{19}H_{31}N_3O_2$: C, 68.43; H, 9.37; N, 12.60. Found: C, 68.32; H, 9.41; N, 12.54.

Dimerization of 3-methyl-2-cyclohexen-1-one. A mixture of 22 g (0.2 mole) of 3-methyl-2-cyclohexen-1-one and 39.2 g (0.6 mole; 85.7 purity) of powdered potassium hydroxide in 200 ml of dry ether was stirred and refluxed for two hours. The reaction mixture was then cooled, filtered and the alkali washed with ether. The combined ether extracts were washed neutral with water, dried and distilled. Product (10.5 g) was collected at 120–125° (0.1 mm). After one crystallization from ether-petrol ether, the diketone dimer (8.6 g, 39%) of the title compound melted at 72–73° (lit. m.p. 73–74°).[2]

Dimerization of 3,5-dimethyl-2-cyclohexen-1-one. A mixture of 24.8 g (0.2 mole) of 3,5-dimethyl-2-cyclohexen-1-one and 39.2 g (0.6 mole; 85.7 purity) of powdered potassium hydroxide in 200 ml of dry ether was stirred and refluxed for two hours. After cooling, the ether layer was separated from the alkali and the alkali washed with ether. The combined ether extracts were washed neutral with water, dried and distilled. Product (21.9 g, 88.5%) was collected at 145–152° (0.1 mm) and crystallized from ether-petrol ether to yield 18.2 g of a mixture of the two diketone dimers of 3,5-dimethyl-2-cyclohexen-1-one[2]. The infrared of this dimer mixture (m. p. 90–110°) showed the absence of hydroxyl groups.

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[4] Melting points and boiling points are uncorrected.
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