FREE-RADICAL ADDITION OF CYCLOPENTANONE AND CYCLOHEXANONE TO α -OLEFINS AND ALLYL ETHERS

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Several variants of the synthesis of aliphatic carboxylic acids by the cleavage of five- and six-membered alicyclic compounds have been used. Fieser [1] proposed to oxidize 1-alkylcyclopentanols and 1-alkylcyclohexanols with chromium trioxide in glacial acetic acid, as a result of which 5- and 6-keto carboxylic acids, respectively, are formed. The 1-alkylcycloalkanols required were synthesized by the reaction of Grignard reagents with cyclic ketones. However, in almost all cases yields of only 10-15% were obtained in the oxidation of 1-alkylcyclopentanols and 1-alkylcyclohexanols to keto acids [2-4]. Much better results were obtained by the ozone oxidation of products of the dehydration of tertiary alcohols, namely 1-alkylcyclohexenes and 1-alkylcyclopentenes [5,6].

Evet	Reac	tants	Amou	it takei	1	Temp °C	Time		Yield		Deciduo
cxhr•	Ketone (A)	Incoturated	(mol.	proport	ion)	remp., C	(hr)	a	Mon B	% on B	Residue,
	Ketone (A)	compound(B)	A	В	per-]	(m)	Б	taken	that re-	Б
		compodite(b)			oxide				LANCH	acted	
1	Cyclopentane	1-Octene	3	0.3	0.06	128-130	6.5	33	57	61	13.5
2	π	1-Decane	3	0.3	0.06	127-130	6,5	47.8	71	-	13.5
3	-	4-Methyl-1-	[.		{						
		decene	3,5	0,35	0.07	128-130	6	51.7	62	68	14
4	*	Allyl octyl									
		ether	3,5	0,35	0,105	128-129	6	47.2	53	59	20
5	=	Allyl decyl									
		ether	3	0.3	0.06	129-130	6	38.1	45	59	19.5
6	Cyclohexanone	1-Octene	3	0.3	0.06	142-150	4,5	37.2	59	76	11.5
7		1-Decene	3	0.3	0.06	146-152	6	44.5	62,3	-	14.5
8	n	4-Methyl-1-									
		decene	3.5	0.35	0.07	149-153	6	54	61.2	-	16
9	-	Allyl octyl	[[[[
		ether	3.5	0.35	0.105	143-152	6	53,5	57	64	23
10		2-(Allyloxy)-			[
		ethanol	5	0.5	0.1	142-153	6	30	30	-	37.5

Another known method for the synthesis of 6- and 7-keto carboxylic acids consists in the acylation of cyclopentanone and cyclohexanone with acid anhydrides [7] and cleavage of the resulting 2-acylcyclopentanones and 2acylcyclohexanones with alkali [8]. An unsatisfactory feature of this last method is the low yield (about 35%) of product at the acylation stage. The synthesis of 2-acylcyclohexanones in 75-85% yield has been developed by Hunig and co-workers [9], who carried out the acylation of not cyclohexanone itself, but the product of its condensation with morpholine or pyrrolidine. In this case the scheme of synthesis is complicated on account of additional stages, namely the formation of the enamine and its hydrolysis. A method of lengthening the chain of a carboxylic acid by five carbon atoms was proposed by Plesek [10]. It consisted in the acylation of ethyl 2-oxocyclopentanecarboxylate with an acid chloride and the subsequent cleavage of the acylated product to a 6-keto acid. Finally, we must

(continued)

TABLE 2.

		B.p. in °C	00	06	W	R	Found	1, 7,0	Calculat	ed, %	M.p. of	M.p. of 2,4-di-
Expt.	T:T A GOUCI	(P in mm)	d_4	Qu	found	calc.	υ	н	ບ ບ	н	semicarb- azone (°C)	nitrophenylhy- drazone (C)
7	0 -C ₁₀ H ₂₁	119—120 (1)	3,8810	1,4606	74,13	74,18	80,32 80.37	12,53 12,53	80,60	12,68	104,5-105	
8	$O = CH_{4}$	122-123 (1)	0,8826	1,4625	78,70	78,83	81,04 81,28	13,11 12,93	80,88	12,78	82	1
	0 -(CH ₄),-O-C ₆ H ₁₇	175—177(2,5)	0,9120	1,4600	80,58	80,61	75,88 75,74	11,85 11,85	76,06	12,01	I	1
10	0 ==	130-132 (1)	1,0464	1,4785	54,27	54,25	65,67	9,98	65,96	10,06	I	ł
	\supset					<u>6 10</u>						

• Data from literature: 1) b.p. 156° (20 mm); d²⁰4 0.8850; n²⁰D 1.4535; semicarbazone, m.p. 185.5-186° [14]; 2) b.p. 182° (20 mm); d²⁰4 0.8791; n²⁰D 1.4559; semicarbazone, m.p. 182° (20 mm); d²⁰4 0.8791; n²⁰D 1.4559; semicarbazone, m.p. 183° [14]; 6) b.p. 75-78° (0.05 mm); d²⁰4 0.88; n²⁰D 1.4580; 2.4-dinitrophenylhydrazone, m.p. 112-113° [12]. The other substances were prepared for the first time.

1926

TABLE 2 (continued)

mention the synthesis developed by Stetter [11] and applied in numerous cases for the synthesis of carboxylic acids by the alkylation of 1,3-cyclohexadione and the cleavage of the resulting 2-alkyl-1,3-cyclohexadiones with hydrazine.

We set ourselves the task of developing another route to keto carboxylic acids which, as we saw it, would be preferable to those described above in quite a number of cases. With this object we studied the free-radical addition of cyclopentanone and cyclohexanone to α -olefins and allyl ethers. The addition of cyclohexanone to 1-octene initiated by ultraviolet radiation was described earlier by Kharasch and co-workers [12]; they showed that, when a 1:8 mixture of cyclohexanone and 1-octene was irradiated for 50-70 hr, a number of products was formed: hexanal, 2octene, octene dimer, 2-octylcyclohexanone, 2:1 and 3:1 adducts, and macromolecular substances. The yield of 2octylcyclohexanone was 20-26% on the cyclohexanone. Using t-butyl peroxide as initiator, we showed that cyclohexanone and cyclopentanone add to undecenoic acid with formation of 11-(2-oxocyclopentyl)undecanoic and 11-(2-oxocyclohexyl)undecanoic acids, respectively [13]. In the present work this reaction was studied in greater detail. The conditions of individual experiments, the yields of 1:1 adducts, and the amounts of high-boiling products are given in Table 1. Table 2 shows the structures of the 2-substituted cyclopentanones and cyclohexanones obtained, and their properties. Experiments 1-10 were all carried out in the same way: a solution of the peroxide and unsaturated compound were added uniformly and continuously throughout the whole reaction to the boiling ketone. Reaction began with homolytic decomposition of t-butyl peroxide into t-butoxy radicals. On reaction with the ketone these abstracted hydrogen from the CH₂ group adjacent to the carbonyl group. Such selectivity in the direction of the attack on the ketone molecule is probably to be explained by the lower dissociation energy of the α -C – H bonds and the greater stability of the resulting radical resulting from the conjugation effect. The radical formed adds at the double bond of the unsaturated compound, after which propagation of the chain proceeds:



As well as the 1:1 adduct, substances of higher molecular weight are obtained, and these are probably products of the addition of the 1:1 adduct to a new olefin molecule and telomerization products. At molar proportions of ketone: unsaturated compound:peroxide of 10:1:0.2, the yields of 1:1 adducts were 50-70%, calculated on the unsaturated compound. In Experiments 1, 3-6, and 9 part of the olefins and allyl ethers taken for reaction were isolated from the reaction mixture, but in the other experiments we did not succeed in doing this. In carrying out the identification of the products we found that the 2,4-dinitrophenylhydrazones of 2-octylcyclohexanone prepared by Kharasch [12] and by us had different melting points (112-113° and 118-118.5°, respectively). To confirm the correctness of the structure that we attributed to the 1:1 adducts (see Table 2), we synthesized 2-octylcyclopentanone in two ways:



The two samples had identical properties and their melting points were identical and were not depressed in a mixture test.

It is evident that under the conditions of irradiating the mixture of 1-octene and cyclohexanone with ultraviolet radiation, cyclohexanone adds not only to 1-octene, but also to the 2-octene formed. As a result, a 1:1 adduct is obtained which consists mainly of 2-octylcyclohexanone contaminated by isomeric products. It is this that explains the low melting point of the 2,4-dinitrophenylhydrazone. Under our conditions the probability of the formation of 2-octene was very low. The 1:1 adducts obtained in Experiments 1-8 were oxidized with chromium trioxide with cleavage of the ring and formation of the corresponding keto acids, e.g.

$$O = (CH_2)_3 - O - C_8H_{17} \rightarrow C_8H_{17} - O - (CH_2)_3 - CO - (CH_2)_3 - COOH;$$

$$O = O = (CH_2)_3 - COOH = C_8H_{17} - C_8H_{17} - CO - (CH_2)_4 - COOH.$$

All the oxidations were carried out under identical conditions; the chromium trioxide was taken in an amount that exceeded the theoretical by about 15%. The highest yield of keto carboxylic acids was obtained in the oxidation of 2-alkylcyclopentanones and 2-alkylcyclohexanones (77-87%). Lower yields of keto acids were obtained when branching or an ether link was present in the side chain.

EXPERIMENTAL

Addition of Cyclopentanone and Cyclohexanone to α -Olefins and Allyl Ethers (Table 1, Experiments 1-10). Cyclopentanone or cyclohexanone, in an amount of 80-85 moles percent of the total calculated quantity, was placed in a flask fitted with stirrer, reflux condenser, calibrated dropping funnel, and thermometer. The ketone was heated to the boiling point and stirred while uniform dropwise addition was made of a solution of the t-butyl peroxide and the olefin (or allyl ether) in the remainder of the ketone. When the addition was complete, the reaction mixture was heated further for 1 hr; excess of ketone and products of the decomposition of the peroxide were then distilled off. From the resulting high-boiling product we vacuum-distilled the 1:1 adduct, and telomerization products remained in the flask; the amounts are given in Table 1 in the column "Residue," The 1:1 adducts were purified by repeated distillation. In Experiments 3-5 and 7-9, they were also passed through a column of silica gel. In Experiments 1, 3-6, and 9 we succeeded in isolating the unsaturated compounds that did not react.

<u>2-Octylcyclopentanone</u>. A well-ground mixture was prepared from 14 g (0.05 mole) of 2-octyladipic acid (the synthesis of this was described earlier [15]) and 1.7 g of barium hydroxide. The mixture was heated in the range 270-300°, and ketone and water distilled off. We obtained 6 g (56%) of 2-octylcyclopentanone; b.p. 122-129° (4 mm); d_{40}^{20} 0.8816; n^{20} D 1.4529. Its 2.4-dinitrophenylhydrazone had m.p. 105.7-106.2° (from alcohol).

5-Oxotridecanoic Acid (11). To a solution of 26 g of concentrated sulfuric acid in 44 ml of water we added 19.6 g (0.1 mole) of 2-octylcyclopentanone and then, with stirring, a solution of 15 g (0.15 mole) of chromium trioxide and 26 g of sulfuric acid in 44 ml of water. During the addition the temperature was kept in the range 45-50°, and the mixture was then kept at the same temperature for 2 hr further and left overnight. By extraction with hot benzene (six portions, each 50-60 ml) and then with ether, the keto acid was isolated from the reaction mixture. Ether and part of the benzene were driven off, and the precipitated crystals of keto acid (16.8 g) were separated from the mother liquid. Distillation of the mother liquid gave a further 1.5 g of the acid. In all we obtained 18.3 g (80%) of 5-oxotridecanoic acid, m.p. 72-72.5° (from benzene). Found: C 68.39, 68.15; H 10.67, 10.64%. $C_{13}H_{24}O_{3}$. Calculated: C 68.38; H 10.60%. The other keto acids were prepared from 2-substituted cyclopentanones and cyclohexanones by an analogous procedure.

5-Oxopentadecanoic Acid (12). On oxidation of 40 g (0.18 mole) of 2-decylcyclopentanone with 27 g (0.27 mole) of chromium trioxide we obtained 35.5 g (77%) of 5-oxopentadecanoic acid, m.p. 82-82.5° (from benzene). Found: C 70.21; 70.23; H 11.31, 11.06%. $C_{15}O_{28}O_{3}$. Calculated: C 70.27; H 11.01%. Semicarbazone m.p. 121 to 121.5° (from alcohol).

<u>9-Methyl-5-oxopentadecanoic Acid (13).</u> From 47.9 g (0.2 mole) of 2-(4-methyldecyl)cyclopentanone we obtained 48 g of crude keto acid. After vacuum distillation and purification through a silica gel column we isolated 36 g (66% on reactant taken, 79% on the amount that reacted) of 9-methyl-5-oxopentadecanoic acid; b.p. 175-17 ° (1 mm), d^{20}_{4} 0.9497, n^{20} D 1.4578; found MR 77.66; calculated MR 77.88;-acid number found 205.5, calculated 207.5. Found: C 70.76; H 11.18%, C₁₆H₃₀O₃. Calculated: C 71.07; H 11.18%, Semicarbazone m.p. 113.5-114° (from al-cohol).

8-(Octyloxy)-5-oxooctanoic Acid (14). On oxidation of 38.2 g (0.15 mole) of 2-[3-(octyloxy)propyl]cyclopentanone we isolated 15.5 g of unchanged reactant and 14.3 g of 8-(octyloxy)-5-oxooctanoic acid. Yield 33.3% on reactant taken and 56% on the amount that reacted; m.p. 49° (from acetone). Found: C 67.20, 67.23; H 10.56,10.66%. $C_{16}H_{30}O_4$. Calculated: C 67.10; H 10.56%. Semicarbazone m.p. 90-90.5° (from alcohol).

<u>8-(Decyloxy)-5-oxooctanoic Acid (15).</u> On oxidation of 28.3 g (0.1 mole) of 2-[3-(decyloxy)propy]]cyclopentanone we isolated 13 g of unchanged reactant and 9.8 g (31% on reactant taken, 58% on the amount that reacted) of 8-decyloxy-5-oxooctanoic acid, m.p. 58.1° (from acetone). Found: C 68.66, 68.67; H 10.70, 10.80%. $C_{18}H_{34}O_4$. Calculated: C 68.75; H 10.90%. Semicarbazone m.p. 108° (from alcohol).

6-Oxotetradecanoic Acid (16). From 17.8 g (0.085 mole) of 2-octylcyclohexanone we obtained 18 g (87%) of 6-oxotetradecanoic acid, m.p. 72.5° (from acetone). Semicarbazone m.p. 129-130° (from alcohol).

For the melting point of the keto acid the literature gives 71.5° [4] and 72° [10]; for the melting point of the semicarbazone it gives 130° [4] and 138° [10].

6-Oxohexadecanoic Acid (17). From 38.2 g (0.16 mole) of 2-decylcyclohexanone we obtained 30 g (69.3% on the reactant taken and 84.7% on the amount that reacted) of 6-oxohexadecanoic acid, m.p. 81.5-82° (from benzene). Found: C 71.29, 71.17; H 11.12, 11.16%. $C_{16}H_{30}O_3$. Calculated: C 71.07; H 11.18%. Semicarbazone m.p. 154° (from alcohol). The literature [4] gives: keto acid m.p. 79°, semicarbazone m.p. 149.5°.

<u>10-Methyl-6-oxohexadecanoic Acid (18).</u> From 46.7 g (0.185 mole) of 2-(4-methyldecyl)cyclohexanone we obtained 45.8 g of crude keto acid. After distillation and purification through a silica gel column we obtained 26 g (50% on the reactant taken and 63% on the amount that reacted) of 10-methyl-6-oxohexadecanoic acid; b.p. 181 to 182° (1 mm); d^{20}_4 0.9439; n^{20} D 1.4587; found MR 82.33; calculated MR 82.53. Found: C 71.61, 71.43; H 11.48, 11.27%. C₁₇H₃₂O₃. Calculated: C 71.78; H 11.34%. Semicarbazone m.p. 103° (from alcohol).

Acids (11), (13)-(15), and (18) were prepared for the first time.

SUMMARY

A new method was developed for the synthesis of 5- and 6-keto carboxylic acids by the addition of cyclopentanone and of cyclohexanone in presence of t-butyl peroxide to α -olefins with subsequent oxidation of the 2alkylcyclopentanones and 2-alkylcyclohexanones with chromium trioxide.

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