OZONOLYSIS OF 1-SUBSTITUTED CYCLOOLEFINS¹

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ABSTRACT

Extension of an aliphatic chain by five, six, or seven carbon atoms may be achieved by adding to it a 5-, 6-, or 7-membered olefinic alicycle and subsequently breaking the double bond. Addition of the ring is achieved by a Grignard reaction between an alkylmagnesium bromide and a cyclic ketone, and the resulting 1-alkylcycloolefin is opened by ozonolysis. The end product is a 5-, 6-, or 7-keto acid.

Methods for extension of the aliphatic chain fall into two main groups; those in which one or two carbon atoms are added, and those in which the starting material and added fragment are of comparable chain length. To the former class belong the familiar cyanide and malonic ester syntheses. These are regarded as inferior in long-chain work because end products and starting materials have similar chain-lengths (and thus similar physical properties) and are difficult to separate from each other. Methods of the latter class include the Robinson (5), Noller and Adams (4), and Blaise (1) syntheses, in which a large increment is added in one step and end product is easily separated from relatively short-chain starting materials. These methods suffer from the limited accessibility of such necessary chain-extending reagents as ω -bromo, -cyano, or -aldehydo esters or ω -carbalkoxy acid halides.

Extension using an alicyclic fragment which is subsequently opened to become part of the chain is a tempting approach. Fieser and Smuszkovicz (2) showed that 1-substituted cycloalkanols (from cycloalkanones and a Grignard reagent) may be oxidized to keto acids by chromic acid at 30° in the presence of large amounts of anhydrous acetic acid. Kelkar, Phalnikar, and Bhide (3) encountered difficulty in an attempt to make a keto acid from a 1-alkylcyclohexene by strong oxidation. Schneider and Spielman (7) concluded that chromic acid oxidation of a 1-alkylcyclohexene was inferior to the alkylzinc synthesis of a keto acid. In all investigations there was evidence of concurrent reactions. If linkages other than those intended are attacked, as may well happen when oxidizing agents of poor selectivity are employed, the same problem of separation of end product from lower homologues may be encountered.

In the present investigation, opening of the alicyclic system was achieved by ozonolysis and the resulting keto aldehydes were oxidized by performic acid to the corresponding keto acids. These are "clean" reagents of high specificity and the end products in all cases were nearly white and reasonably pure. A prerequisite for success of the synthesis is unambiguity of location of the olefinic linkage. Wallach (10) has shown that, in general, dehydration of a 1-alkylcyclohexanol gives the olefin with the cyclic rather than the semicyclic double bond. During ozonolysis of the olefins of this investigation, no evidence of alkylidenecycloalkanes was encountered.

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The use of cyclohexanone is illustrated above in the extension of a chain by six carbon atoms giving a 6-keto acid. It is also found that a 5-keto acid may be obtained from cyclopentanone and a 7-keto acid from cycloheptanone. Yields in the two-step synthesis are indicated in Tables I and II.

TABLE I	
OLEFINS	

Name	Yield, %*		<i>n</i> ²⁰ D	C and H, %				
		B.p., °C./mm.		Calc.		Found		
				С	н	С	н	
1-n-Butylcyclopentene	56	51-53/18	1.4478					
1-n-Butylcyclohexene	40	71-73/18	1.4592					
1-n-Amylcyclopentene	52	176 - 177 / 760	1.4540					
1-n-Butylcycloheptene	40	87-92/19	1.4695^{\dagger}	86.8	13.2	86.7	13.2	
dl-1-(2-Methylbutyl)cyclohexene	25	193 - 194 / 760	1.4600	86.8	13.2	86.6	12.9	
1-Phenylcyclohexene	62	122 - 125/11	1.5669†					
1-n-Hexylcyclohexene	43 📉	104-109/19	1.4560	86.7	13.3	86.6	13.0	
1-n-Octylcyclohexene	36	121 - 127/12	1.4683					
1-(10-Undecenyl)cyclopentene	28	139-151/13	1,4908	87.3	12.7	87.1	13.0	

TABLE II

Keto acids										
Name	Yield, %	м.р., °С. —			Sem	icarbazor	ne			
			Acid equivalent		M.p.,	N analysis, %				
			Cale.	Found	-C.	Calc.	Found			
5-Ketononanoic acid	43	44			132133	18.3	18.2			
6-Ketodecanoic acid	61 - 68	46 - 47			160	17.3	17.2			
5-Ketodecanoic acid	67-73	57			111	17.3	17.1			
7-Ketoundecanoic acid	63	51.5-52	200	202	133	16.3	16.3			
6-Keto-8-methyldecanoic acid	76	33 - 34	200	204	120	16.3	15.9			
5-Benzoylpentanoic acid	69	78			182 - 183					

62.5-63

66

108

214

242

286

216

246

286

130-131

120-121

130

15.4

14.0

15.5

14.0

71

60

27

6-Ketododecanoic acid

6-Ketotetradecanoic acid

4-Ketotridecane-1,13-dicarboxylic acid

Losses in the synthesis of 1-alkylcycloolefins are attributable (cf. 6, 8) to two main causes, "coupling" of the Grignard reagent giving a paraffin hydrocarbon and reduction of the cyclic ketone giving an olefin and cycloalkanol. "Coupling" appears to be more serious when higher alkyl halides are employed, and reduction appears to be favored by branching of the Grignard reagent and by increase in the size of the alicycle. It was found to be least in the reaction involving phenylmagnesium bromide. CANADIAN JOURNAL OF CHEMISTRY. VOL. 33

EXPERIMENTAL

Synthesis of 1-Substituted Cycloolefins

The procedure outlined below in the synthesis of 1-*n*-butylcyclohexene from cyclohexanone and *n*-butylmagnesium bromide is typical for all olefins listed in Table I (cf. Signaigo and Cramer (8)). Cyclohexanone (47 gm., 0.48 mole) was added during eight and one-half hours to the Grignard reagent from *n*-butyl bromide (71 gm., 0.52 mole) and magnesium (12 gm., 0.50 mole) in 200 cc. of dry ether, cooled with solid carbon dioxide to maintain an internal temperature of -40 to -20° C. Next day, the mixture was added to ice and hydrochloric acid in excess, and the ethereal solution was washed with water, three times with a saturated aqueous solution of sodium bisulphite (to remove cyclohexanone), and with potassium carbonate solution before it was dried over sodium sulphate. The product, a tertiary alcohol, was not purified, but used directly in the next stage.

Dehydration of 1-*n*-butylcyclohexanol was achieved by heating with iodine (0.2 gm., cf. 11) at reflux in an apparatus provided with a water separator. The theoretical quantity of water was collected in one and one-half hours, and the liquid remaining was fractionally distilled through a 15 cm. Widmer column. To avoid overheating during dehydration of higher tertiary alcohols it was found desirable to add xylene as a diluent. 1-*n*-Butylcyclohexene (26 gm., 40%) boiled at 71–73° at 17 mm. and had n_p^{20} 1.4592. On standing in air, the liquid darkened somewhat, became more viscous, and had a higher refractive index. This was taken to indicate polymerization, and the olefin was utilized as soon as possible in the next step.

Oxidation of 1-Substituted Cycloolefins to Keto Acids

The general procedure employed is described here for the case in which 1-n-butylcyclohexene was converted, by ozonolysis, to 6-ketodecanal, and this aldehyde was oxidized to the corresponding acid by performic acid, generated in situ. A slow stream of oxygen containing approximately 6% of ozone was passed into 1-n-butylcyclohexene (20 gm., 0.15 mole) in acetic acid (20 cc.) until a test sample failed to decolorize bromine and for 10 min. afterward. A technique similar to that of Noller and Adams (4) was used to decompose the ozonide as follows: The viscous solution was diluted with an equal volume of ether, cooled in ice, and treated cautiously with several cubic centimeters of water and 1 gm. (0.01 mole) of zinc dust. There ensued a violent reaction after an induction period, and next day the solution was filtered and separated. The ether solution was washed with water, and then 20 cc. of hydrogen peroxide (30%, 0.2 mole), 25 cc. of formic acid (90%), and 1 gm. of ammonium acetatewere added. After 24 hr. at room temperature the mixture was diluted with ether and water and separated. The ethereal layer was shaken with several portions of aqueous ferrous sulphate until free from peroxides, and the acidic product was freed from neutral impurities using potassium carbonate solution in the usual manner. After removal of ether, 6-ketodecanoic acid was recrystallized from petroleum ether; the yield was 61-68% in several runs and the acid melted at 46-47°.

A simplification of the oxidation procedure was made possible by the obser-

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vations that formic acid may replace acetic acid as an ozonization solvent and that performic acid oxidation appears to be unaffected by the presence of zinc salts. In the modified procedure, 21 gm. of 1-n-butylcyclohexene in an equal volume of formic acid was treated with ozonized oxygen as before except that care was necessary in using the bromine test as the formic acid gradually decolorized bromine. After treatment with zinc, water, and ether, the reaction mixture was filtered but not washed before treatment with a further 20-cc. portion of formic acid and 20 cc. of 30% hydrogen peroxide. The yield of keto acid was 16.5 gm. (58%).

A neutral fraction was obtained in varying quantity after performic acid oxidation of 6-ketodecanal. It was shown to contain unchanged aldehyde, as a second treatment with performic acid gave some 6-ketodecanoic acid. There remained, however, a residual neutral fraction, corresponding to 10-15% of the starting material, which was not an aldehyde and showed evidence of unsaturation. This material will be further studied.

Ozonolysis of 1-Phenylcyclohexene

A modified procedure was employed in the ozonolysis of the aromatic hydrocarbon 1-phenylcyclohexene. By a technique similar to that of Dawson (9) this substance was ozonized in ethyl acetate at -70° under conditions designed to avoid over-ozonization with attack of the benzene nucleus. Following catalytic hydrogenation of the ozonide, the ethyl acetate solution containing 5-benzoylpentanal was treated with performic acid as previously described. From 11.4 gm. of starting material, the yield of 5-benzoylpentanoic acid was 10.3 gm. (69%), melting at 75°.

Undecenyl Bromide

1.

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1-Bromoundec-10-ene (undecenyl bromide) made by the action of phosphorus tribromide upon the corresponding alcohol must be freed from unchanged alcohol before use in the Grignard reaction. This cannot be achieved by distillation, as the two compounds have similar boiling points. The crude bromide (80 gm.) was taken up in dry ether (150 cc.) and treated with 20 gm. of phosphorus pentoxide. Next day, a further 20-gm. portion of phosphorus pentoxide was added, and the mixture was frequently shaken during the next four hours and then decanted into 250 cc. of 50% aqueous methanol. Concentrated aqueous ammonia was quickly added until the mixture was alkaline to phenolphthalein, and after it was washed with a similar portion of aqueous-methanolic ammonia and with water, the ether solution was dried and distilled.

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