Ozonolysis-Reductive Amination of Olefins

KENNETH A. POLLART AND ROBERT E. MILLER
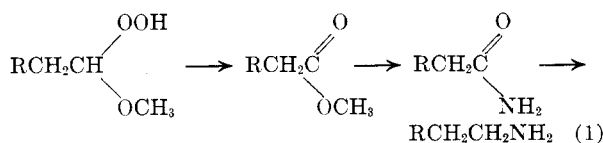
Research and Engineering Division, Monsanto Chemical Company, St. Louis, Missouri

The reductive amination of the mixtures derived from ozonolysis offers a direct route for the synthesis of amines and amino compounds from olefins. The procedure is suitable for the conversion of aliphatic olefins to the desired amino derivatives in nominal yields; cyclohexene, however, yields a complex mixture of products. Particular attention has been devoted to the isolation and identification of by-products. The reaction of ozonized oxygen with 1-ethoxycyclohexene and dicyclohexyl ether is also reported.

The present study was concerned with the fate of the carbonyl and alkoxy hydroperoxide fragments derived from the ozonolysis of olefins subsequent to reductive amination of the total ozonolysis mixture. Our experience has shown that the isolation of the carbonyl compound[1] is not necessary for maximum conversion of the carbonyl compound to the respective amine.

The formation of products derived from the alkoxy hydroperoxide, which is formed by reaction of the zwitterion with the alcoholic solvent, must also be considered. It is believed that esters and amides, rather than amines, are more likely to arise from this intermediate, particularly since ammonolysis of esters is a slow and frequently incomplete reaction (equation 1).

$$ RCH_2CH{\overset{\textstyle OOH}{\underset{\textstyle OCH_3}{\diagup\diagdown}}} \longrightarrow RCH_2C{\overset{\textstyle O}{\underset{\textstyle OCH_3}{\diagup\diagdown}}} \longrightarrow RCH_2C{\overset{\textstyle O}{\underset{\textstyle NH_2}{\diagup\diagdown}}} \longrightarrow $$
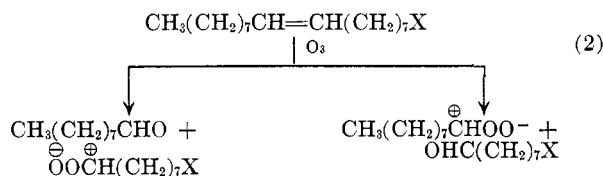
$$ RCH_2CH_2NH_2 \quad (1) $$

The ozonolysis of 1-decene in methanol, followed by reductive amination with Raney nickel at 150°, gave 48–59% conversions to *n*-nonylamine together with 25–33% of the secondary amine. Tertiary amine formation was not observed. With 1-hexadecene the conversions to the desired product, 1-aminopentadecane, were exceptionally high (69–71%). Di-*n*-pentadecylamine (12–15%) was the only by-product. The excellent conversions to the simple amines obtained from this reaction suggested that the zwitterion produced during ozonolysis of the olefin was stabilized by condensation with the formaldehyde[2] fragment, rather than by self-condensation to a polymeric peroxide.

Cleavage of the initial ozonide to the zwitterion and a carbonyl compound appears to be governed by the structure of the original olefin[3]; the zwitter-

ion is usually formed at the carbon atom of the double bond which contains the most effective electron-releasing group.

Because of the insulating effects of the long alkyl chain, the electronic character of a terminal group in derivatives of oleic acid should not significantly influence the products derived from ozonolysis of the double bond. Therefore, approximately equimolar amounts of the two most probable carbonyl compounds expected from cleavage of the double bond (equation 2) should be formed.[4] In agree-

$$ CH_3(CH_2)_7CH{=}CH(CH_2)_7X $$

$$ \Big\downarrow O_3 \qquad\qquad (2) $$

$$ CH_3(CH_2)_7CHO + \qquad CH_3(CH_2)_7CH\overset{\oplus}{O}O^- + $$
$$ \overset{\ominus}{O}O\overset{\oplus}{C}H(CH_2)_7X \qquad OHC(CH_2)_7X $$

ment with these considerations, nearly equivalent conversions of *n*-nonylamine (14–44%) and 9-aminononanoic acid or methyl 9-aminononanoate (17–52%) were obtained from the reductive amination of oleic acid or methyl oleate ozonolysis mixtures.

The principal by-products isolated from these reductive aminations were stearamide, pelargonamide, azelaic acid, and in one case, methyl suberate. Suberic acid had been previously isolated from the ozonolysis of oleic acid by other investigators.[5]

All attempts to identify 9-amino-1-nonanol,[1f] from the ozonolysis-reductive amination of oleyl alcohol failed in spite of the fact that cleavage of the double bond had taken place as evidenced by the isolation of *n*-nonylamine. The reductive amination of cyclohexene ozonolysis mixtures was incomplete below 100°; adipaldehyde or adipaldehydic esters were usually isolated from reactions conducted in alcoholic solvents. If the temperature of the reduction reaction was raised to 150–200°, 1,6-hexamethylenediamine,[1c,d] caprolactam, methyl 6-aminocaproate, and valeramide were isolated. The maximum conversions to the diamine and the lac-

(1) (a) A. B. Brown and J. W. Sparks, U.S. Patent 2,819,279, January 7, 1958; (b) A. S. Carpenter and F. Reeder, British Patents 741,739, December 14, 1955; 743,491, January 18, 1956; (c) E. E. Fisher, U.S. Patent 2,733,270, January 31, 1956; (d) R. E. Foster and H. E. Schroeder, U.S. Patent 2,657,240, October 27, 1953; (e) G. W. Rigby, U.S. Patent 2,657,239, October 27, 1953; (f) H. Otsuki and H. Funahashi, U.S. Patent 2,862,940, December 12, 1958.

(2) (a) R. Criegee, G. Blust, and H. Zincke, *Chem. Ber.*, **87**, 766 (1954); (b) R. Criegee, A. Kerckow, and H. Zincke, *ibid.*, **88**, 1878 (1955).

(3) P. S. Bailey, *ibid.*, **87**, 993 (1954); **88**, 795 (1955).

(4) An elegant substantiation for this premise has been reported by R. G. Ackman, M. E. Reston, L. R. Gallay, and F. A. Vandenheuvel, *Can. J. Chem.*, **39**, 1956 (1961).

(5) (a) B. W. Baker, R. P. Linstead, and B. C. L. Weedon, *J. Chem. Soc.*, 2222 (1955); (b) J. G. Keppler, *Rec. trav. chim.*, **76**, 51 (1957).

TABLE I

OZONOLYSIS-REDUCTIVE AMINATION OF OLEFINS

| Compound	Ozonolysis[a]			Reduction		Products		
	Moles	O_3, moles	Temp., °C	NH_3, moles	Catalyst[b]		B.p. (mm.) [m.p.]	Conversion, %
1-Decene	0.15	0.12	−13	3.0	A	150	n-Nonylamine	90–94 (20)[c]	59.8
Oleic acid	.15	.15	−20	3.3	A	150	n-Nonylamine		24.5
							9-Aminononanoic acid	[185–187]	37.6
							Stearamide	[107–110][d]	15.9
Oleic acid	.15	.28	6	42	A	100	Nonanal	80–82 (13)[e]	22.5
							n-Nonylamine		14.0
							9-Aminononanoic acid		28.9
							Pelargonamide	[94–96][f]	12.9
							Stearic acid	[69–70]	22.0
							Methyl suberate	[10–12][g]	..
							Azelaic acid	[106–107]	22.0
Methyl oleate	.15	.15	−30	3.5	A	150	n-Nonylamine		44.0
							Methyl 9-aminononanoate	95–98 (4)[h]	52.4
							Pelargonamide		33.4
							Stearamide		15.2
Oleyl alcohol	.15	.16	−18	3.1	A	150	n-Nonylamine[i]		42.1
Ethyl undecenoate[j]	.15	.12	−40	3.5	A	150	10-Aminodecanoamide	[58–60][k]	69.8
							10-Undecenoamide	[86–90][l]	16.0
							Residue[m]		..
1-Hexadecene[n]	.15	Excess	4	0.29	B	20	1-Aminopentadecane	[35–37][o]	71.0
							Di-n-pentadecylamine	[57–58][p]	12.0
Cyclohexene	.19	0.17	−12	2.9	A	150	Caprolactam	[68–70][q]	15.8
							1,6-Hexamethylenediamine	[32–36][r]	14.1
							Polymeric amino acid[s]	[124–127]	..
Cyclohexene[t]	.19	0.18	−35	4.1	C	100	6-Aminocaproic acid[u]	[196–200]	33.2
							Polymer[v]		..
1-Ethoxycyclohexene[j]	.2	Excess	−40	1.1	B	100	Adipaldehyde	68–70 (17)[w]	20.6
							Ethyl adipaldehydate	96–98 (4)[x]	20.6
							Ethyl 6-aminocaproate	76–82 (3.5)	15.1
							Unidentified acid	[139–143][y]	..
Dicyclohexyl ether[z]	.11	0.21	8–10	...	..	..	Adipic acid	[141–152]	12.5
							Butyraldehyde[aa]		..
							Butyric acid[bb]		
							Dicyclohexyl adipate[cc]	188 (4)	17.5

[a] Methanol used as solvent except where noted. [b] A = Raney nickel, B = 5% palladium-on-carbon, C = W-4 Raney cobalt. [c] Picrate, m.p. 110–112°. J. v. Braun and W. Sobeski, *Ber.*, **44**, 1469 (1911) give m.p. 111°. [d] F. Krafft and B. Stauffer, *ibid.*, **15**, 1730 (1882) give m.p. 108.5–109°. Infrared spectrum identical with authentic specimen. [e] 2,4-Dinitrophenylhydrazone, m.p. 106–107°. A. M. Gladdis and R. Ellis, *Anal. Chem.*, **30**, 475 (1958) give m.p. 106.5–107°. [f] M. Stolle and A. Rouve, *Helv. Chim. Acta.*, **27**, 950 (1944) give m.p. 97.5–98°. [g] B.p. 153–160° (3 mm.). *Anal.* Calcd. for $C_9H_{16}O_4$: Neut. equiv., 188. Found: Neut. equiv., 188. P. Chuit and J. Hausser, *Helv. Chim. Acta*, **12**, 466 (1929) give b.p. 146–150° (1 mm.), m.p. about 10°. [h] Hydrochloride, m.p. 115–118[1b]. [i] A second component distilled at 118–129° (4 mm.). A portion of this fraction sublimed, m.p. 83–83.5°. *Anal.* Calcd. for $C_{18}H_{35}NO_2$: C, 70.36; H, 12.82; N, 4.13. Found: C, 69.90; H, 13.16; N, 5.12, 5.22. The residue melted at 12–15°. Neither fraction could be conclusively identified. [j] Ethanol solvent. [k] *Anal.* Calcd. for $C_{10}H_{22}N_2O$: C, 64.51; H, 11.82; N, 16.05. Found: C, 64.39; H, 11.06; N, 16.09. [l] E. C. S. Jones and F. L. Pyman, *J. Chem. Soc.*, **127**, 2598 (1925) report m.p. 87°. [m] Converted by acid hydrolysis to 10-aminodecanoic acid, m.p. 187–188°. D. D. Coffman, *et al.*, *J. Poly Sci.*, **3**, 85 (1948) give m.p. 185–188°. [n] Isooctane solvent. [o] Distilled at 110–122° (0.8 mm.); E. Jeffreys, *Ber.*, **30**, 900 (1897) gives b.p. 299–301°, m.p. 36.5°. [p] C. W. Hoerr, H. J. Harwood, and A. W. Ralston, *J. Org. Chem.*, **9**, 201 (1944) give m.p. 63.3°. [q] A. Mueller and P. Bleier, *Monats.*, **50**, 400 (1928) give m.p. 69.2°. [r] Picrate, m.p. 228–224°. V. Solonina, *Bull. soc. chim.*, **16**, 1880 (1896) gives m.p. 220°. [s] *Anal.* Calcd. for $C_{20}H_{41}N_3O_9$: N, 8.99; neut. equiv., 467.6. Found: N, 11.19; neut. equiv., 468.7. [t] Formaldehyde (0.13 mole) added during ozonolysis. [u] Isolated after acid hydrolysis of reaction mixture. *Anal.* Calcd. for $C_5H_{11}NO_2$: C, 51.30; H, 9.41; N, 11.98. Found: C, 51.51; H, 8.81; N, 11.80, 11.84. [v] Amorphous, hydroscopic amino derivative. Infrared analysis was inconclusive. Sulfate. *Anal.* Calcd. for $C_{11}H_{18}N_2·H_2SO_4$: C, 47.86; H, 7.25; N, 10.15. Found: C, 48.61; H, 7.52; N, 10.85, 10.87. Hydrochloride. *Anal.* Calcd. for $C_{11}H_{18}N_2·2HCl·H_2O$: C, 49.20; H, 8.19; N, 10.41; Cl, 26.40; neut. equiv., 269. Found: C, 49.19; H, 8.96; N, 12.36; Cl, 24.03; neut. equiv., 264. [w] Dioxime, m.p. 185–186°. A. Wohl and H. Schweitzer, *Ber.*, **39**, 894 (1906) give m.p. 185–186°. [x] *Anal.* Calcd. for $C_8H_{14}O_3$: C, 60.81; H, 8.97. Found: C, 60.37; H, 9.63; 2,4-dinitrophenylhydrazine, m.p. 55–57°. G. B. Brown, *et al.*, *J. Org. Chem.*, **12**, 160 (1947) give m.p. 58–60°. [y] Sublimes. *Anal.* Calcd. for $C_8H_{17}NO_2$: C, 60.83; H, 10.98; N, 8.80; neut. equiv., 159. Found: C, 60.42; H, 10.68; N, 8.81; neut. equiv., 165.5. [z] Ethyl acetate solvent. [aa] 2,4-Dinitrophenylhydrazone, m.p. 122–123°. [bb] Identified by vapor phase chromatography. [cc] n^{25}D 1.4700. Infrared spectrum is in agreement with this assignment. *Anal.* Calcd. for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.18; H, 9.26. Deutsches Reich Patent 106,013, May 14, 1921, gives b.p. 208–212° (9 mm.); German Patent 763,204 gives n^{25}D 1.4720.

tam were 14–15%. The modification due to Criegee[2a,6] in which formaldehyde is added to the

(6) R. Criegee and G. Lohaus, *Ann.*, **583**, 6 (1953); *Chem. Ber.*, **86**, 1 (1953).

olefin solution prior to ozonolysis, was investigated in the expectation that reductive amination of the intermediate (I) formed by reaction of formaldehyde with the zwitterion (equation 3) would facili-

tate isolation of 6-aminocaproic acid or its derivatives. However, only a viscous water-soluble product was formed, which yielded crude hydrochloride and sulfate salts.

(3)
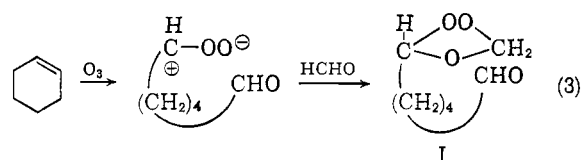
An exothermic decomposition resulted on treatment of this ozonolysis mixture with alcoholic potassium hydroxide. A red solution was formed, which on further heating to 50° deposited variable amounts of potassium carbonate. This characteristic red color was also obtained during the ozonolysis of cyclohexene in a mixture of ammonia and methanol or isooctane at −70°. A red ammonium ozonide has recently been characterized.[7]

A crystalline polymeric acid (m.p. 124–127°) was isolated from the ozonolysis-reductive amination of cyclohexene. The suggested structure of the nitrogen-containing polymeric product (II) is based on earlier proposals by Bailey.[8] The decomposition

II
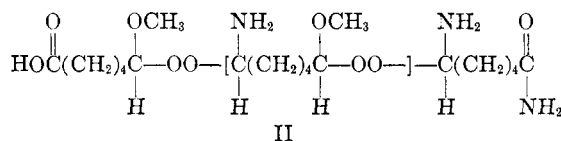
of 1-ethoxycyclohexene ozonolysis mixtures with water or acidified hydroxylamine solution gave 50–54% conversions to cyclohexanone and cyclohexanone oxime, respectively. Yet ethyl adipaldehydate, the expected product from ozonolysis of the double bond, and ethyl 6-aminocaproate, the predicted amino derivative of the aldehyde ester, were isolated from reductive aminations of the ozonolysis mixtures. The most likely source for cyclohexanone formation would involve an acid-catalyzed rearrangement of unreacted 1-ethoxycyclohexene during the work-up procedure. This view is substantiated by the report of Voronov and Rabkina[9] that 1-alkoxycyclohexenes are readily hydrolyzed to cyclohexanone by dilute aqueous acid solutions.

The reaction of dicyclohexyl ether with ozone-oxygen mixtures yielded cyclohexanone, cyclohexanol, and adipic acid. This product composition and the known resistance[10] of the cyclohexane ring to ozonolysis indicate a homolytic cleavage of the carbon-oxygen ether bond, presumably by an ozone initiated oxidation mechanism similar to

that proposed by Schubert and Pease,[11] and further elaborated by Bailey.[12] A trace of dicyclohexyl adipate was also obtained. Larger amounts of this ester, as well as butyric and valeric acids, were obtained from ozonolyses conducted at higher temperatures.

Experimental

Materials.—The purity of the cyclohexene used in these experiments was 99+% (vapor phase chromatographic analysis). *Cyclohexanone diethyl ketal* was prepared by the method of Boeseken and Tellegen,[13] b.p. 60–64° (6 mm.); n^{25}D 1.4376. *1-Ethoxycyclohexene*[14] was synthesized from the ketal in 73% conversion, b.p. 47–49° (10 mm.); n^{25}D 1.4510. Vapor phase chromatographic analysis indicated a purity of 95+%. *Dicyclohexyl ether* was obtained by hydrogenation of diphenyl ether at 175° and 10 hr. over 5% rhodium-on-alumina catalyst. The ether distilled at 101–102° (8 mm.); n^{25}D 1.4736.[15]

Ozonolysis. General Procedure.—The ozone source was a Welsbach T-23 ozonator. Oxygen flow rates to the ozonator were 0.02–0.04 cfm. at 8 p.s.i. The ozone content of the stream was 33–37 mg. ozone/l. oxygen. All ozone concentrations were measured with a Welsbach ozone meter.

The reactor consisted of a cylindrical flask, fitted with a gas inlet tube, stirrer, thermometer and a Dry Ice condenser. The condenser was connected in series with two Dry Ice traps, an ozone meter, and a stainless steel flow meter. After ozonolysis was completed, the mixture was degassed with a dry nitrogen stream.

Ozonolysis reactions were usually conducted in methanol to facilitate direct reductive amination of the products and to avoid formation of polymeric products. When formaldehyde was employed, it was generated by thermal depolymerization of paraformaldehyde and passed into the methanol solution of cyclohexene immediately prior to ozonolysis.

Typical Experiment. Ozonolysis and Reductive Amination of 1-Decene.—1-Decene (21.0 g., 0.15 mole) dissolved in 250 ml. of methanol was cooled to −15°. The oxygen-ozone mixture (37 mg. ozone/l. oxygen) was passed through the solution until 6.04 g. (0.12 mole) of ozone had been generated. The solution was flushed with dry nitrogen and then charged to an autoclave together with 51.0 g. (3.0 moles of liquid ammonia and 10.0 g. of Raney nickel. The sealed clave was pressured with 2900 p.s.i. of hydrogen, and the mixture heated at 150° for 8 hr. The mixture was filtered and distilled. *n*-Nonylamine (12.8 g., 59.8%) distilled at 90–94° (20 mm.). A small fraction distilled at 100–110° (20 mm.). The residue (6.0 g.) was recrystallized to yield 3.0 g. pelargonamide, m.p. 92–94° and 2.0 g. of di-*n*-nonylamine, m.p. 34–35° (hydrochloride, m.p. 230–232° dec.).

Oxidation of Dicyclohexyl Ether.—The reactor was charged with 9.5 g. (0.05 mole) of dicyclohexyl ether and 300 ml. of chloroform. Ozonized oxygen was passed through the mixture for 2.4 hr. at −30°. A total of 4.48 g. (0.09 mole) of ozone was employed. The blue solution was purged with dry nitrogen for 0.5 hr. The solution was washed successively with aqueous sodium sulfite solution and water. The mixture was extracted with ether; the ether extracts were dried (MgSO₄) and distilled. Cyclohexanone 2.5 g. (25.5% conversion), and cyclohexanol, 1.5 g. (15.0% conversion), were isolated. A small ester fraction (0.8 g.) distilled at 164–188° (4 mm.). The residue (3.0 g.) solidified. This was identified as adipic acid by infrared analysis.

(7) I. J. Solomon, K. Hattori, A. J. Kacmarek, G. M. Platz, and M. J. Klein, *J. Am. Chem. Soc.*, **84**, 34 (1962).

(8) P. S. Bailey, *J. Org. Chem.*, **22**, 1548 (1957); *Ind. Eng. Chem.*, **50**, 993 (1958).

(9) M. G. Voronov and J. M. Rabkina, *Izvest. Akad. Nauk, SSR*, **12**, 2240 (1960).

(10) J. R. Durland and H. Adkins, *J. Am. Chem. Soc.*, **61**, 429 (1939), obtained only small amounts of adipic acid from the reaction of cyclohexane with ozone at 0° for 100 hr.

(11) C. C. Schubert and R. N. Pease, *ibid.*, **78**, 2044, 5553 (1956).

(12) P. Bailey, *Chem. Rev.*, **58**, 984 (1958).

(13) J. Boeseken and F. Tellegen, *Rec. trav. chim.*, **57**, 133 (1938).

(14) C. L. Stevens and T. Tazuma, *J. Am. Chem. Soc.*, **76**, 715 (1954).

(15) A. Lacourt, *Bull. soc. chim. Belges*, **36**, 346 (1926).