The Autoxidation of 2-Cyano 3,3-Disubstituted Carboxylate Anions. The Synthesis of 3,3-Disubstituted 2-Oxocarboxylates[1]

NORMAN RABJOHN AND CHARLES A. HARBERT[2]

Department of Chemistry, University of Missouri, Columbia, Missouri 65201

Ethyl 3,3-dipentyl-2-oxooctanoate, **3a**, was isolated in low yields when oxygen was passed into the Grignard complex, 1, $R_1 = R_2 = R_3 = C_5H_{11}$, obtained from the conjugate addition of pentylmagnesium bromide to ethyl 2-cyano-3-pentyl-2-octenoate. The extension of this base-catalyzed autoxidation to ethyl 2-cyano 3,3-disubstituted carboxylates, 2, in polar solvents was found to afford good yields of 2-oxo esters, 3. It was shown that the nitrile group of 2 is lost during the autoxidation as a mixture of cyanate and cyanide ions in the approximate ratio of 4:1. Suggestions are made with regard to the mechanism by which 2 is converted to 3.

The conjugate addition of Grignard reagents to alkylidenecyanoacetates offers one of the best approaches to the formation of quaternary carbon atom systems.[3] We have observed more recently[4] that the highest yields of 1,4-addition products result when an excess (30-40%) of the organometallic reagent is employed, and that extended reaction times, in the presence of air, lead to the diminution of the ir nitrile absorption of the reaction product with concomitant production of materials which absorb at 2000-2050 cm^{-1}. It is thought that the latter is due to the presence of the ketenimine grouping (-C=C=N-) which is known[5] to absorb in this range. The present investigation was undertaken to examine in more detail the nature of the products which result from such prolonged reactions.

When an excess (~25%) of a titrated ether solution of pentylmagnesium bromide was added to a mixture of ethyl 2-cyano-3-pentyl-2-octenoate and cuprous iodide catalyst and the resulting complex, 1, $R_1 = R_2 = R_3 = C_5H_{11}$, stirred at room temperature, the color changed gradually from black to yellow to orange. After several hundred hours, the reaction mixture was hydrolyzed to give a viscous red oil: ir absorptions at 2035 (ketenimine), 1715 and 1750 (carbonyl), and 2255 (nitrile, very weak) cm^{-1}. Vapor phase chromatographic (vpc) analysis indicated the presence of two main components which corresponded to **2a** (35% by area) and an unknown compound (60%) of shorter retention time, as well as six minor constituents. Distillation afforded a small amount of **2a**, considerable
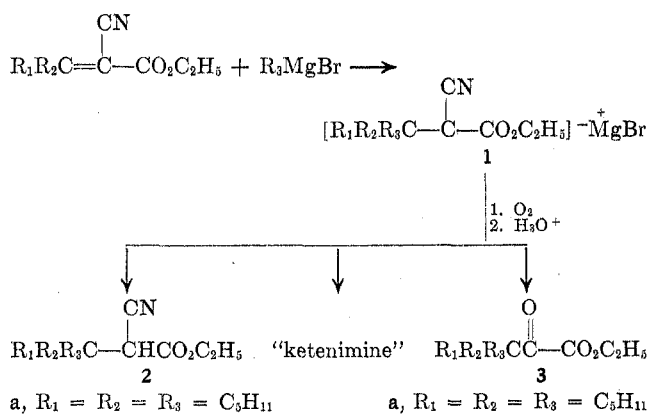
tarry residue, and a colorless oil (33%) which was identified as ethyl 3,3-dipentyl-2-oxooctanoate, **3a**. Efforts to isolate and identify the species responsible for the ketenimine absorption were largely futile and will not be described here.

Apparently **3a** was formed by the oxygenation of the Grignard complex, 1. A similar reaction has been reported by Stork, Herz, and Wendt[6] who oxygenated the conjugate addition complexes of several 16-dehydro-20-oxopregnanes to obtain the corresponding 17α-ols. The isolation of **3a**, rather than a cyanohydrin or a related material, in the present case, indicates that the oxygenated intermediate is unstable and decomposes with the loss of the nitrile group.

In an effort to decrease the reaction time and increase the yield of **3a**, air or oxygen was bubbled into ether solutions of the Grignard complex. The reaction time was lowered to 20 hr, but the yield of **3a** was decreased. Substitution of tetrahydrofuran for ether increased the yield to 41%, whereas the use of anisole led to a complex mixture which was not separated. Also, the solvent combination of benzene-triethylamine[7] was tried, but apparently the 1,4 addition failed in this system. Although the preparation of **3a** by this autoxidative route was novel, the synthetic utility appeared to be limited so attention was turned to an alternative approach.

The base-catalyzed autoxidation of the saturated cyano ester, **2a**, then was investigated since Russell and coworkers[8] have shown that this is an excellent way to oxidize compounds which have active hydrogen atoms. This choice proved to be fortunate since a 71% yield of **3a** was obtained by passing oxygen into a mixture of **2a**, potassium *t*-butoxide, dimethyl sulfoxide, and *t*-butyl alcohol. The use of other solvents was investigated and, since dimethylformamide gave slightly better results, 80% **3a**, it was employed in further autoxidations. *t*-Butyl alcohol was tried without success, and an autoxidation of **2a** in the benzyltrimethylammonium hydroxide-pyridine system[9] afforded the corresponding **3a**, but more volatile by-products were formed also.

The autoxidation was extended to the other 2 in Table I, and the results are recorded in Table II. The yields of 3 were generally good except in the case of ethyl 2-cyano-2-cyclohexylacetate. When the normal

$$R_1R_2C{=}C(CN){-}CO_2C_2H_5 + R_3MgBr \longrightarrow$$

$$[R_1R_2R_3C{-}\overset{CN}{\underset{|}{C}}{-}CO_2C_2H_5]^{-} \overset{+}{MgBr}$$

1

1. O$_2$
2. H$_3$O$^+$

$$R_1R_2R_3C{-}\overset{CN}{\underset{|}{C}}HCO_2C_2H_5 \qquad \text{``ketenimine''} \qquad R_1R_2R_3C\overset{O}{\overset{||}{C}}C{-}CO_2C_2H_5$$

2   **3**

a, $R_1 = R_2 = R_3 = C_5H_{11}$ a, $R_1 = R_2 = R_3 = C_5H_{11}$

(1) Taken from the Ph.D. Thesis of C. A. Harbert, 1967, and presented in part at the 2nd Midwest Regional American Chemical Society Meeting, Lawrence, Kan., Oct 27-28, 1966.

(2) NDEA Fellow, 1963-1966.

(3) N. Rabjohn, L. V. Phillips, and R. J. DeFeo, *J. Org. Chem.*, **24**, 1964 (1959).

(4) N. Rabjohn and C. L. King, unpublished results.

(5) C. L. Stevens and J. C. French, *J. Amer. Chem. Soc.*, **75**, 657 (1953).

(6) G. Stork, J. E. Herz, and M. W. Wendt, U. S. Patent 3,080,393 (1963); *Chem. Abstr.*, **59**, 8835 (1963).

(7) E. C. Ashby and R. Reed, *J. Org. Chem.*, **31**, 971 (1966).

(8) G. A. Russell, E. G. Janzen, A. G. Bemis, E. J. Geels, A. J. Moye, S. Mak, and E. T. Strom, "Selective Oxidation Processes," Advances in Chemistry Series, No. 51, American Chemical Society, 1965, pp 112-169.

(9) Y. Sprinzak, *J. Amer. Chem. Soc.*, **80**, 5449 (1958).

TABLE I

Ethyl 2-Cyano 3,3-Disubstituted Carboxylates **2**

$R_1{}^a$	$R_2{}^a$	$R_3{}^a$	Bp, °C (mm)	n^{25}D	Yield, %	Formula	Calcd, % C	H	Found, % C	H
C_2H_5	C_2H_5	C_5H_{11}	130–133 (2)	1.4513	72	$C_{15}H_{27}NO_2$ (a)^b	71.10	10.74	71.33	10.78
(CH$_2$)$_5$		C_6H_5	118–120 (0.4)	1.5250	76	$C_{17}H_{21}NO_2$ (b)	75.24	7.80	75.34	7.94
C_2H_5	C_7H_{15}	C_4H_9	135–138 (0.4)	1.4530	83	$C_{19}H_{35}NO_2$ (c)	73.73	11.40	73.89	11.25
C_4H_9	C_6H_{13}	C_5H_{11}	117–119 (0.1)	1.4532	77	$C_{21}H_{39}NO_2$ (d)	74.72	11.65	74.64	11.54
C_5H_{11}	C_5H_{11}	C_5H_{11}	119–122 (0.1)	1.4530	85	$C_{21}H_{39}NO_2{}^c$ (e)	74.72	11.65	74.81	11.75
C_5H_{11}	C_5H_{11}	C_6H_5	123–125 (0.05)	1.4940	89	$C_{22}H_{33}NO_2$ (f)	76.92	9.68	76.69	9.72

^{a} All alkyl groups are normal. ^{b} Identification for registry no. ^{c} Nmr (CCl$_4$) δ 4.20 (q, 2, OCH$_2$CH$_3$), 3.37 (s, 1, CH), and 0.7–1.7 (m, 36, CH$_2$, CH$_3$); ir (film) 2250 (CN) and 1750 cm^{-1} (CO).

TABLE II

3,3-Dialkyl-2-oxocarboxylates **3**

$R_1{}^a$	$R_2{}^a$	$R_3{}^a$	Bp, °C (mm)	n^{25}D	Temp, °C	Solvent	Yield, %	Formula	Calcd, % C	H	Found, % C	H
(CH$_2$)$_5$		H	105–107 (6)^b	1.4514	20	DMF^c	21	$C_{10}H_{16}O_3$ (g)^d				
C_2H_5	C_2H_5	C_5H_{11}	112–114 (2)	1.4369	20	DMF	72	$C_{14}H_{26}O_3$ (h)	69.38	10.81	69.58	10.72
(CH$_2$)$_5$		C_6H_5	120–122 (1)	1.5185	20	DMF	60	$C_{16}H_{20}O_4$ (i)	73.82	7.74	74.04	7.74
C_2H_5	C_4H_9	C_7H_{15}	90–93 (0.05)	1.4428	50	DMF	74	$C_{18}H_{34}O_3$ (j)	72.43	11.48	72.43	11.26
C_2H_5	C_4H_9	C_7H_{15}			20	DMSO-t-BuOH^e	61					
C_4H_9	C_5H_{11}	C_6H_{13}	112–115 (0.35)	1.4442	50	DMF	76	$C_{20}H_{38}O_3$ (k)	73.57	11.73	73.77	11.62
C_5H_{11}	C_5H_{11}	C_5H_{11}	94–96 (0.15)	1.4442	20	DMSO-t-BuOH^e	71	$C_{20}H_{38}O_3$ (l)	73.57	11.73	73.66	11.84
C_5H_{11}	C_5H_{11}	C_5H_{11}			20	DMF	80					
C_5H_{11}	C_5H_{11}	C_6H_5	113–115 (0.05)	1.4860	50	DMF	68	$C_{21}H_{32}O_3$ (m)	75.86	9.70	75.90	9.67

^{a} All alkyl groups are normal. ^{b} R. Fischer and T. Wieland, *Chem. Ber.*, **93**, 1387 (1960): bp 117–120° (15 mm). ^{c} Dimethylformamide. ^{d} Identification for registry no. ^{e} Dimethyl sulfoxide-t-butyl alcohol (80:20, v/v).

twofold excess of base was used with the latter, no ethyl cyclohexylglyoxylate was obtained, apparently because of further oxidation at carbon-3 of this initially formed product. This difficulty was alleviated to some extent (21% yield) by employing a stoichiometric amount of potassium *t*-butoxide.

The fate of the cyano group during the autoxidation was of interest since it could leave as cyanide or cyanate ion. Aurich[10] has shown that the base-catalyzed autoxidation of phenylacetonitrile affords cyanide ion, whereas cyanate ion is obtained from diphenylacetonitrile. These results suggest that cyanate ion should be formed on autoxidation of **2**. Accordingly, autoxidation mixtures from **2a** were analyzed by precipitation of the silver salts,[11] and the method was tested against standard solutions of cyanate and cyanide ions. When the method was applied to autoxidation mixtures from diphenylacetonitrile and phenylacetonitrile, the values obtained were 98% cyanate ion from the former and 90% cyanide ion from the latter; these are in good agreement with Aurich's results.[10] The data from the autoxidation of **2a** indicate that cyanate and cyanide ions are produced in the approximate ratio of 4:1.

The mechanism of the autoxidation of **2** has not been established completely, but it obviously must involve peroxy anion, **5** (Chart I). Its formation may be pictured as a direct reaction of **4** with oxygen,[9,12] or as a multistep process through radicals **6** and **7** as suggested by Russell.[8,13] It is not possible to distinguish between these alternative routes on the basis of the present study.[14] The peroxy anion, **5**, might be transformed

to products by at least the three routes shown in Chart I. Path "b" is suggested as the predominant one on the basis of the preferential formation of cyanate ion; similar reactions are well documented.[15] Path "a" seems to be the most likely way by which cyanide ion might arise.

The corresponding 2-oxo acids, **9**, were formed as minor products in the autoxidation of the 2-oxo esters, **3**. A plausible route to these compounds might be by a base-catalyzed elimination as shown.[16] Upon heating,

$$R_1R_2R_3CCOCO_2CH_2CH_3 \xrightarrow{\text{t-BuO}^-} R_1R_2R_3CCOCO_2H + CH_2{=}CH_2$$

3   **9**
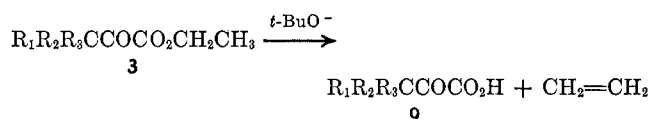
the 2-oxo acids, **9**, lose carbon dioxide and rearrange to ketones. A study of this reaction will be reported separately.

The autoxidation of 2-cyano-3,3-dipentyloctanenitrile was examined briefly during the course of the present investigation. The expected initial product was an acyl cyanide, **8**. It was hoped that the experiment might help to elucidate the fate of any **8** which arose by path "c" during the autoxidation of **2**; however, the autoxidation of the dinitrile produced a complex mixture which by ir analysis contained **8**, unchanged dinitrile, and acidic materials. No attempt was made to separate the oily product.

(10) H. G. Aurich, *Tetrahedron Lett.*, 657 (1964).

(11) G. Charlot, "Quantitative Inorganic Analysis," R. C. Murray, Translator, Wiley, 1954, pp 310–312.

(12) H. R. Gersmann, H. J. Nieuwenhuis, and A. F. Bickel, *Tetrahedron Lett.*, 1383 (1963).

(13) For recent reviews on the relative merits of the one- vs. two-electron transfer mechanism, see ref 8 and G. A. Russell, *J. Pure Appl. Chem.*, **15**, 185 (1967).

(14) Russell[8,13] has cited catalysis of the autoxidation of carbanions by nitro aromatics as evidence for the one-electron transfer mechanism. In a single experiment in the present investigation it appeared that the autoxidation of **2a** in DMSO-*t*-BuOH was not catalyzed significantly by nitrobenzene.

(15) C. Walling and S. A. Buckler, *J. Amer. Chem. Soc.*, **77**, 6032 (1955); M. Avramoff and Y. Sprinzak, *ibid.*, **85**, 1655 (1963).
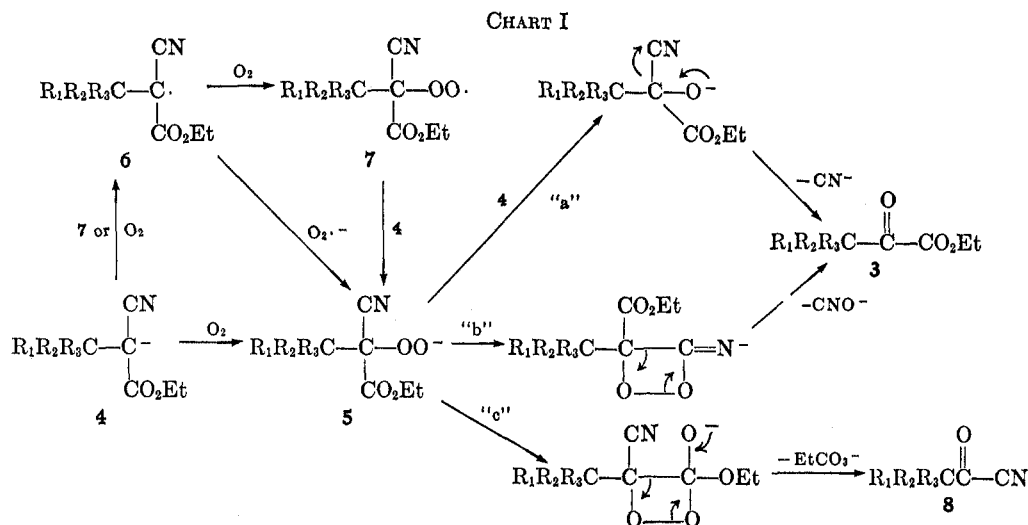
(16) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt, New York, N. Y., 1959, pp 493–494.

CHART I

Experimental Section[17]

Materials.—Unless otherwise stated, reagents were obtained from commercial sources and distilled prior to use. The potassium *t*-butoxide was prepared according to the method of Johnson and Schneider.[18] Magnesium sulfate was employed as the drying agent.

2-Cyano 3,3-Dialkyl Substituted Esters (2).—The compounds listed in Table I were prepared by the addition of Grignard reagents to ethyl alkylidenecyanoacetates in the presence of cuprous iodide according to a previously described procedure.[8] The needed cyanoacetates were synthesized by the method of Cope, *et al.*,[19] and those not described previously in the literature are recorded below.

Ethyl 2-Cyano-3-butyl-2-nonenoate.—This compound was obtained in 88% yield from 5-undecanone and ethyl cyanoacetate: bp 113–115° (0.5 mm); n^{25}D 1.4661.

Anal. Calcd for $C_{16}H_{27}NO_2$: C, 72.41; H, 10.26. Found: C, 72.60; H, 10.41.

Ethyl 2-Cyano-2-cyclohexylacetate.—The method of Marshall and Carroll[20] was adopted. From 50 g (0.26 mol) of ethyl cyclohexylidenecyanoacetate,[19] 3 g (0.08 mol) of sodium borohydride, and 120 ml of ethanol there was obtained 40.7 g (80%) of product: bp 124–125° (3 mm); n^{25}D 1.4580 [lit.[20] bp 112–113° (1.8 mm); n^{25}D 1.4574).

2-Cyano-3-pentyl-2-octenenitrile.—The method of Cope and Hoyle[21] was followed. The condensation of 150 g (0.8 mol) of 6-undecanone with 52.8 g (0.8 mol) of malononitrile afforded 92 g (53%) of material: bp 112–114° (1 mm); n^{25}D 1.4713.

Anal. Calcd for $C_{14}H_{22}N_2$: C, 77.01; H, 10.16. Found: C, 76.87; H, 9.97.

2-Cyano-3,3-dipentyloctanenitrile.—A titrated[22] ether solution of 0.12 mol of pentylmagnesium bromide was added to a mixture of 25 g (0.115 mol) of 2-cyano-3-pentyl-2-octenenitrile and 0.57 g (0.003 mol) of cuprous iodide in 100 ml of anhydrous ether while the temperature was maintained at 24–26°. The mixture was allowed to stir overnight, hydrolyzed with dilute hydrochloric acid, and worked up in the usual manner[8] to give 19.4 g (60%) of product: bp 105–107° (0.1 mm); n^{25}D 1.4550.

Anal. Calcd for $C_{19}H_{34}N_2$: C, 78.56; H, 11.80. Found: C, 78.50; H, 11.65.

---

(17) The ir spectra were recorded on a Perkin-Elmer Model 237-B spectrophotometer and the nmr spectra were run on a Varian A-60 spectrometer employing tetramethylsilane as an internal standard. Elemental microanalyses were performed by Drs. Weiler and Strauss, Oxford, England, and Galbraith Laboratories, Inc., Knoxville, Tenn. Analytical vpc was done on a Wilkens Aerograph A90-P3 and a Microtek 2000-R gas chromatograph. All boiling points are uncorrected.

(18) W. S. Johnson and W. P. Schneider, "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., Wiley, New York, N. Y., 1963 p 132.

(19) A. C. Cope, C. M. Hofmann, C. Wyckoff, and E. Hardenbergh, *J. Amer. Chem. Soc.*, **63**, 3452 (1941).

(20) J. A. Marshall and R. D. Carroll, *J. Org. Chem.*, **30**, 2751 (1965).

(21) A. C. Cope and K. E. Hoyle, *J. Amer. Chem. Soc.*, **63**, 733 (1941).

(22) H. Gilman, P. D. Wilkinson, W. P. Fishel, and C. H. Meyers, *ibid.*, **45**, 150 (1923).

Autoxidation of the Grignard Complex, 1, $R_1 = R_2 = R_3 = C_5H_{11}$, from the Reaction of Pentylmagnesium Bromide with Ethyl 2-Cyano-3-pentyl-2-octenoate. A. Prolonged Exposure to Air.—A titrated[22] ether solution of 0.32 mol of pentylmagnesium bromide was added to a mixture of 70 g (0.26 mol) of ethyl 2-cyano-3-pentyl-2-octenoate[19] and 1.32 g (0.007 mol) of cuprous iodide in 250 ml of dry ether while the temperature was maintained at 24–26°. The drying tube was removed from the condenser and the mixture was allowed to stir for 1000 hr at room temperature. The orange reaction mixture was hydrolyzed with dilute hydrochloric acid and worked up to give 89 g of a red oil whose ir spectrum (neat) showed absorptions at 2035 (ketenimine, m),[5] 1655 (C=C, m), and·1750 and 1715 cm^{-1} (C=O, s). The vpc chromatogram (silicone rubber on Chromosorb W, 45–60) had only two major peaks corresponding to cyano ester 2a (35%) and an unknown (60%) of shorter retention time. A 24-g portion of the crude product was distilled through a spinning-band column to give 7.9 g (33%) of a compound, identified as ethyl 3,3-dipentyl-2-oxooctanoate, 3a, bp 94–96° (0.15 mm), n^{25}D 1.4442; 4 g of cyano ester 2a; and 8 g of a tarry residue. An ir spectrum (neat) of the low-boiling ester had peaks at 1745 and 1715 (C=O, s) and 1270 cm^{-1} (CO$_2$R, s) and the nmr spectrum (neat) had absorptions at δ 4.22 (q, 2, OCH$_2$CH$_3$) and 0.7–1.9 (m, 36, CH$_2$, CH$_3$).

Anal. Calcd for $C_{20}H_{38}O_3$: C, 73.57; H, 11.73. Found: C, 73.66; H, 11.84.

B. Reaction with Oxygen.—A titrated ether solution of 0.08 mol of pentylmagnesium bromide was added dropwise to a mixture of 17.2 g (0.065 mol) of ethyl 2-cyano-3-pentyl-2-octenoate and 0.33 g (0.002 mol) of cuprous iodide in 65 ml of dry ether. The reaction mixture was allowed to stir at room temperature for 2 hr and the flask was fitted with a Dry Ice condenser and a gas-dispersion tube. Oxygen was admitted for 20 hr and the mixture was hydrolyzed with dilute hydrochloric acid and worked up. The resulting black oil was distilled through a spinning-band column to give 3.8 g (18%) of 3a, bp 96–98° (0.25 mm), n^{25}D 1.4450, and a tarry residue.

Autoxidation of Ethyl 2-Cyano 3,3-Disubstituted Alkanoates (2).—The following procedure is a modification of the method of Russell and coworkers[8] and is representative of the method used to obtain the 2-keto esters, 3, recorded in Table II. In a 200-ml three-necked flask equipped with a magnetic stirrer, gas-dispersion tube, and reflux condenser, protected with a drying tube, were placed 16.8 g (0.05 mol) of ethyl 2-cyano-3,3-dipentyloctanoate, 2a, 11.2 g (0.1 mol) of potassium *t*-butoxide, and 150 ml of anhydrous DMF. Oxygen was passed through the solution for 19 hr at room temperature, and then it was quenched with water (100 ml) and extracted with five 50-ml portions of ether. The combined extracts were washed, dried, and concentrated to give an oil which was distilled through a spinning-band column. There was obtained 13.1 g (80%) of 3a: bp 103–108° (0.5 mm); n^{25}D 1.4444.

The autoxidation was repeated several times, both at room temperature and 50°; only 7–9 hr was required at the latter temperature. The yields were comparable at both temperatures and varied from 51 to 80%. Similar autoxidations in DMSO-*t*-

BuOH (80:20 v/v) afforded 3a in 71% yield and in 51–66% yield when carried out at 50 ± 2°, with the balance of the product being a lower boiling ketone.

Autoxidation of Ethyl 2-Cyano-3,3-dipentyloctanoate. Determination of Cyanide and Cyanate Ions.[11]—The determination was carried out several times and the following procedure is representative. Oxygen was passed into a solution of 3.37 g (0.01 mol) of 2a and 2.24 g (0.02 mol) of potassium *t*-butoxide in 60 ml of DMSO-*t*-BuOH (80:20 v/v) for 7 hr at 50 ± 3°. The mixture was quenched with 50 ml of distilled water and extracted with three small portions of ether and the aqueous portion was adjusted to pH 5–7 with dilute nitric acid. A solution of 2 g (0.012 mol) of silver nitrate in 20 ml of distilled water was added and the white precipitate was collected on a tarred, sintered-glass funnel. It was washed with two small portions of water and treated with five 15-ml portions of dilute (1:5) nitric acid. The remaining silver cyanide was washed with distilled water and dried. The solid weighed 0.33 g (0.0025 mol) which corresponds to 25% cyanide ion; the cyanate ion was taken as the difference from 100%.

The results varied from 25 to 27% cyanide ion in DMSO-*t*-BuOH (80:20 v/v) to 14–18% cyanide ion in DMF. These values represent an approximate product ratio of 80:20 cyanate to cyanide ion on the basis of the determinations with standard solutions. The latter contained 20% cyanide and 80% cyanate ions, in the appropriate solvents, and were subjected to the conditions of the autoxidation and work-up procedure prior to precipitation of the silver salts. The average values for cyanide and cyanate were found to be 23 and 77% in DMSO-*t*-BuOH and 15 and 85% in DMF.

Registry No.—Table I—a, 25593-95-7; b, 25593-96-8; c, 25593-97-9; d, 25593-98-0; e, 25593-99-1; f, 25594-00-7; Table II—g, 13275-31-5; h, 25594-02-9; i, 25565-11-1; j, 25565-12-2; k, 25594-03-0; l, 25594-04-1; m, 25565-13-3; ethyl 2-cyano-3-butyl-2-nonenoate, 25594-05-2; 2-cyano-3-pentyl-2-octenenitrile, 13017-59-9; 2-cyano-3,3-dipentyloctanenitrile, 25594-07-4.

Additions to Bicyclic Olefins.   IV.
The Facile Reduction of Labile Epoxides of Bicyclic Olefins by Lithium in Ethylenediamine

HERBERT C. BROWN,[1] SHIRO IKEGAMI,[2] AND JAMES H. KAWAKAMI[3]

Richard B. Wetherill Laboratory, Purdue University, Lafayette, Indiana 47907

The reduction of many hindered and unstable bicyclic epoxides with lithium aluminum hydride is very slow and is often accompanied by rearrangement. In contrast, the addition of lithium metal to an ethylenediamine solution of such epoxides at 50° reduces such epoxides rapidly, without rearrangement. In this way, norbornene oxide is readily reduced to essentially pure *exo*-norbornanol in 87% yield. Similarly, badly hindered and labile epoxides, such as 2-methylene-7,7-dimethylnorbornane oxide and *exo*- and *endo*-7,7-dimethylnorbornene oxides, were readily reduced to the corresponding tertiary and secondary alcohols, respectively.

We were interested in studying the stereochemistry of the epoxidation of norbornene, 7,7-dimethylnorbornene, and related olefins.[4] If the resulting epoxides could be reduced quantitatively to the corresponding known bicyclic alcohols, the stereochemistry of epoxidation could be conveniently established by vapor phase chromatography.

Unfortunately, the usual reduction of epoxides by lithium aluminum hydride is very slow for many of these bicyclic epoxides. Moreover, such reductions are often accompanied by rearrangements. For example, in order to achieve a reasonable rate, Kwart and Takeshita[5] found it necessary to treat norbornene oxide with lithium aluminum hydride in boiling N-ethylmorpholine. They obtained 16% of the rearranged 7-norbornanol in addition to 84% of the expected 2-norbornanol (eq 1). The 7-norbornanol presumably
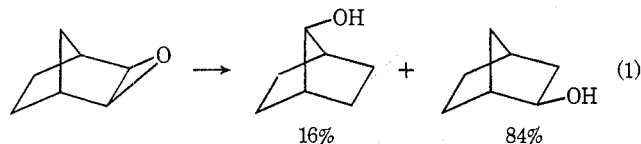
resulted from electrophilic ring opening of the epoxide ring by lithium aluminum hydride.

Data reported by Hallsworth and Henbest[6,7] indicated that some steroidal epoxides, which were quite unreactive to lithium aluminum hydride, were easily reduced with a large excess of lithium in ethylamine. However, they obtained some olefin in the reduction of labile steroidal epoxides.

Consequently, a study was begun to determine whether the various norbornyl epoxides would be reduced quantitatively with lithium–ethylamine to the corresponding alcohols without rearrangements or eliminations occurring to complicate the interpretation of the results.

Results and Discussion

We found ethylenediamine (bp 116°) a more convenient medium to use than the much lower boiling ethylamine (bp 16°) for routine laboratory reduction of hindered epoxides.[8] After some exploratory experiments an exceedingly simple procedure was developed and proved highly satisfactory. This procedure involves dissolving 10 mmol of norbornene oxide in 10 ml of ethylenediamine, adding 30 mg-atoms of lithium wire in 2-mm pieces, and heating at 50° with stirring until a

(1) Author to whom correspondence should be addressed.

(2) Postdoctorate research associate on a grant (GP 6492 X) supported by the National Science Foundation.

(3) Graduate research assistant on grants (G 19878 and GP 6492 X) supported by the National Science Foundation.

(4) H. C. Brown, J. H. Kawakami, and S. Ikegami, *J. Amer. Chem. Soc.*, in press.

(5) H. Kwart and T. Takeshita, *J. Org. Chem.*, **28**, 670 (1963).

(6) A. S. Hallsworth and H. B. Henbest, *J. Chem. Soc.*, 3571 (1960).

(7) A. S. Hallsworth and H. B. Henbest, *ibid.*, 4604 (1957).

(8) (a) The lithium reduction in ethylenediamine is much less vigorous than in ethylamine. We have encountered side reactions in ethylamine when the reaction conditions were not controlled (see Discussion). (b) Isolation of the alcohol from the epoxide reduction in ethylenediamine is simple because the base is very soluble in water where it exists as the hydrate, and is only slightly soluble in ether, whereas ethylamine is miscible both in water and in ether.