TABLE II

ELECTROREDUCTION OF ALIPHATIC KETONES WITH A 6-HR STANDING PERIOD BEFORE ELECTROLYSIS

Entry	Ketone	Yield,[a] % N-Methylalkylamine	Yield,[a] % Alcohol
1[b]	2-Heptanone	73[c]	5
2[b]	Cyclohexanone	70[d]	9
3[e]	Cyclopentanone	70[d]	10
4[f]	Diethyl ketone	52[g]	27
5[f]	Diisopropyl ketone	0	83

[a] Yields are based upon starting ketone. [b] The product was analyzed on an Aerograph gas chromatograph using a 10 ft, 24% silicone oil 200 column at 150°. [c] The nmr spectrum of this compound was identical with its published spectrum (see footnote *b*, Table I). [d] The ir spectrum of this compound was identical with its published spectrum (see footnote *b*, Table I). [e] The product was analyzed on a F & M Model 500 gas chromatograph using a 10 ft, 20% Carbowax 20 M–5% KOH column at 110°. [f] The product was analyzed on a F & M Model 500 gas chromatograph uing a 10 ft, 20% Carbowax 20 M–5% KOH column at 100°. [g] $n^{25}D$ 1.4066 [lit. $n^{25}D$ 1.4060; A. C. Cope, N. A. Le Bel, H. H. Lee, and W. R. Moore, *J. Amer. Chem. Soc.*, **79**, 4720 (1957)].

electrolytically in the normal manner, produced a material which contained 77% of N-methyl-2-heptylamine.

Experimental Section

General Procedure for the Electroreduction of Cyclic and Acyclic Aliphatic Ketones (Ketone Added after the Addition of Solvent, Zero Standing Time before Electrolysis).—Lithium chloride (17 g, 0.4 mol) and anhydrous methylamine (300 ml) were placed in a three-neck, 0.5-l. flask fitted with a Dry Ice condenser and two (2 × 5 cm) platinum electrodes. Immediately after addition of ketone (0.05 mol), the solution wss electrolyzed by passing a current of 2 A through the system for 2 hr and 41 min (19,300 C).[9] Ether was added, and the solvent was allowed to evaporate through a condenser that was kept at −5°. The residue was hydrolyzed with water, and the aqueous solution was extracted with ether. The ether extracts were combined, dried ($MgSO_4$), concentrated, and distilled to give the product. The results obtained for 2-heptanone, cyclohexanone, cyclopentanone, diethyl ketone, and diisopropyl ketone are summarized in Table I.

Electroreduction of 2-Heptanone (Dropwise Addition of Ketone to Cell during Electrolysis).—Into a four-neck, 100 × 170 mm electrolysis cell[10] fitted with a Dry Ice condenser, addition funnel, and two platinum electrodes were placed lithium chloride (34 g, 0.8 mol) and methylamine (600 ml). Current (2 A) was passed through the cell, and 2-heptanone (5.85 g, 0.05 mol dissolved in 150 ml of ether) was added dropwise over a period of 2 hr and 20 min. Solvent was then allowed to evaporate through a water condenser and the resulting residue was hydrolyzed (water). The organic material was worked up in the usual manner. Distillation afforded 3.6 g (62%) of product, bp 83–92° (*ca.* 40 mm). Analysis by glpc (10 ft, 24% silicone oil 200 column, 155°), showed the product to consist of 2-heptanol (97%) and N-methyl-2-heptylamine (3%). The yields based upon starting ketone were: 2-heptanol, 60%; N-methyl-2-heptylamine, 2%.

General Procedure for the Electroreduction of Cyclic and Acyclic Aliphatic Ketones (Ketone Added before the Addition of Solvent, 6-Hr Standing Period before Electrolysis).—Lithium chloride (17 g, 0.4 mol) and ketone (0.05 mol) were placed in a three-neck, 500-ml flask fitted with a Dry Ice condenser and two platinum electrodes. Then 300 ml of methylamine was added, and the resulting solution was allowed to stand (6 hr) before a current (2 A) was passed through the system for 2 hr and 41 min (19,300 C).[11] At the end of this time, ether was added and the solvent was evaporated.[12] The usual work-up, followed by distillation, yielded the product. The results for the reduction of 2-heptanone, cyclohexanone, cyclopentanone, diethyl ketone, and diisopropyl ketone are shown in Table II.

N-Methylimine of 2-Heptanone.—2-Heptanone (24 g, 0.2 mol) and methylamine (600 ml) were placed in a 1-l., three-neck flask fitted with a Dry Ice condenser and a magnetic stirrer. After the solution was allowed to stir for 1 hr, solvent was evaporated through a water condenser. The resulting residue was taken up in ether, dried ($CaSO_4$), and stripped of solvent to give 27 g of product. Analysis by glpc (10 ft, 24% silicone oil 200 column), showed the product to consist of 2-heptanone (34%) and the N-methylimine of 2-heptanone (66%).[13]

Electroreduction of the N-Methylimine of 2-Heptanone.—In a three-neck flask (300 ml) fitted with a Dry Ice condenser and two platinum electrodes were placed lithium chloride (8 g, 0.2 mol), 3 g of material (80% N-methylimine of 2-heptanone and 20% 2-heptanone) obtained by preparative gas chromatography[14] of the above reaction product, and 200 ml of methylamine. Current (1 A) was passed through the system for 1 hr and 15 min (4500 C). The solvent was allowed to evaporate, and the resulting residue was worked up as in the previous experiment to give 2.3 g of residue, which (analysis by glpc[14]) was shown to consist of N-methyl-2-heptylamine (77%), 2-heptanone (13%), and the N-methylimine of 2-heptanone (10%).

Registry No.—2-Heptanone, 110-43-0; N-methylimine of 2-heptanone, 22058-71-5; cyclohexanone, 108-94-1; cyclopentanone, 120-92-3; diethyl ketone, 96-22-0; diisopropyl ketone, 565-80-0.

Acknowledgment.—This research was sponsored by the Air Force Office of Scientific Research, Office of Aerospace Research, U. S. Air Force, under AFOSR Grant 822-67.

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(9) In the reduction of cyclohexanone, current (2 A) was passed for 4 hr (28,800 C) rather than for 2 hr and 41 min.

(10) R. A. Benkeser and E. M. Kaiser, *J. Amer. Chem. Soc.*, **85**, 2858 (1963).

(11) In the reduction of cyclohexanone, current (2 A) was passed for 6 hr (43,200 C) rather than for 2 hr and 41 min.

(12) In the reduction of 2-heptanone and cyclohexanone, a water condenser was used. In the reduction of cyclopentanone, diethyl ketone, and diisopropyl ketone, a condenser that was kept at −5° was used.

(13) The ir spectrum showed imine absorption at 6.1 μ (L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley & Sons, Inc., New York, N. Y., 1958, p 267) and its nmr spectrum (CCl_4) showed a 2.5 H singlet at τ 7.0, a 2 H multiplet at 7.5–8.0, a 3 H multiplet at 8.0–8.3, a 6 H multiplet at 8.3–8.9, and a 3 H multiplet at 9.0–9.2.

(14) An Aerograph Autoprep gas chromatograph with a 10 ft 24% silicone oil 200 column was used. Although the imine could be collected pure, it undergoes rapid hydrolysis in air.

α Anions of Carboxylic Acids. I. Effect of Hexamethylphosphoramide on Metalation and Alkylation

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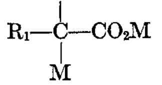
α anions of carboxylic acids (I) offer unique opportunities in synthesis.



$$R_1-\overset{R_2}{\underset{M}{C}}-CO_2M \qquad M = Na, Li$$

I

Unfortunately, their utility has not been investigated with acids other than acetic acid[2] and methyl-branched acids of chain lengths no greater than C_4.[3] Typically, disodio derivatives con-

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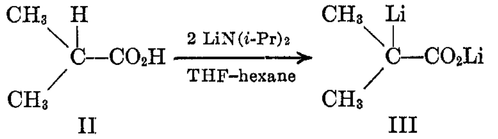
(1) Agricultural Research Service, U. S. Department of Agriculture.

(2) D. O. DePree and R. D. Closson, *J. Amer. Chem. Soc.*, **80**, 2311 (1958).

(3) P. L. Creger, *ibid.*, **89**, 2500 (1967), and references cited therein.

taining saturated β-carbon atoms were found to be unstable at the temperatures necessary for their formation.[2]

Creger[3] has recently prepared lithium α-lithio isobutyrate (III) in high yield by treating isobutyric acid (II) with 2 equiv of lithium diisopropylamide in tetrahydrofuran (THF)-hexane solution. Alkylation of this dianion in homogeneous solution with butyl bromide (iodide) gave 80% (89%) yield of 2,2-dimethylhexanoic acid.



II III

We have made an effort to apply this procedure to the alkylation of straight-chain aliphatic acids and have found it to be quite unsatisfactory. In general, we observed that the reaction mixtures of straight-chain acid dianions are cloudy and heterogeneous, and furthermore, yields of the corresponding α-butyl derivatives of n-aliphatic acids (C_7–C_{18}) are in the low range (29–44%) (Table I). Therefore, in order to effect the alkylation of long straight-chain acids, a modification was essential.

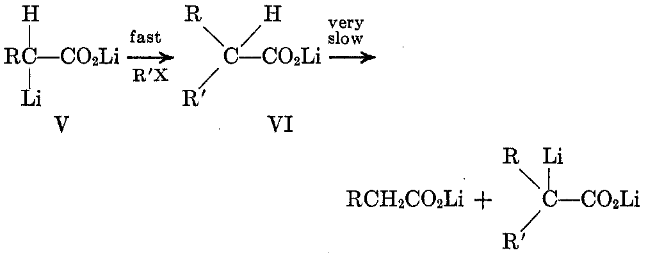
TABLE I

PRODUCT YIELDS FROM REACTIONS OF STRAIGHT- AND BRANCHED-CHAIN METALATED ACIDS WITH BUTYL BROMIDE

	% yield[a]	
Starting acid	THF–hexane	THF–hexane–HMPA
Straight chain	2-Butyl Acid	
Heptanoic	43	93
Pelargonic	34	90
Myristic	29	90
Stearic	44[b]	87[b,c]
Branched chain	2,2-Dibutyl Acid	
Isobutyric	80	75
2-Butylheptanoic	50[d]	15[e]
2-Butylpelargonic	45	9

[a] All yields are based on distilled, recrystallized, or chromatographed product whose purity was determined by gas chromatographic analysis. Satisfactory elemental analyses and consistent ir, nmr, and mass spectra data were obtained for all products and are in accord with their reported values. [b] Best yields were obtained after stirring the dianion solution at room temperature for 1.5 hr. [c] Two equivalents of HMPA used. Some cloudiness was noted in the reaction mixture. [d] Product consisted of 30% 1-octene when the dianion of 2-butylheptanoic acid was treated with 1-bromooctane. [e] Product consisted of 80–85% 1-octene when the dianion of 2-butylheptanoic acid was treated with 1-bromooctane.

The use of hexamethylphosphoramide (HMPA) as cosolvent permitted the preparation of dianions in clear homogeneous solutions. The metalated n-aliphatic acids are then alkylated with n-butyl bromide to give α-butyl acids in yields generally exceeding 90%. Examples of the reaction are recorded in Table I with the corresponding results of the unmodified method. Dialkylated acids were not observed even in trace amounts. One may conclude from this observation that lithium–hydrogen exchange between the straight-chain acid V and the α-branched acid VI to generate the dianion of dialkyl acetic acid (VII) is not competitive with the very rapid nucleophilic attack of V on R′X. This is equally the case for reactions in the absence of HMPA.



V VI IV VII

The unique solvent properties of HMPA have been reviewed.[4a] It has attractive solvation properties, which facilitates the preparation of dianions[4b] and accelerates nucleophilic reactions. Use of HMPA avoids undesired side reactions, since it does not itself metalate or compete for base as do the basic solvents dimethyl sulfoxide and N,N-dimethylformamide.[5,6]

HMPA as a strong basic cosolvent has a yield-lowering effect on alkylation of dianionic α-branched acids, in contrast to its yield-enhancing effect on alkylation of dianionic n-aliphatic acids. Yields are only slightly lowered for α-butylation of isobutyric acid but dramatically lowered (9–15%) in the case of α-butylation of α-butyl acids. Reaction of n-octyl bromide with metalated 2-butyl heptanoic acid in THF–hexane–HMPA allowed isolation of extensive amounts of 1-octene (80–85%). This evidence, along with the trend seen in Table I, indicates that as the extent of chain branching of the acid increases, elimination in THF–hexane–HMPA becomes significant. It is noteworthy that the substitution/elimination ratio shows a much smaller change without the addition of HMPA.[7]

The synthetic possibilities for preparing secondary acids from n-aliphatic acids in HMPA solutions are exceptional. These compounds are normally difficult to prepare in high yields. Typically, these compounds are obtained by free radical addition of aliphatic acids to olefins in yields approximating 50–70%.[8] The preparations are generally inefficient by requiring high acid to olefin ratios (>10:1) and are difficult to purify.

The synthetic utility of metalated straight-chain aliphatic acids prepared in THF–hexane–HMPA solutions is now being examined with such reagents as CO_2, CS_2, alkyl nitrates, O_2, and ethyl formate. Detailed studies of these reactions will be shortly forthcoming.

Experimental Section

Solvent Purification.—THF was dried over sodium, distilled, and then redistilled from a ketyl solution (sodium and benzophenone) before use.

HMPA was distilled from sodium hydride at reduced pressure and stored over molecular sieves.

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[4] (a) H. Normant, *Angew. Chem. Intern. Ed. Engl.*, **6**, 1046 (1967); (b) H. Normant and T. Cuvigny, *Bull. Soc. Chim. Fr.*, 1881 (1965); see this reference for other examples of dianions prepared in HMPA.

[5] T. J. Wallace, H. Pobiner, and A. Schriesheim, *J. Org. Chem.*, **30**, 3768 (1965).

[6] Complete lithium–hydrogen exchange between DMSO and the dianion species is noted at 0°.

[7] Amounts of 1-octene isolated from the reaction of 1-bromooctane and metalated 2-butylheptanoic acid in THF–hexane are in the order of 30%.

[8] (a) A. D. Petrov, G. I. Nikishin, and Yu. N. Ogibin, *Dokl. Akad. Nauk SSSR*, **131**, 580 (1960); (b) T. Perlstein, A. Eisner, W. C. Ault, and P. A. DeHaven, *J. Amer. Oil Chem. Soc.*, **45**, 859 (1968).

Procedure.—The procedure described here for the preparation of 2-butylheptanoic acid is typical of the method used for all the acids mentioned in Table I.

2-Butylheptanoic Acid.—Anhydrous THF (35 ml) and diisopropylamine (4.9 g, 0.049 mol) was added to a dry, nitrogen-flushed flask under an atmosphere of nitrogen. *n*-Butyllithium in hexane (30 ml of 1.6 *M*, 0.048 mol) was added to the magnetically stirred solution at such a rate as to maintain the temperature below 0°. *n*-Heptanoic acid (2.95 g, 0.0227 mol) was then added to the cold basic solution and again the temperature was kept below 0°. After 15 min, HMPA (9 ml, 0.050 mol) was added to the milky white solution, which became transparent and light yellow after 5 min of stirring at 5°. The solution was stirred for an additional 15 min at 5°, and *n*-butyl bromide (3.3 g, 0.024 mol) was added at once at 0°. The reaction temperature immediately rose to 18°. After 2 hr of additional stirring at room temperature, the reaction was worked up in the following manner. Dilute hydrochloric acid (10%) was added at 0° until the mixture became acidic. The aqueous layer was separated and extracted with petroleum ether (bp 30–60°). The combined organic layers were washed five times with 100-ml portions of dilute hydrochloric acid, H_2O, and saturated sodium chloride solutions. The organic layer was then dried and the solvent was stripped off. The residue was distilled through a 5-in. Vigreux column to give 4.06 g (96%) of a colorless oil, bp 175–177° (30 mm). Examination of this oil on a gas chromatographic column (0.25 in. × 6 ft, 25% DEGA, phosphoric acid treated 60–80 Chromosorb A) at 180° showed this product to be 96.5% 2-butylheptanoic acid and 3.5% *n*-heptanoic acid.

Registry No.—HMPA, 680-31-9; 2-butylheptanoic acid, 22058-70-4.

An Improved Synthesis of 2,4,6-Octatriene

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The title compound has been prepared previously *via* a coupling reaction followed by a dehydration.[1] The yields are low (20–40%) and the product is often contaminated with its isomers.[1c,d,h] Recently, 1,3,6- and 1,3,7-octatriene (I and II, respectively) have become available in high yield by the metal-catalyzed dimerization of the butadiene.[2] Attempts at converting I and II to 2,4,6-octatriene (III) have shown that the bases studied which are strong enough to isomerize II will catalyze a cyclization of the octatrienyl anion, forming a mixture of methylcycloheptadienes.[3,4]

We wish now to report that some hydroxide bases in dimethyl sulfoxide (DMSO) are specific for the isomerization of I and II, giving 70–85% yields of III with little or no accompanying cyclization. Triton B and tetramethylammonium hydroxide catalyze the reaction smoothly, and <5% cyclic products are obtained even with prolonged reaction times. Cyclization is obtained with KOH; however, the reaction time may be controlled to give an 84% yield of 95% pure 2,4,6-octatriene. Other alkali metal hydroxides give a less clear-cut reaction.

Thus, 2,4,6-octatriene may be obtained as a mixture of stereoisomers[3] in 70% overall yield from butadiene.

Experimental Section

All boiling points are uncorrected. Analyses by gas–liquid partition chromatography (glpc) were performed on an F & M Model 720 chromatograph using a 20-ft column packed with 20% tris(cyanoethoxy)propane on 35/80 mesh Chromosorb P. The octatrienes were prepared by the dimerization of butadiene in the presence of a zero-valent nickel complex and a hydroxylic solvent,[2c] and consisted of a 1:3 mixture of 1,3,6-octatriene and 1,3,7-octatriene contaminated with *ca.* 6% of 4-vinylcyclohexene and 1–2% of other unidentified materials.

Preparative Isomerization of the Octatriene Mixture. A. With Triton B in DMSO at 90°.—The octatriene mixture (0.82 g) and DMSO (10.0 ml) were sealed under N_2 in a glass-walled pressure vessel equipped with a septum through which liquids could be injected. After the mixture had equilibrated at 90°, 0.25 ml of Triton B (40% benzyltrimethylammonium hydroxide in methanol, K & K Laboratories) was added. The reaction mixture was stirred for 10 min, cooled briefly, and quenched in 20 ml of ice–water. Following work-up, 0.67 g (81.8%) of material was distilled at 58° (30 mm). Glpc analysis showed the presence of 2,4,6-octatriene (85.3%), methylcycloheptadienes (3.6%), 4-vinylcyclohexene (5.8%), 1,3,7-octatriene (1.3%), and unidentified materials (4.0%). Fractional distillation may be employed to give III in >95% purity

B. With KOH in DMSO at 80°.—Potassium hydroxide pellets (5.0 g) and DMSO (30 ml) were sealed in a pressure vessel. When equilibrium was established, 2.28 g of octatrienes was added *via* a syringe and stirring was continued for 2 hr at 80°. The reaction vessel was allowed to cool at room temperature for 30 min, at which time the contents were quenched in 150 ml of ice–water. After work-up, 1.91 g (84%) of 95% pure 2,4,6-octatriene was distilled at 66° (44 mm). In a separate experiment the reaction temperature and time were extended to 105° and 4 days, respectively, and a 53% yield of methylcycloheptadienes[3] (96% pure) was obtained.

Registry No.—III, 764-75-0.

Acknowledgment.—The author wishes to express his gratitude to Dr. E. A. Zuech for generously supplying authentic samples as well as for invaluable discussions.

[1] (a) R. Kuhn and C. Grundmann, *Chem. Ber.*, **71**, 442 (1938); (b) P. Nayler and M. C. Whiting, *J. Chem. Soc.*, 3037 (1955); (c) G. F. Woods and A. Viola, *J. Amer. Chem. Soc.*, **78**, 4380 (1956); (d) K. Alder and H. von Brachel, *Ann.*, **608**, 195 (1957); (e) J. Normant, *Bull. Soc. Chim. Fr.*, 1868 (1963); (f) V. L. Bell, *J. Polym. Sci., Part A*, **2**, 5291 (1964); (g) E. N. Marvell, G. Caple, and B. Schatz, *Tetrahedron Lett.*, 385 (1965); (h) C. W. Spangler and R. D. Feldt, *Chem. Commun.*, 709 (1968).

[2] (a) S. Takahashi, T. Shibano, and N. Hagihara, *Tetrahedron Lett.* 2451 (1967); *Bull. Chem. Soc. Jap.*, **41**, 454 (1968); (b) E. J. Smutney, *J. Amer. Chem. Soc.*, **89**, 6793 (1967); E. J. Smutney and H. Chung, *Preprints, Div. Petrol. Chem., Amer. Chem. Soc.*, **14**, No. 2, B112 (1969); (c) see, for example, J. Feldman, O. Frampton, B. Saffer, and M. Thomas, *ibid.*, **9**, No. 4, A55 (1964).

[3] E. A. Zuech, D. L. Crain, and R. F. Kleinschmidt, *J. Org. Chem.*, **33**, 771 (1968).

[4] H. Takahasi, T. Kimata, and M. Yamaguchi, *Tetrahedron Lett.*, 3173 (1964).

The Meerwein–Ponndorf–Verley Reduction of 1,2-Cyclopentanedione. Stereochemical Evidence for Dual Reductive Paths

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Reduction of 1,2-cyclohexanedione[1] with aluminum isopropoxide in toluene has been shown to produce *cis*- and *trans*-1,2-cyclohexanediols in a stoichiometrically

[1] Although both 1,2-cyclohexanedione and 1,2-cyclopentanedione have been shown to exist largely as the tautomeric enolones (footnote 14, ref 2), the dione nomenclature will be used here because both compounds behave as diones in this study.