($CHCl_3$, *c* 5%) and D-(−)-*erythro*-1,2-diphenyl-1-propanol, $[\alpha]D$ −70.0° ($CHCl_3$, *c* 5%).

The alcoholic mixture (1.0 g.) from the solvolysis of run 1 was added dropwise to 10 ml. of thionyl chloride at 10°. The solution was held at room temperature for six hours and worked up by the procedure reported previously (procedure A)[4e] to give 0.128 g. of D-*erythro*-1,2-diphenyl-1-propyl chloride, m.p. 138–139.5°, $[\alpha]^{25}D$ −94.7° ($CHCl_3$, *c* 5%). The combined filtrates from the crystallization of this material was shaken with a mixture of water and pure pentane. The pentane layer was washed three times with water, dried and the pentane was evaporated to an oil. This oil was submitted to formolysis in dry solvent under the conditions of the formolyses of the 1,2-diphenyl-1-propyl chlorides (25°).[4e] The reaction mixture was worked up as follows. The solution was shaken with a mixture of pure pentane and water, the organic layer was washed twice with water and once with dilute base. The solution was dried, the solvent was evaporated until 5 ml. of solution remained, and the mixture was cooled to −10°. The formate that crystallized (D-*erythro*-1,2-diphenyl-1-propyl formate)[4e] was recrystallized from pentane to give 0.27 g. of ester, m.p. 87.5–87.8°, $[\alpha]^{25}D$ −85.9° ($CHCl_3$, *c* 10%).

The acetolyses reported in runs 2 and 3 were carried out under conditions identical to those employed for the solvolyses of the *p*-bromobenzenesulfonate esters of *erythro*- and *threo*-1,2-diphenyl-1-propanol reported previously,[4e] except that the times were longer (see Table III), and not all of the starting material was consumed. What starting material remained, however, was converted to hydrocarbon during the lithium aluminum hydride treatment. The residues from the flash distillations of the alcohols were nonacidic. In run 2, from 4.9 g. of starting ester, 1.15 g. of alcoholic mixture was obtained, $[\alpha]^{25}D$ +32.6° ($CCHl_3$, *c* 5%). The synthetic mixture that served as model (for rotations) was prepared from the same samples of alcohol that were used for the model for run 1.

Control Experiments for Acetolysis.—A solution of 1.35 g. of L-1,1-diphenyl-2-propyl acetate, $n^{25}D$ 1.5462, $\alpha^{24}D$ −80.7° (neat, *l* = 1 dm.), in 26.5 ml. of dry acetic acid (containing 2% of acetic anhydride and 0.05 *N* in potassium acetate) was held at 75° for 19 hours. The mixture was then cooled and shaken with a mixture of pure pentane and water. The organic layer was washed with water (three times), and with dilute base. The solution was dried, the solvent was evaporated, and the residual oil was twice flash distilled at 25 mm. to give 1.27 g. of starting material, $n^{25}D$ 1.5462, $\alpha^{24}D$ −79.9° (neat, *l* = 1 dm.).

The compound D-*threo*-1,2-diphenyl-1-propyl acetate[4e] (1.35 g.), $[\alpha]^{25}D$ −7.1° ($CHCl_3$, *c* 8.5%), $n^{25}D$ 1.5412, was submitted to the above procedure to give 1.23 g. of starting material, $[\alpha]^{25}D$ −7.0° ($CHCl_3$, *c* 8%), $n^{25}D$ 1.5411.

Acknowledgment.—A number of rotations and isolation experiments were carried out with the assistance of Mrs. Theodora W. Greene.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Reductive Polymerization of α,β-Unsaturated Amides. I. N,N-Diethylcrotonamide

BY H. R. SNYDER AND ROBERT E. PUTNAM[1]

RECEIVED JULY 6, 1953

The treatment of N,N-diethylcrotonamide with lithium aluminum hydride, in molar equivalent of one-half or less, brings about reductive dimerization and polymerization of the amide. The structure of the dimeric reduction product is proved to to be that of N,N,N′,N′-tetraethyl-α-ethyl-β-methylglutaramide. The carbon chains of the polyamides produced probably are of the same type as the chain in the glutaramide. Especially when a relatively high molar proportion of the reducing agent is employed some reduction of amide groups occurs leading to mixtures of amines.

The reduction of amides by lithium aluminum hydride has proved useful for the preparation of amines.[2,3] In general the reduction of amides is carried out with an excess of the hydride and over a long reaction time. Under such conditions amides of unsaturated acids are reduced to saturated amines.[4]

It now has been found that upon treatment with small amounts of lithium aluminum hydride, N,N-diethylcrotonamide undergoes reductive *coupling* yielding N,N,N′,N′-tetraethyl-α-ethyl-β-methylglutaramide (I) along with a low molecular weight polymeric amide, probably of the structure shown by II. Reduction of amide groups also occurs, especially at relatively high ratios of the hydride to the amide, leading to a complex mixture of amines. The course of the reaction can be controlled within certain limits as shown in Table I.

$$CH_3CH{=}CHCONEt_2 \xrightarrow[\text{Ether}]{LiAlH_4}$$

$$\begin{array}{l} CH_3CHCH_2CONEt_2 \quad CH_3CHCH_2CONEt_2 \\ \quad | \qquad\qquad\quad | \\ CH_3CH_2CHCONEt_2 + (CH_3CHCHCONEt_2)x + \text{amines} \\ \qquad\qquad\quad | \\ \qquad\quad CH_3CH_2CHCONEt_2 \end{array}$$

I II, $x > 0$

When one-half of a molar equivalent of lithium aluminum hydride is used all three products (dimer, polymer and amines) are produced, but with one-twentieth of an equivalent of the hydride, only the polymeric amide can be isolated.

The structure of the dimeric coupling product was proved by hydrolysis to the disubstituted glutaric acid III. After two recrystallizations the acid melted at 97–99°, and subsequent recrystallizations did not affect this value. Since the melting point is near that (101°) reported by Michael and Ross[5] for one of the diastereoisomeric α-ethyl-β-methylglutaric acids, the preparation described by these authors was repeated, with certain modifications. The synthesis consists in the addition of ethyl cyanoacetate to ethyl crotonate to yield diethyl α-cyano-β-methylglutarate (IV). Ethylation of IV with ethyl iodide yielded diethyl α-cyano-α-ethyl-β-methylglutarate (V), which on hydrolysis and decarboxylation with 20% hydrochloric acid gave a mixture of the diastereoisomeric α-ethyl-β-methyl-

(1) National Science Foundation Fellow, 1952–1953.

(2) W. E. Brown, R. Adams, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 469; U. Solms, *Chimia*, **5**, 25 (1951).

(3) For an extensive study of the reduction of amides with this reagent, which appeared while this paper was in press, see V. Mićović and M. Mihailović, *J. Org. Chem.*, **18**, 1190 (1953).

(4) A. Uffer and E. Schlittler, *Helv. Chim. Acta*, **31**, 1397 (1948).

(5) A. Michael and J. Ross, THIS JOURNAL, **53**, 1150 (1931).

glutaric acids. By repeated fractional crystallizations from a mixture of chloroform and low-boiling petroleum ether the desired isomer melting at 97–99° was obtained.

$$\begin{array}{l} CH_3CHCH_2CONEt_2 \\ \quad | \\ CH_3CH_2CHCONEt_2 \end{array} \xrightarrow[HCl]{20\%} \begin{array}{l} CH_3CHCH_2COOH \\ \quad | \\ CH_3CH_2CHCOOH \end{array}$$

III

This was identical with III as shown by a mixed melting point (97–99°) and by comparison of the infrared spectra (Fig. 1).

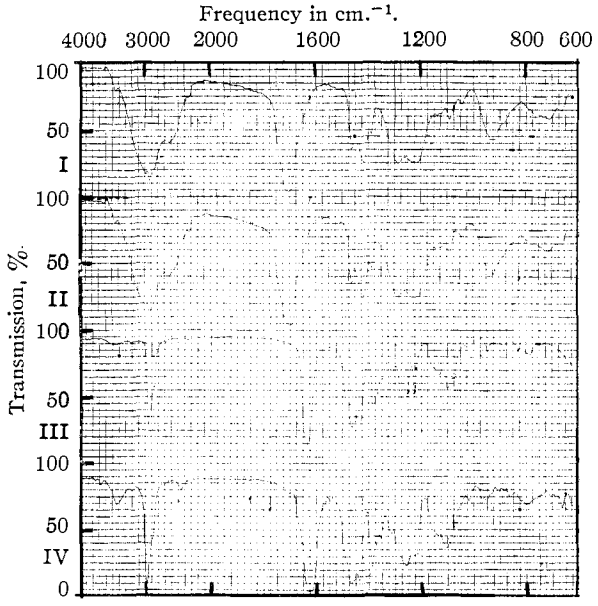

Fig. 1.—Infrared spectra: I, α-ethyl-β-methylglutaric acid (in chloroform); II, synthetic α-ethyl-β-methylglutaric acid (in chloroform); III, N,N,N′,N′-tetraethyl-α-ethyl-β-methylglutaramide (smear); IV, polymer (in chloroform).

The union of the two crotonic units in the dimer by junction between the α-position of one and the β-position of the other suggests that the reaction involves conjugate addition of an organometallic intermediate to the second molecule of the unsaturated amide. Presumably the addition product at this stage could attack another unsaturated amide molecule, yielding, after hydrolysis, the trimer II ($x = 1$). That the polyamides produced do have structures of the type II is indicated by the close similarity of the infrared absorption of such a polymer to that of the dimer I (Fig. 1). The process may be related to the Ziegler polymerization of olefins.[6]

Initial observations have shown that the amines formed in the reaction arise by partial reduction of amides of types I and II. The structures of these amines are being further investigated, as is the scope of the reduction itself.

TABLE I

REDUCTION OF N,N-DIETHYLCROTONAMIDE WITH LITHIUM ALUMINUM HYDRIDE

$LiAlH_4$, mole	$C_8H_{15}ON$, mole	Products, yield, % Dimer (I)	Polymers (II)	Amines
0.1	0.2	10.6	17.7	55.5
.026	.14	29.3	37[a]	18.4
.013	.12	0[b]	66[c]	17.8
.007	.14	0[b]	86	0[b]

[a] The average molecular weight, measured cryoscopically in benzene, was 629. [b] The amount of the product, if present at all, was insufficient for isolation. [c] The average molecular weight, measured cryoscopically in benzene, was 405; some dimer probably was present in this product.

Experimental[7]

N,N-Diethylcrotonamide.[8]—To 100 g. of crotonic acid was added 190 g. (115 ml.) of thionyl chloride. The mixture was heated gradually and was refluxed gently for two hours. The crude reaction product was fractionated and the fraction distilling at 120–123° was collected. In this way 93 g. (67.4%) of crotonyl chloride was obtained.

To a solution of 105 g. of diethylamine in 300 ml. of C.P. benzene was added dropwise a solution of 75 g. of crotonyl chloride in 200 ml. of C.P. benzene over a period of several hours. The reaction mixture was stirred and cooled in an ice-bath during the addition. The diethylamine hydrochloride which precipitated was filtered off and the filtrate was washed once with 10% sodium hydroxide, once with 10% hydrochloric acid and once with a saturated salt solution. After the benzene solution had been dried over anhydrous sodium sulfate the solvent was distilled and the residual oil was fractionated under reduced pressure. The N,N-diethylcrotonamide distilling at 131–134° (52 mm.) weighed 77 g. (76%).

Lithium Aluminum Hydride Reduction of N,N-Diethyl Crotonamide.—In a flask equipped with a Soxhlet extractor were placed 20 g. of N,N-diethyl crotonamide and 500 ml. of anhydrous ether (dried over sodium hydride). The system was flushed with nitrogen and a paper thimble containing 1 g. of lithium aluminum hydride was placed in the extractor. Refluxing was begun immediately. After refluxing for 3 hours the reaction mixture was treated with wet ether and filtered immediately to remove inorganic material. The ether filtrate was extracted with 10% hydrochloric acid and dried over anhydrous sodium sulfate; the ether was removed on a steam-cone. The residual viscous oil (15.9 g.) was fractionated under reduced pressure. In this way 5.8 g. (29.3%) of N,N,N′,N′-tetraethyl-α-ethyl-β-methylglutaramide distilling at 162° (0.6 mm.) was obtained.

Anal. Calcd. for $C_{16}H_{32}N_2O_2$: C, 67.56; H, 11.34; N, 9.85. Found: C, 67.38; H, 11.04; N, 9.85.

A colorless glassy residue (7.4 g.) remained in the distillation pot. Its average molecular weight, determined cryoscopically in benzene, was 629, corresponding to an average chain length of 4.4.

The hydrochloric acid extract was neutralized with 10% sodium hydroxide and extracted with ether. The ether layer was dried over anhydrous sodium sulfate and the ether was distilled leaving 3 g. of an oil with a strong amine odor. This oil proved to be a mixture of at least three amines, the structures of which are being investigated.

α-Ethyl-β-methylglutaric Acid (III).—A solution of 2.35 g. of N,N,N′,N′-tetraethyl-α-ethyl-β-methylglutaramide in 50 ml. of 20% hydrochloric acid was refluxed for five hours. The hot solution was cooled and extracted with ether. The ether layer was separated and extracted with 10% sodium hydroxide. The basic layer was neutralized with 10% hydrochloric acid and extracted with ether. The ether was removed on a steam-bath and the residual colorless oil was kept in a vacuum desiccator overnight. The solid obtained in this fashion weighed 1 g. (70%). After two recrystallizations from a mixture of petroleum ether and chloroform it had a melting point of 97–99°. A mixed melting point with an authentic sample of α-ethyl-β-methylglutaric acid (melting point 97–99°) showed no depression. The infrared spectra of the two acids in chloroform solution were identical (Fig. 1).

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.27; H, 8.14.

(6) K. Ziegler, *Angew. Chem.*, **64**, 323 (1952).

(7) Analyses performed by Mrs. Esther Fett, Mrs. Katherine Pih and Mr. Joseph Nemeth. Infrared spectra determined by Miss Helen P. Miklas and Mrs. Rosemary Hill and interpreted by Miss Helen P. Miklas.

(8) N. Maxim, *Bull. soc. chim. Romania*, **10**, 97 (1928) [*C. A.*, **23**, 2697 (1929)].

Diethyl α-Cyano-β-methylglutarate (IV).—To a solution of 11.5 g. of sodium in 250 ml. of absolute alcohol were added 56.5 g. of ethyl cyanoacetate and 57 g. of ethyl crotonate. The red reaction mixture was heated on a steam-cone for 21 hours, cooled and poured into 1 l. of water containing 50 ml. of acetic acid. The water solution was extracted with ether and the ether extract was dried over anhydrous sodium sulfate. The ether was removed on a steam-cone and the residual deep red oil was fractionated. Diethyl α-cyano-β-methylglutarate distilled at 115° (0.5 mm.) and weighed 52 g. (45.8%).

Diethyl α-Cyano-α-ethyl-β-methylglutarate (V).—To 5.75 g. of finely pulverized sodium was added 25 ml. of absolute alcohol. When the mixture became too viscous for further reaction 52 g. of diethyl α-cyano-β-methylglutarate was added. After the initial violent reaction 5 ml. of absolute alcohol was added to facilitate complete solution of the sodium. Then 39 g. of ethyl iodide was added and the mixture was stirred at room temperature for three hours and heated on a steam-cone for one half hour. The viscous mass was poured into 400 ml. of water containing 20 ml. of acetic acid. The cloudy water solution was extracted with ether. The ether layer was dried over anhydrous sodium sulfate and the ether was removed on a steam-cone. The residual oil was fractionated at reduced pressure and the fraction distilling at 112° (0.3 mm.) was collected (45 g., 76%). The diethyl α-cyano-α-ethyl-β-methylglutarate obtained, as reported by Michael and Ross,[5] had the same boiling point as diethyl α-cyano-β-methylglutarate and since physical constants were not available the former was analyzed to prove its identity.

Anal. Calcd. for $C_{13}H_{21}O_4N$: C, 61.15; H, 8.29. Found: C, 60.88; H, 8.31.

α-Ethyl-β-methylglutaric Acid.—A mixture of 44 g. of ethyl α-cyano-α-ethyl-β-methylglutarate and 500 ml. of 20% hydrochloric acid was refluxed for 24 hours. By this time, complete solution of the oil had occurred. The cooled solution was thoroughly extracted with ether and the ether extract was washed with three 80-ml. portions of 10% sodium hydroxide. The basic aqueous layer was made acidic with 20% hydrochloric acid and was extracted with ether. The ether was removed on a steam-cone and the residual viscous oil was kept in a vacuum desiccator overnight. In this way 18.2 g. (62.8%) of a mixture of the diastereoisomeric α-ethyl-β-methylglutaric acids were obtained. The desired isomer was obtained by repeated crystallization from a chloroform–petroleum ether mixture. It melted at 97–99° and further recrystallizations failed to raise its melting point.

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[CONTRIBUTION FROM THE CONVERSE LABORATORIES OF HARVARD COLLEGE AND THE HUNTINGTON LABORATORIES OF THE MASSACHUSETTS GENERAL HOSPITAL]

The Alkaline Rearrangement of α-Haloketones. III.[1] Effect of Changing the Halogen

BY ROBERT BERNER LOFTFIELD AND LAWRENCE SCHAAD[2]

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When α-haloketones react with base, a mixture of rearrangement and substitution products results. On the basis of the proposed reaction mechanism, it is predicted that the proportion of rearrangement product will be greater as the halogen is changed from Br to Cl to F. This prediction is confirmed for the case of bromo- and chloromethyl cyclohexyl ketone. Contrary to Mousseron's report,[7] no ester of cyclohexylacetic acid was obtained from chloromethyl cyclohexyl ketone on treatment with sodium methoxide.

A large number of α-haloketones react with sodium alkoxides to yield mixtures of varying proportions of a rearrangement product (esters IV and V), and a substitution product (ketal IX). The ketal results from the attack of alkoxide ion on the carbonyl carbon followed by cyclization to an alkoxyepoxide.[3] This is then solvolyzed to yield the ketal. We have proposed that the rearrangement proceeds through an entirely different (and competing) course beginning with attack on the α′-hydrogen and proceeding through a cyclopropanone intermediate which is solvolyzed to yield one or both of two esters.[1]

If the postulated reaction mechanisms are correct, we may make some predictions regarding the effect of changing halogen (F, Cl, or Br) on the proportion of rearrangement *vs.* substitution product. There would be some change in k_{II}, k_{III} and K_{VI}, but the major effect would probably be in K_{VII}. McCabe and Warner[4] have shown in the quite comparable case of ring closure from ethylene halohydrin anions to ethylene oxide that the rate for halogen = Br is about 100 times greater than for halogen = Cl and about 60,000 times greater than for halogen = F. By analogy, we would expect to find a series of halo ketones where it would be possible to vary the products from all substitution to all rearrangement by changing the halogen, *i.e.*, the rate of substitution might be changed by a factor of 60,000 while the rate of the rearrangement was substantially constant. In addition to the theoretical interest, such control over product composition would be of enormous preparative value.[5]

We chose the halomethyl cyclohexyl ketones for Wagner and Moore[6] had just reported that the bromo derivative gave only the substitution product IX. After the investigation was begun it gained significance when Mousseron, *et al.*,[7] reported that chloromethyl cyclohexyl ketone gives a mixture of esters IVa and Va on treatment with sodium methoxide. Methyl bromocyclohexyl ketone, which presumably rearranges through the same cyclopropanone III, had been reported to give only the ester IVa.[6] It is not reasonable to suggest that in one case III can solvolyze exclusively to IVa and in another give mostly Va. If these observations were confirmed, the theory would need to be revised.

(1) R. B. Loftfield, THIS JOURNAL, **73**, 4707 (1951); **72**, 632 (1950).

(2) From a thesis submitted by Mr. Schaad in partial fulfillment of the requirements for the Bachelor of Science degree in Biochemical Sciences, Harvard College, 1952. Contribution 803 from the Cancer Commission of Harvard University.

(3) T. I. Termnikova and E. N. Kropacheva, *Zhur. Obshchei Khim.* (*J. Gen. Chem.*), **19**, 1917 (1949); *C. A.*, **44**, 1929 (1950); C. L. Stevens, W. Malik and R. Pratt, THIS JOURNAL, **72**, 4758 (1950).

(4) C. L. McCabe and J. C. Warner, *ibid.*, **70**, 4031 (1948).

(5) B. Tchoubar, *Compt. rend.*, **235**, 720 (1952), has achieved some of this control by substituting silver salts for alkali in these reactions.

(6) R. B. Wagner and J. A. Moore, THIS JOURNAL, **72**, 2884 (1950).

(7) M. Mousseron, R. Jacquier and A. Fontaine, *Compt. rend.*, **232**, 1562 (1951).