Solution a, originally containing 3.0 $M \alpha$ -methylbenzyl alcohol-OD, 0.50 M acetophenone, and 0.011 M mesityl disulfide, was treated in this way. The difference spectrum showed C-D $\,$ absorption at 4.7 μ , absorbancy 0.14. The infrared spectrum indicated the presence in the distillate of 15% acetophenone, 85% a-methylbenzyl alcohol. The extinction coefficient of the C-D bond was estimated to be 7.0 from examination of the infrared spectrum of 2-octanol-2-D in chloroform. On this basis the concentration of α -methylbenzyl alcohol- α -D in the distillate was estimated to be 2.0 \dot{M} , 28% deuterium exchange. In another similar run the recovered distilled α -methylbenzyl alcohol (1.05 g., 0.0086 mole) was diluted to 10 ml. with pyridine and treated with a solution of 2 g. (0.02 mole) of chromium trioxide in 20 ml. of pyridine at room temperature for 16 hr. The mixture was filtered, diluted with water, and extracted with ether. The extract was washed with 6 N hydrochloric acid, and with water, dried, and distilled, leading to acetophenone, b.p. 40° (0.1 mm.), 0.43 g., 42% yield. A difference spectrum against acetophenone showed no infrared absorption at $4.7 \ \mu$.

Solution b, containing initially 3.0 $M \alpha$ -methylbenzyl alcohol-OD and 0.5 M acetophenone in benzene, was irradiated and treated in the same way. The difference spectrum of the recovered, water-equilibrated α -methylbenzyl alcohol showed no C-D absorption at 4.7 μ .

Solution c, containing initially 3.0 M α -methylbenzyl alcohol and 0.017 M 2-mercaptomesitylene, was irradiated and worked up in the same way. The difference spectrum of the recovered water-equilibrated α -methylbenzyl alcohol showed absorption at 4.7 μ , indicating 12% deuterium exchange. Solution d, 3.0 M α -methylbenzyl alcohol and 0.011 M mesityl disulfide, led, after irradiation and work-up, to recovered alcohol with absorption at 4.7 μ , indicating 19% deuterium exchange.

Acetophenone-2-Propanol (Table VII).-Aliquots (5 ml.) of 0.5 M acetophenone in 2-propanol were transferred to Thunberg tubes, degassed, and irradiated for 3 to 24 hr. The rate of reaction of acetophenone was followed by ultraviolet spectrophotometry and by vapor phase chromatography. The rate of formation of acetone was followed by vapor phase chromatography. In ultraviolet analyses for acetophenone, the irradiated solutions were diluted, absorbancies were measured at 310, 320, and 330 m μ , averaged, and converted to concentrations from a calibration curve. Chromatographic analyses for acetophenone were made with p-chloroacetophenone as internal standard, with a 3 ft. imes 0.5 in. column packed with 10% Dow-Corning QF-1 on 80-100 Chromosorb W. Column, detector, and injector temperatures were 150, 200, and 305°, respectively. Analyses for acetone were carried out with 2-butanol as internal standard, with a 6 ft. \times 0.25 in. column packed with 20% adipate resin (R. C. Polymeric B.G.A., Rubber Corporation of America) on 80-100 Celite. Column, detector, and injector temperatures were 50, 100, and 130°, respectively.

Acetophenone–Pinacol.—(a) Acetophenone (120 ml., 1 mole) was diluted to 1 l. with 2-propanol and irradiated under nitrogen for 192 hr. with a Hanovia mercury are 100 w. 16A-13 lamp with an interposed Vycor heat shield. 2-Propanol was removed and unreacted acetophenone was distilled out, b.p. 46° (0.1 mm.), 80 ml. The pinacol residue, 40 g., 100% yield, was triturated with $60-110^\circ$ petroleum ether, and the insoluble fraction was crystallized three times from $60-110^\circ$ petroleum ether, leading to 10 g. of the mess diastereomer, m.p. 123–124°, reported¹⁰ 123°. The remainder was a mixture of the diastereomers, melting over a range.

(b) Samples of the pinacol were isolated from the kinetic runs under conditions examined. Vields were determined, and the products were characterized by infrared spectra.

[CONTRIBUTION FROM THE KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE UNIVERSITY, EAST LANSING, MICH.]

A Versatile Ketone Synthesis. The Reduction of α -Diketones and α -Ketols by Hydriodic Acid¹

By William Reusch and Ronald LeMahieu

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When treated with hydriodic acid in refluxing acetic acid, α -diketones and α -ketols are reduced to saturated ketones. This provides a general ketone synthesis, which in certain cases may be used to shift a carbonyl group to an adjacent position. Thus, 4-acetoxycholestan-3-one was converted to cholestan-4-one; 3,5,5-trimethylcyclohexane-1,2-dione gave 2,4,4-trimethylcyclohexanone and 2,4,4-trimethylcyclohex-2-en-1-one in a ratio of 4:1; 3,3-dimethylcyclohexane-1,2-dione gave 3,3-dimethylcyclohexanone; 4-hydroxy-4-ethyl-3-hexanone gave 4-ethyl-3-hexanone; and both sebacoin and sebacil were reduced to cyclodecanone. Since benzoin and benzil require more vigorous conditions for reduction to deoxybenzoin and since pivaloin cannot be reduced at all, we suggest an enolic carbonium ion intermediate to explain these findings.

In a recent paper² we described the reduction of cholestan-3,4-dione and the derived enol methyl ethers to cholestane-4-one by hydriodic acid in refluxing acetic acid (eq. 1). Hydrogen iodide is well known for its ability to reduce a variety of organic substrates including aryl olefins. arylcarbinols, aryl ketones, benzils, glycols, α -haloketones, and α,β -epoxyketones. In some of these reactions the reduction is believed to proceed by a direct hydride transfer from hydrogen iodide to a carbonium ion intermediate.³ At first, reaction 1 appeared to parallel the reduction of substituted benzils reported by Japp, Klingeman,⁴ and Fuson⁵ (reactions 2, 3, and 4); however, the conditions required for satisfactory reduction of these latter compounds are more vigorous than those employed in the reductions of A and the aliphatic α -diketones dis-

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$$C_6H_5COCOC_6H_5 \xrightarrow{HI} C_6H_5COCH_2C_6H_5$$
 (2)



cussed in this paper. Thus, an acetic acid solution of benzil containing 4 to 5 equivalents of 48% hydriodic acid gave, after 1 hr. at reflux, an excellent yield of benzoin but no deoxybenzoin; benzoin was recovered unchanged after similar treatment. Furthermore, the formation of D from A and B does not correspond to the reduction of the most hindered carbonyl group observed for unsymmetrically substituted benzils (eq. 4).

We now wish to report additional work (Table I) which concerns the scope and mechanism of this remarkable reaction. The reduction of the alkylated



^a Based upon pure ketone actually isolated. ^b Corrected for recovered starting material. ^c Based upon analysis (*e.g.*, v.p.c., infrared, ultraviolet, etc.) of the crude neutral products.

acyloin N is particularly noteworthy since it illustrates the general ketone synthesis outlined in eq. $5.^6$ The

$$2RCO_{2}CH_{3} \xrightarrow{Na} R \xrightarrow{R} COCH(OH)R \xrightarrow{HI} RCOCH_{2}R$$

$$(5)$$

$$R \xrightarrow{Na} R \xrightarrow{C} C \xrightarrow{C} R$$

$$R \xrightarrow{C} R \xrightarrow{C} R \xrightarrow{(5)} RCOC(OH)RR' \xrightarrow{HI} RCOCHRR'$$

success of the acyloin condensation in forming medium and large carbocyclic systems adds to the attractiveness of this method. In this respect, a comparison of the hydriodic acid reduction of sebacoin (P) and sebacil (R) with the currently favored⁷ zinc dust-hydrochloric acid reduction⁸ of sebacoin should be made.

(6) The alkylation of acyloin salts has been described by J. C. Speck, Jr., and R. W. Bost, J. Org. Chem., 11, 788 (1946). We are indebted to Prof. Speck for calling this method to our attention and for a generous gift of compound N.

The very good yields of cyclodecanone (Q) reported for the latter reduction require that the published procedure be carefully followed. Thus, sebacil-free sebacoin must be used and the temperature must be held between 75 and 80° during the hydrochloric acid addition. Failure to observe these requirements may lead to incomplete reduction, overreduction to cyclodecane, or contamination of the cyclodecanone with sebacil. We find that comparable yields of Q are obtained from both sebacoin and sebacil by reduction with hydriodic acid in refluxing acetic acid, thus obviating the problem of temperature control.

The course of the reduction of asymmetrically substituted diketones and ketols (e.g., A, C, H, K) suggests that this reaction will provide a valuable method for shifting a carbonyl group to an adjacent position, particularly within a six-membered ring. For example, substituted cyclohexanones having a quaternary α carbon (S) can be oxidized to the corresponding α diketone⁹ and then reduced to the isomeric β -quaternary ketone (T). Alternatively, the $\Delta^{1,9}$ -octalone-2 system (U) can be converted to a 1-decalone (V) by epoxidation followed by alkaline rearrangement² and reduction.



Reduction of 3-hydroxycholest-3-en-2-one (E) yields cholestan-2-one (F) accompanied by the isomeric cholestan-3-one (G). Although the isolation of pure F requires chromatography, this simple approach compares favorably with a recently reported¹⁰ general synthesis of 2-keto steroids.

Theoretical Discussion.—The isolation of benzoin and ketol M from the hydriodic acid reduction of benzil and α -diketone K, respectively, suggests that the reduction of α -diketones proceeds in at least two stages. Since α -ketols are also reduced to ketones, it is attractive to assume that their formation constitutes the first stage. Although this reduction conceivably proceeds by β -addition of hydrogen iodide to a diosphenol tautomer followed by deiodination¹¹ of the iodoketol tautomer (eq. 6), the facile reduction of benzil to benzoin under mild conditions implies that a geminal iodohydrin intermediate may be involved (eq. 7).

The second stage in the reduction of α -diketones to ketones necessarily becomes the reductive dehydroxylation of a ketol. In the case of benzoin, this is most

(8) Zinc dust in acetic acid will not usually reduce α -ketols (e.g., i and ii) unless a neighboring hydroxyl group is present (e.g., iii): J. K. Norymberski, J. Chem. Soc., 517 (1956). The use of hydrochloric acid in the reduc-



tion of sebacoin 7 results in reaction conditions which approach those of the Clemmensen reduction.

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⁽⁷⁾ A. C. Cope, J. W. Barthel, and R. D. Smith, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons. Inc., New York, N. Y., 1963, p. 218.



reasonably accomplished by a sequence of steps involving nucleophilic attack by iodide ion upon a conjugate acid of benzoin or some closely related species (eq. 8). The α -iodoketone thus formed is then reA or C where, in contrast with H, retention of the most hindered carbonyl function is observed. In any event, the advantage of direct displacement on enol derivatives, as compared with the ketols themselves, is not immediately apparent.

The second mechanism for ketol reduction is characterized by ionization of the enol conjugate acids to isomeric allylic carbonium ions. From compound H, for example, conjugate acids a and b are precursors to the intermediate ions c and d, respectively. The subsequent reduction of these ions may proceed by combination with iodide ion followed by reduction of the resulting α -iodoketone,¹¹ or by direct hydride transfer from hydrogen iodide itself.^{3,12} Loss of a proton from ion c would also account for the unsaturated ketone J observed as a minor product from the reduction of H. Since ion c is more stable than ion d,



duced¹¹ to desoxybenzoin. The high concentration of hydrogen iodide and vigorous conditions required for the reduction of benzoin may be an indication that a doubly protonated intermediate is involved. On the other hand, the severe conditions required for benzoin reduction, relative to the reductions of the diketones and ketols described here, may be attributed to carbonyl deactivation by the conjugated phenyl group and/or preferred reduction *via* enol intermediates. Since pivaloin is not reduced by vigorous treatment with hydrogen iodide, we favor the latter interpretation.

Two mechanisms for the second stage in the reduction of enolizable α -diketones will now be examined. First, iodide ion may effect a nucleophilic displacement on the conjugate acid of an enol tautomer (or an acetate derivative of an enol) yielding an enol form of an α iodoketone. In an unsymmetrical system two isomeric ketols, and hence two enol forms, must be considered. This point is illustrated for the reduction of H by structures a and b. Nucleophilic displacement of water by an SN2 mechanism is more favorable in structure b, as a consequence of steric compressions in the transition states associated with a. Reduction via structure b does not lead to the observed product, and this mechanism is therefore considered improbable. Even if an argument favoring displacement for structure a could be advanced, it is unlikely that this same argument would successfully rationalize the reduction of



reduction via c will be favored and the major product will be I. A similar argument will account for the major products from all the reductions studied so far. The only case in which this is not immediately clear is the reduction of E. An inspection of models discloses that the β -side of intermediate ion f is blocked by the C-10 angular methyl group, whereas ion e may



be freely solvated from both sides. Reduction *via* the latter intermediate will therefore predominate.

An intermediate allylic ion of the type suggested above was proposed by Turner, *et al.*,¹³ to account for the conversion of the cyclic ether W to bromoketone X upon treatment with hydrobromic acid. The



⁽¹²⁾ Our attempts to effect reduction of N by other hydride donors (e.g., triphenylmethane, cycloheptatriene, and 3,7,10-trimethyltriptychsiloxazolidine) have not been successful and we conclude either that reduction by direct hydride transfer is unimportant in these reactions, or that the acid strength of the reducing medium must be higher than that employed with these donors.

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formation of Z from Y under similar conditions¹⁴ may also be interpreted in this manner. The α -bromoketones isolated in these reactions are less prone to reductive dehalogenation than are α -iodoketones.

Experimental

The following instruments were used in the work described below: Perkin-Elmer Model 21 infrared spectrophotometer; Beckman DK-2 ultraviolet and visible spectrophotometer; Beckman DB ultraviolet and visible spectrophotometer; Varian Associates A-60 high resolution nuclear magnetic resonance spectrometer; Consolidated Engineering Model 21-103c mass spectrometer; Aerograph A-90-P gas chromatograph.

The melting points were taken on a Kofler hot stage microscope and the microanalyses were by Spang Microanalytical Laboratory, Ann Arbor, Mich.

General Procedure.--Reduction of an α -ketol requires 2 equivalents of hydrogen iodide while α -diketones demand 4 equivalents. A 100% excess of the reducing agent, in the form of 47% hydriodic acid, is added to a 2- to 30-fold quantity (by volume) of glacial acetic acid containing the organic substrate. The red color of free iodine is usually apparent upon mixing the reactants and becomes quite deep when the mixture is heated to reflux. After refluxing for 1 to 3 hr., the reaction mixture is chilled and quickly poured into a 2- or 3-fold quantity (by volume) of cold sodium hydroxide solution containing sufficient sodium bisulfite to reduce all the iodine present. The combined organic layers from three or four ether extractions of the resulting mixture are washed first with dilute bisulfite solution and then with several portions of 5% sodium hydroxide solution until the wash remains alkaline. A final wash with distilled water followed by drying over magnesium sulfate (anhydrous) and removal of the solvent gives the crude reduction product.

Reduction of Benzil.—A 2.0-g. sample of benzil in a solution of glacial acetic acid (30 ml.) and 47% hydriodic acid (12 g.) was refluxed for 1 hr. The usual work-up gave 1.25 g. of a colorless solid. Two crystallizations from ethanol yielded needles, m.p. 133–134°, which were identified as benzoin by mixture melting point and a comparison of the infrared spectrum with authentic material.

Treatment of benzoin (1.0 g.) with hydriodic acid (5.4 g.) in acetic acid (30 ml.) under similar conditions gave 0.96 g. of recovered benzoin.

Reduction of 4-Acetoxycholestan-3-one (**C**).—A solution of 4acetoxycholest-4-en-3-one¹⁶ (500 mg.) in glacial acetic acid was hydrogenated in the presence of Pt. One equivalent of hydrogen was taken up and an infrared spectrum of the residue from an aliquot of the resulting solution supported the assignment of structure C to the solute. The filtered solution was refluxed with 2 ml. of 47% hydriodic acid for 1 hr., and following the usual work-up gave 310 mg. of cholestan-4-one, identified by mixture melting point and infrared spectrum.

Reduction of 3-Hydroxy-5 α -cholest-3-en-2-one (E).—A solution of E (400 mg.) in glacial acetic acid (30 ml.) was treated with 47% hydriodic acid (2 ml.) and refluxed for 30 min. The usual work-up gave 370 mg. of semisolid material which was chromatographed on 15 g. of neutral alumina using a 1:1 benzene-ether eluting mixture and gave 310 mg. of a colorless solid, m.p. 95–102°. Since further crystallizations did not improve this melting point, the material was rechromatographed and yielded two fractions. Crystallization of the first fraction from aqueous ethanol gave 140 mg. of 5 α -cholestan-2-one, m.p. 127–128° (reported¹⁶ m.p. 130–131°), identified by mixture melting point and comparison of the infrared spectrum with authentic material. The second fraction, m.p. 103–110°, λ_{max}^{CCl} 5.88, 9.74, and 10.46 μ , appeared to be a mixture of 5 α -cholestan-3-one and 5 α -cholestan-2-one.

Reduction of 3,5,5-Trimethylcyclohexan-1,2-dione (**H**).— A solution of 3,5,5-trimethylcyclohexan-1,2-dione¹⁷ (1.79 g.) in glacial acetic acid (35 ml.) was treated with 47% hydriodic acid (13 g.) at reflux for 2 hr. The work-up of this reaction was modified so that the product was washed first with sodium bicarbonate solution (to remove acetic acid) followed by 20% potassium hydroxide (to remove unreacted diosphenol). Acidification of the latter wash solutions gave 500 mg. of recovered H. The neutral oil remaining (1.18 g.) was analyzed by v.p.c., using a 15% neopentyl glycol succinate column at 123°, and two major components were found. These materials were isolated by preparative v.p.c. and were identified in the following manner. The first material to be eluted (81% of the neutral product) proved to be 2,4,4-trimethylcyclohexanone (I) from a consideration of the infrared spectrum,¹⁸ $\lambda_{\rm Lex}^{\rm CCl4}$ 5.84 μ , and the 2,4-DNP derivative, m.p. 149–150° (reported¹⁹ m.p. 150–151°).

The second material to be eluted was identified as 2,4,4-trimethyl-2-cyclohexen-1-one (J) on the strength of the ultraviolet spectrum, $\lambda_{\max}^{C2HOH} 233.5 \text{ m}\mu$ (log ϵ 4.0); the infrared spectrum,²⁰ $\lambda_{\max}^{CCl4} 5.95$ and 6.08 μ ; the nuclear magnetic resonance spectrum; and the 2,4-DNP derivative, m.p. 163–165° (reported²¹ m.p. 163–164°).

3,3-Dimethylcyclohexane-1,2-dione (K).—A solution of 2benzal-6,6-dimethylcyclohexanone (7 g.) in acetone (140 ml.) was chilled in an ice bath while a solution of potassium permanganate (5.2 g.) and magnesium sulfate (3.9 g.) in water (105 ml.) was slowly added with stirring. The addition of the oxidizing reagent required 1 hr. and the mixture was agitated at room temperature for another 30 min. The reaction mixture was filtered and extracted with ether several times, following which the combined ether extracts were washed with 20% sodium hydroxide solution to remove acidic substances. After acidification of the basic wash portions, the organic acids were extracted with ether, and the combined ether extracts were washed with 5% sodium bicarbonate to remove carboxylic acids. The remaining ether solution gave 800 mg. of a thick oil; $\lambda_{\max}^{CCl_4}$ 2.95, 6.00, and 11.89 μ ; λ_{\max}^{CHoH} 265 m μ (log ϵ 3.8). This material proved to be homogeneous with respect to v.p.c. on a 20%S.E.-30 column at 165° and was assigned structure K, since it gave a scarlet di-2,4-DNP derivative, m.p. 239-240°, λ_{max}^{CH} 352 (4.4) and 388 m μ (log ϵ 4.3), which appears to be identical with that reported for K by Ramirez and Kirby,²² m.p. 237-238°, $\lambda_{\max}^{CHCl_3}$ 351 (4.5) and 388 m μ (log ϵ 4.4).

Reduction of 3,3-Dimethylcyclohexane-1,2-dione (**K**).—A solution of K (620 mg.) in glacial acetic acid (30 ml.) was refluxed with 47% hydriodic acid (6 g.) for 2 hr. The usual work-up gave 460 mg. of a neutral oil, which proved to be a mixture of two components by v.p.c. on a 15% neopentyl glycol succinate column. The material first eluted (78% of the total product) was shown to be 3,3-dimethylcyclohexanone (L) by a comparison of its infrared spectrum and v.p.c. retention time with an authentic sample. The 2,4-DNP derivative gave no depression of a mixture melting point with authentic material.

The second substance to be eluted was an α -ketol—either 2-hydroxy-6,6-dimethylcyclohexanone (M) or 2-hydroxy-3,3-dimethylcyclohexanone—as demonstrated by the infrared spectrum, λ_{max}^{CCL} 2.90, 5.83, and 9.03 μ , and conversion to the di-2,4-DNP derivative derived from 3,3-dimethylcyclohexane-1,2-dione.

Further reduction of the product mixture described above decreased the amount of ketol and gave an oil which was 90% L by v.p.c. analysis.

Reduction of 4-Hydroxy-4-ethyl-3-hexanone (**N**).⁶—To a solution of N (7.0 g.) in glacial acetic acid (100 ml.) was added 55 ml. (4 molar equivalents) of 47% hydriodic acid, and the resulting mixture was refluxed 2 hr. The deep red solution was worked up as previously described and yielded 6.0 g. of a light yellow oil. Distillation of this oil through a Vigreux column at atmospheric pressure gave a small fraction boiling under 150° followed by a 5.0-g. fraction, b.p. 152–157°. Analysis of this material by v.p.c. using a 15% Ucon Polar column (8 ft. × 1/s in.) at 155° showed it to be >95% a single substance. A strong sharp absorption band at 5.84 μ in the infrared indicated we were dealing with a saturated ketone; however, all attempts to prepare a crystalline derivative were unsuccessful.²³ Consequently, the assignment of structure O to this substance rests upon nuclear magnetic resonance and mass spectroscopic measurements.

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TABLE II

NUCLEAR MAGNETIC RESONANCE ASSIGNMENTS (CH₃CH₂)₂CHCOCH₂CH₃

с a a b

| Proton grouping | Position, τ | Multiplicity | Integration |
|--------------------|------------------|-----------------|-------------|
| а | Near 7.6 | Quartet | 2 0 |
| a' | Near 7.8 | Quintet | 3.0 |
| b | 9.02 | Triplet | 0.0 |
| b′ | 9.18 | Triplet | 9.0 |
| с | Near 8.5 | Broad multiplet | 4.1 |

Reduction of Sebacoin (P) .- A 12-g. sample of crude sebacoin²⁴ was dissolved in 100 ml. of glacial acetic acid and refluxed 2 hr. with 45 g. of 47% hydriodic acid (2.3 molar equivalents), Following the usual work-up, distillation of the crude product (10.9 g.) gave three fractions ranging in color from very light yellow to light orange. The first fraction (0.9 g.) was shown to be 50% cyclodecanone by v.p.c. analysis using a 15%phenyldiethanolamine succinate column (8 ft. \times 0.25 in.) at 165°. The second fraction (6.7 g), b.p. 103-109° (17 mm.), was 90% cyclodecanone contaminated with sebacil and two other substances present in only minor quantities. The third fraction (1.2 g.), b.p. $109-115^{\circ}$ (17 mm.), was mainly cyclodecanone with sebacil (12%) as the main contaminent. These assignments were made by comparing v.p.c. retention times and infrared spectra with corresponding values for authentic cyclodecanone (Aldrich Chemical Co.) donated by Prof. Harold Hart.

TABLE III

MASS SPECTROSCOPIC ASSIGNMENTS OF ALL PEAKS HAVING an Intensity Greater than 10% of the Base Peak

| | Rel. | | | |
|-----|-----------|----------|-------------------------------------|--|
| m/e | abundance | Meta | astable transitions | |
| 128 | 11 | 51.0 | $(99^+) \rightarrow (71^+)$ | |
| 100 | 11 | | | |
| 99 | 15 | 39.3 | $(128^+) \rightarrow (71^+)$ | |
| 71 | 90 | | | |
| 57 | 96 | 37.0 | | |
| 55 | 25 | | | |
| 43 | 100 | 26.2 | $(71^+) \rightarrow (43^+)$ | |
| 41 | 29 | | | |
| 39 | 20 | 25.2 | $(128^+) \twoheadrightarrow (99^+)$ | |
| 29 | 87 | | | |
| 28 | 12 | lnten | Intensity of $P + 1$ peak | |
| 27 | 58 | Caled. f | Calcd. for $C_8H_{16}O: 8.94\%P$ | |
| | | Found: | 9.3%P | |

Reduction of Sebacil (R).—A solution of crude sebacil²⁵ (3.2 g.) in glacial acetic acid (40 ml.) and 47% hydriodic acid (35 g.) was refluxed for 2.5 hr.; after the usual work-up, 2.5 g. of a yellow oil was isolated. This material proved to be 94% cyclodecanone by v.p.c. analysis.

Acknowledgment.--We wish to thank Mr. Robert Guynn for his help with some of these experiments, and Dr. M. Russell of this department for making the mass spectrum analysis, and to acknowledge gratefully the support of the National Institutes of Health by way of research grant AM 04936-03.

(25) Prepared by the oxidation of sebacoin by the procedure of A. T. Blomquist and A. Goldstein, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p. 838. The crude sebacil used in this experiment is greater than 92% pure.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY, NEW YORK 21, N. Y.]

Competitive Elimination-Substitution Reactions. Some Dramatic Differences between Bromides and Tosylates

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Typical examples of primary alkyl bromides and tosylates were treated with alkoxides under preparative conditions. Under conditions that usually lead to elimination rather than substitution, tosylates gave surprisingly good yields of substitution products while the corresponding bromides underwent predominantly the elimination reaction. This sharp difference between bromides and tosylates can be of enormous significance in the development of synthetic procedures.

A primary alkyl halide or tosylate possessing at least one hydrogen at carbon 2 can, simultaneously, undergo bimolecular substitution and elimination on treatment with a nucleophilic reagent. The relative extents of substitution and elimination depend on the nature of the alkyl group of the substrate,⁴⁻⁶ the leaving group,⁷⁻⁹ the attacking nucleophilic reagent,^{6,10} the solvent,¹¹ and temperature.¹² Of these various fac-

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tors which influence competitive elimination-substitution reactions, the effect of the nature of the leaving group appears to have received little attention.

In the case of alkyl chlorides, bromides, and iodides, it is known⁷ that the SN2/E2 ratio is not markedly dependent on the nature of the halide, although the ratio is reported to decrease in the order RCl > RBr > RI. Previous kinetic studies with 2-phenylethyl bromides and tosylates^{8,9} have led to suggested differences between bromides and tosylates in their tendency to undergo substitution and elimination but no uniform pattern,13 useful to the synthetic organic chemist, has evolved: Since 2-phenylethyl halides and tosylates represent special cases, elimination being promoted in each of these by the phenyl group, we report here the

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