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THE FACILE CLEAVAGE OF NON-ENOLIZABLE KETONES IN DIMETHYL SULFOXIDE SOLUTION (1,2)

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The advent of dimethyl sulfoxide as a commercially available chemical has spawned many investigations of this compound both as a solvent and as a reagent. These investigations in turn have resulted in the discovery of useful new methods for carrying out various reactions. In addition, many heretofore unknown reactions have been discovered in which dimethyl sulfoxide is either the critical solvent or the reagent.

We wish to report a new reaction in dimethyl sulfoxide (DMSO), (3) the cleavage of non-enolizable ketones with base at room temperature to acid and hydrocarbon moieties.

This novel reaction offers several advantages over other methods of cleavage. In comparison with the classical Haller-Bauer reaction (4) (the only well investigated ketone cleavage with base) the conditions for our reaction require a much lower temperature and give a higher yield of cleavage product. As is shown in Table 1, nortricyclanone yields 65% of II and dehydronorcamphor gives IV in 80% yield at room temperature. In contrast, nortricyclanone yields only 27% of the amide of II, m.p. 200-201°, after refluxing for 3.5 hours with sodium amide in xylene, while dehydronorcamphor is converted to the amide of IV in 33% yield after refluxing with sodium amide in dioxane. (5)

In a typical experiment 0.0046 moles of ketone was added in a nitrogen atmosphere to a solution of 4.0 g. (0.035 moles) of sublimed potassium *tert*-butoxide in 11 ml. of dimethyl sulfoxide containing 0.01 mole of water. The reaction mixture was stirred at room temperature for periods of up to four hours, carefully neutralized with concentrated hydrochloric acid and extracted with ether. Removal of the solvent was followed by either recrystallization or distillation of the product. Under optimum conditions the yields listed in Table 1 were obtained.

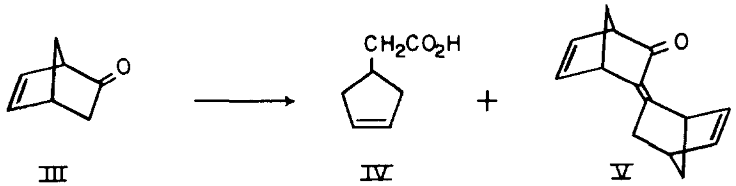
Table 1

Ketone	Product	Percent yield
Nortricyclanone (I)	bicyclo[3.1.0] hexane-3-carboxylic acid (II)	65
Dehydronorcamphor (III)	Δ^3-cyclopentenylacetic acid (IV)	80
7-Ketonorbornene	Δ^1-cyclohexene carboxylic acid Δ^3-cyclohexene carboxylic acid	18 32
Camphenilone	β-camphoceenic acid	9
Benzopinacolone	triphenylmethane, benzoic acid	99, 100

The facile cleavage of non-enolizable ketones in dimethyl sulfoxide solution is extremely sensitive to water and to *tert*-butanol. Maximum yields were obtained when the DMSO solution of potassium *tert*-butoxide was first reacted with *ca.* 0.3 equivalents of water (potassium *tert*-butoxide, water ratio of 10:3). When all of the potassium *tert*-

butoxide was reacted with water (potassium *tert*-butoxide, water ratio of 1:1) the yield was negligible. The extreme solvent dependency of this reaction was further demonstrated by the preparation of the potassium dimethyl sulfoxide anion from potassium hydride and DMSO, followed by the addition of varying amounts of *tert*-butanol and water. Maximum yields were again obtained when the potassium hydride, *tert*-butanol, water ratio was 10:10:3 (equivalent to a potassium *tert*-butoxide, water ratio of 10:3). Thus when there was a molar deficiency of *tert*-butanol in comparison to the moles of potassium ion the yield dropped proportionately. The question of the relative roles of alcohol and water in this reaction are emphasized by the results quoted above.

There are many interesting facets to this facile cleavage. Whereas Cristol and Freeman have shown (5) that dehydronorcamphor (III) reacts with potassium *tert*-butoxide in refluxing *tert*-butanol to yield 19% cleavage product, IV, and 31% self-condensation product, V, we observe only the cleavage reaction, which occurs under our conditions



III IV V

in 80% yield after a reaction time of four hours.

The rate at which the cleavage reaction proceeds deserves particular mention. In the case of the easily cleaved benzopinacolone a

97.5% yield of triphenylmethane was obtained in 135 seconds at room temperature when sublimed potassium tert-butoxide was the base used. When the only base present was the dimethyl sulfoxide anion (6) the cleavage gave a quantitative yield of triphenylmethane in four minutes.

Investigations are continuing on the scope and mechanism of this facile cleavage of non-enolizable ketones.

REFERENCES

1. Presented in part before the Division of Organic Chemistry, 147th National Meeting of the American Chemical Society, Philadelphia, Pa., April, 1964; Abstracts, p. 7N.

2. We wish to thank the National Science Foundation for partial support of this research.

3. The dimethyl sulfoxide used in this study was obtained from the Crown Zellerbach Corp., distilled under reduced pressure from calcium hydride and stored over Linde 13 x molecular sieves.

4. For a review see K. E. Hamlin and A. W. Weston, "The Cleavage of Non-enolizable Ketones with Sodium Amide" in Organic Reactions, Vol. IX, John Wiley and Sons, Inc., New York, 1957, p. 1.

5. S. J. Cristol and P. K. Freeman, J. Amer. Chem. Soc., **83**, 4427 (1962).

6. The dimethyl sulfoxide anion was prepared according to the procedure of E. J. Corey and M. Chaykovsky, J. Amer. Chem. Soc., **84**, 866 (1962).