[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

STUDIES ON THE NEF REACTION. III. BICYCLO[2•2•2]-5-OCTEN-2-ONE

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Current research on the scope and mechanism of the Nef reaction has shown that most primary and secondary aliphatic nitro compounds can be converted to the corresponding aldehydes or ketones in 20–90% yield (1–7). The molecular weight of the compound does not affect the yield, but molecules in which the nitro group is hindered sterically or which allow for resonance stabilization of the anion of the *aci* salt undergo the conversion with difficulty if at all (4, 6).[3] While the presence of a double bond usually does not interfere with the reaction, compounds related to 2-nitrobicyclo[2•2•1]heptene-5 do not undergo the Nef reaction unless the double bond is removed by reduction (3–7). This fact seems to indicate that the geometry of the bicyclo[2•2•1]heptene-5 ring system as a whole prevents the reaction from proceeding. To determine whether the failure of the Nef reaction in this series was due to the particular ring system or to bicyclic systems in general, it seemed desirable to extend the reaction to the next higher homolog, the bicyclo[2•2•2]octene ring system.

This paper describes the synthesis of 2-nitrobicyclo[2•2•2]octene-5 (I) and the conversion of I to II by the Nef reaction. Condensation of cyclohexadiene and nitroethylene gave a 33% yield of the adduct I. It is a waxy semi-solid that decomposes on prolonged standing and during distillation. No suitable solvent was found for recrystallization.

Rapid addition of the sodium salt of I to dilute acid gave a 68% yield of ketonic material which was shown to possess structure II by the following transformations. Catalytic reduction of II gave III, the oxime of which was identical with that previously prepared by Komppa (9). Lithium aluminum hydride reduction of II gave IV which had been prepared by Alder and Rickert (10) by saponification of the adduct from cyclohexadiene and vinyl acetate. However, they characterized IV only by means of the phenylurethan derivative, m.p. 125°. In this laboratory it was not possible to obtain from IV the same phenylurethan as reported by Alder and Rickert. To prove unequivocally the structure of IV, the synthesis of Alder and Rickert was repeated and the crude alcohol obtained upon saponification of the adduct was converted to its *p*-nitrobenzoate derivative, m.p. 108.5–109.5°. The *p*-nitrobenzoate of IV melted at 108.5–110°.

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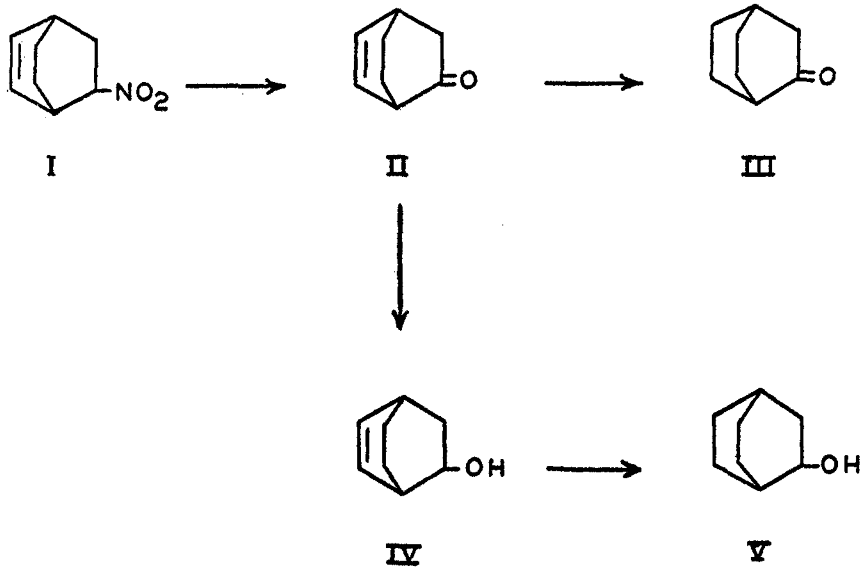
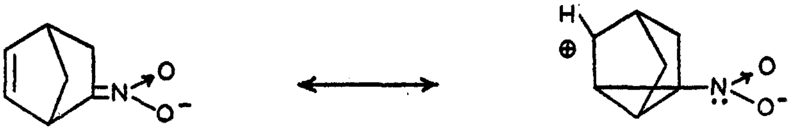
[2] Abstracted from a thesis submitted by D. R. Saunders in partial fulfillment of the requirements for the degree of Bachelor of Arts, Princeton University, May, 1953.

[3] In a study of the regeneration of nitroparaffins from their salts, Kornblum and Graham (8) found that those salts least stabilized by resonance gave the poorest yields of nitro compounds upon acidification and the Nef reaction proceeded more readily than did regeneration.



The infrared spectra of the two samples were identical. Further evidence for the authenticity of IV (and II) was provided by catalytic reduction of IV to V. The melting points of V and its phenylurethan were in agreement with the values found previously by Komppa (9).



A possible explanation for the facts outlined above may be that derivatives of 2-nitrobicyclo[2•2•1]heptene-5 are stabilized by resonance in a manner similar to that of phenylnitromethane.[4] In the present case the molecule is stabilized by a resonance form with the nortricyclene structure. Several conversions of derivatives of bicyclo[2•2•1]heptene-5 to the nortricyclene structure are known (3, 11, 12). Reduction of the double bond would eliminate this stabilization and the Nef reaction then could proceed readily. In the bicyclo[2•2•2] octene-5 series, no tricyclic derivatives homologous with nortricyclene are known[5] and hence this type of stabilization would not be present.

EXPERIMENTAL[6]

2-Nitrobicyclo[2•2•2]octene-5 (I). A solution of 12.0 g. (0.15 mole) of cyclohexadiene and 9.9 g. (0.14 mole) of nitroethylene was heated under reflux for one hour. The reaction mix-

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[4] As suggested by a referee and in reference (7), steric differences between the various compounds may also be responsible for this effect.

[5] An attempt to prepare such a compound is described in reference (18).

[6] All melting points are corrected. All boiling points are uncorrected. Analyses by Clark Microanalytical Laboratories, Urbana, Illinois. We are indebted to Mrs. Iris Siewers of the National Heart Institute, Bethesda 14, Maryland for infrared spectra of several of these compounds.

ture was steam-distilled and the distillate was extracted with ether. The ethereal solution was dried and concentrated to an orange oil that distilled with slight decomposition, 6.9 g. (33%), b.p. 85–87° (1.0 mm.).

Bicyclo[2•2•2]-5-octen-2-one (II). A solution of the *aci* salt was prepared by dissolving 6.9 g. (0.045 mole) of I in an ethanolic solution containing 3.6 g. (0.09 mole) of sodium hydroxide. The solution was allowed to stand one hour and then was added rapidly to a well-stirred solution of 30 ml. of concentrated hydrochloric acid in 200 ml. of water at 0°. The ice-bath was removed and the reaction mixture was stirred until it became colorless (about two hours). After steam-distillation of the total mixture, the distillate was saturated with sodium chloride and extracted three times with ether. The ethereal solution was dried and the ether was removed through a fractionating column packed with glass helices. The residue was a pale yellow oil from which 3.72 g. (68%) of waxy semi-solid was obtained, b.p. 84–85° (13 mm.). The ketone was sublimed for analysis.

Anal. Calc'd for $C_8H_{10}O$: C, 78.65; H, 8.25.

Found: C, 78.60; H, 8.35.

The *2,4-dinitrophenylhydrazone* was prepared in quantitative yield according to the method of Shriner and Fuson (13). Two recrystallizations from ethanol gave golden-yellow prisms, m.p. 150.5°.

Anal. Calc'd for $C_{14}H_{14}N_4O_4$: C, 55.63; H, 4.67; N, 18.53.

Found: C, 55.90; H, 4.78; N, 18.42.

Bicyclo[2•2•2]octan-2-one (III). A solution of 1.66 g. (0.014 mole) of II in 10 ml. of ethanol was mixed with 100 mg. of 30% palladium-on-charcoal and hydrogenated at atmospheric pressure and room temperature. The catalyst was removed by filtration. Removal of the solvent under an air jet yielded 1.41 g. (83%) of a white, waxy solid, m.p. 166–167° [reported (9) 176°; (14) 178–179°] which was not further purified but was converted to the *oxime* of III by the method of Shriner and Fuson (15). Recrystallization from ethanol-water gave colorless prisms, m.p. 117–118° [reported (9) 117–118°].

Bicyclo[2•2•2]-5-octen-2-ol (IV). A solution of 2.40 g. (0.02 mole) of II in 100 ml. of anhydrous ether was heated under reflux with 350 mg. of lithium aluminum hydride for four hours. The ethereal solution was cooled to 0° and 50 ml. of 4 *M* sulfuric acid was added with vigorous stirring until effervescence ceased. The reaction mixture was extracted with ether. The ethereal solution was dried and the ether was removed through a fractionating column packed with glass helices. The residue was dissolved in hot petroleum ether which upon cooling and scratching afforded 2.07 g. (83%) of a fluffy, white solid, m.p. 162–164°. A sample was recrystallized from petroleum ether for analysis, m.p. 166–167°.

Anal. Calc'd for $C_8H_{12}O$: C, 77.37; H, 9.74.

Found: C, 77.59; H, 9.84.

The *p-nitrobenzoate* of IV was prepared by the method of Shriner and Fuson (16). Recrystallization from ethanol-water gave pale yellow plates, m.p. 108.5–109.5°.

Anal. Calc'd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13.

Found: C, 66.06; H, 5.62; N, 5.20.

A sample of IV, prepared by the method of Alder and Rickert (10), was converted to the *p*-nitrobenzoate derivative by the same technique and was recrystallized from ethanol-water, m.p. 108.5–110°. The infrared spectra of the two derivatives were identical.

Bicyclo[2•2•2]octan-2-ol (V). A solution of 145 mg. (1.17 millimoles) of IV in 10 ml. of ethanol absorbed 110% of the theoretical amount of hydrogen when reduced at atmospheric pressure and room temperature with 30% palladium-on-charcoal. The catalyst was separated and about half of the ethanol was removed by evaporation under an air jet. The residue was diluted with water and the solid that formed was removed by filtration, 120 mg. (82%), m.p. 216–217° (sealed capillary) [reported (9) 216–217° (sealed capillary)].

The *phenylurethan* of V was prepared by the method of Shriner and Fuson (17) and recrystallized once from petroleum ether and once from ethanol-water, m.p. 137–138° [reported (9) 138–139°].

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SUMMARY

The conversion of 2-nitrobicyclo[2•2•2]octene-5 to bicyclo[2•2•2]-5-octen-2-one by the Nef reaction is reported. An explanation is advanced for the success of this conversion and the failure of a similar reaction in the bicyclo[2•2•1] heptene-5 series.

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