crystalline precipitate and crystallization from absolute ethanol yielded 0.76 g. of the methiodide IId, m.p. 202–204°.

Anal. Calcd. for $C_{11}H_{22}ONI$: C, 42.45; H, 7.13; N, 4.50. Found: C, 42.53; H, 7.14; N, 4.54.

Treatment of the Salt IId with Alkali. A.—An intimate mixture of 300 mg. of the salt IId and 1.0 g. of sodium carbonate was heated at 230° and 7 mm. of pressure for 1 hr. The distillate, collected on a cold finger cooled with Dry Ice–acetone, was dissolved in ether and extracted with 5% hydrochloric acid. The ether solution contained no appreciable quantity of solute. The aqueous extract was made alkaline with sodium hydroxide and extracted with ether. The organic solution was dried over sodium sulfate, evaporated, and the residue, 135 mg., distilled. The product, 100 mg., proved to be the amino ketone IIc, b.p. 85–95°/7 mm.

Anal. Found: C, 71.29; H, 11.30; N, 8.63.

Its methiodide, prepared as before, m.p. 201–203°, mixed m.p. 202–204°.

B.—A mixture of 311 mg. of the salt IId and silver oxide, freshly prepared from 0.2 g. of silver nitrate, was stirred at room temperature for 45 min. The mixture was filtered, the water removed under vacuum, and the residue heated at 230° and 7 mm. of pressure for 30 min. The distillate on the cold finger was dissolved in ether and extracted with 5% hydrochloric acid. Again, no neutral product was found in the ether solution. The acidic solution was made alkaline with sodium hydroxide and extracted with ether. This organic solution was dried over sodium sulfate and evaporated. The residual oil, 40 mg., was converted to its methiodide, 45 mg., m.p. 197–200°, mixed m.p. 198–201°.

2-Methyl-2-carbethoxycyclohexanone Ethylene Ketal (IIIc).—The above ketalation procedure was repeated with 60.4 g. of the keto ester IIe, b.p. 90–91°/4 mm. (lit.,[5] b.p. 85–86°/3 mm.), 5 mg. of *p*-toluenesulfonic acid, 100 ml. of ethylene glycol, and 750 ml. of benzene. It led to 64.1 g. of the ketal IIIc, b.p. 123–124°/8 mm., infrared spectrum (chloroform): 5.77 (s)μ.

Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 62.80; H, 9.01.

2-Methyl-2-hydroxymethylcyclohexanone Ethylene Ketal (IIId).—The above hydride reduction procedure was repeated with 64.1 g. of the ketal ester IIIc in 250 ml. of ether and 20 g. of lithium aluminum hydride in 500 ml. of ether. It led to 44.2 g. of the hydroxy ketal, b.p. 114–115°/6 mm., infrared spectrum (chloroform): 2.70 (m), 9.15 (s)μ.

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.12; H, 10.00.

2-Methyl-2-*p*-toluenesulfonoxymethylcyclohexanone (IIf).—*p*-Toluenesulfonyl chloride, 47.5 g., was added to a solution of 42.3 g. of hydroxy ketal in 470 ml. of dry pyridine at −5°, the mixture stirred and then allowed to stand at −15° for 13 hr. The mixture was added to 1 l. of water and ice and extracted with chloroform. The organic solution was extracted with 200-ml. portions of ice-cold 20% sulfuric acid, until the extract remained acidic. The chloroform solution then was washed successively with water, dilute sodium bicarbonate solution and water and was dried over anhydrous sodium sulfate. Evaporation of the solvent under vacuum gave 70.5 g. of oily crude ketal tosylate. The latter and 1 ml. of concd. hydrochloric acid were dissolved in 635 ml. of acetone and heated on a steam bath for 2 hr. The residue was taken up in water and extracted with ether. The extract was dried over sodium sulfate and evaporated under vacuum. The oily residue was crystallized from petroleum ether–ether cooled in a Dry Ice-acetone bath. Recrystallization gave 19.7 g. of solid, m.p. 55–58°. The oily residues from the crystallizations were retosylated by the above procedure and yielded 7.6 g. more of the same solid product. Several further crystallizations from petroleum ether–ether afforded the ketotosylate IIf, m.p. 57–59°, infrared spectrum (chloroform): 5.85 (s), 7.37 (s), 8.51 (s) μ.

Anal. Calcd. for $C_{15}H_{20}O_4S$: C, 60.78; H, 6.80; S, 10.82. Found: C, 60.94; H, 7.09; S, 10.87.

1-Methylbicyclo[3.1.1]heptan-6-one (I).—A solution of 5.0 g. of the ketotosylate IIf and 0.73 g. of sodium hydroxide in 250 ml. of 1:1 methanol–water was refluxed for 12 hr. The solution was acidified and extracted with ether. The extract was washed successively with water, 5% sodium bicarbonate, and water and was dried over anhydrous sodium sulfate. Evporation of the solvent and distillation of the residue gave 1.57 g. of crude product which on redistillation yielded 1.17 g. of the bicyclic ketone I, b.p. 79–80°/35 mm., spectra: ultraviolet (95% ethanol), λ_{max} 290 mμ (ϵ 30): infrared (chloroform), 5.66 (s)μ.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.54; H, 9.90.

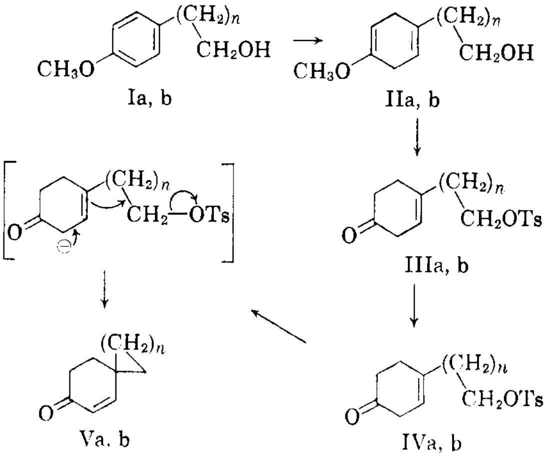
Preparation of Spiran Ring Systems by Intramolecular Alkylation

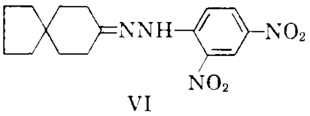
John H. Fassnacht and Norman A. Nelson[1]

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Mass.

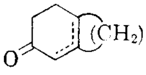
Received December 1, 1961

Of the numerous methods for the preparation of carbocyclic spiran ring systems, one of the newer procedures involves intramolecular alkylation. We have prepared the spirans Va and Vb by utilizing an intramolecular alkylation reaction similar to that reported by Winstein and Baird.[2,3]

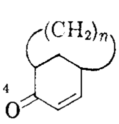




VI



VII



VIII

Series a. $n = 1$
Series b. $n = 3$
Ts = $CH_3C_6H_4SO_2$—

---

[1] Department of Chemistry, The Upjohn Company, Kalamazoo, Mich., to whom inquiries should be addressed.

[2] The present work was initiated as an extension of our previous intramolecular alkylations of ketones and esters [N. A. Nelson and G. A. Mortimer, *J. Org. Chem.*, **22**, 1146 (1957)].

[3] S. Winstein and R. Baird, *J. Am. Chem. Soc.*, **79**, 756, 4238 (1957).

The starting alcohols (Ia and b) were converted to the dihydrophenyl derivatives IIa and b by Birch-type reductions using lithium and alcohol in liquid ammonia. The best conversions to the dihydrophenyl compounds were obtained when excesses of lithium large enough to cause a *bronze* phase in the liquid ammonia were used.[4] The dihydrophenyl derivatives are somewhat unstable toward heat but were obtained pure by distilling them rapidly under reduced pressure.

The dihydrophenyl compounds IIa and b were hydrolyzed to the ketones IIIa and b in good yields by stirring them with sulfuric acid in aqueous tetrahydrofuran at room temperature. While these ketones were not obtained pure by distillation, they were characterized as their 2,4-dinitrophenylhydrazone derivatives and were of sufficient purity to be used in the next step.

The tosylates IVa and b were prepared at 0° from the corresponding keto alcohols and *p*-toluenesulfonyl chloride (recrystallized) using redistilled anhydrous pyridine as the solvent. Good yields of the tosylates, as oils, could be obtained. However, since they were unstable on standing and were not obtained crystalline, they were used in the crude state in the displacement reaction. Infrared spectral analyses indicated that the compounds were essentially free of solvents and unchanged starting material.

The tosylates IVa and b were best converted to the corresponding spirans Va and b, respectively, with sodium hydride in dioxane. Spiro[2.5]oct-1-en-3-one (Va) was obtained in 29% yield. The ultraviolet spectrum [$\lambda_{\max}^{C_2H_5OH}$ 256 mμ (ε 10,550)] shows an elevation in $\lambda_{\max}$ of 31 mμ over that observed for 2-cyclohexenone.[5] This bathochromic shift is indicative of conjugation with a 3-membered ring.[3,6,7] The nuclear magnetic resonance spectrum of the product is fully consistent with structure Va.

Spiro [4.5]dec-1-en-3-one (Vb) was obtained in 28% yield and was characterized as its 2,4-dinitrophenylhydrazone derivative. A portion of Vb was hydrogenated and the product was converted to its 2,4-dinitrophenylhydrazone derivative VI, which was shown to be identical to an authentic sample of VI, supplied by Professor S. Winstein.

The alkylation of α,β- or β,γ-unsaturated carbonyl compounds occurs chiefly at the α-position.[8] That considerable *intermolecular* alkylation did occur in our case at the α-position(s) of the unsaturated ketones was indicated by the large amounts of higher molecular weight residues remaining after distillation of the desired products. However, the formation of the spirans Va and b occurs by alkylation at a position γ to the ketone carbonyl. Products of the type VII and VIII (representing possible *intramolecular* α-alkylations with appropriate double bond rearrangements) were not detected in the products by spectroscopic or gas chromatographic techniques.

Experimental[9]

β-(2,5-Dihydro-4-methoxyphenyl)ethyl Alcohol (IIa).—Lithium wire (4.53 g., 0.66 g.-atom) was added over a 10-min. period to a stirred solution of 10 g. (0.066 mole) of β-(4-methoxyphenyl)ethyl alcohol,[10] 80 ml. of ether, 30 g. (0.66 mole) of absolute ethanol and 400 ml. of liquid ammonia. This solution was stirred for 30 min. after which 13.8 g. (0.30 mole) of absolute ethanol was added followed by 2.07 g. (0.30 g.-atom) of lithium. After stirring the mixture for an additional 30 min., the ammonia was allowed to evaporate and enough water was added just to dissolve all of the solid material remaining. The resulting layers were separated and the water layer was extracted with ether. The ether layers were combined and dried over magnesium sulfate. Distillation of the crude product through an apparatus previously soaked in dilute sodium hydroxide solution gave 7.2 g. (72%) of β-(2,5-dihydro-4-methoxyphenyl)ethyl alcohol, b.p. 80° (0.2–0.15 mm.), $\nu_{\max}^{CCl_4}$ 1695 (m) and 1665 (s) cm.$^{-1}$ (C=C stretching of unconj. enol ether),[11] $\lambda_{\max}^{C_2H_5OH}$ 278 (ε 269) and 284 mμ (ε 235). The ultraviolet spectrum indicates the presence of about 15% unchanged starting material.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.12; H, 9.09. Found: C, 69.86; H, 9.40.

β-(4-Keto-1-cyclohexenyl)ethyl Alcohol (IIIa).—A solution of 10 g. (0.064 mole) of β-(2,5-dihydro-4-methoxyphenyl)ethyl alcohol, 50 ml. of tetrahydrofuran, 25 ml. of water, and 2.5 ml. of concentrated sulfuric acid was stirred for 45 min. at room temperature. The product was extracted with ether after saturation of the reaction mixture with ammonium sulfate. The ether layers were combined and washed twice with a saturated sodium bicarbonate solution (which in addition was saturated with ammonium sulfate), twice with a saturated ammonium sulfate solution, and dried over magnesium sulfate. Distillation of the product gave 4.93 g. (53%) of IIIa, b.p. 85–87° (0.006 mm.), which contained about 18% of β-(4-methoxyphenyl)ethyl alcohol as ascertained from the infrared and ultraviolet spectra, $\lambda_{\max}^{C_2H_5OH}$ 278 (ε 314) and 284 mμ (ε 267). Compound IIIa was characterized as its *2,4-dinitrophenylhydrazone*, made in the usual way, and recrystallized from absolute ethanol, m.p. 102–104.7°, $\lambda_{\max}^{C_2H_5OH}$ 361 mμ (ε 21,866).

Anal. Calcd. for $C_{14}H_{16}N_4O_5$: C, 52.50; H, 5.00; N, 17.50. Found: C, 52.52; H, 5.30; N, 17.54.

Spirol[2.5]oct-1-en-3-one (Va).—4-(β-Tosyloxyethyl) 3-cyclohexenone (IVa) was obtained as an oil in 79% yield

---

[4] W. S. Johnson, B. Bannister, and R. Pappo, *J. Am. Chem. Soc.*, **78**, 6331 (1956).

[5] N. A. Nelson, R. S. P. Hsi, J. M. Schuck, and L. D. Kahn, *J. Am. Chem. Soc.*, **82**, 2573 (1960).

[6] E. N. Trachtenberg and G. Odian, *J. Am. Chem. Soc.*, **80**, 4018 (1958), and references cited therein.

[7] D. S. Irvine, J. A. Henry, and F. S. Spring, *J. Chem. Soc.*, 1316 (1955).

[8] See, for example, A. C. Cope, H. L. Holmes, and H. O. House, *Organic Reactions*, **9**, 107 (1957); R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives, and R. B. Kelley, *J. Chem. Soc.*, 1131 (1957); and A. J. Birch, J. A. K. Quartey, and H. Smith, *J. Chem. Soc.*, 1768 (1952).

[9] Melting points and boiling points are uncorrected. The infrared spectra were determined with a Baird (Model B) spectrophotometer fitted with a sodium chloride prism. In reporting infrared spectra, (s) denotes strong, (m) medium, and (w) weak absorption. Ultraviolet spectra were determined with a Cary (Model 11MS) recording spectrophotometer. We are indebted to Prof. J. S. Waugh for the NMR spectrum which was determined with a Varian V-4300B spectrometer and stabilized magnetic system operating at a frequency of 40.0 mc. The microanalyses were performed by Dr. S. M. Nagy and his associates.

[10] K. H. Slotta and H. Heller, *Ber.*, **63**, 3029 (1930).

[11] G. Stork, *J. Am. Chem. Soc.*, **73**, 504 (1951).

from β-(4-keto-1-cyclohexenyl) ethyl alcohol and *p*-toluenesulfonyl chloride in anhydrous pyridine at 0°. The product was obtained by adding benzene to the reaction solution after 24 hr., neutralizing the pyridine with ice cold 1 *N* hydrochloric acid, and removing the benzene from the dried organic solution. The alkylation was carried out under a nitrogen atmosphere in a dry flask which was equipped with a magnetic stirring bar, nitrogen inlet tube, and a condenser with a calcium chloride drying tube. A mixture of 15.0 g. (0.05 mole) of 4-(β-tosyloxyethyl)-3-cyclohexenone, 400 ml. of anhydrous dioxane, 1 drop of anhydrous *t*-butyl alcohol, and 1.22 g. (0.05 mole) of sodium hydride was stirred at reflux for 17 hr. Ether and 200 ml. of water with sufficient ammonium sulfate to saturate the aqueous layer were added. The water layer was separated and extracted with ether. The ether layers were combined, dried over magnesium sulfate, and filtered. The solvents were distilled through a 2-foot helix-packed column. The residue (7.78 g.) was distilled through a semimicro column[12] giving 1.81 g. (29.2%) of spiro[2.5]oct-1-en-3-one, b.p. 59° (1.5 mm.), n_D^{29} 1.5170, $\nu_{max}^{CCl_4}$ 1675 (s, conj. C═O) and 1612 cm.$^{-1}$ (m, conj. C═C $\lambda_{max}^{C_2H_5OH}$ 256 mμ (ε 10,550). Vapor phase chromatographic analysis[13] showed the presence of only one material. The NMR spectrum[9,14] exhibits peaks at 986, 1006, 1015, and 1025 c.p.s. for the vinyl protons; 1156, 1162, 1174, and 1180 c.p.s. for the methylene protons of the six-membered ring; and 1220 c.p.s. for the methylene protons of the three-membered ring.

Anal Calcd. for $C_8H_{10}O$: C, 78.68; H, 8.19. Found: C, 78.46; H, 8.13.

Spiro[2.5]oct-1-en-3-one 2,4-dinitrophenylhydrazone was prepared in the usual way, chromatographed on acid-washed alumina using 95% hexane-5% ether as eluent, and recrystallized from absolute ethanol to give a pure sample, m.p. 172–172.5°, $\lambda_{max}^{C_2H_5OH}$ 380 mμ (ε 30,200).

Anal. Calcd. for $C_{14}H_{14}N_4O_4$: C, 55.62; H, 4.63; N, 18.54. Found: C, 55.62; H, 4.69; N, 18.45.

4-(2,5-Dihydro-4-methoxyphenyl)-1-butanol (IIb).—The general procedure outlined by Johnson and co-workers was followed.[4] A solution of 20 g. (0.11 mole) of 4-(*p*-methoxyphenyl)-1-butanol[15] and 250 ml. of anhydrous ether was stirred while 1 l. of liquid ammonia was added. Rapid stirring was continued while 520 ml. of absolute ethanol was added followed by rapid addition of 27.6 g. (4.0 g.-atoms) of lithium wire. Then, 250 ml. of absolute ethanol was added, in conjunction with sufficient liquid ammonia to maintain a *bronze* phase throughout the reaction while at the same time keeping the bulk of the solution medium to light grey in color. After the lithium had reacted (total time about 1 hr.), the ammonia was allowed to evaporate. Water was added to dissolve the solid, and the solution was extracted with ether The ether extracts were combined, washed with water, dried over magnesium sulfate, and filtered. Distillation of the product through dry apparatus previously soaked in sodium hydroxide solution gave 16 g. (80%) of 4-(2,5-dihydro-4-methoxyphenyl)-1-butanol, b.p. 74–99° (0.1–0.2 mm.), mostly at 97–99° (0.1–0.2 mm.), $\lambda_{max}^{CCl_4}$ 3400 (m, O—H), 1693 (m) and 1665 (s C═C stretching of unconj. enol ether),[11] and 1223 cm.$^{-1}$ (s, ether C—O—C), $\lambda_{max}^{C_2H_5OH}$ 268–274 mμ (ε 25) indicating about 1% aromatic impurity.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.52; H, 9.89. Found: C, 72.23; H, 10.18.

4-(4-Keto-1-cyclohexenyl)-1-butanol (IIIb).—Using the procedure described above for the preparation of β-(4-keto-1-cyclohexenyl)ethyl alcohol, the hydrolysis of 10 g. (0.055 mole) of 4-(2,5-dihydro-4-methoxyphenyl)-1-butanol gave 7.3 g. (79%) of material, b.p. 78–115° (0.03–0.015 mm.), which was not obtained pure since polymerization hindered fractionation of the material. The *2,4-dinitrophenylhydrazone* of IIIb was obtained in the usual way—by cooling the reaction solution in Dry Ice–isopropyl alcohol to ensure complete precipitation of the derivative. The filtered crystals had to be washed immediately with water to avoid decomposition. Repeated recrystallization of the derivative from absolute ethanol gave a pure sample, m.p. 49.5–51° $\lambda_{max}^{C_2H_5OH}$ 361 mμ (ε 25,520).

Anal. Calcd. for $C_{16}H_{20}N_4O_5$: C, 55.17; H, 5.74; N, 16.09. Found: C, 55.35; H, 5.82; N, 16.09.

Spirol[4.5]dec-1-en-3-one (Vb).—4-(4-Tosyloxybutyl)-3-cyclohexenone (IVb) was obtained as an oil in 77% yield from 4-(4-keto-1-cyclohexenyl)-1-butanol and *p*-toluenesulfonyl chloride as described above for the preparation of compound IVa. The same procedure used in the preparation of spiro[2.5]oct-1-en-3-one (Va) gave from 14.7 g. (0.045 mole) of 4-(4-tosyloxybutyl)-3-cyclohexenone and 1.08 g. (0.045 mole) of sodium hydride, 2.2 g. (32%) of a colorless oil, b.p. 82–84° (1.0 mm.), $\nu_{max}^{CCl_4}$ 1678 (s, conj. C═O) and 1612 cm.$^{-1}$ (w, conj. C═C), $\lambda_{max}^{C_2H_5OH}$ 231 mμ (ε 9,344). Vapor phase chromatographic analysis[13] showed the presence of 13.4% of an impurity. The crude spiro[4.5]dec-1-en-3-one was converted directly to its *2,4-dinitrophenylhydrazone* derivative which was recrystallized from absolute ethanol m.p. 150–151.2° (softening at 147°), $\lambda_{max}^{C_2H_5OH}$ 376 mμ (ε 30,640).

Anal. Calcd. for $C_{16}H_{18}N_4O_4$: C, 58.18; H, 5.45; N, 16.96. Found: C, 58.16; H, 5.68; N, 16.90.

Spiro[4.5]decan-3-one 2,4-dinitrophenylhydrazone (VI).—A hydrogenation was carried out with 0.50 g. (0.003 mole) of spiro [4.5]dec-1-en-3-one (approximately 86% pure by vapor phase chromatographic analysis) in 10 ml. of absolute ethanol, using 75 mg. of 10% palladium-on-carbon catalyst. At the completion of the reaction 88.7% of the theoretical amount of hydrogen had been absorbed. The mixture was filtered and converted directly to its 2,4-dinitrophenylhydrazone derivative, which was recrystallized several times from absolute ethanol, m.p. 161°, $\lambda_{max}^{C_2H_5OH}$ 363 mμ (ε 24,260).

Anal. Calcd. for $C_{16}H_{20}N_4O_4$: C, 57.83; H, 6.02; N, 16.86. Found: C, 57.97; H, 5.99; N, 16.90.

A mixed melting point with an authentic sample of IV, m.p. 161–161.9°, kindly supplied by Professor S. Winstein, showed no depression.

---

[12] Of a type similar to that described by C. W. Gould, Jr., G. Holzman, and C. Niemann, *Anal. Chem.*, **20**, 361 (1948).

[13] Gas-chromatographic columns were 9-mm. Pyrex tubes, 190 cm. long, containing 30% by weight of Dow-Corning Silicone oil No. 550 on a 50–100 mesh firebrick support. Helium was used as the carrier gas and thermistors were employed for the detection of sample peaks.

[14] Determined in carbon tetrachloride solution using tetramethylsilane as an internal standard. Positions of peaks are expressed in cycles per second relative to the proton resonance band of benzene at 1000 c.p.s. or the band of tetramethylsilane at 1255 c.p.s.

[15] R. Heck and S. Winstein, *J. Am. Chem. Soc.*, **79**, 3105 (1957).

Reactions of 2-(*p*-Toluenesulfonoxy)lepidine with Nucleophilic Reagents[1]

J. F. BUNNETT[2] AND J. Y. BASSETT, JR.[3]

Venable Chemical Laboratory, University of North Carolina, Chapel Hill, N. C.

Received December 22, 1961

We have shown[4] that 2,4-dinitrophenyl *p*-toluenesulfonate is cleaved by nucleophilic re-

---

[1] Supported in part by the Army Research Office (Durham).

[2] Brown University, Providence, R. I.

[3] R. J. Reynolds Fellow, 1956–1957. This manuscript is based on the Ph.D. thesis of J. Y. Bassett, Jr., October, 1957.

[4] J. F. Bunnett and J. Y. Bassett, Jr., *J. Am. Chem. Soc.*, **81**, 2104 (1959).