The Preparation of Spiro[2.5]octan-6-one. Catalytic Hydrogenation of a Vinylcyclopropane

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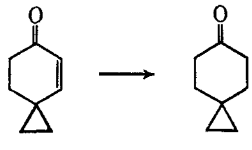
In connection with other work, we required a sample of the unknown spiro ketone **2**. The preparation of **2** appeared to be straightforward, involving reduction of the unsaturated spiro ketone **1** available from the procedure of Fassnacht and Nelson.[2] Preliminary experiments indicated, however, that even under very mild conditions of catalytic hydrogenation, considerable cleavage of the cyclopropane ring accompanied double-bond reduction. Since the hydrogenolysis product proved difficult to separate from **2**, various conditions were examined to effect the desired reduction; some of the results are shown in Table I.



1 **2**

TABLE I

REDUCTION OF SPIRO[2.5]OCT-4-EN-6-ONE (1) AT 25° [a]

Catalyst	Solvent	% **2**	% 4-ethylcyclohexanone (**4**)
5% Pd/C	50% aqueous EtOH	23	77
5% Pd/C	Absolute EtOH	43	57
5% Pd/C	THF	47	53
5% Pd/C	Hexane	68	32
5% Pd/C	94% aqueous EtOH 0.12 *N* NaOH	60	40
5% Pd/C	85% aqueous EtOH 0.01 *N* NaOH	84	16
PtO_2	THF	91	9
Raney Ni[b]	THF	100	0

[a] Reductions were carried out at a constant pressure of 1 atm (H_2 plus solvent vapor pressure) and were carried to completion. Weight ratios of ketone to catalyst were in most cases about 20:1; reaction times ranged from 13 to 63 min. For reduction using Raney Ni, the ketone to catalyst ratio was 4.5:1, and reaction time was 175 min. [b] W-2.

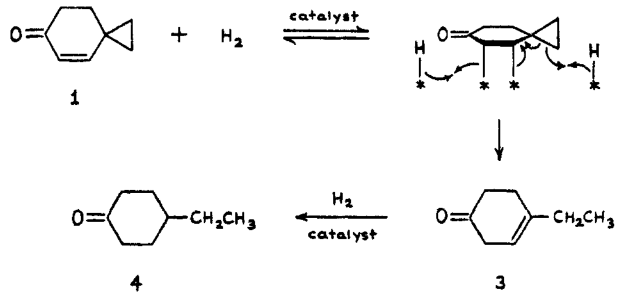
Hydrogenolyses of vinyl-substituted cyclopropane derivatives have often been observed,[3] but relatively little work has been directed toward selective reduction of the double bond. Exceptions are found in the work of Slabey and Wise,[3b] who reported such selectivity in the high-pressure reduction of isopropenylcyclopropane using Ba–Cu–CrO catalyst; considerable hydrogenolysis occurred, however, when the double bond was more highly substituted. The use of mercury-poisoned Raney nickel, first reported by Corner and Pease in 1945,[4] seemed more promising for the present purpose. The catalyst did indeed prove effective in preventing hydrogenolysis of **1**, although hydrogenation to **2** proceeded very slowly. However, unpoisoned Raney nickel was found to be equally effective. This result was unexpected since Raney nickel has been found to cause the hydrogenolysis of vinylcyclopropanes under comparable conditions.[3c,5] The only complication (which also occurred with poisoned Raney nickel) was a relatively slow reduction of the product, **2**, to the corresponding alcohol. Hydrogenation using Raney nickel was examined in various solvents; production of the alcohol was found to be slowest, relative to hydrogenation of the double bond, when tetrahydrofuran was used. This combination of catalyst and solvent is therefore considered optimal for preparation of the title spiro ketone.

The hydrogenolysis of **1** observed with palladium or platinum catalysts (Table I) gave 4-ethylcyclohexanone as the only cleavage product, with no trace of 4,4-dimethylcyclohexanone being found (vpc); spiro[2.5]-octane itself is catalytically reduced to 1,1-dimethylcyclohexane.[6]

Cleavage of the bond adjacent to the point of substitution is the usual mode of hydrogenolysis of vinylcyclopropanes,[3] and is thought to result from initial adsorption at the double bond, followed by migration of the point of adsorption to the three-membered ring.[3a]

Interestingly, in several runs stopped short of completion (using catalysts which gave hydrogenolysis), an intermediate was found which proved to be 4-ethyl-3-cyclohexenone (**3**), demonstrating that under these conditions the complete reduction does not occur in a single step. A possible mechanism involving **3** is outlined in Scheme I (arrows represent movements of single electrons).

SCHEME I



Experimental Section

2-(4-Methoxyphenyl)ethanol.—A solution of 150 g (0.90 mol) of *p*-methoxyphenylacetic acid in 350 ml of tetrahydrofuran (THF) was added to a stirred solution of 35 g (0.92 mol) of lithium aluminum hydride in 650 ml of THF under nitrogen over a period of 1.5 hr. After stirring at room temperature for 5 hr, the thick slurry evolved heat and became less viscous; stirring was continued for an additional 5 hr. The excess hydride was decomposed with 15 ml of ethyl acetate, after which 750 ml of 6 *N* sulfuric acid was added. Several hours of stirring led to a clear two-phase system. The aqueous phase was extracted with THF, and the combined THF solutions were washed with 5% base and saturated salt solution, then dried with anhydrous potassium carbon-

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(1) N D E A Title IV Predoctoral Fellow, 1964–1967.

(2) J. H. Fassnacht and N. A. Nelson, *J. Org. Chem.*, **27**, 1885 (1962).

(3) (a) J. Newham, *Chem. Rev.*, **63**, 123 (1963); (b) V. A. Slabey and P. H. Wise, *J. Amer. Chem. Soc.*, **74**, 3887 (1952); (c) R. Van Volkenburgh, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *ibid.*, **71**, 172 (1949); (d) M. Hanack, H. J. Schneider, and H. Schneider-Bernlöhr, *Tetrahedron*, **23**, 2195 (1967).

(4) E. S. Corner and R. N. Pease, *Ind. Eng. Chem., Anal. Ed.*, **17**, 564 (1945).

(5) R. Van Volkenburgh, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *J. Amer. Chem. Soc.*, **71**, 3595 (1949).

(6) R. W. Shortridge, R. A. Craig, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *ibid.*, **70**, 946 (1948).

ate. Solvent was removed by distillation (last traces at 1 mm) to give a residue of 108 g (0.71 mol, 79%) of light yellow oil, initial bp 101° (0.8 mm),[7] which was used without further purification. The nmr and ir spectra of this material indicated that it contained no appreciable impurities.

The general procedure of Fassnacht and Nelson[2] was used for the preparation of 1, with modifications to accommodate a larger scale reaction. As these modifications led to improved yields, they are presented below.

2-(2,5-Dihydro-4-methoxyphenyl)ethanol.—To a stirred solution of 304 g (2.0 mol) of 2-(4-methoxyphenyl)ethanol and 450 g of methanol in 2.5 l. of liquid ammonia, 75 g (10.8 g-atoms) of lithium was added at a rate sufficient to maintain reflux and a blue color in solution. An additional 160 g of methanol and 15 g (2.2 g-atoms) of lithium were added alternately in portions. Treatment as previously described[2] followed by rotary evaporation gave a light orange residue weighing 298 g (1.94 mol, 97%). Nmr and ir analyses indicated that this material was substantially pure and free from starting alcohol; it was used without further purification. Attempted distillation[2] on this scale led to extensive decomposition.

4-(2-Hydroxyethyl)-3-cyclohexenone.—A solution of 285 g (1.85 mol) of 2-(2,5-dihydro-4-methoxyphenyl)ethanol, 1 l. of THF, 550 ml of water, and 55 ml of concentrated sulfuric acid was stirred for 1.5 hr at 25°. A mixture of 300 g of ice and 300 ml of 6 *N* sodium hydroxide was then added with stirring, after which the solution was saturated with salt. The aqueous layer was separated, extracted with THF, and the combined organic phases washed and dried as described previously.[2] Solvent and residual water were removed by rotary evaporation at 40–50°, to give 241 g (1.72 mol, 93%) of product. The nmr spectrum of this material showed no appreciable differences from that of a sample collected by vpc (5 ft × 0.25 in. 20% SF-96 on Chromosorb W, 158°), and it was used without further purification.

The tosylate of this alcohol was prepared in the usual manner in pyridine solution, yielding 319 g of viscous oil. Nmr analysis indicated a purity of >80%, and no further purification was attempted.

Spiro[2.5]oct-4-en-6-one.—To a stirred solution, under nitrogen, of 98.0 g (0.33 mol) of the crude tosylate in 3.3 l. of anhydrous dioxane (distilled from sodium metal after 20-hr reflux), 10 drops of anhydrous *t*-butyl alcohol were added, followed by 12.9 g (0.54 mol) of sodium hydride. The mixture was then stirred at high speed while it was heated to reflux for 11 hr, allowed to cool to room temperature, and treated with 1 l. of saturated ammonium chloride solution. The aqueous layer was separated and extracted with ether, and the combined organic phases were dried with anhydrous magnesium sulfate. Solvents were removed by distillation through a 2-ft Vigreux column (final bp 101°). The residue was distilled through a short Vigreux column, giving 22.4 g of material of bp 69–73° (3 mm). Gas chromatography (20 ft × 0.25 in. 15% Carbowax 6000 on Chromosorb W, 175°) showed this material to contain impurities with retention times (RT) of 40, 42, and 73 relative to the major product of RT 100. Since previous experiments had shown that the impurities of RT 40 and 42 would be difficult to separate from the saturated spiro ketone, the mixture was redistilled through a spinning-band column to give 14.0 g of material containing 96% RT 100 and 4% RT 73, bp 86–87° (8 mm). The nmr spectrum of pure RT 100, obtained in the final distillation fractions, demonstrated it to be the compound previously described.[8] The ir spectrum (CCl_4) had characteristic bands[8] at 860 (s), 910, 935, 970, 1010, 1035 (w), 1055 (w), 1120, 1190, 1615, 1680 (vs), and 3070 cm^{-1}.

Spiro[2.5]octan-6-one.—The 14.0 g of material described above was dissolved in 200 ml of THF and hydrogenated over 1.5 g of W-2 grade Raney nickel in a Parr apparatus at room temperature and 10–50 psig. Contamination of the mixture by THF-soluble compounds in the stopper was eliminated by inserting a tight-fitting Teflon disk between stopper and solution. The pressure was carefully monitored and the hydrogenation stopped when the theoretical hydrogen uptake had been achieved. The time required was 7 hr. After filtration of the solution, traces of remaining catalyst were collected on a magnetic stirring bar. Solvent was removed by distillation through a 2-ft Vigreux column at atmospheric pressure, and the residue was distilled through a spinning-band column to give 11.1 g (0.09 mol, 81%) of 99.5% pure spiro[2.5]octan-6-one, bp 93.5° (33 mm). The characteristic bands[8] in the ir spectrum (CCl_4) occurred at 880 (w), 920 (w), 1010, 1045 (w), 1140, 1715 (s), and 3065 cm^{-1}; the nmr spectrum (CCl_4) had bands at δ^9 0.47 (s, 4 H), 1.63 (t, J = 6.5 cps, 4 H), and 2.32 (t, J = 6.5 cps, 4 H).

Anal. Calcd for $C_8H_{12}O$: C, 77.4; H, 9.7. Found: C, 77.0; H, 9.8.

Identification of the Intermediate (3).—Small-scale hydrogenations (Table II), duplicating conditions given in Table I, were stopped prior to completion and analyzed by vpc on the Carbowax column described above. In every case, a broad peak was observed which was not present in mixtures from hydrogenations carried to completion. This peak was collected and found by its nmr spectrum to consist of approximately equal parts of **3** and 4-ethyl-2-cyclohexenone (**5**). Reinjection of the mixture into the gas chromatograph caused further isomerization, greatly increasing the percentage of **5**. Attempted purification by vpc of the product of an independent synthesis of **3** (described below) also produced a mixture of **3** and **5**. These data suggest that the actual hydrogenation intermediate, before partial isomerization to **5** on the vpc column, is compound **3**.

Table II

Partial Reduction of Spiro[2.5]oct-4-en-6-one

Catalyst	Solvent	Percentage of total products **2**	**4**	**3**	% starting material consumed
5% Pd/C	THF	50	35	15	57
5% Pd/C	THF	47	26	27	32
5% Pd/C	Absolute EtOH	38	42	20	54

4-Ethyl-3-cyclohexenone (3).—A small sample of the *p*-toluenesulfonate of 4-(2-hydroxyethyl)-3-cyclohexenone was reduced with lithium aluminum hydride in ether. After removal of the ether, the product was oxidized by the Jones procedure.[10]

Registry No.—2, 15811-21-9.

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

[8] H. E. Simmons, E. P. Blanchard, and H. D. Hartzler, *J. Org. Chem.*, **31**, 295 (1966).

[9] Expressed in parts per million (ppm) from TMS = 0.

[10] A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *J. Chem. Soc.*, 2548 (1953).