Hamann and Straus[19] have determined equilibrium constants at 25° and 45° for reaction III, finding the values: $K_{25°} = 6.1 \times 10^{-6}$ mole kg.$^{-1}$ and $K_{45°} = 2.8 \times 10^{-6}$ mole kg.$^{-1}$ for $K = (a_{C_5H_{10}NH_2^+}) \times (a_{CH_3O^-})/(a_{C_5H_{10}NH})$ in which a are molal activities.

For pure piperidine, $a_{C_5H_{10}NH} \cong 11.7$ mole kg.$^{-1}$; hence for solutions of piperidine in methanol such as those employed in experiments of Table III, this term is smaller and therefore $a_{CH_3O^-}$ at 45° is smaller than $[K(a_{C_5H_{10}NH})]^{1/2} = [2.8 \times 10^{-6} \times 11.7]^{1/2} = 5.7 \times 10^{-3}$ mole kg.$^{-1}$. From this figure and from the known rates of reaction of *o*- and *p*-chloronitrobenzenes with sodium methoxide in methanol (Table I) and with piperidine in the same solvent (Table III), it can be seen that aminolysis is the only reaction that takes place under the experimental conditions of Table III, due to the very low concentration of methoxide ion.

(19) S. D. Hamann and W. Straus, *Disc. Faraday Soc.*, **22**, 70 (1956).

Acknowledgments.—Our thanks are offered to Dr. Mauricio Bühler, head of the Organic Chemistry Laboratories, Comisión Nacional de Energía Atómica de la República Argentina, who afforded W.G. the hospitality of his laboratories, to him and Dra. Josefina Rodríguez for their guidance and advice on radioactive technique and to Professor J. F. Bunnett and Dr. C. A. Bunton for helpful discussions. Thanks are also offered to Mrs. B. B. de Deferrari for the microanalyses.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF VERMONT, BURLINGTON, VT.]

Ionic Reactions in the Spirane Series. I. Effect of Adjacent Ring Size on the Acetolysis of Neopentyl-type Tosylates of the Spirane Series

BY A. PAUL KRAPCHO AND MERRILL BENSON

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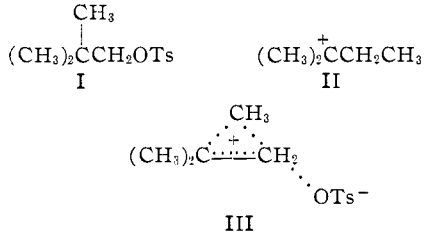
The acetolysis of several spirane tosylates (VI, n = 2, 3 and 4) of the neopentyl-type has been studied. The acetolysis rate was found to be dependent on adjacent ring size and the products of the acetolysis were predominantly olefins resulting from rearrangement. The results are discussed in terms of the effect of ring strain on anchimeric assistance in rearrangements of the Wagner–Meerwein type.

Introduction.—The Wagner–Meerwein rearrangement of neopentyl-type systems (I) to *t*-amyl systems (II) under solvolytic conditions has been investigated.[1] The fact that the formolysis of neopentyl tosylate is as rapid as that of ethyl tosylate has been attributed to anchimeric assistance of the neighboring methyl group and the transition state would have a bridged-ion structure (III).[2] The acetolysis of *cis*- and *trans*-9-decalyl-



carbinyl tosylates (IV and V), which represent a neopentyl system wherein the migrating group is an integral part of a fused ring system, has been

investigated by Dauben.[3] These compounds solvolyze at the same rate at 90° and are five times faster than neopentyl tosylate, corresponding to a slight rate enhancement. The product in each case is predominantly the rearranged olefin and bridged-ion transition states are proposed.

It has also been reported that cyclopropylcarbinyl sulfonate and methylcyclobutylcarbinyl brosylate undergo solvolysis under ionizing conditions at rates which exceed those for non-cyclic substrates by factors of several hundred or more.[1,4] Here it is probable that the solvolysis is being assisted by a combination of field and anchimeric effects due to the neighboring cyclopropyl and cyclobutyl groups.

The favorable geometry of spirane tosylates (VI), in which the neopentyl system is also part of an alicyclic ring, seems well suited for a systematic study designed to assess ring strain *versus* anchimeric assistance as a driving force in rearrangements of the Wagner–Meerwein type.[5] The dehydration with accompanying rearrangement of spiranols has been the subject of many investigations.[6]

In order to obtain some preliminary information with regard to the effect of ring strain, the acetolysis rates of the spirane tosylate systems (VI) were investigated where n = 2, 3 and 4. As a model system the acetolysis rate of 2,2-dimethylcyclopentyl tosylate (VII) was measured for comparative purposes.

Synthesis.—The preparation of the spiranols followed standard routes previously described in

(1) A. Streitwieser, Jr., *Chem. Revs.*, **56**, 571 (1956).

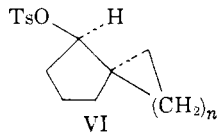
(2) S. Winstein and H. Marshall, *J. Am. Chem. Soc.*, **74**, 1120 (1952).

(3) W. G. Dauben and J. B. Rogan, *ibid.*, **79**, 5002 (1957).

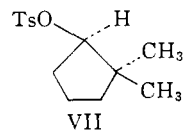
(4) E. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., Inc., New York, N. Y., 1959, pp. 588–591, and references cited therein.

(5) S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, *J. Am. Chem. Soc.*, **74**, 1113 (1952).

(6) (a) P. A. Naro and J. A. Dixon, *ibid.*, **81**, 1681 (1959), and references cited therein; (b) A. C. Cope, J. M. Grisar and P. E. Peterson, *ibid.*, **82**, 4299 (1960).

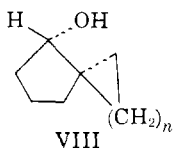


VI

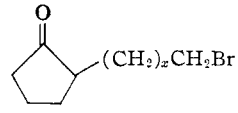


VII

the literature. Spiro[3,4]octan-5-ol (VIII, n = 2) was prepared by lithium aluminum hydride reduction of the corresponding ketone, which was prepared by pinacol rearrangement of 1,1′-dihydroxybicyclobutyl according to the procedure described by Vogel.[7] Spiro[4,4]nonan-1-ol(VIII, n = 3) and spiro[4,5]decan-1-ol (VIII, n = 4) were prepared by a similar reduction from the corresponding ketones, which were obtained by cyclization of 2-(ω-bromobutyl)-cyclopentanone (IX, x = 3) and 2-(ω-bromopentyl)-cyclopentanone (IX, x = 4), respectively, following the procedure of Mayer, Wenshuh and Topelmann.[8] The



VIII



2,2-dimethylcyclopentanol was prepared from 2,2-dimethylcyclohexanone following the procedure of Wilcox and Mesirov,[9] which consisted of the nitric acid oxidation of 2,2-dimethylcyclohexanone to 2,2-dimethyladipic acid, pyrolysis of this diacid with barium hydroxide to yield 2,2-dimethylcyclopentanone, and reduction of this ketone with lithium aluminum hydride. The corresponding tosylates could readily be prepared from the spiranols by the procedure described by Tipson.[10]

Solvolysis Results.—The specific first-order rate constants for acetolysis of the three spirane tosylates and for the model system 2,2-dimethylcyclopentyl tosylate are summarized in Table I along with the temperature interval studied and the calculated activation energy. In each experiment the reaction was followed to at least 75% completion and six or more values of the first-order rate constant were determined from appropriately spaced titrations. No trends in these values were observed and the rate constants were reproducible. In the Experimental section a typical kinetic run is listed. All acetolysis procedures and conditions were similar to those described previously[11] and all kinetic runs were run in anhydrous acetic acid (1% in acetic anhydride) containing a slight excess of sodium acetate. The rate constants were determined by the infinity titer technique and all infinity titers checked to within a few per cent. of the calculated values.

The activation parameters were calculated in the usual manner[12] and are listed in Table II along with the relative rates for comparative purposes.

TABLE I

System, n =	Temp., °C.	k_1, sec.$^{-1}$[a]	E_a, kcal.
VI, 2	16.00 ± 0.02	1.24 ± 0.04 × 10^{-3}	21.7
	20.00 ± .01	2.08 ± .01 × 10^{-3}	
VI, 3	20.00 ± .02	9.59 ± .13 × 10^{-5}	22.0
	30.00 ± .02	3.34 ± .08 × 10^{-4}	
VI, 4	40.00 ± .02	1.86 ± .03 × 10^{-5}	25.5
	50.00 ± .03	6.63 ± .14 × 10^{-5}	
VII	50.00 ± .03	2.83 ± .02 × 10^{-5}	26.6
	60.00 ± .05	9.82 ± .04 × 10^{-5}	

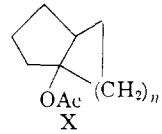
[a] The rate constants are average values and deviations from the average of two or three independent kinetic experiments.

TABLE II

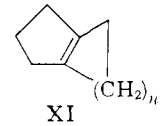
System, n =	$\Delta H\ddagger$[a]	$\Delta S\ddagger$[b]	25° calcd. $k \times 10^5$[c]	Relative k (25°)
VI, 2	21.1	+1.2	3890	4440
VI, 3	21.4	−3.9	151	172
VI, 4	24.9	−0.6	2.36	2.7
VII	26.0	+0.5	0.875	1.0

[a] Probable error of ±1 kcal. with the exception of n = 2 where probable error of ±1.5 kcal. due to rapid solvolysis rate and small temperature interval studied. [b] Probable error of ±2 e.u. except for n = 2 where probable error is ±3 e.u. [c] Extrapolated or interpolated from data at other temperatures.

Product Analysis.—The products of the acetolysis of the spirane tosylates were predominantly the rearranged olefins with small amounts (5 to 8%) of presumably rearranged acetates (determined by micro saponification of the crude acetolysis product) as depicted in structure X. In each case the major product was the bicyclic olefin with the tetrasubstituted double bond (structure XI) as could readily be shown by infrared comparisons with the olefinic samples obtained from acid-catalyzed rearrangements of the spiranols.[3] All acetolysis products had small amounts of olefinic material present with a trisubstituted double bond exocyclic to one of the rings.



X



XI

Discussion.—Rate enhancements due to participation of adjacent small ring systems have been reported in several cases.[1] The ethanolysis of cyclopropylcarbinyl benzenesulfonate at 20° has been found to be 14 times as rapid as that of allyl benzenesulfonate and 500 times as rapid as that of ethyl benzenesulfonate.[13] The acetolysis of nortricyclyl brosylate at 25° is about 200 times as fast as that of *endo*-norbornyl brosylate.[14] Both of these examples have been interpreted as a rate enhancement due to participation by the neighboring cyclopropyl ring.

The acetolysis rates for dicyclobutylcarbinyl brosylate, methylcyclobutyl brosylate and isopropyl brosylate have been found to be in the ratio 220:510:1,[1,15] indicative of a rate enhancement due to the neighboring cyclobutyl ring.

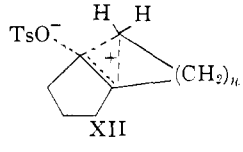
(7) E. Vogel, *Chem. Ber.*, **85**, 25 (1952).
(8) R. Mayer, G. Wenshuh and W. Topelmann, *ibid.*, **91**, 1916 (1958).
(9) C. F. Wilcox, Jr., and M. Mesirov, *J. Org. Chem.*, **25**, 1841 (1960).
(10) R. S. Tipson, *ibid.*, **9**, 235 (1941).
(11) P. D. Bartlett and W. P. Giddings, *J. Am. Chem. Soc.*, **82**, 1240 (1960), and references cited therein.
(12) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," J. Wiley and Sons, Inc., New York, N. Y., 1961, Second Edition.
(13) C. G. Bergstrom and S. Siegel, *J. Am. Chem. Soc.*, **74**, 145, 254 (1952).
(14) S. Winstein, H. M. Walborsky and K. Schreiber, *ibid.*, **72**, 5795 (1950).
(15) S. Winstein and N. J. Holness, *ibid.*, **77**, 3054 (1955).

In the cases of adjacent five- or more-membered saturated ring systems the acetolysis rates of cycloalkylmethyl *p*-bromobenzenesulfonates have been measured by Felkin and Le Ny.[16] At 79.9° the acetolysis rates for isobutyl brosylate, cyclopentanemethyl brosylate and cyclohexanemethyl brosylate are listed as 1.35×10^{-6}, 7.65×10^{-6}, and 1.19×10^{-6} sec^{-1}, respectively, pointing to a slight rate enhancement due to the neighboring cyclopentyl ring.

A comparison of the relative rate of 2,2-dimethylcyclopentyl tosylate to pinacolyl tosylate (k approximately 2×10^{-7} $sec.^{-1}$ from one-third the rate of the brosylate)[2] shows a slight rate enhancement(factor of 4), indicating that any assistance from participation is small. The relative rate of spiro[4,5]decan-1-yl tosylate ($n = 4$) to 2,2-dimethylcyclopentyl tosylate, a factor of 2.7, again shows a very slight rate enhancement and points to a slight anchimeric acceleration by the neighboring cyclohexane ring. A comparison of the relative rates of spiro[3,4]octan-5-yl tosylate ($n = 2$), factor of 4440, and spiro[4,4]nonan-1-yl tosylate ($n = 3$), factor of 172, with 2,2-dimethylcyclopentyl tosylate exhibits a pronounced rate enhancement.

The main trend in the rates in the series appears to be due to $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$ being -1.3 ± 2.5 e.u. This would seem to indicate that the large acceleration of rate observed in the systems with adjacent cyclobutyl and cyclopentyl ring systems is primarily due to relief of ring strain by anchimeric assistance.

In the case of spiro[3,4]octan-5-yl tosylate the angular strain of the cyclobutane ring, combined with a field effect based on the premise that the regions of high electron density lie slightly outside the square of the carbon nuclei, is ideal for participation. One of the electron-rich regions outside the cyclobutane ring approaches C_α from the side opposite –OTs, thus facilitating the departure of the group with the formation of a bridged-ion transition state of the type XII where $n = 2$.



XII

This transition state closely resembles the products of the reaction; much progress has been made along the reaction coördinate.

The spiro[4,4]nonan-1-yl tosylate with the cyclopentyl ring adjacent to the tosylate group, although certainly possessing less angular strain than the analogous cyclobutyl ring, is strained somewhat by torsional forces attributed to hydrogen–hydrogen repulsions.[17] Release of this torsional strain can be envisioned by participation with the formation of a bridged-ion transition state where $n = 3$.

In the case of the spirane possessing the cyclohexane ring adjacent to the tosylate group, the cyclohexane ring is unstrained, with hydrogen–hydrogen repulsions reduced to a minimum in the chair conformation. Very little difference in rate would be expected on this basis in comparison to 2,2-dimethylcyclopentyl tosylate. Anchimeric assistance in these latter cases would be expected to be the smallest, although bridged-ion transition states may be involved.

Further investigations of the acetolysis of other spirane tosylates are currently under investigation and will be reported shortly.

Acknowledgment.—This investigation was supported by a grant from the Research Corporation and an NSF Institutional Grant from the University of Vermont, whose assistance is gratefully acknowledged.

Experimental

All melting points (capillary tubes) and boiling points are uncorrected. Infrared spectra were recorded on a Perkin–Elmer model 21 recording spectrometer.

Spiro[3,4]octan-5-ol(VIII, $n = 2$).—Spiro[3,4]octan-5-one was obtained in 70% yield by pinacol rearrangement of 1,1′-dihydroxybicyclobutyl following the procedure described by Vogel[7]; b.p. 56–58° (7 mm.), reported 69–70° (18 mm.). The quantitative reduction of the spiranone to the spiranol was effected by refluxing an ethereal solution with excess lithium aluminum hydride, decomposing the excess lithium aluminum hydride with water, drying the ethereal solution with magnesium sulfate and then distilling the product: b.p. 139–140° (750 mm.), reported 140–141° (760 mm.). An examination of the infrared spectrum showed no carbonyl band present and strong hydroxyl absorption at 3400 $cm.^{-1}$.

Spiro[3,4]octan-5-yl Tosylate (VI, $n = 2$).—The tosylate was prepared from 1.83 g. (0.0145 mole) of spiranol by allowing it to stand in a solution of 6 ml. of anhydrous pyridine and 2.78 g. (0.0145 mole) of *p*-toluenesulfonyl chloride for 24 hours at 0°. The mixture was poured into ice-water and the tosylate was extracted with cold pentane. The pentane extract was washed three times with portions of 5% hydrochloric acid, once with dilute sodium bicarbonate solution, and once with water. The pentane extract was dried over anhydrous sodium sulfate and the pentane concentrated to 25 ml. under reduced pressure. Crystals separated from the pentane solution on cooling to −20°. The sample was very unstable at room temperature (decomposition resulted in about 12 minutes). For the kinetic runs the sample was recrystallized twice at low temperature from pentane. The material was used directly on removal of the pentane at 0° under reduced pressure. The acetolysis equivalent was found to be 273, calcd. 280.

Spiro[4,4]nonan-1-ol (VIII, $n = 3$).—Spiro[4,4]nonan-1-one was prepared in 73% yield from 2-(ω-bromobutyl)-cyclopentanone by the procedure described by Mayer, Wenshuh and Topelman[8]; b.p. 68–70° (5 mm.), reported b.p. 82.5–83° (13 mm.). The reduction of the spiranone to the spiranol was effected using ethereal lithium aluminum hydride in 87% yield, b.p. 77° (4 mm.).

Spiro[4,4]nonan-1-yl Tosylate (VI, $n = 3$).—The tosylate was prepared from 5.16 g. (0.037 mole) of spiranol by allowing it to stand in a solution of 25 ml. of anhydrous pyridine and 7.07 g. (0.037 mole) of *p*-toluenesulfonyl chloride for 36 hours at 0°. The mixture was poured into ice-water, the precipitated solid was filtered, and the solid washed thoroughly with cold water. The sample readily decomposed on standing at room temperature for a short time (15 minutes). The crude white solid was taken up in petroleum ether (30–60°) at room temperature, the solution was dried over anhydrous sodium sulfate, and the solution was decanted from the drying agent. On cooling, the solution deposited fluffy white crystals which were filtered and rapidly air-dried. In this manner there was obtained 8 g. (73% yield) of the tosylate. The solid was again taken up in petroleum ether and recrystallization at low temperature yielded the pure tosylate melting at 43–44°. The acetolysis equivalent was found to be 300, calcd. 294.

Anal. Calcd. for $C_{16}H_{22}O_3S$: C, 65.27; H, 7.53. Found: C, 65.61; H, 7.76.

(16) H. Felkin and G. Le Ny, *Bull. soc. chim. France*, **24**, 1169 (1957).

(17) H. C. Brown, R. S. Fletcher and R. R. Johannesen, *J. Am. Chem. Soc.*, **73**, 212 (1951), and references cited therein.

Spiro[4,5]decan-1-ol (VIII, $n = 4$).—Spiro[4,5]decan-1-one was obtained in 65% yield from 2-(ω-bromopentyl)-cyclopentanone by the procedure described by Mayer, Wenshuh and Topelmann,[8] the only modification being that 50% aqueous potassium hydroxide was utilized in place of the 35% solution suggested by the above authors. The colorless liquid boiled at 82–83° (2 mm.), reported 105–106° (3 mm.).

The spiranol was prepared in 91% yield from the spiranone by lithium aluminum hydride reduction and boiled at 93° (4.5 mm.), reported[18] b.p. 107–108° (10 mm.).

Spiro[4,5]decan-1-yl Tosylate (VI, $n = 4$).—The tosylate was prepared from 1.94 g. (0.013 mole) of spiranol by allowing it to stand in a solution of 10 ml. of anhydrous pyridine and 2.5 g. (0.013 mole) of *p*-toluenesulfonyl chloride for 15 hours at 0°. On pouring into ice-water an oil formed which solidified on standing. The solid was filtered, washed thoroughly with water and quickly air-dried. This yielded 3.3 g. (85% yield) of a white solid which on two crystallizations from hexane at low temperature melted at 52–53°. The sample was fairly stable at room temperature for a few days. The acetolysis equivalent was found to be 310, calcd. 308.

Anal. Calcd. for $C_{17}H_{24}O_3S$: C, 66.20; H, 7.84. Found: C, 65.95; H, 7.66.

2,2-Dimethylcyclopentyl Alcohol.—The 2,2-dimethylcyclopentyl alcohol was prepared in 92% yield by the lithium aluminum hydride reduction of the corresponding ketone following the procedure of Wilcox and Mesirov.[9] The sample had b.p. 153–154°, reported b.p. 154–155°. The ketone was prepared in 67% yield by pyrolysis of 2,2-dimethyladipic acid with barium hydroxide and boiled at 142–144°, reported[9] 140–143°.

2,2-Dimethylcyclopentyl Tosylate (VII) was prepared as in the previous case and after three crystallizations from hexane there was obtained a 79% yield of a white crystalline solid of m.p. 49.5–50.5°. The acetolysis equivalent was found to be 279, calcd. 268.

Anal. Calcd. for $C_{14}H_{20}O_3S$: C, 62.65; H, 7.51; S, 11.95. Found: C, 62.95; H, 7.29; S, 12.14.

Kinetic Procedures.—Acetolysis procedures and conditions were chosen to be similar to those of Bartlett and Giddings,[11] which were similar to those utilized by Winstein, *et al.*,[19] and by Roberts, *et al.*[20] Anhydrous acetic acid containing 1% excess acetic anhydride was prepared by refluxing reagent grade acetic acid with the calculated amount of acetic anhydride.[14] The tosylate samples were weighed into 10-ml. volumetric flasks so that solutions 0.092 molar in ester would be obtained, then 10.0 ml. of 0.0971 molar sodium acetate–acetic acid was added (slight excess of acetate was present in all runs). The reactions were carried out in the volumetric flasks and the rate constants were determined by the infinity titer technique. The first aliquot after thermal equilibrium had been established was called zero time. Aliquots of 1.0 ml. were pipetted directly from the volumetric flask in the constant temperature bath and quenched by cooling in ice-water or by drainage into pentane. A few drops of a saturated solution of crystal violet in acetic acid were added and the residual sodium acetate was immediately titrated with 0.0208 *M* perchloric acid. The infinity titers were obtained by heating the volumetrics at 70–80° for a period corresponding to at least ten-half lives, returning to the bath to equilibrate, and titration of the 1.0-ml. aliquot as usual. The experimentally determined infinity titer was utilized in all calculations of the first-order rate constants. As a check on procedure the first-order rate constant for cyclopentyl tosylate at 50° was found to be $4.07 \pm 0.07 \times 10^{-5}$ sec.$^{-1}$ which compared favorably with the value of $3.84 \pm 0.06 \times 10^{-5}$ sec.$^{-1}$ reported by Winstein, *et al.*[21]

In one run sealed ampoules were utilized and the first-order rate constant obtained was $1.86 \pm 0.07 \times 10^{-5}$ sec.$^{-1}$ at 40° which compared favorably with the value of $1.86 \pm 0.03 \times 10^{-5}$ sec.$^{-1}$ obtained from the infinity titer method using the volumetrics. In all runs the infinity titers checked to within at least 4%. The data for a typical kinetic run are listed in Table III.

TABLE III

ACETOLYSIS OF SPIRO[4,4]NONAN-1-YL TOSYLATE AT 30.00° ± 0.02°; SOLUTION 0.0917 *M* IN TOSYLATE AND 0.0971 *M* IN SODIUM ACETATE

Time, sec.	Titer, ml.	10^4k, sec.$^{-1}$
0	3.42	..
600	2.90	3.12
1263	2.38	3.40
1915	2.02	3.31
2722	1.66	3.28
4422	1.16	3.21
7066	0.74	3.25
Infinity (22 hr.)	0.44	..
		Av. 3.26 ± 0.07

Acetolysis Products. (a) Acetolysis of Spiro[3,4]octan-5-yl Tosylate(VI, $n = 2$).—The unstable tosylate (1.8 g., 6.4 mmoles) was weighed directly into hexane and the hexane removed by concentration on a Rinco rotary evaporator at 0°. To this residual oil was added a solution of 0.56 g. (6.8 mmoles) of sodium acetate dissolved in 7 ml. of anhydrous acetic acid. A clear solution resulted which was allowed to stand for 9 hours at room temperature and finally heated at 50° for 5 minutes. The solution was cooled, poured into ice-water and the aqueous layer extracted four times with pentane. The pentane extract was washed twice with sodium bicarbonate solution, twice with water, and dried over anhydrous sodium sulfate. The pentane was carefully distilled through a Nester–Faust spinning band column and there was obtained 0.5 g. (72% yield if all olefin) of a nearly colorless oil. No further purification was effected.

The infrared spectrum of the undistilled product was recorded in the pure liquid phase and the main component could readily be identified as bicyclo[3.3.0]oct-1(5)-ene by comparison of the spectrum with that of one kindly supplied by Cope.[6b] The by-products present were approximately 6% of a presumably rearranged acetate (as determined by micro-saponification), which exhibited an absorption band at 1740 cm.$^{-1}$, and a small amount of bicyclo[3.3.0]oct-1(2)-ene identified by weak bands at 3070 and 793 cm.$^{-1}$.[6b]

(b) Acetolysis of spiro[4,4]nonan-1-yl Tosylate (VI, $n = 3$) was run as in the previous acetolysis in (a) above using 2.76 g. (9.39 mmoles) of tosylate and 0.874 g. (10.3 mmole) of sodium acetate in 20 ml. of anhydrous acetic acid. The solution was warmed at 60–75° for 2 hours and worked up as previously. There was obtained after removal of the pentane 0.7 g. (61% if all olefin) of a nearly colorless liquid.

The infrared spectrum of the undistilled product was recorded in the neat liquid phase and the main component could readily be identified as bicyclo[4.3.0]non-1(6)-ene by comparison of the spectrum with that of the product obtained from the dehydration of spiro[4,4]nonan-1-ol according to the procedure of Christol *et al.*,[22] which produces this olefin as the major component. The by-products present were 8% of a presumably rearranged acetate (as determined by micro saponification), which exhibited a weak absorption band at 1740 cm.$^{-1}$, and a small amount of olefinic material with the double bond exocylic to one of the ring systems as could be identified by weak bands at 3070 and 793 cm.$^{-1}$. The olefinic material from the acetolysis exhibited a relatively weaker band at 793 cm.$^{-1}$ than did the product obtained from the acid-catalyzed rearrangement of the spiranol.

(c) Acetolysis of Spiro[4,5]decan-1-yl Tosylate (VI, $n = 4$).—The acetolysis was run as in procedure (a) using 2.2 g. (7.23 mmoles) of tosylate and 0.65 g. (7.95 mmoles) of sodium acetate dissolved in 10 ml. of anhydrous acetic acid. The solution was warmed at 90° for 2 hours and was worked up as previously. There was obtained after removal of the pentane 0.85 g. (87% yield if all olefin) of a yellow liquid.

The infrared spectrum of the undistilled product was recorded in the pure liquid phase and the main component could readily be identified as bicyclo[5.3.0]dec-1(7)-ene by

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(19) (a) S. Winstein, C. Hanson and E. Grunwald, *J. Am. Chem. Soc.*, **70**, 812 (1948); (b) S. Winstein, E. Grunwald and L. L. Ingraham, *ibid.*, **70**, 821 (1948).

(20) J. D. Roberts and V. C. Chambers, *ibid.*, **73**, 5034 (1951).

(21) S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse D. Trifan and H. Marshall, *ibid.*, **74**, 1127 (1952).

(22) H. Christol, R. Jacquier and M. Mousseron, *Bull. soc. chim. France*, **24**, 1027 (1957).

comparison of the infrared spectrum with that of the product obtained from the zinc chloride dehydration of spiro-[4,5]decan-1-ol according to the procedure of Mayer,[14] which has been shown to yield this olefin as the major product. The by-products present were 7% of a presumably rearranged acetate (determined by micro saponification), which exhibited a weak absorption band at 1740 cm.$^{-1}$, and weak bands appeared in both samples at 3070 and 743 cm.$^{-1}$ which possibly is indicative of olefinic material with a double bond exocyclic to one of the ring systems.

[CONTRIBUTION FROM THE DEPARTMENTS OF PHARMACEUTICAL CHEMISTRY OF THE UNIVERSITY OF KANSAS, LAWRENCE, KANS., AND THE UNIVERSITY OF WISCONSIN, MADISON, WIS.]

A Stereospecific Synthesis of D(−)-Shikimic Acid[1,2]

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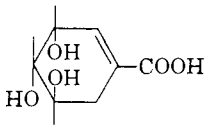
A stereospecific synthesis of *dl*-shikimic acid (I) from the Diels–Alder adduct of *trans,trans*-1,4-diacetoxy-1,3-butadiene (II) and methyl acrylate is reported. The optical resolution also was effected.

Naturally occurring shikimic acid was first isolated in 1885.[3] Fischer and Dangschat reported its structure to be I.[4] No total synthesis of shi-

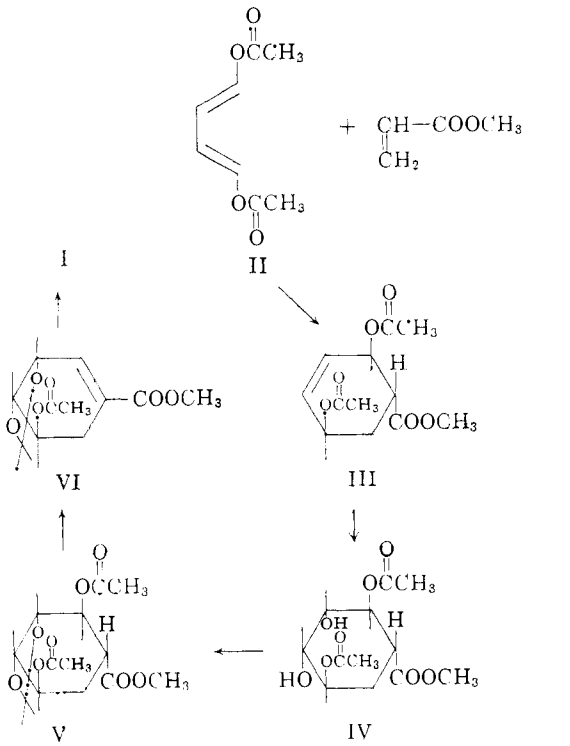


I

kimic acid had previously been described, although Grewe and co-workers had reported the synthesis of quinic acid[5] which Fischer and Dangschat had previously converted to shikimic acid.[6] This acid has been shown to be the biological precursor of phenylalanine, tyrosine and tryptophan,[7] which, in turn, are the parents of the majority of plant alkaloids. It is also involved in the biosynthesis of lignin,[8] one of the major constituents of wood, flavonoids,[9] and of other important aromatic compounds.[10] The enzymatic synthesis of shikimic acid from D-erythrose-4-phosphate and phosphoenolpyruvate was reported by Srinivasan, Katagiri and Sprinson.[11]

Since the acid has been shown to be an important link in aromatic biogenesis, it was desirable to devise a complete synthetic scheme whereby carbon-14 could be introduced into specific positions of the molecule. If this could be accomplished, the pathways of formation of various naturally occurring aromatic compounds could be followed.

The route to shikimic acid which proved successful was based on a Diels–Alder reaction of *trans,trans*-1,4-diacetoxy-1,3-butadiene[12,13] (II) with methyl acrylate to afford methyl 2β,5β-diacetoxy-3-cyclohexene-1α-carboxylate (III) in 93% yield. Although attempted hydroxylation of the double bond in III with potassium permanganate led to a mixture of compounds, *cis*-hydroxylation *anti* to the two acetoxy groups was successfully achieved by employing osmium tetroxide. The product obtained in this reaction was designated as methyl 2β,5β-diacetoxy-3α,4α-dihydroxycyclohexane-1α-carboxylate (IV). The stereochemical assignment of the carbomethoxy function at 1 differs from that proposed by McCrindle, Overton and Raphael,[2] but is in accord with the results of pyrolysis of the corresponding acetonide V.



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(2) This work was initially reported in a Communication to the Editor, *J. Am. Chem. Soc.*, **81**, 2909 (1959), and was later corroborated by R. McCrindle, K. H. Overton and R. A. Raphael, *J. Chem. Soc.*, 1560 (1960), utilizing a similar synthesis.

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