to boiling and then allowed to stand overnight at 25°. The mixture was filtered into excess dilute hydrochloric acid, diluted with water, and filtered; the product was washed with water. The wet acid IIa was melted in a 50-ml. erlenmeyer flask on a hot plate, cooled, taken into ether and filtered. The filtrate on evaporation gave an orange oil IIIa which was treated with 250 mg. of potassium hydroxide in 25 ml. of methanol and boiled for 15 min. The reaction was diluted with water to yield a crystalline solid, 400 mg., m.p. 170–174°. The product was purified by passing it over 10 g. of alumina in dichloromethane–ether. The first eluates gave white crystalline material which was crystallized from ether to give 180 mg. of VIIa: 15% yield; m.p. 190–193° (FJ); λ_{max} 240.5 mμ (ε 26,800); ν_{max} 2215 (cyano), 1688, 1624 cm.$^{-1}$; $[\alpha]^{23}D$ −18.5° (*c* 0.54, $CHCl_3$).

Anal. Calcd. for $C_{22}H_{27}NO_2$ (337.4): C, 78.30; H, 8.08. Found: C, 78.33; H, 8.22.

16α17α-[3-Carboxy-3,1-(2-isoxazolino)]pregn-4-ene-3,20-dione (IIa).—A solution of 4.0 g. (0.01 mole) of II in 1 l. of acetone (distilled over $KMnO_4$) was treated at ice-bath temperature and under nitrogen with 5 ml. of 8 *N* chromic acid (Jones reagent)[10] during 7 min., stirred for an additional 5 min., and quenched in 1.5 l. of ice–water. Most of the acetone was evaporated under reduced pressure, and the precipitated solid was separated by filtration, washed with water, and dried, 2.9 g., 72% crude. The crude product was refluxed for 25 min. in 200 ml. of 95% ethanol with 900 mg. of oxalic acid dihydrate. The mixture was evaporated under reduced pressure at 50–60° and crystallized from dioxane–water to give 2.37 g. (60% yield): m.p. 210–212° (TH); λ_{max} 240 mμ (ε 18,700); $[\alpha]^{24}D$ +102° (*c* 0.51, $CHCl_3$); ν_{max} 1741, 1719, 1675, 1633, 1587 cm.$^{-1}$.

Anal. Calcd. for $C_{23}H_{29}NO_5$ (399.5): C, 69.15; H, 7.32; N, 3.51. Found: C, 69.05; H, 7.13; N, 3.60.

17α-Hydroxy-3,20-dioxopregn-4-ene-16α-carbonitrile (IIIa).—A sample (1.0 g.) of IIa was melted at 250° until all foaming ceased. The melt was cooled and stirred with methanol to yield 280 mg. of a solid product, m.p. 245° (FJ). Two crystallizations from methanol and ether gave 80 mg.: m.p. 245–247° (FJ); λ_{max} 240 mμ (ε 16,000); $[\alpha]^{23}D$ +92.2° (*c* 0.51, $CHCl_3$); ν_{max} 3440 (hydroxyl), 2250 (cyano), 1710 (keto), 1655 (keto), 1616 cm.$^{-1}$.

Anal. Calcd. for $C_{22}H_{29}NO_3$ (355.5): C, 74.33; H, 8.22. Found: C, 74.14; H, 8.22.

(10) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon *J. Chem. Soc.*, 39 (1946).

A Novel 2.2.1-Bicyclic Elimination of a N-Tosylpyrazoline

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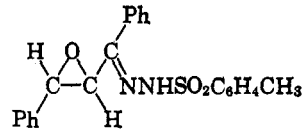
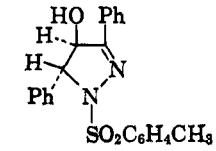
The pyrolytic decomposition of the alkali salts of tosylhydrazones of aldehydes and ketones in aprotic solvents has been reported to give products expected to arise from intermediate carbenes.[1,2] In view of our interest in heterocyclic small-ring compounds, we sought to define further the reactivity of a carbenoid center adjacent to a three-membered oxirane ring.

In an attempt to prepare the tosylhydrazone of *trans*-chalcone oxide (I), two different approaches were tried. Treatment of *trans*-chalcone oxide with tosylhydrazide in acidic ethanol for 5 min. at 50° gave a product identical with that obtained by treating benzalacetophenone tosylhydrazone with 10% sodium hydroxide and 30% hydrogen peroxide in methyl alcohol. That the product from both reactions was not the desired tosylhydrazone I was evidenced by a strong peak



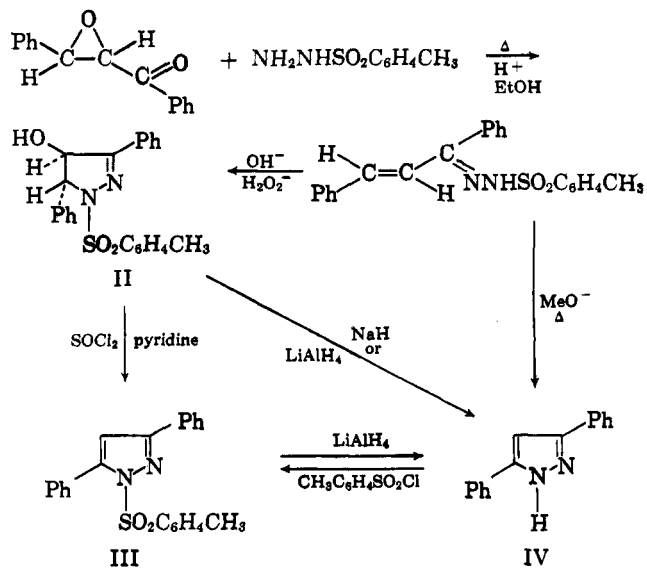
I



II

at 3.0 μ in its infrared spectrum. This material is instead assigned structure II on the basis of chemical and physical data cited below. The elemental analysis of II, m.p. 225–226°, indicates that it is an isomer of I. Dehydration with thionyl chloride–pyridine in benzene afforded in excellent yield 1-*p*-toluenesulfonyl-3,5-diphenylpyrazole (III). Treatment of III with lithium aluminum hydride in tetrahydrofuran readily gave rise to 3,5-diphenylpyrazole (IV). Structure III was further confirmed by its unequivocal synthesis from 3,5-diphenylpyrazole and *p*-toluenesulfonyl chloride. The various transformations leading to the products described above are outlined in Chart I.

CHART I

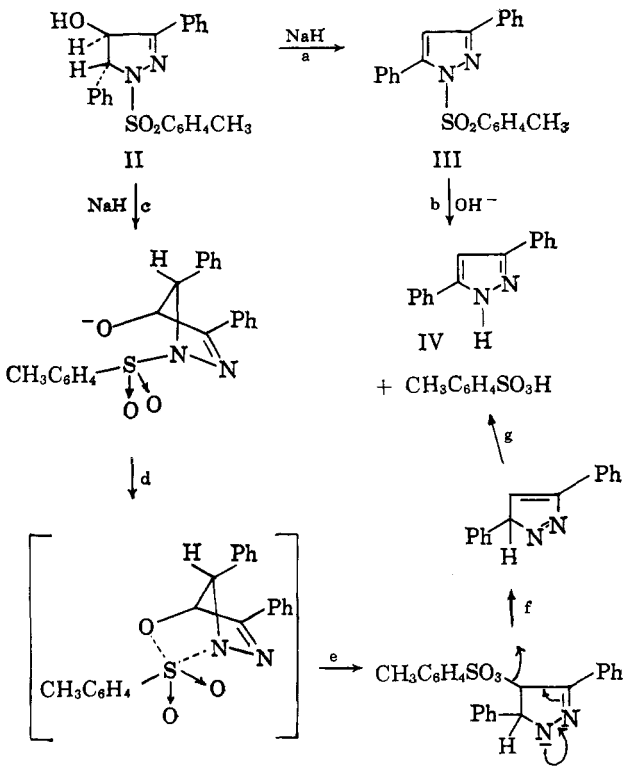


Even with the mildest conditions, 4-hydroxypyrazoline (II) resulted from the reaction of tosylhydrazide with the *trans* oxide of benzalacetophenone. The mechanism of its formation probably involves the intermediate formation of tosylhydrazone (I) which then undergoes an intramolecular ring opening and closure to form II. The configuration of II is such that the hydroxyl group on C-4 and the hydrogen on C-5 are on the same side of the pyrazoline ring. A related study of the reaction of hydrazine with an epoxy ketone[3] has shown that the epoxide ring is opened to give a similar intermediate, which, on heating, loses water to yield the corresponding pyrazole. It has also been reported[4] that the related *trans*-ethylenimine ketones and phenylhydrazine produce the analogous 4-aminotrialkylpyrazolines.

Treatment of II with sodium hydride in diglyme or tetrahydrofuran led to an unexpected result. Under the basic conditions employed, II was converted in almost quantitative yield to 3,5-diphenylpyrazole (IV)

(1) J. W. Powell and M. C. Whiting, *Tetrahedron*, **7**, 305 (1959).
(2) L. Friedman and H. Shechter, *J. Am. Chem. Soc.*, **81**, 5512 (1959).
(3) Jorlander, *Ber.*, **49**, 2782 (1916).
(4) N. H. Cromwell and H. Hoeksema, *J. Am. Chem. Soc.*, **71**, 716 (1949).

SCHEME I



and *p*-toluenesulfonic acid. Scheme I is a summary of a possible sequence capable of describing pyrazole formation.

The basic dehydration (path a) of an analogous 4-hydroxypyrazoline to the corresponding pyrazole[5] demanded that particular attention be paid to this possibility (*i.e.*, paths a and b). This sequence, however, is eliminated by the finding that III was stable under conditions at which pyrazole formation from II proceeded smoothly. This result caused III to be rejected as a possible precursor of the pyrazole. The formation of IV can therefore be regarded as occurring directly from compound II and may be rationalized by sequence c through g. The scheme consists of the initial formation of an alkoxide anion followed by intramolecular migration of the *p*-toluenesulfonyl group from nitrogen to oxygen. This step involves a transition state which is geometrically comparable to a bicyclo[2.2.1]heptane and suggests that a minimum of strain energy would be required for the migration. Once the *p*-toluenesulfonyl group has migrated, the resulting species eliminates a tosylate anion and is followed by subsequent tautomerization to the stable pyrazole. Treatment of II with hot alcoholic base resulted in a 20% conversion to IV only after refluxing for 24 hr. Presumably the alkoxide anion of II in a protic solvent is well solvated, and achieving the 2.2.1-bicyclic transition state becomes increasingly difficult.

Experimental

Attempted Preparation of the Tosylhydrazone of *trans*-Chalcone Oxide.—A mixture of *trans*-chalcone oxide (4.47 mmoles) and tosylhydrazide (4.50 mmoles) in 15 ml. of acidic ethanol (1% H_2SO_4–95% ethanol) was refluxed in a nitrogen atmosphere for 30 min. On cooling, the product crystallized in small white plates, m.p. 225–226°, 0.89 g., 47%.

Anal. Calcd. for $C_{22}H_{20}N_2O_3S$: C, 67.32; H, 5.14; N, 7.14; S, 8.17. Found: C, 67.15; H, 4.94; N, 7.26; S, 8.40.

The infrared spectrum of the 4-hydroxypyrazoline (II) has bands at 3.00, 6.27, 7.41, and 8.60 μ.

To 1.0 g. of benzalacetophenone tosylhydrazide dissolved in 10 ml. of methanol was added 1.20 ml. of 2 *N* NaOH and 1.60 ml. of 30% hydrogen peroxide. The mixture was allowed to stand at room temperature for 12 hr. It was then diluted with an equal volume of water, saturated with sodium chloride, and thoroughly extracted with ether. The ethereal extracts were washed over sodium thiosulfate solution and were dried over sodium sulfate. Evaporation of the solvent left 0.42 g. (40%) of a colorless solid, m.p. 225–226°. The infrared spectrum of this solid was identical in every detail with the solid described above.

Preparation of 1-*p*-Toluenesulfonyl-3,5-diphenylpyrazole (III).—A solution of 1.0 g. of 4-hydroxypyrazoline (II) and 3 ml. of pyridine in 50 ml. of benzene was cooled to 0° and 2.0 g. of thionyl chloride in 25 ml. was added dropwise over 10 min. The solution was stirred for an additional 30 min. during which time the temperature was allowed to rise to 20°. The mixture was then heated under reflux for 1 hr. and then filtered to remove the pyridine hydrochloride. The solution was washed twice with water and dried over sodium sulfate. Evaporation of the solvent left 0.89 g. of a pale yellow oil. This material was taken up in hexane–benzene and a crystalline solid soon precipitated. The solid amounted to 0.78 g. (74%), m.p. 108–114°, and was recrystallized from hexane–benzene to give a solid of m.p. 118–119°.

Anal. Calcd. for $C_{22}H_{18}N_2O_2S$: C, 70.58; H, 4.85. Found: C, 70.76; H, 4.72.

The infrared spectrum is characterized by bands at 7.30, 8.41, and 8.5 μ. The n.m.r. spectrum ($CDCl_3$) shows a multiplet centered at τ 2.59, a singlet at 3.41 and a singlet at 7.68. The peak areas are in the ratio of 14:1:3. The infrared spectrum of the solid was superimposable on that of an authentic sample of 1-*p*-toluenesulfonyl-3,5-diphenylpyrazole (prepared by heating equimolar quantities of 3,5-diphenylpyrazole and *p*-toluenesulfonyl chloride in pyridine for 4 hr. on a steam bath). This material can be readily reduced with lithium aluminum hydride to give 3,5-diphenylpyrazole and *p*-toluenesulfonic acid.

Lithium Aluminum Hydride Reduction of the 4-Hydroxypyrazoline Derivative.—To 75 mg. of fresh lithium aluminum hydride in 10 ml. of ether, stirred magnetically, was added a solution of 500 mg. of 4- ydroxypyrazoline in 10 ml. of ether. There was slight warming on addition. The mixture was stirred for 1 hr. at room temperature and was then hydrolyzed with saturated ammonium chloride. The aqueous layer was extracted with ether and the organic extracts were dried over sodium sulfate. Evaporation of the solvent left a colorless solid, m.p. 183–190°, 0.82 g. Successive recrystallizations from methanol gave white needles, m.p. 201–202°.

Anal. Calcd. for $C_{15}H_{12}N_2$: C, 81.79; H, 5.49; N, 12.72. Found: C, 81.87; H, 5.64; N, 12.48.

The infrared spectrum of this material was identical in every detail with an authentic sample of 3,5-diphenylpyrazole.[6]

Reaction of 1-*p*-Toluenesulfonyl-3,5-diphenyl-4-hydroxypyrazoline with Sodium Hydride.—In 5 ml. of tetrahydrofuran was dissolved 100 mg. of the 4-hydroxypyrazoline (II). To the mixture was added 15 mg. of sodium hydride. The solution was heated under reflux for 10 min. and was then poured onto ice. The mixture was extracted with ether and the extracts were dried over sodium sulfate. Evaporation of the ether afforded 70 mg. of 3,5-diphenylpyrazole.

Treatment of 1-*p*-toluenesulfonyl-3,5-diphenylpyrazole (III) under identical conditions with those described above gave, as the only isolated product, 95% yield of recovered starting material.

Acknowledgment.—The author wishes to acknowledge the excellent technical assistance of Miss Linda Norling. This investigation was supported in part by The Petroleum Research Fund, administered by the American Society, through a Type G grant.

(5) T. L. Jacobs, "Heterocyclic Compounds," Vol. 5, R. C. Elderfield, Ed., John Wiley and Sons, New York, N. Y., 1957, p. 68.

(6) An authentic sample of 3,5-diphenylpyrazole was prepared by the procedure of A. Dornow and W. Bartsch, *Ann.*, **602**, 23 (1957).