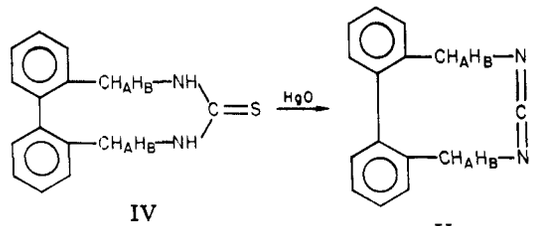
Scheme II



IV V

(s, 3 H), 3.20 (m, 2 H), 5.70 (m, 1 H), and 7.63 (m, 4 H).

**Preparation of 1,3-Diazacyclonona-1,2-diene (I).** In scrupulously dried equipment under nitrogen, III (5.00 g, 0.0169 mol), potassium *tert*-butoxide (MSA Research, 2.37 g, 0.0211 mol), and freshly distilled (from $P_2O_5$) methylene chloride (225 mL) were refluxed for 1 h. After the mixture was filtered, solvent was removed, and the resulting yellow liquid was distilled. I (1.54 g, 73.3%) was obtained [bp 48 °C (0.85 mm)]: IR (neat) 3000–2850, 2100 (s) $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.30 (m, 4 H), 1.80 (s, 8 H). Anal. Calcd for $C_7H_{12}N_2$: C, 67.70; H, 9.74. Found: C, 67.55; H, 9.55.

**Low-Temperature NMR Experiments and $\Delta G^{\ddagger}$ Calculations.** The low-temperature NMR experiments were carried out on a JEOL PS-100 (most of the experiments) and a Varian FX-100 (a few experiments). The solvent used was $CF_2Cl_2$, and the temperature ranged between ambient temperature and −160 °C. The probe temperature was calibrated by placing a thermocouple in a tube of $CF_2Cl_2$ (without spinning). Frequent thermocouple measurements were made; we feel our temperatures are accurate to ±2 °C.

Free energy of activation ($\Delta G^{\ddagger}$) calculations were made by using $\Delta G^{\ddagger} = -RT_c \ln (k_c h/kT_c)$, where $R$, $h$, and $k$ are the gas, Planck's, and Boltzmann's constants, respectively, and $k_c$ is the rate constant at the coalescence temperature, $T_c$. Values for $k_c$ were obtained either from (1) visual comparison of the simulated[10] and experimental spectra or (2) $k_c = (\pi/2^{1/2})(\Delta\nu^2 + 6J^2)^{1/2}$, where $\Delta\nu$ is the separation of $H_A$ and $H_B$ at the slow-exchange limit, and $J$ is $J_{AB}$. Because the slow-exchange spectra are not as definitive as we would like, we can only estimate $\Delta\nu$ and $J$. This is a common problem,[4] and we have dealt with it by calculating $\Delta G^{\ddagger}$ for the ranges of $\Delta\nu$ and $J$ which are possible. These are 55–60 Hz for $\Delta\nu$ and 12–15 Hz for $J$. All $\Delta G^{\ddagger}$ values calculated are between 6.6 and 6.8 kcal/mol. Uncertainties in our temperature measurements have also been considered; a ±2 °C range leads to only minor effects. We feel confident that a $\Delta G^{\ddagger}$ of 6.7 ± 2 kcal/mol is quite reasonable.

**Acknowledgment.** We thank Professor S. S. Eaton for simulating the spectra and for helpful discussions, M. Ashley for running most of the low-temperature spectra, the Regional NMR Center for running some low-temperature spectra, and the Research Corp. for partial support of this work.

**Registry No.** I, 6248-74-4; II, 1889-06-1; III, 72796-10-2; 2-azacyclooctanone, 673-66-5; hydroxylamine hydrochloride, 5470-11-1.

## Novel Rearrangement of a Diaziridine

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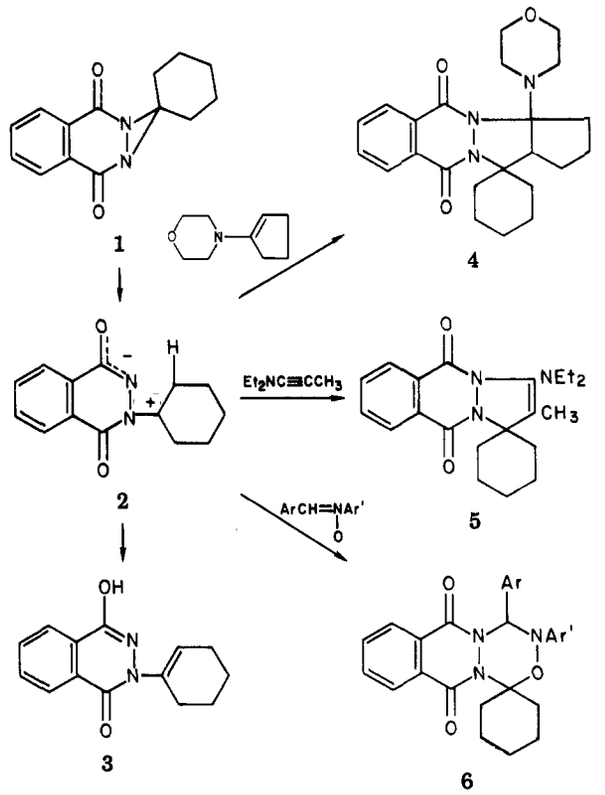
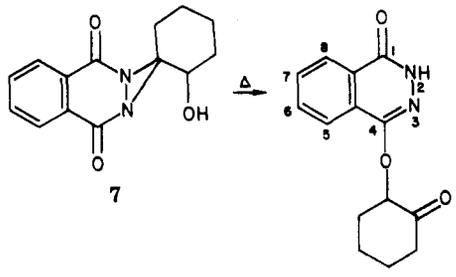
Recent work in these laboratories established that 1,1-dialkyl-1*H*-diazirino[1,2-*b*]phthalazine-3,8-diones isomerize in refluxing toluene into 2-(1-alken-1-yl)-4-hydroxy-1-

Scheme I



(2*H*)-phthalazinones. For example, **1** in refluxing toluene formed **3**. Presumably an azomethine imine, **2**, was initially formed which subsequently stabilized itself by loss of a proton (Scheme I). It was possible to intercept **2** by heating **1** with enamines,[1] ynamines,[1] and nitrones[2] to yield compounds **4**–**6**, respectively (Scheme I). We now report that a derivative of **1**, namely, **7**, in refluxing toluene or in $Me_2SO$ containing potassium *tert*-butoxide undergoes an unusual isomerization.

Heating of **7** in anhydrous toluene for 2 h caused gradual precipitation of compound **8** (55%). The same product



was obtained in 85% yield when **7** was treated with potassium *tert*-butoxide in $Me_2SO$ at ambient temperature. The constitution of **8** was established by $^{13}C$ NMR and $^1H$ NMR spectroscopy, chemical degradation, mass spectroscopy, and elemental analysis. That **8** was a 4-alkoxy-1(2*H*)-phthalazinone was indicated by its acid and alkaline hydrolysis. In hot hydrochloric acid **8** formed 4-hydroxy-1(2*H*)-phthalazinone (**9**) in 95% yield. Compound **8** in hot aqueous 10% sodium hydroxide followed by acidification of the reaction mixture gave **9** (95%) and 2-hydroxycyclohexanone (35%, isolated as the 2-4-dinitrophenylhydrazone). The alkaline hydrolysis probably occurred through the intermediacy of **10** (Scheme II). The

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(2) H. W. Heine and L. Heitz, *J. Org. Chem.*, **39**, 3192 (1974).

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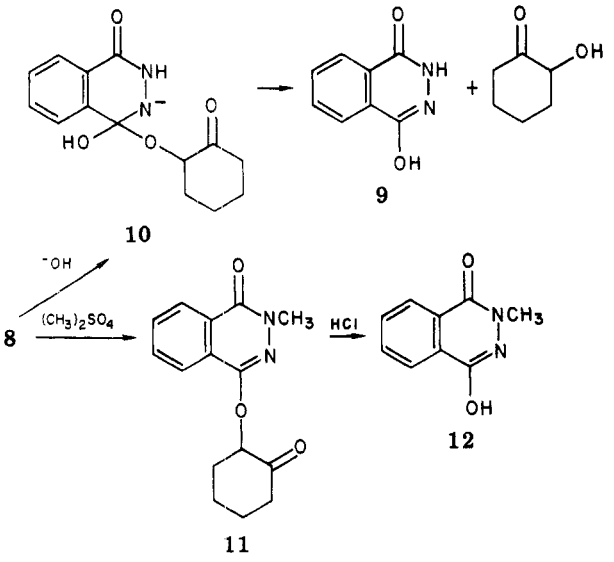
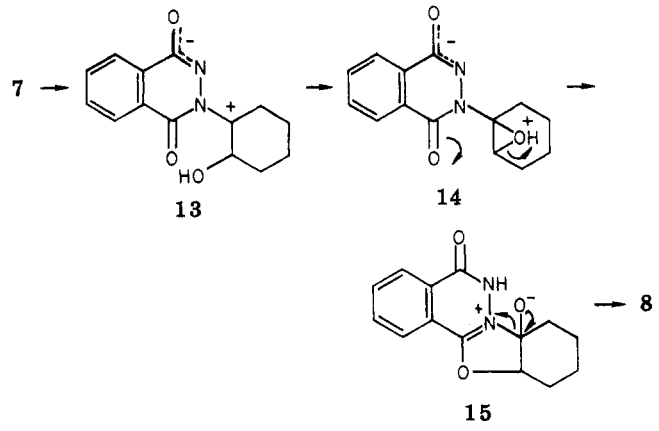
Scheme II



Scheme III



presence of the O=C—NH moiety in 8 was proved by N-methylation with dimethyl sulfate. Acid hydrolysis of the methylated product 11 leads to the known 2-methyl-4-hydroxy-1(2*H*)-phthalazinone (12, Scheme II). The N-methylation of 4-methoxy-1(2*H*)-phthalazinone with dimethyl sulfate has been described.[3]

The $^{13}C$ NMR spectrum of the isomerized product suggested structure 8. A resonance observed at 205.5 ppm is consistent with a ketone carbonyl. An absorption peak at 78.1 ppm is indicative of a methine carbon with a direct bonding C–H coupling of 149 Hz which is most likely of a type –OCH< and not –NCH<. Two resonances at 158.8 and 148.6 ppm which were assigned to the amido carbonyl and imino functions, respectively, exhibited long-range spin coupling to a $D_2O$-exchangeable hydrogen; in the latter case the splitting was fairly large (~8 Hz). This value is appropriate to a planar three-bond pathway as is present in 8 between $C_1$ and the NH.

Features in the proton NMR supportive of structure 8 were a multiplet at $\delta$ 5.46 (OCH), a broad singlet at $\delta$ 11.8 (NH), and the fact that just one of the four aromatic hydrogens exhibited a uniquely low-field shift relative to the others as expected for the 8-position of 8 due to magnetic effects of the proximate 1-carbonyl function.

A rationalization for the isomerization of 7 to 8 involves the initial formation of the azomethine imide 13. Interaction of the alcohol group with the positive center of 13 generates the protonated epoxide 14. Nucleophilic ring opening by the amido oxygen yields 15, the immediate precursor to 8 (Scheme III).

## Experimental Section

**Preparation of 2-Hydroxyspiro[cyclohexane-1,1′-[1*H*]-diazirino[1,2-*b*]phthalazine]-3′,8′-dione (7).** A suspension of 1.92 g (15 mmol) of 3,3-(α-hydroxypentamethylene)diaziridine[4] in 250 mL of dry $Et_2O$ containing 3.03 g (30 mmol) of $Et_3N$ was cooled to 5–10 °C. To the suspension was added dropwise a solution of 3.04 g (15 mmol) of *o*-phthaloyl chloride in 100 mL of dry $Et_2O$. The reaction mixture was stirred for 5 h, the $Et_3N$·HCl was filtered, and the solvent was evaporated to give 7. Some 7 was occluded in the precipitate of $Et_3N$·HCl and was reclaimed by dissolving the $Et_3N$·HCl in water and filtering. The total yield of crude 7 was 3.68 g (95%), mp 129–133 °C. Recrystallization from ethyl acetate gave 2.85 g of pure 7, mp 136–138 °C. Anal. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.11; H, 5.46; N, 10.85. Found: C, 64.84; H, 5.06; N, 11.01.

**Thermal Isomerization of 7 to 4-[(2-Oxocyclohexyl)-oxy]-1(2*H*)-phthalazinone (8).** A mixture of 0.80 g (3.1 mmol) of 7 and 40 mL of anhydrous toluene was refluxed for 2 h. The crude 8 (440 mg, 55%, mp 233–238 °C) that had precipitated was filtered. Recrystallization from commercial absolute ethanol gave 8: mp 236–238 °C; molecular ion at *m/e* 258. Anal. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.11; H, 5.46; N, 10.85. Found: C, 65.06; H, 5.67; N, 10.95.

**Base-Catalyzed Isomerization of 7 to 8.** To a solution of 304 mg (2.71 mg) of potassium *tert*-butoxide in 3.50 g of $Me_2SO$ was added 700 mg (2.71 mmol) of 7. The reaction mixture immediately turned yellow and was stirred overnight. Approximately 4 mL of $H_2O$ was added to the mixture followed by the addition of 5% HCl until the mixture was acid to litmus. The crude 8 (597 mg, 85%, mp 224–277 °C) was filtered. Recrystallization from commercial ethanol gave 8, mp 235–238 °C.

**Basic Hydrolysis of 8 to 9 and 2-Hydroxycyclohexanone.** A mixture of 8 (500 mg, 1.93 mmol) and 20 mL of 20% aqueous sodium hydroxide was refluxed for 0.5 h. Addition of 5% hydrochloric acid precipitated 300 mg (95%) of 9. A solution of 2,4-dinitrophenylhydrazine was added to the acid filtrate and the 205 mg (35%) of the corresponding hydrazone (19) filtered. The infrared spectra of 19 obtained by the above method and from an authentic sample of 2-hydroxycyclohexanone were identical. The melting point of 19 after recrystallization from 95% EtOH was 185–188 °C. Anal. Calcd for $C_{12}H_{14}N_4O_5$: C, 48.96; H, 4.72; N, 19.03. Found: C, 49.32; H, 4.77; N, 19.21.

**Acid Hydrolysis of 8.** A mixture of 8 (500 mg, 1.93 mmol) and 10 mL of concentrated hydrochloric acid was refluxed for 1.5 h. The cooled reaction mixture was filtered to give 300 mg (95%) of 9, mp 340 °C.

**Preparation of 2-Methyl-4-[(2-oxocyclohexyl)oxy]-1-(2*H*)-phthalazinone (11).** A mixture of 400 mg (1.54 mmol) of 8, 5 mL of methanol, 700 mg (5.5 mmol) of $(CH_3)_2SO_4$, and 2 mL of 20% aqueous KOH was refluxed for 1 h. The mixture was concentrated by evaporation of the solvents under reduced pressure and the residue neutralized with 5% HCl. The crude 11 (300 mg, 71%) was filtered. Recrystallization from 90% aqueous EtOH gave 11: mp 184–184.5 °C; molecular ion at *m/e* 272. Anal. Calcd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.28. Found: C, 66.25; H, 6.06; N, 10.39.

**Hydrolysis of 11 to 2-Methyl-4-hydroxy-1(2*H*)-phthalazinone (12).** A mixture of 500 mg (1.83 mmol) of 11 and 10 mL of concentrated hydrochloric acid was refluxed for 1 h. The reaction mixture was filtered to give 300 mg (98%) of the known 12, mp 238–240 °C (lit.[5] mp 238 °C). The infrared spectra of 12 prepared from the hydrolysis of 11 and from the reaction of methylhydrazine and phthalic anhydride were identical.

**Acknowledgment.** Acknowledgment is made to the Camille and Henry Dreyfus Foundation for support of this research and to Dr. William VandenHeuvel of Merck Sharp & Dohme Research Laboratories for the mass

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spectra of several compounds. We thank Mr. Steve M. Bonser who first prepared compound 7 and treated it with potassium *tert*-butoxide.

**Registry No.** 7, 72866-28-5; 8, 72881-42-6; 9, 1445-69-8; 11, 72866-29-6; 12, 18393-54-9; 19, 24847-86-7; 3,3-(α-hydroxypentamethylene)diaziridine, 4469-71-0; *o*-phthaloyl chloride, 88-95-9; 2-hydroxycyclohexanone, 533-60-8.

## Mechanisms of Elimination Reactions. 31. Stereochemistry of Elimination Reactions of 3-Phenyl-2-butyl Tosylates[1]

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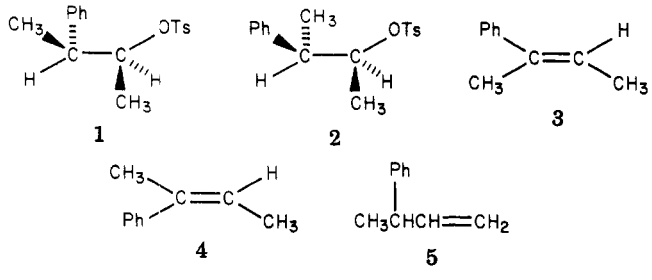
An often-quoted piece of evidence for the anti rule in E2 reactions is the report of Cram[3] that *erythro*-3-phenyl-2-butyl tosylate (1) gives only *cis*-2-phenyl-2-butene (3) and *threo*-3-phenyl-2-butyl tosylate (2) gives only *trans*-2-phenyl-2-butene (4) on treatment with sodium



ethoxide in ethanol, in both cases the products of exclusive anti elimination. The presence of some 3-phenyl-1-butene (5) was deduced from the fact that chiral substrate gave a crude product mixture retaining some optical activity, but none of this olefin was isolated. More recent studies have revealed significant extents of syn elimination in E2 reactions of secondary alkyl tosylates.[4-7]

Because of these results, and because sensitive methods of analysis for minor products were not available at the time of the original work, we felt it advisable to reinvestigate this reaction by using GLC to analyze the product mixtures. The results are given in Table I. There is clearly no detectable syn elimination with 1, either under Cram's[3] conditions or with the stronger base sodium *tert*-butoxide. While small percentages of the product (3) of syn elimination from 2 are found with both base/solvent pairs, the same product is shown to result from isomerization of 5 (previously observed by Cram and Uyeda with *tert*-butoxide[8]). Closer examination of the figures strongly suggests that 3 does result from isomerization rather than

Table I. Product Proportions from E2 Reactions of the Diastereomeric 3-Phenyl-2-butyl Tosylates[a]

| | | % yield | | |
|---|---|---|---|---|
| reactant | base/solvent | 3 | 4 | 5 |
| 1 | EtONa/EtOH[b] | 90.9 | 0 | 9.1 |
| 2 | | 2.7 | 84.1 | 13.2 |
| 5[d] | | 18.1 | 0 | 81.9 |
| 1 | *t*-BuONa/*t*-BuOH[c] | 56.4 | 0 | 43.6 |
| 2 | | 7.4 | 36.3 | 56.3 |
| 5[d] | | 14.5 | 0 | 85.5 |

[a] Substrate 0.06–0.08 M, base 0.4–0.5 M. [b] Conditions: 4 h at 110 °C and then overnight at 80 °C. [c] Conditions: 5 h at 80 °C. [d] Isomerization of pure 5; 3 and 4 were stable under the reaction conditions.

syn elimination. With sodium ethoxide, the ratio of 3 to 5 is 0.22 in the isomerization and 0.20 in the elimination. The corresponding figures with sodium *tert*-butoxide are 0.17 and 0.13, respectively. The similarity of the ratios strongly suggests that the 3 obtained in the eliminations from 2 arises predominantly or exclusively from isomerization. The upper limit for syn elimination from 2 thus seems to be a few percent and that for syn elimination from 1 much less than 1%.

There are several possible reasons why syn elimination is so unimportant in this system. It is known that simple secondary alkyl tosylates give cis olefin almost entirely by anti elimination, even when there is substantial syn elimination in the formation of the corresponding trans olefins,[7] the difference presumably being due to greater eclipsing interactions in the transition state for syn than for anti elimination. The transition states for syn elimination from 1 and 2 must have methyl–phenyl and methyl–methyl eclipsing, respectively, and are thus sterically analogous to the transition states for the formation of the cis isomers of simple straight-chain alkenes.

It is also possible that the β-phenyl group is less activating toward syn than anti elimination. The trans olefin from the reaction of stereospecifically deuterated 2-chloro-1-phenylpropane-*1-d* with alkoxides in the corresponding alcohols is formed exclusively or nearly exclusively by anti elimination,[9] a case where eclipsing interactions cannot significantly hinder syn elimination. In addition, anti elimination from *cis*-2-phenylcyclopentyl tosylate is 9 times as fast as syn elimination from *trans*-2-phenylcyclopentyl tosylate with potassium *tert*-butoxide in *tert*-butyl alcohol as base.[10] On the other hand, this rate effect could simply reflect steric differences between the reactants, and the Hammett ρ is actually larger for syn than for anti elimination.[10] Thus the experimental evidence is ambiguous on the possibility of an adverse electronic effect of a β-phenyl group on syn elimination.

### Experimental Section

***erythro*- and *threo*-3-Phenyl-2-butyl *p*-Toluenesulfonates.** 3-Phenyl-2-butanol was prepared and separated into the pure racemic diastereomers, and the *p*-toluenesulfonates of the diastereomers were prepared by the method of Cram.[11]

**3-Phenyl-1-butene** was obtained by the method of Cram.[12] It was purified by preparative GLC on an 8 ft × 0.25 in. column of 15% Carbowax 1540 on Chromosorb W (60/80 mesh).

***cis*- and *trans*-2-Phenyl-2-butenes.** The dehydration of methylethylphenylcarbinol by refluxing for 10 h with 4 N sulfuric

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