SCHEME IV

$$Mn(II) + S \rightleftharpoons Mn(II)\text{-}S \quad (17)$$

$$Cr(VI) + 3Mn(II)\text{-}S \rightleftharpoons Cr(III) + 3Mn(III)\text{-}S \quad (18)$$

$$Mn(III)\text{-}S \xrightarrow{k} Mn(II) + P \quad (19)$$

However, in our study chromium(III) definitely did not exhibit any influence on the reaction rate. Therefore, any mechanism which would require an equilibrium involving chromium(III) to be established prior to the rate-limiting step of the oxidation has to be rejected, and we therefore cannot apply the mechanism proposed by Kemp and Waters to rationalize our results. Further, while the formation of a complex between manganese and an α-hydroxy acid was an entirely plausible assumption, it would be much less justified to propose the formation of an intermediate complex in the case of the oxidation of cyclobutanol.

Registry No.—Vanadium, 7440-62-2; manganese, 7439-96-5; cyclobutanol, 2919-23-5; 1-deuteriocyclobutanol, 22696-02-2; 1-methylcyclobutanol, 20117-47-9.

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The Synthesis of Substituted Hydroazulenes

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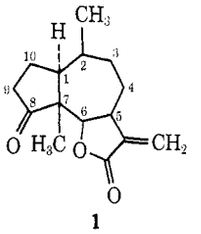
The conversion of 1(9)-octalin-2-one derivatives to isomeric 9-octalin-2-one derivatives by way of ketal formation and subsequent acid hydrolysis has been examined. Construction of substituted diketo hydroazulenes from these 9-octalin-2-one derivatives has been studied, and the chemistry of the resulting compounds investigated.

A large variety of techniques are currently available for the stereoselective construction of substituted decalins and hydrindanes. In addition, conformational analysis is useful in predicting the relative stability of isomers in such systems.[1] Unfortunately, a similar body of information is not available for the stereoselective construction of substituted hydroazulenes, and the application of conformational analysis to substituted seven-membered rings is relatively difficult.[2] Recently, a large and relatively important group of sesquiterpenes, the pseudoguaianolides, has been shown to possess the hydroazulene ring system.[3] Damsin (**1**) is a typical representative of this family of



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compounds.[4] As a result of our interest in these sesquiterpenes, this work was initiated to develop stereoselective methods for the preparation of substituted and functionalized hydroazulenes, with particular reference to the substitution patterns typical of the pseudoguaianolides.

In order to provide a method for direct introduction of oxygen functionality at C-6 and C-8 of the hydroazulene ring system, we have examined the transannular condensation of two unstable 1,3,6-cyclodecatriones **5a** and **5b**, which are conveniently prepared by ozonolysis of the corresponding β,γ-unsaturated ketones **4a** and **4b**[5] (Scheme I).

The methods available in the literature for construction of β,γ-unsaturated ketones, such as **4**, are essentially twofold: kinetic protonation of the enolate anion derived from the corresponding α,β-unsaturated ketone[6] and Birch reduction of a suitably substituted 6-methoxytetralin followed by careful hydrolysis.[7] Unfortunately, these methods require vigorous and strongly basic reaction conditions, which are not compatible with a variety of functional groups. It is well known, however, that conversion of an α,β-unsaturated ketone to a ketal affords a product in which the double bond has moved to a β,γ position.[8] We, therefore, chose to examine the possibility of careful hydrolysis of such a ketal to the corresponding β,γ-unsaturated ketone.

Treatment of octalone **2a** with ethylene glycol in the presence of *p*-toluenesulfonic acid afforded ketal **3a** as the only product. Careful hydrolysis of **3a** with oxalic acid in aqueous methanol then afforded an 81% yield of **4a**. Ozonolysis of **4a** followed by a reductive work-up would be anticipated to yield triketone **5a**. This compound proved to be extremely reactive, however, and could not be isolated. Hydroazulene **6a** was obtained instead, presumably by way of spon-

(1) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, N. Y., 1962.

(2) (a) N. L. Allinger, *J. Amer. Chem. Soc.*, **81**, 5727 (1959); (b) R. Pauncz and D. Ginsburg, *Tetrahedron*, **9**, 40 (1960); (c) J. B. Hendrickson, *J. Amer. Chem. Soc.*, **83**, 4537 (1961); (d) J. B. Hendrickson, *Tetrahedron*, **19**, 1387 (1963); (e) J. B. Jones, J. M. Zander, and P. Price, *J. Amer. Chem. Soc.*, **89**, 94 (1967).

(3) J. Romo and A. R. de Vivar, *Progr. Chem. Org. Natur. Prod.*, **25**, 90 (1967).

(4) (a) L. Bernardi and G. Büchi, *Experientia*, **13**, 466 (1957); (b) W. Herz, H. Watanabe, M. Miyazaki, and Y. Kishida, *J. Amer. Chem. Soc.*, **84**, 2601 (1962); (c) M. Suchy, V. Herout, and F. Šorm, *Collect. Czech. Chem. Commun.*, **28**, 2257 (1963).

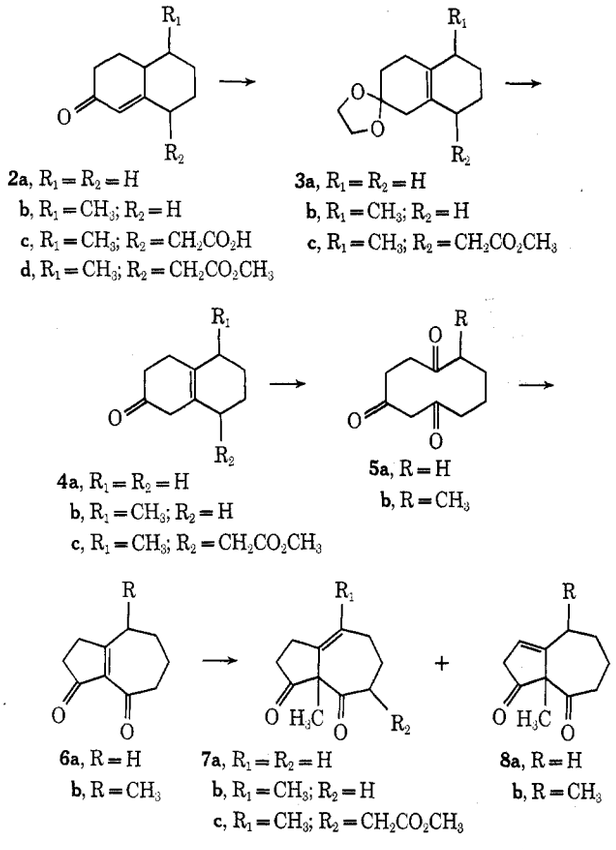
(5) *Cf.* L. Velluz, G. Muller, J. Mathieu, and A. Poittevin, *C. R. Acad. Sci.*, **252**, 4084 (1961).

(6) (a) H. J. Ringold and S. K. Malhotra, *Tetrahedron Lett.*, 669 (1962); (b) J. A. Marshall and S. F. Brady, *ibid.*, 1387 (1969); (c) J. Meinwald and L. Hendry, *J. Org. Chem.*, **36**, 1446 (1971).

(7) *Cf.* A. J. Birch, *J. Chem. Soc.*, 593 (1946).

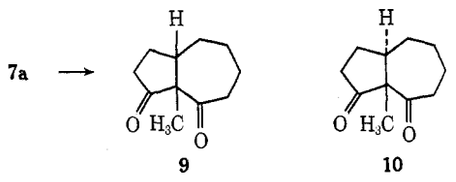
(8) (a) J. A. Zderic, D. C. Limon, H. J. Ringold, and C. Djerassi, *J. Amer. Chem. Soc.*, **81**, 3120 (1959); (b) C. Djerassi and M. Gorman, *ibid.*, **75**, 3704 (1953).

SCHEME I

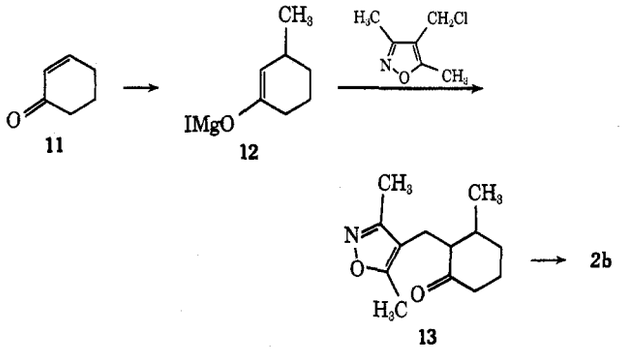


taneous transannular bond formation followed by loss of water. Subsequent alkylation of **6a** with methyl iodide and potassium carbonate then afforded a 68:32 mixture of **7a** and **8a**, from which pure **7a** could be obtained by fractional crystallization.

Catalytic hydrogenation of an intermediate such as **7** offers a potential method for control of the relative stereochemistry at C-1 and C-2 of the hydroazulene ring, if hydrogen is delivered in a cis fashion from the catalyst surface. Since all of the known pseudoguaianolides appear to possess a trans ring junction at C-1 and C-7,[3] there is also an additional requirement that hydrogen be delivered from the side of the molecule opposite the C-7 methyl group. Unfortunately, hydrogenation of **7a** over platinum afforded the cis-fused compound **9** in 67% yield, while none of the trans-fused compound **10** could be isolated. It appears likely, however, that additional substituents on the ring system may be utilized to control the stereochemistry of this reaction.[4b]

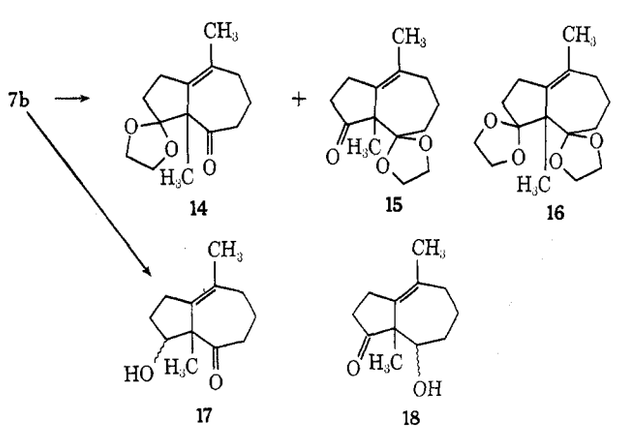


The introduction of a C-2 methyl group on the hydroazulene ring system was next examined. Cuprous chloride catalyzed conjugate addition of methylmagnesium iodide to 2-cyclohexenone (**11**) in ether solution was carried out to give magnesium enolate **12**. Enolate **12** was then alkylated[9] with 3,5-dimethyl-4-chloromethylisoxazole[10] in the presence of hexamethylphosphoramide to give stereospecifically keto isoxazole **13** in 41% overall yield. Hydrogenolysis of **13** followed by treatment with sodium methoxide and finally aqueous base[11] afforded 5-methyl-1(9)-octalin-2-one (**2b**), which contained 12% of the β,γ-unsaturated isomer **4b**.



Acid-catalyzed ketalization of this equilibrium mixture with ethylene glycol gave **3b** as the only product. Subsequent hydrolysis with oxalic acid in aqueous methanol yielded a 12:3:85 mixture of **2b**, **3b**, and **4b**, respectively, from which pure **4b** was obtained by column chromatography. Ozonolysis of **4b** also failed to produce a stable 1,3,6-cyclodecatrione. Spontaneous condensation of the presumed intermediate **5b** afforded the enolic diketo hydroazulene **6b** directly in 80% yield. Alkylation of **6b** with methyl iodide and potassium carbonate then afforded **7b** as the only isolable product. In contrast with **6a**, the C-2 methyl group of **6b** apparently provides enough additional stabilization of the intermediate enolate anion so that **7b** is obtained to the complete exclusion of **8b**.

Since C-5 of **7b** is activated by a carbonyl group, in principle an additional substituent could be introduced at this position by alkylation. This, however, requires a method for differentiation between the two carbonyl groups. This was accomplished by monoketalization of **7b** with ethylene glycol to give a 4:6



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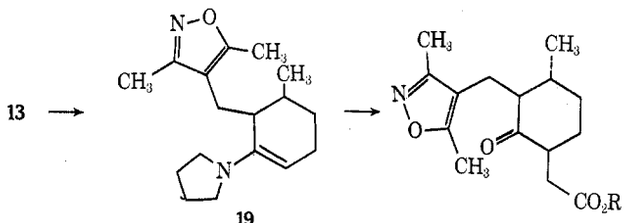
(10) (a) N. K. Kochetkov, E. D. Khomutova, and M. V. Bazilevskii, *J. Gen. Chem. USSR*, **28**, 2762 (1958); (b) J. E. McMurry, Ph.D. Thesis, Columbia University, New York, N. Y., 1967.

(11) *Cf.* (a) G. Stork, S. Danishefsky, and M. Ohashi, *J. Amer. Chem. Soc.*, **89**, 5459 (1967); (b) G. Stork and J. E. McMurry, *ibid.*, **89**, 5463 (1967); (c) *ibid.*, **89**, 5464 (1967).

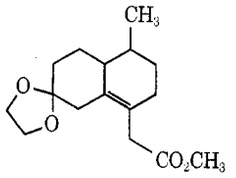
mixture of **14** and **15**, respectively, which was separated by column chromatography. Although monoketal formation was very facile, diketal **16** was not observed as a product. Relief of the unfavorable interaction between the dipoles of the carbonyl groups of **7b**, whose orientation is fixed by the hydroazulene ring system, may be responsible. In addition, hydrogenation of **7b** over platinum resulted in reduction of the C-8 carbonyl group to give **17** in 36% yield. None of the isomeric product **18** could be isolated.

In an effort to introduce substitution at C-5 of the hydroazulene ring system, without resorting to alkylation of an intermediate such as **14**, an attempt was made to construct **4c**. Reaction of pyrrolidine with **13** afforded the corresponding enamine **19**, which was



19 **20a**, R = C_2H_5; **b**, R = H

treated with ethyl bromoacetate to give **20a**. Saponification then gave the crystalline acid **20b**, which presumably possesses the more stable all-equitorial configuration. Utilization of the isoxazole annelation procedure[11] permitted conversion of **20b** to **2c**, and subsequent Fischer esterification with methanol afforded **2d**. Ketalization of **2d** with ethylene glycol proceeded smoothly to give a product which contained no vinyl protons in the nmr. Therefore, this represents either **3c**, **21**, or a mixture of the two. Careful hydrolysis of this product with oxalic acid afforded a 58% recovery of α,β-unsaturated ketone **2d**. In addition, an inseparable 23:77 mixture of ketal and β,γ-unsaturated ketone was also obtained. On the assumption that the unconjugated ketone thus obtained possessed structure **4c**, the ketone–ketal mixture was ozonized, and the crude product was treated with methyl iodide and potassium carbonate. The anticipated product, **7c**, would be expected to show infrared absorption near 1745 cm^{-1} for the carbonyl group contained in a five-membered ring. This was not observed in the crude product. The implication appears to be that the β,γ-unsaturated ketone obtained in this series of reactions was **22** and not the desired **4c**.[12]



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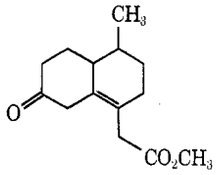

22

(12) The preparation of β,γ-unsaturated ketone **4c** has been accomplished by an alternate route. A manuscript describing its synthesis and conversion to substituted hydroazulenes is in preparation.

Experimental Section[13]

2,2-Ethylenedioxy-9-octalin (3a).—To a solution of 9.595 g (63.9 mmol) of enone **2a**[14] and 0.1022 g (0.54 mmol) of *p*-toluenesulfonic acid monohydrate in 75 ml of benzene was added 25 ml of ethylene glycol. The resulting mixture was heated at reflux in a nitrogen atmosphere under a Dean-Stark water separator for 25 hr. After cooling, the mixture was diluted with 150 ml of benzene and washed once with 50 ml of saturated $NaHCO_3$ solution and three times with 50-ml portions of water, then dried. Concentration *in vacuo* followed by distillation afforded 11.317 g (91%) of pure ketal **3a** as a colorless liquid: bp 75.5–80.0° (0.10–0.20 mm); nmr (CCl_4) δ 3.84 (4 H, s, OCH_2CH_2O).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 75.76; H, 7.42. Found: C, 75.58; H, 7.53.

9-Octalin-2-one (4a).—To a solution of 1.000 g (5.15 mmol) of ketal **3a** in 50 ml of methanol was added a solution of 0.852 g (9.46 mmol) of oxalic acid in 30 ml of water, and the resulting mixture was allowed to stir at room temperature for 4 hr. The mixture was then diluted with 200 ml of half-saturated NaCl solution and extracted with 200 ml of ether. The ether extract was washed twice with 50-ml portions of water, once with 25 ml of saturated $NaHCO_3$ solution, once with 50 ml of water, and once with 25 ml of saturated NaCl, and dried. Concentration *in vacuo* afforded 0.748 g of oil, which was put on a 20-g column of silica gel. Elution with 400 ml of benzene afforded 0.627 g (81%) of **4a**, which was identified by spectroscopic comparison with an authentic sample.[7]

Bicyclo[5.3.0]dec-1(7)-ene-6,8-dione (6a).—A solution of 6.217 g of β,γ-unsaturated ketone **4a** in a mixture of 40 ml of dichloromethane and 40 ml of absolute methanol was cooled at Dry Ice–acetone bath temperature and treated with a stream of ozone in oxygen for 2.1 hr (until the blue coloration of excess ozone developed). After the solution was purged with nitrogen, 20 ml of trimethyl phosphite[15] was added and the mixture was allowed to stir at room temperature for 21.3 hr. Concentration *in vacuo* followed by distillation afforded 4.896 g (72%) of **6a** as a yellow liquid, bp 89.5–97.0° (0.4 mm). Redistillation afforded the analytical sample: bp 86–87° (0.6 mm); uv max (CH_3OH) 234 nm (ϵ 8380); ir (neat) 1720, 1668, and 1611 cm^{-1}.

Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 72.95; H, 7.23.

7-Methylbicyclo[5.3.0]dec-1-ene-6,8-dione (7a).—To a solution of 2.66 g (16.2 mmol) of **6a** in 100 ml of acetone was added 108 g (761 mmol) of methyl iodide and 2.38 g (17.2 mmol) of potassium carbonate. After reflux for 23 hr, the mixture was filtered and the filtrate was concentrated *in vacuo*. Chromatography of the residue on silica gel with 2:98 ether–benzene elution afforded 0.571 g (20%) of a mixture of **7a** and **8a**, which was obtained as a colorless liquid after short-path distillation (121° bath at 0.50 mm). Integration of nmr signals (CCl_4 solution) at δ 1.23, 1.30, and 2.96 indicated a 32:68 ratio of **8a** and **7a**.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.31; H, 7.77.

Crystallization of the isomer mixture from ether–hexane at −20° afforded 0.165 g of oily, white solid. Two recrystallizations yielded pure **7a** as colorless prisms: mp 49.5–50.0°; ir (KBr) 1739 (five-membered ring C=O), 1697 (seven-membered ring C=O), and 1672 cm^{-1} (C=C); nmr (CCl_4) δ 1.30 (3 H, s, CH_3) and 5.84 (1 H, t, J = 6 Hz, vinyl H).

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.02; H, 8.02.

***cis*-7-Methylbicyclo[5.3.0]decane-6,8-dione (9).**—To a solution of 0.0593 g of enedione **7a** in 6.0 ml of absolute ethanol was added 0.0216 g of 83% platinum oxide, and the mixture was stirred under a hydrogen atmosphere for 3 hr. Catalyst was then filtered off and washed with ethanol. Concentration *in vacuo*

(13) Melting points are uncorrected. Unless otherwise stated, magnesium sulfate was employed as a drying agent. Uv spectra were determined either on a Cary Model 11PM or a Beckman DB-G spectrophotometer. The infrared spectra were determined with a Beckman IR-8 infrared spectrophotometer. Nmr spectra were determined with a Varian A-60 spectrometer using tetramethylsilane as internal standard. The mass spectra were obtained with a Varian MAT CH7 mass spectrometer. Microanalyses were performed by M-H-W Laboratories, Garden City, Mich. Baker reagent silica gel, 60–200 mesh, was used as adsorbent for column chromatography.

(14) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

(15) W. S. Knowles and Q. E. Thompson, *J. Org. Chem.*, **25**, 1031 (1960).

of the combined filtrate and washings afforded 0.0598 g of colorless oil, which was chromatographed on 10.0 g of silica gel. Elution with 1:9 ether–benzene afforded 0.0399 g (67%) of **9**, identical with an authentic sample[16] by comparison infrared and nmr spectra and also by comparison thin layer chromatography (silica gel G, elution with 2:8 ethyl acetate–benzene).

3-Methyl-2-(3,5-dimethyl-4-isoxazolylmethyl)cyclohexanone (13).—A solution of methylmagnesium iodide was prepared under nitrogen by dropwise addition of a solution of 31.248 g (0.220 mol) of methyl iodide in 400 ml of anhydrous ether into a flask containing 5.596 g (0.230 g-atom) of magnesium turnings, over a period of 1.9 hr with mechanical stirring, and at ice-bath temperature. After addition was completed, stirring was continued at room temperature for 1 hr. The resulting mixture was cooled at ice-bath temperature, and 0.991 g (0.010 mol) of cuprous chloride was added. A solution of 19.228 g (0.200 mol) of 2-cyclohexenone in 400 ml of anhydrous ether was then added dropwise over a period of 3.25 hr with stirring. When addition was complete, a solution of 29.136 g (0.200 mol) of 3,5-dimethyl-4-chloromethylisoxazole[10] in 90 ml of hexamethylphosphoramide (distilled from CaH_2) was added rapidly at ice-bath temperature. After the mixture was stirred at ice bath temperature for 1 hr and at room temperature for an additional 13 hr, the mixture was decomposed with 400 ml of saturated NH_4Cl solution. The ether layer was separated, washed nine times with 200-ml portions of water and once with 200 ml of saturated brine, and dried. Concentration *in vacuo* followed by distillation through a 10-cm Vigreux column afforded 18.202 g (41%) of keto isoxazole **13** as a pale yellow oil: bp 128.0–133.0° (0.15–0.27 mm); ir (neat 1712 cm^{-1} (C=O). Redistillation afforded the analytical sample as a colorless, viscous liquid which partially crystallized after prolonged storage at 0°, bp 129.0–130.0° (0.25 mm).

Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.73; H, 8.71; N, 6.33.

5-Methyl-1(9)-octalin-2-one (2b).—A solution of 16.924 g (0.0765 mol) of keto isoxazole **13** in 200 ml of absolute ethanol was stirred with 23 g of W-4 Raney nickel[17] under a hydrogen atmosphere and at room temperature. After 5.6 hr, an additional 20 g of W-4 Raney nickel[17] was added and stirring at room temperature under hydrogen was continued for 19.4 hr (the reaction was monitored by following disappearance of the isoxazole uv band at 224 nm). Catalyst was filtered off and the nickel residues were washed well with absolute ethanol. Concentration *in vacuo* of the combined filtrate and washings afforded a yellow resin, which was dissolved in 250 ml of anhydrous methanol. After the solution was purged with nitrogen, 40.0 g (0.740 mol) of sodium methoxide was added, and the mixture was heated at reflux under nitrogen for 5 hr. The mixture was then diluted with 350 ml of water, and refluxing under nitrogen was continued for an additional 14.5 hr. After cooling, the mixture was diluted with 500 ml of water and extracted four times with 250-ml portions of ether. The combined ether extracts were washed once with 250 ml of water, three times with 100-ml portions of 3 *M* HCl, once with 250 ml of water, once with 100 ml of saturated $NaHCO_3$, once with 250 ml of water, and once with 100 ml of saturated NaCl, and dried. Concentration *in vacuo* followed by distillation through a 10-cm Vigreux column afforded 7.633 g (61%) of an equilibrium mixture of **2b** and **4b** as a colorless oil which partially crystallized on standing at 5°: bp 71.0–76.0° (0.12–0.15 mm); ir (neat) 1708 (C=O), 1669 (conjugated C=O), and 1619 cm^{-1} (C=C); nmr (CCl_4) δ 5.68 (1 H, s, CH=C). Integration of a small signal in the nmr at δ 2.61 indicated the presence of *ca.* 12% β,γ-unsaturated ketone **4b**. This material was characterized by conversion to the 2,4-dinitrophenylhydrazone, which crystallized from ethyl acetate–ethanol as small red needles, mp 188.0–189.0°.

Anal. Calcd for $C_{17}H_{20}N_4O_4$: C, 59.29; H, 5.85; N, 16.27. Found: C, 59.21; H, 6.08; N, 16.22.

5-Methyl-9-octalin-2-one (4b).—To a solution of 2.263 g (13.8 mmol) of enone **2b** and 0.100 g (0.53 mmol) of *p*-toluenesulfonic acid monohydrate in 75 ml of benzene was added 25 ml of ethylene glycol. The resulting mixture was heated at reflux in a nitrogen atmosphere under a Dean-Stark water separator for 20 hr. After cooling, the mixture was diluted with 200 ml of benzene, washed once with 50 ml of saturated $NaHCO_3$ and three times with 50-ml portions of water, and dried. Concentration *in vacuo* followed by distillation afforded 2.498 g (87%) of ketal **3b** as a colorless liquid: bp 77.0–79.0° (0.14 mm); nmr (CCl_4) δ 1.00 (3 H, d, J = 6.5 Hz, $CHCH_3$) and 3.88 (4 H, s, OCH_2CH_2O).

To a solution of 2.415 g (11.6 mmol) of ketal **3b** in 75 ml of absolute methanol was added a solution of 1.272 g of oxalic acid in 45 ml of water. After it was stirred at room temperature for 3.5 hr, the solution was diluted with 200 ml of half-saturated NaCl solution and extracted with 200 ml of ether. The ether extract was washed twice with 50-ml portions of water, once with 50 ml of saturated $NaHCO_3$, once with 50 ml of water, and once with 50 ml of saturated NaCl, and dried. Concentration *in vacuo* afforded 1.908 g of pale yellow oil. Integration of the nmr signals at δ 2.63, 3.86, and 5.68 indicated the presence of **2b**, **3b**, and **4b** in a ratio of 12:3:85. The crude product was put on a 40-g column of silica gel and eluted with 840 ml of benzene. Concentration *in vacuo* followed by distillation afforded 1.532 g (80%) of pure **4b** as a colorless oil: bp 59.5–64.5° (0.12 mm); ir (neat) 1720 cm^{-1} (C=O); nmr (CCl_4) δ 1.02 (3, H, d, J = 6.5 Hz, $CHCH_3$) and 2.63 (2 H, br, W_H = 5 Hz, $R_2C{=}CRCH_2CO$).

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.21; H, 9.85.

2-Methylbicyclo[5.3.0]dec-1(7)-ene-6,8-dione (6b).—A solution of 1.464 g (8.91 mmol) of β,γ-unsaturated ketone **4b** in a mixture of 10 ml of absolute methanol and 10 ml of methylene chloride was cooled at Dry Ice–acetone bath temperature and treated with a stream of ozone in oxygen for 52 min (until the solution became blue in color from the presence of excess ozone). After the solution was purged with nitrogen, 5.0 ml of trimethyl phosphite[15] was added and the mixture was allowed to stir at room temperature for 19 hr. Concentration *in vacuo* followed by short-path distillation (110° bath at 0.07 mm) afforded 1.268 g (80%) of **6b** as a yellow liquid which crystallized on standing at −12° overnight and gave a purple color with ferric chloride. Material from a similar preparation was redistilled to give the analytical sample: bp 107–108° (1.0 mm); uv max (CH_3OH) 233 nm (ϵ 13,300); ir (neat) 1715, 1637, and 1605 cm^{-1}; nmr (CCl_4) δ 1.68 (3 H, s, vinyl CH_3).

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.08; H, 7.94.

2,7-Dimethylbicyclo[5.3.0]dec-1-ene-6,8-dione (7b).—To a solution of 2.99 g (16.8 mmol) of **6b** in a mixture of 30 ml of acetone and 5.25 ml (84.3 mmol) of methyl iodide was added 2.68 g (19.4 mmol) of potassium carbonate (dried overnight at 140°). After reflux under nitrogen for 5 hr, the mixture was diluted with 40 ml of ether and filtered. Concentration *in vacuo* afforded 3.10 g of tan oil, which partially crystallized on standing at −12°. Chromatography on 60 g of silica gel afforded 2.81 g of solid on elution with benzene. Recrystallization from hexane yielded 1.68 g (52%) of **7b** as a white solid, mp 68.5–70.0°. Repeated recrystallization from hexane afforded the analytical sample: mp 70.0–71.0°; ir (KBr) 1744 (five-membered ring C=O) and 1696 cm^{-1} (seven-membered ring C=O); nmr (CCl_4) δ 1.25 (3 H, s, CH_3) and 1.85 (3 H, s, vinyl CH_3).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.18; H, 8.25.

Preparation of Monoketals 14 and 15.—To a solution of 0.1681 g (0.874 mmol) of **7b** in 35 ml of benzene was added 5 ml of ethylene glycol and 0.0525 g of *p*-toluenesulfonic acid monohydrate. The resulting mixture was heated at reflux under a Dean-Stark water separator for 1.5 hr. After cooling, the mixture was diluted with 65 ml of benzene and washed once with 50 ml of saturated $NaHCO_3$ solution and three times with 50-ml portions of water, then dried. Concentration *in vacuo* afforded 0.2111 g of pale yellow oil which was chromatographed on 10 g of silica gel. Elution with 5:95 ether–benzene afforded 0.0462 g (22%) of monoketal **14** as a white solid, mp 90.5–93.0°. Recrystallization from hexane afforded the analytical sample: mp 92.0–93.0°; ir (KBr) 1696 cm^{-1} (seven-membered ring C=O); nmr (CCl_4) δ 1.15 (3 H, s, CH_3), 1.71 (3 H, s, vinyl CH_3), and 3.77 (4 H, multiplet, OCH_2CH_2O).

Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.14; H, 8.60.

Continued elution with 5:95 ether–benzene afforded 0.0810 g (39%) of monoketal **15** as a white solid: mp 60.0–63.0°; ir (KBr) 1742 cm^{-1} (five-membered ring C=O); nmr (CCl_4) δ 1.21 (3 H, s, CH_3), 1.75 (3 H, s, vinyl CH_3), and 3.75 (4 H, s, OCH_2CH_2O); mass spectrum (70 eV) *m/e* (rel intensity) 236 (M^+, 29), 100 (25), 99 (100).

Elution with ether afforded 0.0546 g of pale yellow oil which appears to be a ketal ester derived from cleavage of the β-diketone system of **7b**: ir (neat) 3410 (OH) and 1733 cm^{-1} (ester C=O);

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nmr (CCl_4) δ 1.13 (3 H, d, J = 7 Hz, $CHCH_3$), 1.70 (3 H, s, vinyl CH_3), 3.5–4.3 (8 H, multiplet, OCH_2), and 7.31 (1 H, s, OH); mass spectrum (70 eV) m/e (rel intensity) 298 (M^+, 6), 100 (13), 99 (100).

2,7-Dimethylbicyclo[5.3.0]dec-1-en-8-ol-6-one (17).—To a solution of 0.1520 g of **7b** in 10.0 ml of absolute ethanol was added 0.0306 g of 81% platinum oxide, and hydrogenation was allowed to proceed at atmospheric pressure for 3 hr. Catalyst was then removed by filtration and washed well with ethanol. Removal of solvent *in vacuo* from the combined filtrate and washings afforded 0.1588 g of colorless resin, which was chromatographed on 10.0 g of silica gel. Elution with 1:9 ether–benzene afforded 0.0705 g of white solid, which was recrystallized from hexane to give 0.0552 g (36%) of **17**, mp 101.5–102.5°. Two recrystallizations from ether–hexane afforded the analytical sample: mp 103.0–104.0°; ir (KBr) 3306, 1108 (OH), and 1681 cm^{-1} (seven-membered ring C=O); nmr (CCl_4) δ 1.08 (3 H, s, CH_3), 1.66 (3 H, s, vinyl CH_3), and 4.07 (1 H, multiplet, W_H = 20 Hz, CH_2CHOH); mass spectrum (70 eV) m/e (rel intensity) 194 (M^+, 10), 176 (58), 161 (65), 123 (100), 98 (26), 97 (43).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.55; H, 9.83.

3-Methyl-2-(3,5-dimethyl-4-isoxazolylmethyl)cyclohexan-1-one-6-acetic Acid (20b).—A solution of 55.21 g (0.249 mol) of keto isoxazole **13** and 0.0732 g of *p*-toluenesulfonic acid monohydrate in a mixture of 70 ml of pyrrolidine and 200 ml of benzene was heated at reflux under a Dean-Stark water separator in a nitrogen atmosphere for 65 hr. Concentration *in vacuo* afforded the crude product as a viscous amber oil (a weak carbonyl band at 1714 cm^{-1} indicated incomplete conversion to the enamine).

The oil was dissolved in 200 ml of benzene, 64.6 g (0.387 mol) of ethyl bromoacetate was added, and the resulting mixture was heated at reflux in a nitrogen atmosphere for 40 hr. A solution of 5.0 ml of glacial acetic acid in 75.0 ml of water was then added and refluxing was continued for an additional 2 hr. After cooling, the mixture was extracted with 1 l. of ether. The ether extract was washed four times with 100-ml portions of 3 *M* HCl. The combined aqueous washes were then extracted with 250 ml of ether. The combined ether extracts were washed twice with 100-ml portions of saturated NaCl, dried, and concentrated *in vacuo*. The residual amber oil was dissolved in 600 ml of 10% ethanolic KOH and allowed to stir at room temperature for 21.5 hr. After the resulting mixture was concentrated *in vacuo*, the residue was taken up in 3 l. of water and extracted four times with 500-ml portions of ether. The combined ether extracts were washed once with 250 ml of water and once with 250 ml of saturated NaCl, dried, and concentrated *in vacuo* to give 22.42 g (41%) of recovered **13**. The combined aqueous layers were acidified with 100 ml of concentrated HCl and extracted four times with 500-ml portions of benzene. The combined benzene extracts were washed once with 200 ml of saturated NaCl, dried, and concentrated *in vacuo* to give 21.01 g of crude **20b** as a dark amber resin which partially crystallized on standing at room temperature for several days. Crystallization from ether–hexane afforded 9.23 g (13%) of **20b** as a yellowish-brown solid, mp 127.5–131.5°. Repeated recrystallization and treatment with activated carbon afforded the analytical sample as small white prisms: mp 135.0–135.5°; ir (KBr) 1707 cm^{-1} (carboxyl and ketone C=O); nmr ($CDCl_3$) δ 11.57 (1 H, s, COOH).

Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58; N, 5.01. Found: C, 64.63; H, 7.64; N, 4.75.

Methyl 5-Methyl-1(9)-octalin-2-one-8-acetate (2d).—To a solution of 16.607 g (59.5 mmol) of crude acid **20b** in 100 ml of absolute ethanol was added 2.0 ml of concentrated H_2SO_4, and the mixture was heated at reflux for 5 hr. After cooling, the mixture was diluted with 300 ml of water and extracted three times with 75-ml portions of benzene. The combined benzene extracts were washed once with 100 ml of water, twice with 100-ml portions of 5% Na_2CO_3, and twice with 100-ml portions of water, and dried over anhydrous Na_2SO_4. After concentration *in vacuo*, the residue was chromatographed on a 50-g column of silica gel. Elution with 400 ml of benzene and 500 ml of 1:9 ether–benzene afforded 13.895 g of ester **20a** as a viscous, amber oil: ir (neat) 1734 (ester C=O) and 1713 cm^{-1} (ketone C=O); nmr (CCl_4) δ 2.12 (3 H, s, CH_3) and 2.30 (3 H, s, CH_3).

A solution of 13.627 g (44.3 mmol) of **20a** in 200 ml of absolute ethanol was stirred with 8.6 g of W-4 Raney nickel[17] under a hydrogen atmosphere at room temperature. After 25.7, 40.2, and 67.1 hr, additional 6.7-, 11.4-, and 9-g quantities of W-4 Raney nickel[17] were added. After a 71.1-hr reaction period (the reaction was monitored by following disappearance of the isoxazole uv band at 229 nm), the mixture was filtered, and the nickel residues were washed well with absolute ethanol. Concentration *in vacuo* of the combined filtrate and washings afforded an amber-colored resin, which was dissolved in 100 ml of absolute ethanol. The solution was diluted with 500 ml of 10% NaOH solution, purged with nitrogen, and heated at reflux under nitrogen for 4 hr. After cooling, the mixture was diluted with 1.5 l. of water and washed twice with 250-ml portions of ether, then acidified with 150 ml of concentrated HCl and extracted four times with 250-ml portions of ether. The combined ether extracts were washed once with 250 ml of saturated NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give 7.509 g of **2c** as a viscous, amber resin: ir ($CHCl_3$) 1714 (carboxyl C=O) and 1670 cm^{-1} (ketone C=O).

The crude acid **2c** was dissolved in 80 ml of absolute methanol, 4.0 ml of concentrated H_2SO_4 was added, and the resulting mixture was heated at reflux for 3 hr. After cooling, the mixture was diluted with 250 ml of water and extracted three times with 75-ml portions of benzene. The combined benzene extracts were washed once with 100 ml of water, twice with 100-ml portions of 5% K_2CO_3, and once with 100 ml of water, and dried over anhydrous Na_2SO_4. Concentration *in vacuo* followed by distillation of the residue afforded 4.413 g (31% overall) of **2d** as a pale yellow liquid, bp 128–138° (0.2 mm). Redistillation afforded the analytical sample: bp 144.0–144.5° (0.45 mm); ir (neat) 1736 (ester C=O), 1675 (ketone C=O), and 1619 cm^{-1} (C=C); nmr (CCl_4) δ 5.58 (0.5 H, s, C=CH) and 5.78 (0.3 H, s, C=CH); mass spectrum (70 eV) m/e 236 (M^+).

Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.32; H, 8.44.

Methyl 2,2-Ethylenedioxy-5-methyl-8-octalin-8-acetate (21).—To a solution of 1.982 g (8.39 mmol) of α,β-unsaturated ketone **2d** in 75 ml of benzene was added 20 ml of ethylene glycol and 0.077 g (0.40 mmol) of *p*-toluenesulfonic acid monohydrate. The resulting mixture was heated at reflux in a nitrogen atmosphere under a Dean-Stark water separator for 2 hr. After cooling, the mixture was diluted with 75 ml of benzene, washed once with 50 ml of saturated $NaHCO_3$ and five times with 50-ml portions of water, and dried. Concentration *in vacuo* afforded 2.253 g of pale yellow oil which was chromatographed on 50 g of silica gel. Elution with benzene and 2:98 ether–benzene afforded 1.686 g (72%) of **21**. Short-path distillation (160° bath, 0.55 mm) afforded the analytical sample as a colorless liquid: ir (neat) 1738 cm^{-1} (ester C=O); nmr (CCl_4) δ 1.01 (3 H, br, W_H = 5.5 Hz, $CHCH_3$), 3.60 (3 H, s, OCH_3), and 3.86 (4 H, br, W_H = 2.3 Hz, OCH_2CH_2O).

Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.75; H, 8.81.

Hydrolysis of Ketal 21.—To a solution of 0.537 g (1.92 mmol) of ketal **21** in 40 ml of methanol was added a solution of 0.700 g (7.77 mmol) of oxalic acid in 25 ml of water. After the mixture was stirred at room temperature for 2.5 hr, it was diluted with 150 ml of half-saturated NaCl solution and extracted with 200 ml of ether. The ether extract was washed once with 75 ml of saturated $NaHCO_3$ solution, twice with 75-ml portions of water, and once with 50 ml of saturated NaCl solution, and dried. Concentration *in vacuo* afforded 0.444 g of pale yellow oil, which was chromatographed on 30 g of silica gel. Elution with 5:95 ether–benzene afforded 0.1578 g of a mixture of ketal **21** and β,γ-unsaturated ketone **22**, which was homogeneous by thin layer chromatography (silica gel G, elution with 2:8 ethyl acetate–benzene). Integration of nmr signals (CCl_4 solution) at δ 3.86 and 3.62 indicated the presence of **21** and **22** in a ratio of 23:77. The mass spectrum (70 eV) showed m/e (rel intensity) 280 (10), 236 (19), and 99 (100).

Further elution with 5:95 ether–benzene and 1:9 ether–benzene afforded 0.260 g (57%) of α,β-unsaturated ketone **2d**.

Attempted Preparation of Methyl 2,7-Dimethylbicyclo[5.3.0]-dec-1-ene-6,8-dione-5-acetate (7c).—A solution of 0.062 g of the crude β,γ-unsaturated ketone, prepared by ketalization and hydrolysis of **17b**, in a mixture of 5.0 ml of methylene chloride and 5.0 ml of methanol was cooled at Dry Ice–acetone bath temperature and treated with a stream of ozone in oxygen for 4 min (until a blue coloration developed from the presence of excess ozone). After the solution was purged with nitrogen, 0.50 ml of trimethyl phosphite[15] was added and the resulting mixture was allowed to stir at room temperature for 23 hr. The mixture was then concentrated at water-pump pressure, and the remaining volatile material was removed by short-path distillation (107°

bath, 0.20 mm) to give 0.091 g of residual yellow oil. This was dissolved in a mixture of 5.0 ml of acetone and 1.0 ml of methyl iodide, 0.0438 g of anhydrous K_2CO_3 was added, and the mixture was heated at reflux for 3 hr. After cooling, the mixture was diluted with 15 ml of ether and filtered. Removal of solvent *in vacuo* then afforded 0.094 g of yellow oil which showed infrared absorption at 1734, 1716, 1652, and 1607 cm^{-1}.

Registry No.—**2b**, 36873-61-7; **2d**, 36873-62-8; **3a**, 36873-63-9; **3b**, 36873-64-0; **4b**, 36873-65-1; **4b** dinitrophenylhydrazone, 36873-66-2; **6a**, 36873-67-3; **6b**, 36873-68-4; **7a**, 36873-69-5; **7b**, 36873-70-8; **13**, 36873-71-9; **14**, 36873-72-0; **15**, 36873-73-1; **17**, 36873-74-2; **20b**, 36873-75-3; **21**, 36873-76-4.

Mechanism for the Peracetic Acid Oxidation of *trans*-α-Iodo-α′-acetoxystilbene to Benzil[1]

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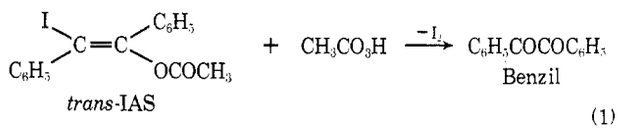
The mechanism for the reaction of *trans*-α-iodo-α′-acetoxystilbene (*trans*-IAS) with peracetic acid to form benzil has been studied by means of its kinetics and the examination of related reactions. The rate is expressed as $v = (k_2 + k_2'h_0)$[*trans*-IAS]$[CH_3CO_3H]$. The reaction is accelerated in a more acidic solvent, but it is retarded by addition of sodium acetate and stopped in strongly basic solvents. *trans*- and *cis*-α,α′-diacetoxystilbene (DAS) are stable against peracetic acid alone, but they are oxidized to benzil by a mixture of peracetic acid and iodine or alkyl iodide. *trans*-IAS gives on treatment with peracetic acid in the presence of anisole *trans*-DAS, benzoin and its acetate together with other products. The reaction of *trans*-α,α′-diiodostilbene (*trans*-DIS) with peracetic acid in propionic acid gives *trans*-α-iodo-α′-propionyloxystilbene (*trans*-IPS) by introduction of solvent carboxylate group. These results suggest a mechanism involving a rate-determining electrophilic attack by peracetic acid on the iodine atom of IAS to give vinylic cation, which yields DAS by the reaction with solvent acetic acid. Then DAS reacts with produced acetyl hypoiodite, the adduct being further oxidized and hydrolyzed to give benzil.

In our previous paper,[2] we reported that *trans*-α-iodo-α′-acetoxystilbene (*trans*-IAS), a product by iodoacetoxylation of tolan, gave benzil on oxidation with peracetic acid (eq 1). The mechanism of this reaction



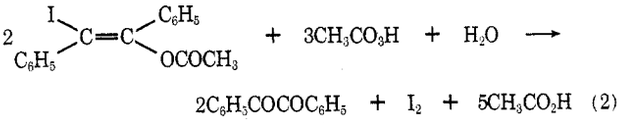
(1)

is of interest in comparison to the solvolysis of vinyl halides, since a vinyl cation may be an intermediate in the oxidation. There are many examples of solvolysis of a vinyl halide involving an intermediary vinyl cation.[3-7] Thus, acetolyses of both *cis*- and *trans*-1-iodo-1-cyclopropylpropenes in the presence of silver acetate at 25° gave equal amounts of stereoisomeric acetates as major products, pointing to the conclusion that the products arising from both cis and trans iodides are formed from the same intermediate, which is most likely a linear vinyl cation.[7] The calculations on 1-cyclopropylvinyl cations by means of the extended Hückel molecular orbital method also suggest that the ions are most stable in the linear, bisected conformation.[8]

There are some obscurities in the mechanism for oxidation of *trans*-IAS to benzil (eq 1). (1) Where is the initial attacking site of peracid? (2) Is the attacking species an electrophile? (3) Is a vinyl cation involved? (4) Is α,α′-diacetoxystilbene (DAS) an intermediate in analogy with the formation of IAS from *trans*-α,α′-diiodostilbene (*trans*-DIS)? For the elucidation of these questions, we carried out the kinetic studies and then examined the related reactions, *i.e.*, oxidations of DAS and DIS with peracetic acid in the presence or absence of iodine or alkyl iodide. Further, we attempted to detect a hypothetical intermediate, DAS. The present paper describes a probable mechanism for the oxidation of *trans*-IAS with peracetic acid as well as of related reactions.

Results and Discussion

Stoichiometry.—The reaction of *trans*-IAS with peracetic acid gives benzil together with iodine.[2] Since the main products are benzil (based on tlc analysis) and iodine, the stoichiometry may be as follows.



(2)

However, it must be taken into account that peracetic acid is consumed also by the further oxidation of iodine and/or hypoiodous acid probably present in the reaction mixture, and by the decomposition of peracid itself. Hence, for the examination of the stoichiometry, the conversion of IAS to benzil, the consumption of peracetic acid, and the formation of iodine should be studied simultaneously at appropriate time intervals. Figure 1 shows conversion curves, which indicate that more than 2 mol of peracetic acid is consumed and less than 0.5 mol of iodine is formed by consuming 1 mol of IAS (or by formation of benzil). This result means that more than 0.5 mol of peracetic acid is consumed by further oxidation of iodine compounds or by decomposition.

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