talline precipitate appeared. The reaction mixture was cooled and filtered to give 7.3 g. (96%) of colorless needles, m.p. 270–272° dec. A sample of the product was recrystallized from water and dried *in vacuo* over P_2O_5 at 100° for 3 hours; m.p. 270–272° dec.

Anal. Calcd. for $C_6H_6N_6O \cdot {}^1/_3H_2O$: C, 39.12; H, 3.65; N, 45.62. Found: C, 39.19; H, 3.61; N, 45.59.

6-Aminomethylpurine (XIX).—A solution of 6-cyanopurine (XV) (0.29 g., 0.002 mole) in 15 ml. of absolute methanol was hydrogenated at room temperature and atmospheric pressure in the presence of 0.2 g. of 5% palladium-charcoal. The suspension was filtered, the precipitate washed with methanol and the combined filtrates evaporated *in vacuo* to yield 0.23 g. (75%) of needles, m.p. 181–183° dec. The reaction product, which turned pink on exposure to air, was very soluble in water, ethanol, methanol and acetic acid and sparingly soluble in ether and benzene. A sample was purified by pouring a concentrated ethanol solution into ether. This treatment was repeated twice to yield a pale pink product, m.p. 183–185° dec. An ethanolic solution of this compound produced an intense crimson coloration on acidification. The picrate of XIX was prepared from aqueous solution in cold water. After four crystallizations from water, a light yellow product, m.p. 190° dec. was obtained.

Anal. Calcd. for $C_6H_7N_5 \cdot C_6H_3N_3O_7$: C, 38.10; H, 2.66; N, 29.62. Found: C, 37.94; H, 2.86; N, 29.47.

Spectrophotometric and Dissociation Studies.—Spectrophotometric measurements were made with a Cary model 11 ultraviolet recording spectrophotometer (Applied Physics Corporation, Pasadena, Calif.) using matched 1-cm. silica cells and techniques and buffers previously described.[37] The apparent pK_a values were determined using the methods described by Fox and Shugar,[38,39] and Parke and Davis.[40]

Acknowledgments.—The authors wish to thank Dr. George B. Brown, Dr. J. J. Fox, Dr. C. Chester Stock and Dr. D. A. Clarke for valuable advice and discussion. They wish to express their gratitude to Mr. Janis Vitols and Mr. Herbert S. Rosenkranz for assistance.

(37) J. J. Fox, L. F. Cavalieri and N. Chang, THIS JOURNAL, **75**, 4315 (1953).

(38) J. J. Fox and D. Shugar, *Bull. soc. chim. Belg.*, **61**, 44 (1952).

(39) D. Shugar and J. J. Fox, *Biochim. et Biophys. Acta*, **9**, 199 (1952).

(40) T. V. Parke and W. W. Davis, *Anal. Chem.*, **26**, 642 (1954).

NEW YORK 21, N. Y.

[CONTRIBUTION FROM THE MERCK SHARP & DOHME RESEARCH LABORATORIES]

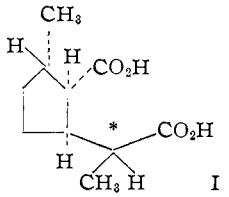
Studies in the Iridomyrmecin Series. Abnormal Ring Closure of a 1,6-Keto Aldehyde

BY N. L. WENDLER AND H. L. SLATES

RECEIVED MARCH 6, 1958

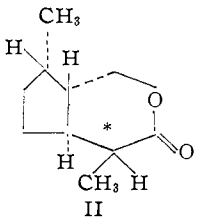
An unusual ring closure of a 1,6-keto aldehyde derivative of a tetrahydrofuran is described.

The original work by Fusco, Trave and Vercellone[1] on the structure of iridomyrmecin and related terpenoid compounds isolated from various *Iridomyrmex* species of ants led these authors to the proposal of a part structure for this substance. This part structure was based on the oxidation of iridomyrmecin to a nepetalinic acid whose structure had presumably been established by McElvain and Eisenbraun[2] to be I (unknown configuration at carbon designated by asterisk). Some time there-

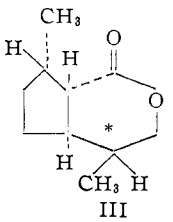


I

after Cavill, Ford and Locksley[3] reported summary findings permitting the assignment of either structure II or III to iridomyrmecin and its epimer (epimeric at the carbon designated by an asterisk).



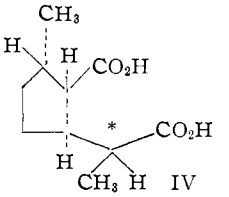
II



III

Recently McElvain[4] succeeded in converting nepetalic acid to isoiridomyrmecin in such a way as presumably to have established structure II for these substances.

On the basis of structure II we undertook to synthesize iridomyrmecin as well as its epimer, and the present account reports our experience in this direction. Since the inception of our work, however, a further article by Cavill[5] has appeared in which it is now disclosed that through private communication with McElvain a change of group configurations in nepetalinic acid is necessary whereby formula IV now represents the structure of this key compound. Details concerning the chemistry necessitating revision of the previously



IV

accepted structure I for nepetalinic acid which would have greatly enlightened this rather confused field were not revealed.

We prepared the Diels–Alder adduct V[6] from isoprene and maleic anhydride and reduced it with lithium aluminum hydride to the diol VI.

(1) R. Fusco, R. Trave and A. Vercellone, *Chim. e Industr.*, **37**, 958 (1955); **37**, 251 (1955).

(2) S. M. McElvain and E. J. Eisenbraun, THIS JOURNAL, **77**, 1599 (1955); **77**, 3383 (1955).

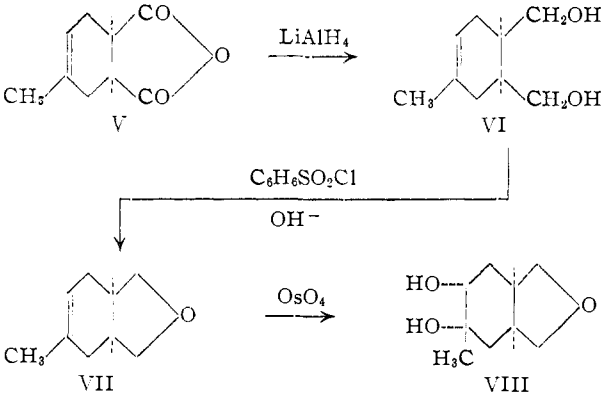
(3) G. W. K. Cavill, D. L. Ford and H. D. Locksley, *Chemistry & Industry*, 465 (1956).

(4) S. M. McElvain and E. J. Eisenbraun, *J. Org. Chem.*, **22**, 976 (1957).

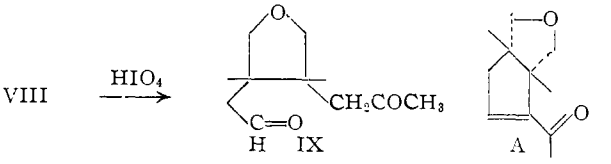
(5) G. W. K. Cavill and H. D. Locksley, *Australian J. Chem.*, **10**, 352 (1957).

(6) J. Böeseken and W. J. F. van der Gracht, *Rec. trav. chim.*, **56**, 1203 (1937); see also E. A. Farmer and F. L. Warren, *J. Chem. Soc.*, 3221 (1931).

It had been observed previously[7] that a 1,4-diol system is converted to the corresponding cyclic oxide by treatment of the mono- or dimesylate derivatives variously with basic reagents or lithium aluminum hydride, respectively. The latter of these techniques was unrewarding in the case of our diol VI, whereas esterification with one equivalent of methanesulfonyl chloride in pyridine followed by treatment of the crude product with methanolic potassium hydroxide afforded 40–50% of the desired tetrahydrofuran derivative VII. On the other hand by employing Schotten–Baumann conditions, whereby a stirred ether solution of VI containing *p*-toluenesulfonyl chloride was treated dropwise with aqueous potassium hydroxide, yields of 75–80% of the cyclic oxide VII could be realized. Hydroxylation of VII with osmium tetroxide produced the crystalline diol VIII, m.p. 95–98°.



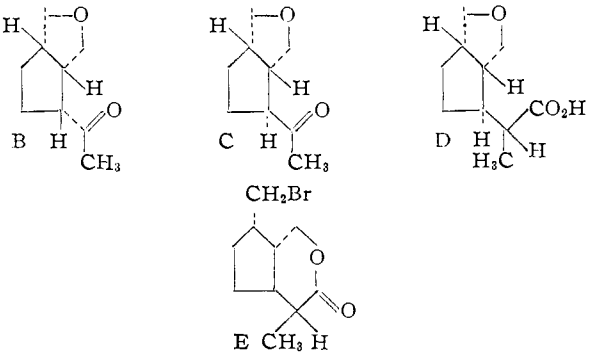
It had been anticipated that periodate cleavage of VIII to the intermediate ketoaldehyde IX would, in keeping with precedent, ring close to the bicyclic $\Delta^{\alpha,\beta}$-ketone A. The latter might then have been successively hydrogenated to the *cis-syn-cis*-



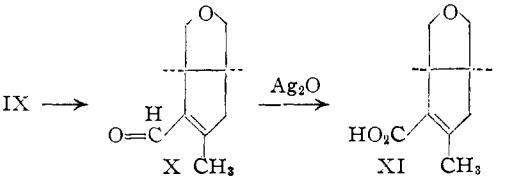
saturated ketone B and epimerized to the *cis-syn-trans*-ketone C. Homologation of C would have led to the bicyclic acid D capable of conversion with hydrogen bromide to the bromolactone E. Reductive debromination of E should in turn have provided II. Since the position alpha to the lactone carbonyl is epimerizable to what is most probably the equatorial configuration, the above sequence would have constituted a stereo-selective synthesis of isoiridomyrmecin (and correspondingly iridomyrmecin).

In actuality, cleavage of the diol VIII with sodium metaperiodate followed by cyclization under a variety of conditions consistently produced the $\Delta^{\alpha,\beta}$-unsaturated aldehyde X, instead of the ketone A, as the only volatile product that could be characterized. The crude aldehyde exhibited ultraviolet absorption with $\lambda_{max}^{CH_3OH}$ 248 mμ

(7) G. Stork, L. J. Friedman, E. E. van Tamelen and A. W. Burgstahler, THIS JOURNAL, **75**, 384 (1953).



(9,800) instead of 237 mμ expected for a ketone with structure A. The infrared spectrum exhibited a band at 3.67 μ associated with the aldehydic function (C–H). Nuclear magnetic resonance measurements on this material also indicated unmistakably the C–H absorption at 196 cycles on the low field side characteristic of the aldehyde group with no evidence of an olefinic hydrogen; X formed a semicarbazone, m.p. 215–220°, and a red 2,4-dinitrophenylhydrazone derivative, m.p. 214–214.5°. Finally oxidation of X with silver oxide proceeded smoothly with formation of the carboxylic acid XI, m.p. 100–102°, conclusively establishing structure X for the cyclization products.



The somewhat surprising consequence of cyclization of the 1,6-ketoaldehyde IX to give X is in some measure mitigated by the low yield in which it was formed. Cyclizations were effected variously employing potassium hydroxide, potassium *t*-butoxide, piperidine acetate and basic alumina and all gave essentially the same result.

Experimental[8]

1-Methyl-4,5-bis-hydroxymethylcyclohex-1-ene (VI).—A solution of 25 g. of adduct V (m.p. 63.5–64.5°) in 300 cc. of ether was added to 25 g. of lithium aluminum hydride in 1 l. of ether at room temperature at such a rate as to maintain reflux. After the addition was complete the reaction mixture was refluxed for 2 hours, then chilled in ice and decomposed with 75 cc. of ethyl acetate followed by 450 cc. of saturated sodium sulfate solution. The ether solution of VI was decanted from the salts, dried over magnesium sulfate and evaporated to a viscous oil, wt. 20 g. An analytical sample was obtained by distillation at 140° and 0.7–0.8 mm.

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.23; H, 10.25. Found: C, 69.09; H, 10.22.

Formation of the Bicyclic Oxide VII. (A).—A solution of 25 g. of the diol VI in 100 cc. each of benzene and pyridine at 0° was treated dropwise with stirring with 18.4 g. (1 equiv.) of methanesulfonyl chloride in 50 cc. of benzene. The reaction mixture was allowed to stand overnight at 0–5° then diluted with water and the benzene layer separated and diluted with ether. The organic layer was washed successively with dilute hydrochloric acid and sodium bicarbonate, dried over magnesium sulfate and concentrated at 30–40° to an oil. The latter was dissolved in 100 cc. of methanol and treated with 20 g. of potassium hydroxide in 20 cc. of water

(8) Melting points were taken on a micro hot-stage apparatus and are corrected.

causing an immediate precipitation of sodium methanesulfonate. The reaction mixture was refluxed for 1 hour and then the methanol distilled *in vacuo* to the point of turbidity. The reaction mixture at this stage was diluted with saturated salt solution and extracted with petroleum ether which dissolved VII away from other insoluble organic impurities. The petroleum ether extract was dried and evaporated to a mobile oil with a terpene-like odor. Distillation of this oil afforded 11.1 g. of VII, b.p. 110° at 45 mm. (54%).

Anal. Calcd. for $C_9H_{14}O$: C, 78.26; H, 10.15. Found: C, 78.28; H, 10.28.

(B).—A solution of 10 g. of diol VI and 15 g. of *p*-toluenesulfonyl chloride in 50 cc. of ether was treated dropwise with stirring with a solution of 15 g. of potassium hydroxide in 50 cc. of water. After addition was complete the reaction mixture was heated for 1 hour on the steam-bath and worked up as in part A; yield 7 g. (80%) of VII.

Preparation of Diol VIII by Osmium Tetroxide Hydroxylation of Oxide VII.—A solution of 10 g. of oxide VII in 25 cc. of dioxane was treated with 25 g. of osmium tetroxide and allowed to stand at room temperature for 2 days. At the end of this period the dark reaction mixture was decomposed by hydrogen sulfide,[9] filtered through Celite and concentrated to a water-soluble oil, wt. 7.5 g. This oil crystallized on standing and could be recrystallized from ether, m.p. 95–98°.

Anal. Calcd. for $C_9H_{10}O_3$: C, 62.81; H, 9.30. Found: C, 62.60; H, 9.38.

Cleavage of VIII to IX and Formation of the Bicyclic $\Delta^{\alpha,\beta}$-Aldehyde X. (A).—A solution of 575 mg. of crystalline diol VIII in 2 cc. of tetrahydrofuran at room temperature was treated with 750 mg. of sodium metaperiodate in 5 cc. of water. The reaction mixture was cooled slightly to offset the heat of reaction which was accompanied by the separation of sodium iodate. The reaction mixture was allowed to stand 1 hour, then concentrated *in vacuo* and the water-soluble keto aldehyde intermediate IX thoroughly extracted with ether. Evaporation of the ether left 360 mg. of a colorless oil which gave an immediate yellow precipitate with 2,4-dinitrophenylhydrazone reagent. This oil was dissolved in 15–20 cc. of benzene treated with 3 drops of pyridine and 2 drops of acetic acid and refluxed with a water separator for 1 hour. The reaction mixture was diluted with ether and washed successively with dilute hydrochloric acid, potassium bicarbonate and saturated salt solution. The dried ether solution was concentrated and distilled at 100° and 0.7 mm. to afford 100 mg. of crude aldehyde X with a $\lambda_{max}^{CH_3OH}$ 248 mμ, *E* 9800, λ_{max} 5.99 μ (conj C=O), 6.08 μ (C=C), 3.67 μ (ald. C-H); n.m.r. 196 ∼.

2,4-Dinitrophenylhydrazone red crystals from ethyl acetate–methanol, m.p. 214–214.5°. *Anal.* Calcd. for $C_{15}H_{16}O_5N_4$: C, 54.22; H, 4.82; N, 16.87. Found: C, 54.48; H, 5.02; N, 16.70.

Semicarbazone from methanol, m.p. 215–220°. *Anal.* Calcd. for $C_{10}H_{10}O_2N_3$: C, 57.42; H, 7.18; N, 20.10. Found: C, 57.45; H, 7.01; N, 19.73.

(B).—A solution of 1.72 g. of diol VIII was cleaved in 20 cc. of water with 3 g. of sodium metaperiodate for 1 hour. The reaction solution was made alkaline with potassium hydroxide and warmed on the steam-bath to the appearance of turbidity. Extraction with ether afforded 150 mg. of crude X, $\lambda_{max}^{CH_3OH}$ 244 mμ, *E* 9800.

(C).—A solution of 2 g. of diol VIII was cleaved with 3 g. of sodium metaperiodate for 1 hour and the product continuously extracted with ether. The ether solution was evaporated and the residue treated with 50 cc. of *t*-butyl alcohol containing 0.39 g. of potassium metal dissolved. The reaction mixture turned yellow and finally orange-red. After 15 minutes the reaction was quenched with 10% hydrochloric acid, evaporated and worked up as described above. The product obtained in low yield exhibited $\lambda_{max}^{CH_3OH}$ 248 mμ, *E* 7448.

(D).—Results comparable to the foregoing were experienced when the ether solution of the cleavage product IX was allowed to stand several hours on basic alumina and then eluted.

Oxidation of the Bicyclic Aldehyde X to the Acid XI.—A solution of 100 mg. of the aldehyde X in 2 cc. of ethanol was treated with silver oxide freshly prepared from 200 mg. of silver nitrate and 100 mg. of potassium hydroxide. The oxidation was allowed to proceed for 30 minutes with stirring and then filtered, evaporated and dissolved in ether. The acidic material was extracted with potassium bicarbonate. Acidification of the bicarbonate extract precipitated the acid XI in crystalline form. The latter was extracted with ether and crystallized from the same solvent, m.p. 100–102°.

Anal. Calcd. for $C_4H_{12}O_3$: C, 64.29; H, 7.14. Found: C, 64.09; H, 7.08.

RAHWAY, N. J.

(9) Method of D. H. R. Barton and D. Elad, *J. Chem. Soc.*, 2085 (1956).

[CONTRIBUTION FROM CHEMICAL DIVISION, AEROJET-GENERAL CORPORATION]

The Synthesis of 1,1'-Biaziridine. A New Bicyclic System[1]

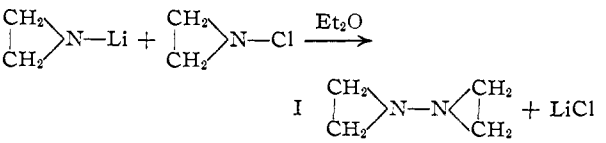
BY ALLEN F. GRAEFE AND RALPH E. MEYER

RECEIVED JANUARY 24, 1958

The preparation of 1-haloaziridines from ethylenimine and hypohalite is described. The reaction of 1-chloroaziridine with 1-lithiumaziridine in ether was investigated, and evidence is presented that the isolated product is 1,1'-biaziridine. Some properties of this new bicyclic compound are presented.

Introduction

During the course of an investigation of the lower alkyl hydrazines in this Laboratory, it became a matter of importance to synthesize the as yet unknown bicyclic compound, 1,1'-biaziridine (I). A method of preparation of the compound became available when it was found that 1-chloroaziridine could be obtained from ethylenimine and aqueous hypochlorite. 1,1'-Biaziridine was then prepared from the reaction of 1-chloroaziridine with the known 1-lithiumaziridine.[2]



I

To our knowledge, no other hydrazine derivative has been prepared by this method. This may be the result of the ready dehydrohalogenation of alkylchloramines by alkylamide anions since, in an attempt to prepare tetramethylhydrazine from dimethylchloramine and dimethylamidomagnesium halide, Klages and co-workers reported amines as the only basic products.[3] In the present synthesis

(1) This investigation was carried out under a contract with the Office of Naval Research.

(2) H. Gilman, *et al.*, THIS JOURNAL, **67**, 2106 (1945).

(3) F. Klages, *et al.*, *Ann.*, **547**, 1 (1941).