Brèves communications - Kurze Mitteilungen
Brevi comunicazioni - Brief Reports

The Acid Catalyzed Rearrangement of Ambreinolide * [1]

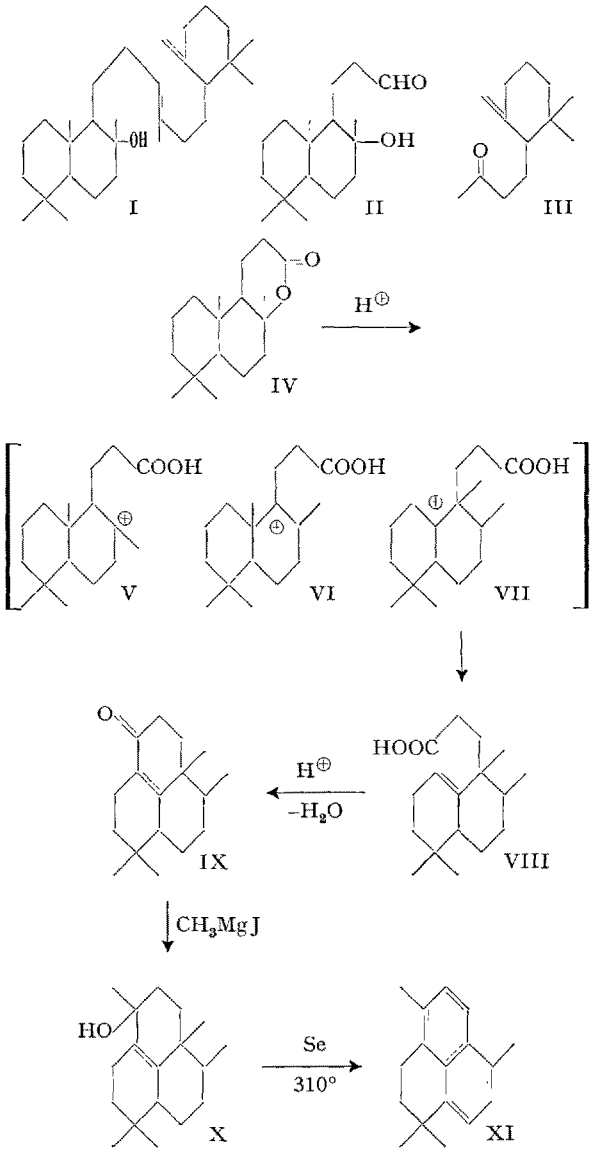
Ambergris, an excretion product of the sperm whale and of considerable importance to perfumery, has been the subject of several chemical investigations during the last decade. The structure of ambrein (I), a constituent of the non-volatile fraction of ambergris, has been elucidated by RUZICKA and JEGER and their collaborators in Zurich and by LEDERER and his school in Paris[2]. A chemical analysis of the volatile fraction of ambergris, which is mainly responsible for the odor of the product, has led to the isolation of dihydro-γ-ionone (III), a ketone, $C_{13}H_{20}O$, of unknown constitution and a hydroxy aldehyde (II), $C_{17}H_{30}O_2$[3]. Noting that all of these naturally occuring substances are products of oxidative degradation of ambrein (I), LEDERER has made efforts to develop procedures for converting the odorless ambrein to products with ambergris odor. One of the products isolated by LEDERER *et al.*[4] from the acid catalyzed isomerization of ambreinolide (IV), a key degradation product of ambrein, is a tricyclic ketone $C_{17}H_{26}O$,

$$\lambda_{max}^{EtOH} 252\,m\mu \ (\log \varepsilon\ 4\cdot1)$$

which has an odor reminiscent of ambergris. A previous attempt to elucidate the structure of this ketone appears to have been unsuccessful[4] (see Formulae I–XI).

We now wish to report work which establishes the structure of the tricyclic ketone $C_{17}H_{26}O$ as IX. The ultraviolet spectrum of this compound indicates the presence of a tetrasubstituted s-trans-α,β-unsaturated carbonyl system, and the infrared spectrum (absorption bands at 6·05 and 6·17 μ) points to a cyclohexenone rather than a cyclopentenone structure. The formation of such a ketone from IV can be satisfactorily explained if it is assumed that a Wagner-Meerwein rearrangement is involved in the acid catalyzed reaction. Such a rearrangement has been observed previously in the closely related conversion of dihydroabietic acid to "hydroxytetrahydroabietic acid"[5], and the formation of the tricyclic ketone can then easily be visualized as proceeding through the sequence IV→ VIII→IX.

Inspection of structure IX shows its close similarity to the hydrocarbon (XI), $C_{17}H_{20}$, which has been obtained by dehydrogenation of the diterpenes agathic acid[6] and cativic acid[7]. The structure XI has recently been established by synthesis[8]. In order to prove the proposed structure IX we have carried out the following conversions: A solution of ambreinolide (IV) (2 g) in 20 ml of dioxane containing 30 ml of 80% H_2SO_4 was heated at 60° for 1·5 h in an atmosphere of nitrogen,



whereby the tricyclic ketone was isolated in 32% yield. (Analysis calculated for $C_{17}H_{26}O$: C 82·87; H 10·64. Found: C 83·37; H 10·62; λ_{max} 251·6 mμ, log ε 4·07; 6·05 and 6·17 μ.) The compound was characterized by a 2,4-dinitrophenylhydrazone (m.p. 196·5–198°, dec. lit.[4]: 196–200°) a phenylsemicarbazone (m.p. 218·2 to 219·6°, lit.[4]: 215–219°), and a semicarbazone (m.p. 207·1–208·6°, lit.[4]: 123–125°;Analysis calculated for $C_{18}H_{29}ON_3$: C 71·24; H 9·63. Found: C 71·33; H 9·64).

* Terpenes III.

[1] Part II, G. BÜCHI and R. E. ERICKSON, J. Amer. chem. Soc. *76*, 3493 (1954).

[2] E. LEDERER, *Odeur et parfums des animaux*, in: *Fortschritte der Chemie organischer Naturstoffe*, vol. 6, p. 88 (Springer, Wien) 1950).

[3] L. RUZICKA and C. F. SEIDEL, Helv. chim. Acta *33*, 1285 (1950). – L. RUZICKA, C. F. SEIDEL, and M. PFEIFFER, Helv. chim. Acta *31*, 827 (1948).

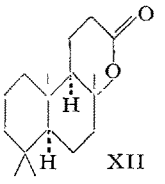
[4] C. COLLIN-ASSELINEAU, E. LEDERER, D. MERCIER, and J. POLONSKY, Bull. Soc. chim. France 720 (1950).

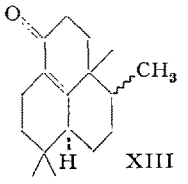
[5] D. H. R. BARTON, Chem. and Ind. 638 (1948). – L. A. SUBLUSKEY and T. F. SANDERSON, J. Amer. chem. Soc. *76*, 3512 (1954).

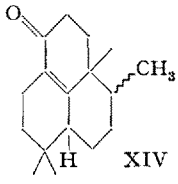
[6] L. RUZICKA and J. R. HOSKING, Ann. Chem. *469*, 147 (1929); Helv. chim. Acta *13*, 1402 (1930); *14*, 203 (1931).

[7] F. W. GRANT, Jr. and H. H. ZEISS, J. Amer. chem. Soc. *76*, 5001 (1954).

The ketone IX (1·3 g) was allowed to react with excess methylmagnesiumiodide to give the corresponding alcohol (X) (1·2 g). Dehydrogenation of X (820 mg) by heating with selenium (1·2 g) at 310° for 19 h yielded 205 mg of XI. (λ max./cyclohexane 233, 283, 294, 328 mμ, log ε 4·51, 3·57, 3·49, 3·05. Picrate, red needles m.p. 135–136°, lit.[8]: 135·5–136·0. Analysis calculated for $C_{23}H_{23}O_7N_3$: C 60·92; H 5·11. Found: C 60·89; H 5·18. Admixture with an authentic sample did not depress this value. Styphnate m.p. 152·6–153·6°, lit.[8]: 151·6 to 152·4°. No melting point depression on admixture with an authentic sample.)


XII


XIII


XIV

According to KLYNE[9] the stereochemistry of ambreinolide is represented by formula XII, from which, however, an unequivocal deduction of a complete stereochemical formula for the tricyclic ketone IX is not possible on the basis of the available evidence. The main uncertainty resides in the assignment of the configuration of the methyl group at C-8. The spatial arrangement of this methyl group in IX may be expected to depend on the mechanism of the transformation V→VI; *a priori* VI could be formed either by a 1,2-hydride shift or by way of the intermediate formation of the corresponding $\Delta^{8,9}$-unsaturated compound.

The configuration of the hydrogen at C-5 may on the other hand be assumed to have changed from α to β in the course of the reaction sequence IV→IX. Conformational considerations indicate that XIV should be thermodynamically more stable than the epimer XIII, regardless of the configuration of the methyl group at C-8. The conditions under which the tricyclic ketone is formed should allow the formation of the more stable epimer, the epimerization at C-5 taking place either at the bicyclic stage or by acid catalyzed isomerisation of XIII to XIV.

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G. BÜCHI, W. S. SAAR, and
A. ESCHENMOSER[10]

Department of Chemistry Massachusetts Institute of Technology, Cambridge, Mass., USA, January 29, 1956.

Zusammenfassung

Die Struktur eines durch säurekatalytische Isomerisation von Ambreinolid entstehenden tricyclischen Ketons $C_{17}H_{26}O$ wurde aufgeklärt.

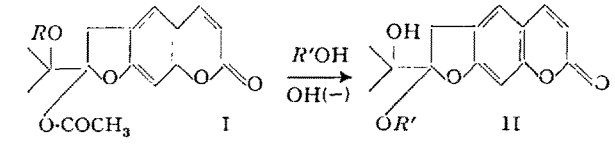
[8] G. BÜCHI and J. J. PAPPAS, J. Amer. chem. Soc. *76*, 2963 (1954).

[9] W. KLYNE, J. chem. Soc. 3072 (1953).

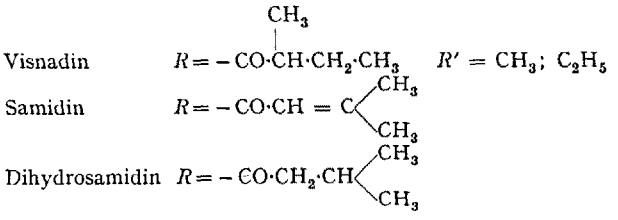
[10] Organisch-chemisches Laboratorium der ETH, Zürich.

Über die Konstitution der Visnagane und Khellactone aus *Ammi visnaga* L.

Vor kürzerer Zeit ist es SMITH, HOSANSKY und BYWATER[1] gelungen, das zuerst von SAMAAN[2] beschriebene, amorphe und koronardilatorisch wirksame Visnagan aus den Samen von *Ammi visnaga* L. in eine Reihe von sehr ähnlichen, kristallisierten Verbindungen aufzutrennen, unter denen sich Visnadin ($C_{21}H_{24}O_7$), Samidin ($C_{21}H_{22}O_7$) und Dihydrosamidin ($C_{21}H_{24}O_7$) finden. Die drei Substanzen stellen Diester eines Glykols dar, in welchem eine Hydroxylgruppe stets mit Essigsäure, die andere mit α-Methylbuttersäure, Seneciosäure bzw. Isovaleriansäure verestert ist. Mit alkoholischer Lauge geben die drei Stoffe neben den erwähnten Fettsäuren die gleiche Verbindung, in welcher eine der in den Visnaganen vorkommenden Acyloxygruppen durch eine aus dem zur Verseifung verwendeten Alkohol stammenden Alkoxygruppe ersetzt ist. Letztere Verbindungen sind offensichtlich identisch mit den sogenannten Alkylkhellactonen von unbekannter Struktur, die schon früher von SPÄTH, GRUBER und MATZKE[3] bei der Behandlung des rohen Ätherextraktes von *Ammi visnaga* mit methyl- bzw. äthylalkoholischer Lauge erhalten worden sind. Die amerikanischen Autoren haben den Visnaganen und Alkylkhellactonen die Formeln I bzw. II zugeschrieben.



I II



Wir möchten jetzt für diese Substanzen etwas modifizierte Formeln vorschlagen. Aus kristallisiertem Visnagangemisch entstand mit KOH-Dioxan ein Gemisch der beiden am C-Atom 4' stereoisomeren Khellactone IA (Smp. 186° [− 18°])[4] und IB (Smp. 174–175° [+ 81°]), in welchem IA stark überwiegt. Beide Stoffe gaben kristallisierte Diazetate, mit Chromsäure Azeton, mit Kaliumpermanganat α-Oxyisobuttersäure und durch säure-katalysierte Wasserabspaltung das optisch inaktive Keton II (Smp. 156,6–157,5°, λ_{max} des 2,4-Dinitrophenylhydrazons etwa 346 mμ; Alkohol). Auch II lieferte bei der Oxydation Azeton bzw. α-Oxyisobuttersäure. II wurde über das Diäthylthioketal III in das bekannte Dihydroseselin[5] (IV) umgewandelt. Oxydation von IA mit Perjodsäure bei pH ~ 4 führte zum Dialdehyd V (Smp. 128–130°), dessen Oxydation mit Perjodsäure bei pH ~ 7 den bekannten Umbelliferon-8-aldehyd[6] (VI), Ameisensäure und Azeton gab. Mit Hydroxyl-

[1] Abstr. of Paper 126th Meeting American Chemical Society, New York, Sept. 12–17 (1954), S. 24N. Vgl. auch E. SMITH, L. A. PUCCI und W. G. BYWATER, Science *115*, 520 (1952).

[2] K. SAMAAN, Quart. J. Pharm. Pharmacol. *4*, 14 (1931).

[3] E. SPÄTH, W. GRUBER und O. MATZKE, Canad. J. Chem. *31*, 715 (1953).

[4] Auf ganze Grade abgerundet $[\alpha]_D$-Werte in Chloroform.

[5] E. SPÄTH, P. K. BOSE, J. MATZKE und N. C. GUHA, Ber. dtsch. chem. Ges. *72*, 821 (1939).

[6] E. SPÄTH und M. PAILER, Ber. dtsch. chem. Ges. *68*, 940 (1935).