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SHORT COMMUNICATION

ON THE NATURAL OCCURRENCE AND RELATIVE CONFIGURATIONS OF THE TETRAHYDROACTINIDIOLIDE ISOMERS

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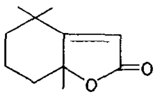
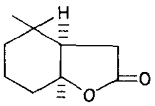
Abstract—The isolation from tobacco of *trans*-tetrahydroactinidiolide and a one-step synthesis of this isomer are reported. Confirmation of the assignments of relative configuration was obtained through examination of the NMR spectra for both of the tetrahydroactinidiolide isomers and model compounds.

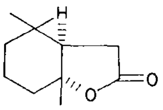
A NUMBER of reports have described the isolation[1] and synthesis[2] of dihydroactinidiolide (I). More recently, tetrahydroactinidiolide (IIa) was found to be a constituent of cigar tobacco leaves.[3] Furthermore, IIa was shown to be identical with the product obtained by catalytic hydrogenation of I. We wish to describe herein the isolation of a tobacco constituent (IIb) isomeric with IIa and the assignments of relative configuration for both isomers.



I

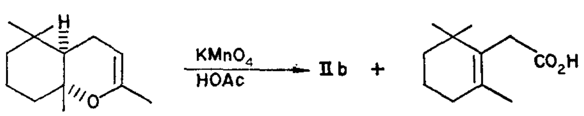


IIa



IIb

During the early 1960's, while pursuing characterization of constituents from Turkish tobacco, both I and a component assigned a gross structure corresponding to either IIa or IIb were isolated. Compound IIb (m.p. 75–80°; i.r. (liquid film) 1767, 1241, 1224, 1170,



IIIb

bp 125–127° (20mm)

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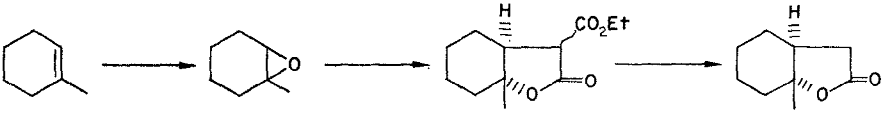
[1] (a) J. BRICOUT, R. VIANI, F. MÜGGLER-CHAVAN, J. P. MARION, D. REYMOND and R. H. EGLI, *Helv. Chim. Acta* **50**, 1517 (1967); (b) K. INA, Y. SAKATO and H. FUKAMI, *Tetrahedron Letters* 2777 (1968); (c) S. FUKUSHIMA, Y. AKAHORI and T. TSUNEYA, *Yakugaku Zasshi* **88**, 646 (1968); (d) W. C. BAILEY, JR., A. K. BOSE, R. M. IKEDA, R. H. NEWMAN, H. V. SECOR and C. VARSEL, *J. Org. Chem.* **33**, 2819 (1968); (e) T. SAKAN, S. ISOE and S. B. HYEON, *Tetrahedron Letters* 1623 (1967).

[2] (a) M. MOUSSERON-CANET, J. C. MANI and J. P. DALLE, *Bull. Soc. Chim. France* 608 (1967); (b) S. ISOE, S. B. HYEON, H. ICHIKAWA, S. KATSAMURA and T. SAKAN, *Tetrahedron Letters* 5561 (1968); (c) E. DEMOLE and P. ENGGIST, *Helv. Chim. Acta* **51**, 481 (1968).

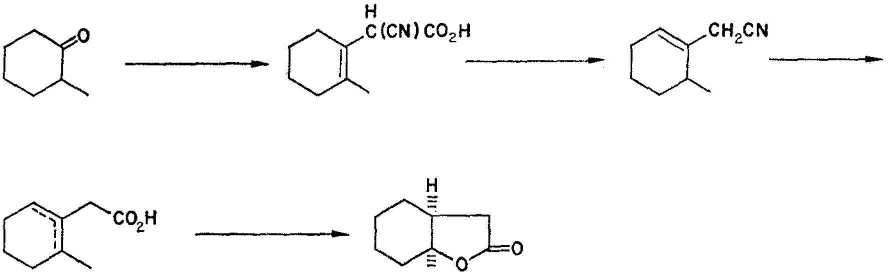
[3] H. KANEKO and K. HOSHINO, *Agri. Biol. Chem.* **33**, 969 (1969).

1149, 1029, 1005, 954, 922, 914, 883 cm^{-1}) was readily synthesized from the unsaturated oxide IIIb previously prepared by Smit *et al.*[4] from geranyl acetone. Surprisingly, none of IIa was obtained, even though a by-product, β-cyclohomogeranic acid, yields IIa exclusively on acid-catalyzed cyclization.[1c,2c] Similar treatment of the geometrical isomer of IIIb (IIIa, b.p. 111–114° (20 mm)) afforded exclusively IIa.

Further confirmation of the above assignments was obtained by inspection of the NMR spectra for the model compounds IV and V. Lactone IV was obtained by the stereospecific method of Ficini and Maujean.[5] With regard to the synthesis of V, a required intermediate (6-methyl-1-cyclohexen-1-yl)-acetonitrile was prepared from 2-methylcyclohexanone by the method used previously for the preparation of cyclohexen-1-acetonitrile from cyclohexanone.[6] Saponification gave a 3:1 mixture of olefinic acids enriched in the required positional isomer for formation of V. Cyclization of the mixture of acids using aqueous, ethanolic hydrochloric acid gave rise to a single lactone, V. Exclusive formation of the *cis*-fused lactone was expected in light of a report by Klein regarding the lactonization of 1-cyclohexene-1-acetonitrile under strongly acid conditions.[7]



IV



V

Perhaps the most diagnostic features concerning stereochemistry in the NMR spectra of lactones IIa, IIb, IV, and V are the chemical shifts of the angular methyl groups. These data are as follows:

TABLE 1

	τ (CDCl$_3$)	$\Delta\nu$ (ppm)
IIb	8·68	0·16
IIa	8·52	
IV	8·77	0·15
V	8·62	

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[4] V. A. SMIT, V. A. SEMENOVSKII, A. V. RUDENKO and V. F. KUCHEROV, *Izv. Akad. Nauk. SSR, Otd. Khim Nauk* 1782 (1963).

[5] J. FICINI and A. MAUJEAN, *Comptes Rend.* **263**, 425 (1966).

[6] A. C. COPE, A. A. D'ADDIECO, D. E. WHYTE and S. A. GLICKMAN, *Organic Synthesis*, Coll., Vol. IV, p. 234, John Wiley and Sons, New York (1963).

[7] J. KLEIN, *J. Org. Chem.* **23**, 1209 (1958).

In both pairs of isomers the chemical shift value was higher for the *trans* lactone than for the *cis* isomer. That this empirical correlation is most likely meaningful for isomeric pairs is indicated by the nearly equal values of Δv.

In summation, the assignments of configuration for IIa and IIb reside in several experimental facts; (a) the NMR data previously mentioned, (b) hydrogenation of I yields only IIa, which, a priori, would be expected for *cis* addition of hydrogen from the least hindered side of I, and (c) cyclization of β-cyclohomogeranic acid (HCO_2H–H_2SO_4) affords IIa. The formation of the more stable *cis* lactones under these conditions is well-precedented.[5,8,9] We acknowledge the recent work of Demole and Enggist (2c) who, on thermodynamic grounds, have proposed the same configuration for IIa. Hopefully, our corroboration of stereochemistry for IIa and IIb will facilitate future work in this area. The absolute configurations of actinidiolide and dihydroactinidiolide ($[\alpha]_D^{15}$ + 7·1°, isolated from *Actinidia polygama*) (1e) evidently are still unknown.*

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* Dihydroactinidiolide isolated from various tobaccos was found in this laboratory to have a specific rotation of zero degrees at a variety of wavelengths. We have not accumulated any information concerning the optical activities of IIa or IIb.

[8] M. F. Ansell and M. H. Palmer, *Quart. Rev. London* **18**, 211 (1964).

[9] W. Herz and L. A. Glick, *J. Org. Chem.* **28**, 2970 (1963).