

STEREOCHEMISTRY OF DIELS-ALDER ADDITION TO
LEVOPIMARIC ACID. MAGNETIC SHIELDING BY THE
CARBON-CARBON DOUBLE BOND

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DIELS-Alder adducts of levopimaric acid (I) with many dienophiles are known.² With symmetrical dienophiles, for example maleic anhydride, the reaction seems to be highly stereoselective, only one of four possible isomers (IIa-d) being formed in high yield. Although it has been hypothesized,^{2d, 3} on the basis of the Alder rules⁴ and steric hindrance by the angular methyl group to β -face approach of the dienophile, that the adduct corresponds to IIa, no evidence on this point has heretofore been reported. We wish to record such evidence.

¹ Contribution No. 1044.

^{2a} H. Wienhaus and W. Sandermann, Ber. 69, 2202 (1936);

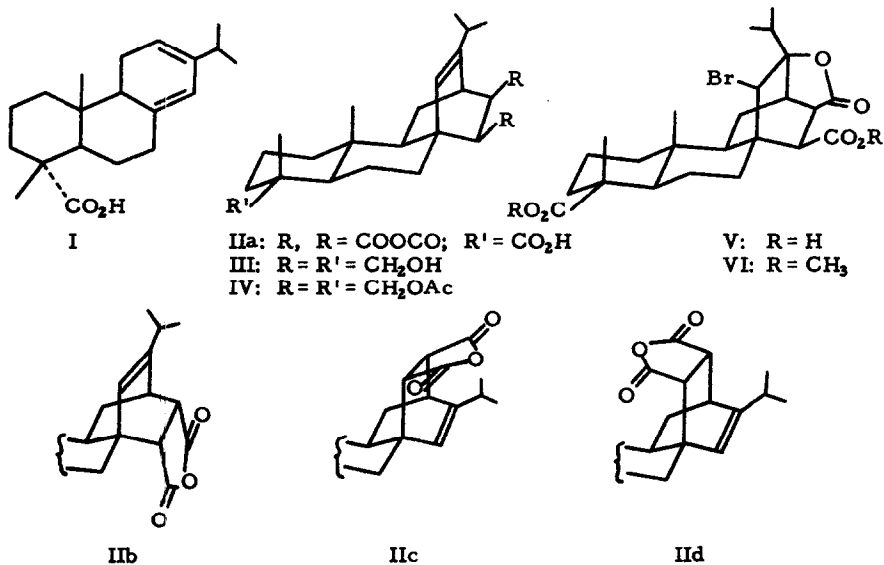
b R. V. Lawrence and N. J. Halbrook, Ind. Eng. Chem. 50, 321 (1958);
J. Amer. Chem. Soc. 80, 368 (1958);

c B. A. Arbuzov and A. G. Khismatullina, Izvest. Akad. Nauk S. S. S. R.,
Otdel. Khim. Nauk 2126 (1959);

d N. J. Halbrook, J. A. Wells and R. V. Lawrence, J. Org. Chem. 26,
2641 (1961).

³ W. D. Lloyd and G. W. Hedrick, J. Org. Chem. 26, 2029 (1961).

⁴ K. Alder and G. Stein, Angew. Chem. 50, 510 (1937).



The NMR spectrum⁵ of the maleic anhydride adduct II contains the expected vinyl proton singlet at 4.47 τ , and has four sharp lines in the C-methyl region. Two of these are the doublet ($\tau = 8.99$, $J = 7$ c. p. s.) from the two equivalent methyls of the isopropyl group, and the 8.82 τ singlet corresponds to the C-4 methyl.⁶ The C-10 methyl group resonance falls

⁵ Nuclear magnetic resonance line positions were determined by the audiofrequency sideband method on a Varian DP-60 spectrometer operating at 60 mc., using tetramethylsilane as internal standard.

⁶ The peaks are observed at 71, 64, 57, and 37 c. p. s. Assignments follow from the observation that $\text{CH}(\text{CH}_3)_2$ coupling constants should be about 7 c. p. s. (ref. 7), and thus the isopropyl doublet is observed at either 71 and 64 or 64 and 57 c. p. s. It has been found that in several series conversion of a C-4a (A/B trans) diterpenic function from carboxyl to methylol or methylol acetate produces a 0.4 τ upfield shift in the resonance of the C-4 methyl (unpublished observations in our laboratories and those of Professor E. Wenkert), and when II is so altered (III and IV), the 71 c. p. s. peak shifts to 50 c. p. s. while the positions of the other three methyl resonances are unchanged. This marks 71 c. p. s. as C-4 methyl, 37 c. p. s. as C-10 methyl, and 64 and 57 c. p. s. for the isopropyl.

at abnormally high field,⁷ 9.38 τ , indicating that the C-10 methyl group is unusually magnetically shielded.⁸ Structure IIc provides no mechanism for such shielding, but the anhydride carbonyl groups in IId or the olefinic bond in IIa or IIb could produce such an effect. That the former is not the explanation is seen from NMR spectra of the triol III, m. p. 181-182°, (Found: C, 76.6; H, 10.8. $C_{24}H_{40}O_3$ requires: C, 76.55; H, 10.71%) formed by lithium aluminum hydride reduction of II, and the corresponding amorphous triacetate IV (Found: C, 71.5; H, 9.0. $C_{30}H_{46}O_6$ requires: C, 71.68; H, 9.02%). Both III and IV also have the C-10 methyl resonance at 9.38 τ , and had it been the carbonyl groups which shielded the methyl, their removal should have resulted in a downfield shift of the methyl resonance. Thus only IIa and IIb, in which the C-10 methyl group is held directly above the plane of the double bond and is shielded by its π -system, are compatible with these NMR data.⁹

It has been shown¹⁰ that on bromination in aqueous base II is converted to a bromolactone diacid V (R=H), and that a number of other lactonic derivatives can be prepared. Formation of these lactones involves interaction of the anhydride carboxyls with the double bond, and thus supports exclusion of IId and further excludes IIb in which the functionality is not suitably oriented to interact.¹⁰ That the remaining structure IIa is

⁷ J. C. W. Chien, *J. Amer. Chem. Soc.* **82**, 4762 (1960) reports that the C-10 methyl resonance of a series of saturated resin acid derivatives falls very near 9.20 τ .

⁸ See H. Conroy in "Advances in Organic Chemistry", Vol. 2. Interscience Publishers, New York, 1960, pp. 285-286.

⁹ For recent examples see R. R. Fraser, *Can. J. Chem.* **40**, 78 (1962), and G. Slomp, F. A. MacKellar and L. A. Paquette, *J. Amer. Chem. Soc.* **83**, 4472 (1961).

¹⁰ L. H. Zalkow and R. A. Ford, Abstracts of Papers, 140th American Chemical Society Meeting, Chicago, Illinois, Sept. 3-8, 1961, p. 83Q. L. H. Zalkow, R. A. Ford and J. P. Kutney, *J. Org. Chem.* in press. Professor Zalkow has informed us that he and his collaborators have independently concluded that the adduct is IIa.

indeed correct is further supported by examination of the dimethyl ester VI, m.p. 225-226° (Found: C, 58.7; H, 7.1; Br, 15.7. $C_{26}H_{37}BrO_6$ requires: C, 59.42; H, 7.10; Br, 15.21%) prepared from the bromolactone V. This ester has infrared absorption at 5.60μ , substantiating the γ -lactone structure, and at 5.71 and 5.81μ corresponding to the ester groups. The NMR spectrum of VI is consistent with the functionality,¹¹ showing a singlet resonance from one proton (CHBr) at 5.47τ , a single sharp line from two methoxyls at 6.37τ , a series of lines corresponding to four C-methyls in the 8.75 - 9.08τ region, and no resonance from vinyl hydrogen. The angular methyl resonance occurs at 8.98τ , well downfield from its position in the unsaturated derivatives II-IV. This shift of the C-10 methyl resonance on saturation of the olefinic bond and introduction of a bromine atom in the vicinity of the methyl supports the conclusion that it is indeed the olefinic group which shields the methyl group. Only structure IIa is compatible with all the data.

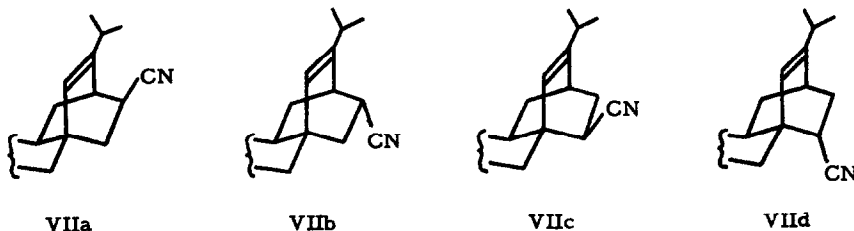
It is worth noting that an α -orientation at C-9 is required to allow the methyl group and the double bond to be in the necessary juxtaposition for the observed shielding to occur. Since conditions for the Diels-Alder reaction are unlikely to cause epimerization of levopimaric acid at C-9, this lends support to the 9α -H configuration recently assigned to the latter molecule.¹²

Diels-Alder reaction of I with acrylonitrile affords a mixture of two adducts.^{2d} In both of these the C-10 methyl resonance occurs at 9.38τ ,

¹¹ An alternate formulation with bromine at C-13 and γ -lactone at C-14 is not excluded by this evidence, but seems less likely mechanistically.

¹² W. H. Schuller and R. V. Lawrence, *J. Amer. Chem. Soc.* **83**, 2563 (1961); A. W. Burgstahler, H. Ziffer and U. Weiss, *J. Amer. Chem. Soc.* **83**, 4660 (1961).

and thus like II both correspond to structures resulting from α -face attack of dienophile, the isomers differing in the location or orientation of the cyano group (VIIa-d). Although the positions of C-10 and C-4 methyl resonances are identical in the two isomers, differences in the vinyl (4.47 and 4.58 τ) and isopropyl (8.94 and 8.99 τ) resonances are clearly observed. These differences are best interpreted in terms of proximity of the cyano group to one or the other of these substituents, leading to a preference for structures VIIa and VIIc over VIIb and VIId where the cyano, regardless of its position, is too distant from the vinyl and isopropyl groups to shield or deshield their protons. Complete structural assignments to these and other adducts will be the subject of a future communication.



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