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# Geometrical isomerism in $\beta$-methyl-$\alpha$-$\beta$-unsaturated diterpenic acids by NMR spectroscopy

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# SEZIONE II

## (Fisica, chimica, geologia, paleontologia e mineralogia)

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**Chimica.** — *Geometrical isomerism in β–methyl–α–β–unsaturated diterpenic acids by* NMR *spectroscopy* (*). Nota di FRANCO DELLE MONACHE, GIULIANO DELLE MONACHE e GIOVANNI BATTISTA MARINI BETTOLO, presentata (**) dal Corrisp. G. B. MARINI BETTOLO.

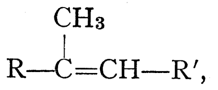
RIASSUNTO. — Sono stati esaminati gli spettri di RMN, in $CCl_4$ ed in $C_6H_6$, di vari acidi diterpenici β–metil–α–β–insaturi.

La determinazione dello spostamento chimico subito dal metile adiacente al carbonio insaturo ha permesso di stabilire l'isomeria geometrica del doppio legame in 13–14.

We have recently described the isolation the structure and configuration of three β–methyl–α–β–unsaturated diterpenic acids, i.e. copaiferic A (I ; $R=CH_3$, $R'=H$), copaiferolic (I ; $R=CH_2OH$, $R'=H$) and 11,hydroxy-labd-8(20)-13-dien-15-oic acids (I ; $R=CH_3$, $R'=OH$) found in the oleoresin of *Copaifera multijuga* [1], [2].

We now report new data which enable us to establish the geometrical isomerism at $\Delta^{13-14}$ double bond.

NMR spectroscopy provides a suitable method for this purpose. In the case of system $R—CH=CH—R'$ the determination of the coupling constants of the two protons [3] (J *cis* = 6–14 *cps*; J *trans* = 11–18 *cps*) is sufficient.

This is not possible in the case of systems  $R—\overset{\overset{CH_3}{|}}{C}=CH—R'$, because the costants of allylic coupling between the methyl and the proton are very small and no correlations can be made.

L. M. Jackman and R. H. Wiley [4] have shown that β–methyl group in α–β–unsaturated esters are specifically "deshielded" by about 0.25 *ppm* when *cis* to a carboxy group, and their signals are invariably found at lower fields than in *trans* compounds.

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(**) Nella seduta del 14 novembre 1970.

This require the availability of both isomers in order to establish the double bond geometry for any particular case.

J. Ronayne and D. H. Williams [5] have studied the "solvent shift" ($\Delta = \delta_{CCl_4} — \delta_{C_6H_6}$) of the β–methyl in a series of α–β–unsaturated aliphatic esters and have observed a preferential "shielding" in benzene solution of the $CH_3/COOCH_3$ *trans*: Δ *cis* = + 0.26 *ppm*, Δ *trans* = + 0.61 *ppm*, Δ *trans*—Δ *cis* = + 0.35 *ppm*.

The method could enable us to establish the double bond configuration on a single isomer, but it cannot be generalized to any class of substances.

TABLE I.

| | $CH_3/COOCH_3$ | $CH_3—C = C—COO$ | |
|---|---|---|---|
| | | $\delta_{CDCl_3} — \delta_{C_6H_6}$ | Δ |
| Copaiferic acid A (I ; R = $CH_3$, R′ = H) . . . . . | *trans* | 1.88–1.64 | + 0.24 |
| Labd–13–en–8α–ol–13–oic acid (II), isomer m.p. 130° | *trans* | 1.91–1.64 | + 0.27 |
| Copaiferic acid B (I ; R = $CH_3$, R′ = H) . . . . . | *cis* | 2.15–2.20 | — 0.05 |
| Labd–13–en–8α–ol–13–oic acid (II), isomer m.p. 98. | *cis* | 2.16–2.28 | — 0.12 |
| Copaiferolic acid (I ; R = $CH_2OH$, R′ = H) . . . . | *cis* | 2.17–2.20 | — 0.03 |
| Copaiferalic acid (I ; R = CHO, R′ = H) . . . . . | *cis* | 2.17–2.20 | — 0.03 |
| Acetyl–copaiferolic acid (I ; R = $CH_2—O—CO—CH_3$, R′ = OH) . . . . . . . . . . . . . . . . . | *cis* | 2.17–2.20 | — 0.03 |
| 11–Hydroxy–labd–8–(20)–13–dien–15–oic acid (I ; R = $CH_3$, R′ = OH) . . . . . . . . . . . | *cis* | 2.17–2.20 | — 0.03 |
| 11–Acetoxy–labd–8–(20)–13–dien–15–oic acid (I ; R = $CH_3$, R′ = $OCOCH_3$) . . . . . . . . . | *cis* | 2.17–2.20 | — 0.03 |
| Labd–8–(20)–13–dien–15–19 dioic acid (I ; R = $COOCH_3$ , R′ = H) . . . . . . . . . . | *cis* | 2.17–2.21 | — 0.04 |
| Agathic acid (I ; R = $COOCH_3$, R′ = H; $C_4$–epimer) | *cis* | 2.14–2.21 | — 0.07 |
| Kolavic acid (III) . . . . . . . . . . . . . . . . | *cis* | 2.17–2.20 | — 0.03 |

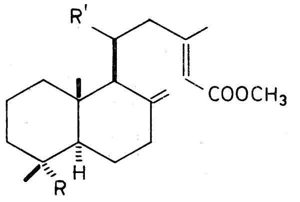
In the case of the above reported, diterpene acids of "*Copaifera multijuga*" and their derivatives, the *cis* methyl was *always* subject to a slight "deshielding effect" in benzene solution ($\Delta = \delta_{CCl_4} — \delta_{C_6H_6} = — 0.05$ *ppm*), in disagreement with the finding on simple acids [5] which show *always* a "shielding" effect of the β–methyl in benzene solution.

Having available both isomers, i.e. copaiferic B and A acids, and labd-13-en-8 α-ol-15-oic isomer *mp* 98° and *mp* 130° [6], it was possible to show (Table I) that, whereas in the case of $CH_3/COOCH_3$ *trans* the methyl group shows in benzene solution a "shielding" effect ($\Delta_{trans} = \delta_{CDCl_3} - \delta_{C_6H_6} = + 0.24$ *ppm*), in the case of $CH_3/COOOH_3$ *cis* shows a slight "deshielding" effect ($\Delta_{cis} = \delta_{CDCl_3} - \delta_{C_6H_6} = - 0.05$ *ppm*).

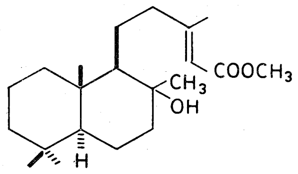
Moreover in the first case the methyl group appears at ~ 1.88 *ppm*; in the second at ~ 2.17, in agreement with Jackman's observations [4].

On the basis of the NMR spectra of similar diterpene acid, i.e. agathic acid and kolavic [6] we may therefore attribute to these substances a *cis* relationship between the C–13 methyl and C–14 ester groups.

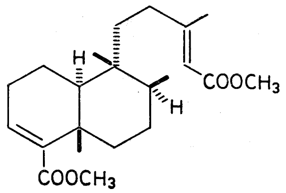
Furthermore the methylene group at $C_8$ shows a particular effect, i.e. two broad singlets always. In the case of $CH_3/COOCH_3$ *cis* are not subject to "solvent shift" or to slight "shielding" solvent shift, whereas with $CH_3/COOCH_3$ *trans* (copaiferic A acid) the two protons show a different "deshielding solvent shift" (— 0.13 and — 0,23 *ppm* respectively).



I



II



III

Also the $CH_3$ at $C_8$ of the labd-13-en-8-α-ol-15 oic acids shows a "shielding solvent shift" (+ 0.15 *ppm*) in the case of the isomer *mp* 98° ($CH_3/COOCH_3$ *cis*) whereas the isomer *mp* 130° ($CH_3/COOCH_3$ *trans*) shows a "deshielding effect" (— 0,06 *ppm*).

The above reported results indicate that the "solvent shift" observed in aliphatic α–β–unsaturated esters ($\Delta_{cis} = + 0.26$; $\Delta_{trans} = + 0.61$) [5] cannot be *generalized* to all α–β–unsaturated esters. In effect the application of the above criteria to copaiferic A acid would have let to assign to this compound a *cis* isomerism whereas it has clearly demonstrated a *trans* geometry.

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[3] L. M. JACKMAN and S. STERNHELL, Application of NMR Spectroscopy in Org. Chem. Pergamon Press.

[4] L. M. JACKMAN and D. H. WILEY, « J. Chem. Soc. », 2886 (1960).

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[6] We are indebted to Prof. C. DJERASSI for labd–13–en–8 α–ol–15–oic acids, to Prof. C. ENZELL for agathic acid and to Prof. S. DEV for kolavic acid.