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I N D I C E

NARDI R., PUCCINELLI A., PATELLA D. - Applicazione del metodo del sondaggio dipolare profondo lungo una sezione dalle Alpi Apuane all'Appennino pistoiese <i>The deep dipolar electric sounding method application along a section from the Alpi Apuane to the Apennines, north Pistoia</i>	Pag. 1
BAGNOLI G. - Segnalazione di Conodonti Devoniani nel Paleozoico della Ma- remma senese (Nota preliminare) <i>First discovery of Devonian Conodonts in the Paleozoic Basement of the Siena Region (Tuscany) (Preliminary report)</i>	» 23
TORRE D. - Orientamenti attuali della tassonomia <i>Recent views on the Taxonomy</i>	» 27
DE MUNNO A., BERTINI V. - Action of N-bromosuccinimide on 3-methyl-1, 2, 5- thiadiazole <i>Azione della N-bromosuccinimide sul 3-metil-1, 2, 5-tiadiazolo</i>	» 43
MENESINI E. - Echinidi fossili dell'Arcipelago maltese. I. <i>Maltese Fossil Echinoids. I.</i>	» 51
RAPETTI F., VITTORINI S. - Il deflusso liquido e torbido del T. Roglio (Bacino dell'Arno), relativi al 1977, in relazione ai processi di erosione nelle argille plioceniche <i>Liquid and solid transport in the T. Roglio (Arno Basin) of the year 1977, related to the processes of erosion into pliocenic clays</i>	» 65
SALA B. - La faune pré-würmienne des grands Mammifères de la Grotte du Poggio (Marina de Camerota, Salerne) <i>Le faune prewürmiane a grandi Mammiferi della Grotta del Poggio (Marina di Camerota, Salerno)</i>	» 77
MORELLI I., CATALANO S., SCARTONI V., PACCHIANI M., MARSILI A. - Boron tri- fluoride-catalysed rearrangements of some tetrasubstituted neotriter- pene epoxides. V - Fragmentation of 21,22-epoxy-A'-neogammaceranes <i>Trasposizioni catalizzate da trifluoruro di boro di alcuni epossidi neo- triterpenoidici tetrasostituiti. Nota V. Frammentazione dei 21, 22-epos- si-A'-neogammacerani</i>	» 101
CARMIGNANI L., GIGLIA G. - Large scale reverse « drag folds » in the late alpine building of the Apuane Alps (N. Apennines) <i>Pieghe di trascinamento a grande scala e a simmetria inversa nell'edi- ficio alpino tardivo delle Alpi Apuane (Appennino Settentrionale)</i>	» 109
DALLEGNO A., GIANELLI G., LATTANZI P., TANELLI G. - Pyrite deposits of the Gavorrano area, Grosseto <i>I depositi di pirite della zona di Gavorrano (Grosseto)</i>	» 127
GRAZZINI M. - Identification et analyse de petits globes dans certaines brèches ophiolithiques <i>Identificazione e analisi di globuli in brecce ofiolitiche</i>	» 167

FRAVEGA P., VANNUCCI G. - Facies di retroscogliera nei calcari giurassico-cretacei di Punta Garavano (Balzi Rossi - Ventimiglia) <i>Back-reef facies in Punta Garavano limestones (Balzi Rossi - Ventimiglia)</i>	» 177
GIUSTIZIA F. - Il deposito musteriano nel riparo i Grottoni presso Calascio (L'Aquila). Nota preliminare <i>The mousterian deposit of « I Grottoni » rock shelter near Calascio (L'Aquila, Italy). Preliminary report</i>	» 189
RADMILLI A. M., MALLEGGNI F., LONGO E., MARIANI R. - Reperto umano con industria acheuleana rinvenuto presso Roma <i>Human femoral fragment with acheulean industry discovered near Rome</i>	» 203
SAITTA M. - Automatizzazione della elaborazione dei dati relativi ad un sistema di analisi di routine in campioni di rocce <i>Automatic processing of data produced in a system of routine analyses of rock samples</i>	» 215
LEONI L., ORLANDI P. - La thaumasite della miniera del Temperino (Campiglia M.ma) <i>Thaumasite from Temperino mine (Campiglia M.ma)</i>	» 241
ORLANDI P., CHECCHI F. - L'ulmannite del M.te Corchia (Alpi Apuane). <i>Ulmannite from Apuan Alps</i>	» 245
MARTINI F. - Segnalazione di un'industria musteriana presso Impruneta (Firenze) <i>A Mousterian lithic industry found near Impruneta (Florence)</i>	» 249
BORGOGNINI TARLI S., PALMA DI CESNOLA A. - Su alcuni resti umani rinvenuti nel deposito Gravettiano della Grotta Paglicci nel Gargano <i>Human skeletal remains from the Gravettian layers of Pagli cave (Gargano headland, Foggia, Italy)</i>	» 261
CIONI O., GAMBASSINI P., TORRE D. - Grotta di Castelcivita: risultati delle ricerche negli anni 1975-77 <i>Results of recent researches (1975-77) in the Castelcivita Cave (Salerno)</i>	» 275
GALIBERTI A., BARTOLI G. - Proposta di una scheda tipo per la classificazione e lo studio dei bifacciali del Paleolitico inferiore mediante elaborazione meccanografica <i>Proposal of a standard card for the study of handaxes of lower paleolithic by mechanographic elaboration</i>	» 297
BARGAGLI R., GALIBERTI A., ROSSI C., SARTI L. - Il giacimento musteriano di Montemileto (Avellino) <i>The mousterian site of Montemileto (Avellino, Italy)</i>	» 341
RADI G. - Resti di un villaggio neolitico a Villa Badessa (Pescara) <i>Remains of a neolithic village found near Villa Badessa (Pescara)</i>	» 405
PENNACCHIONI M. - Nuovi dati e precisazioni sull'insediamento preistorico di Torre Crognola (Vulci - Viterbo) <i>New data and specifications about the prehistoric settlement of Torre Crognola (Vulci, Viterbo, Italy)</i>	» 415
ACCORSI C. A., AIELLO E., BARTOLINI C., CASTELLETTI L., RODOLFI G., RONCHITELLI A. - Il giacimento Paleolitico di Serino (Avellino): stratigrafia, ambienti e paletnologia <i>The paleolithic site of Serino (Avellino - Italy): stratigraphy, environment, palaethnology</i>	» 435

I. MORELLI, S. CATALANO, V. SCARTONI, M. PACCHIANI,
A. MARSILI (*)

BORON TRIFLUORIDE-CATALYSED REARRANGEMENTS
OF SOME TETRASUBSTITUTED NEOTRITERPENE EPOXIDES
V. - FRAGMENTATION OF 21, 22-EPOXY-A'-
NEOGAMMACERANES (**)

Riassunto — *Trasposizioni catalizzate da trifluoruro di boro di alcuni epossidi neotriterpenoidici tetrasostituiti. Nota V. Frammentazione dei 21, 22-epossidi-A'-neogammacerani.* Il 21 β , 22-epossidi-A'-neogammacerano (1) e il suo epimero (2), per azione del complesso trifluoruro di boro-etere, si frammentano per dare acetone e 22, 29, 30-trisnor-B':A'-neogammacer-13(18)-ene (3). L'olefina trisostituita (6), che dovrebbe essere il primo prodotto della frammentazione, è stata preparata per disidratazione del bisnoradiantolo (5a) o dell'isobisnoradiantolo (5b). Trattando (6) con trifluoruro di boro si ha rapida conversione nell'olefina tetrasostituita (3). Un'ulteriore prova della struttura di quest'ultimo prodotto è stata ottenuta per trasformazione del corrispondente epossido (7) nel biciclononanone (8), nell'alcool (9), nell'olefina trisostituita (10) e, infine, nel diene (11). Sulla base dei presenti risultati, e di risultati analoghi ottenuti precedentemente da composti simili, viene proposto un meccanismo, per la frammentazione, che comporta la formazione di un intermedio ossetanico.

Abstract — 21 β , 22-Epoxy-A'-neogammacerane (1) and its epimer (2), undergo fragmentation to acetone and 22, 29, 30-trisnor-B':A'-neogammacer-13(18)-ene (3) on treatment with boron trifluoride-ether complex. The trisubstituted olefin (6), which should be the primary fragmentation product, was prepared by dehydration of either bisnoradiantol (5a) or isobisnoradiantol (5b); boron trifluoride converted (6) into (3). A further proof of the structure of the latter product was obtained by conversion of the corresponding epoxide (7) into the bicyclononanone (8), alcohol (9), olefin (10), and, finally, diene (11). On the basis of the present results, and of results previously obtained from similar compounds, a mechanism involving formation of an oxetane intermediate is proposed for the fragmentation reaction.

Key words — Hopane and trisnor-hopane derivatives.

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In a previous paper (MORELLI et Al., 1979) a novel fragmentation reaction, caused by the action of boron trifluoride-ether complex on the two epimeric epoxides derived from 3-(1-methylethylidene)-A-norcholestane was described. Evidence about the possibility that an oxetane should be the most likely reaction intermediate was also provided.

In order to obtain further proofs that this fragmentation is really peculiar of epoxides derived from olefins having the 1-isopropylidenehydrindane nucleus as structural unit, the behaviour of the A'-neogammacerane epoxides (1) and (2) has been investigated also.

RESULTS AND DISCUSSION

As it was previously reported (MORELLI and MARSILI, 1970), A'-neogammacer-21-ene, on treatment with *p*-nitroperbenzoic acid, gives the two epimeric epoxides (1) and (2) in the ratio 33:67. The reactions of these two products with pyridinium chloride and with hydrochloric acid in ethanol were described (MORELLI and MARSILI, 1970).

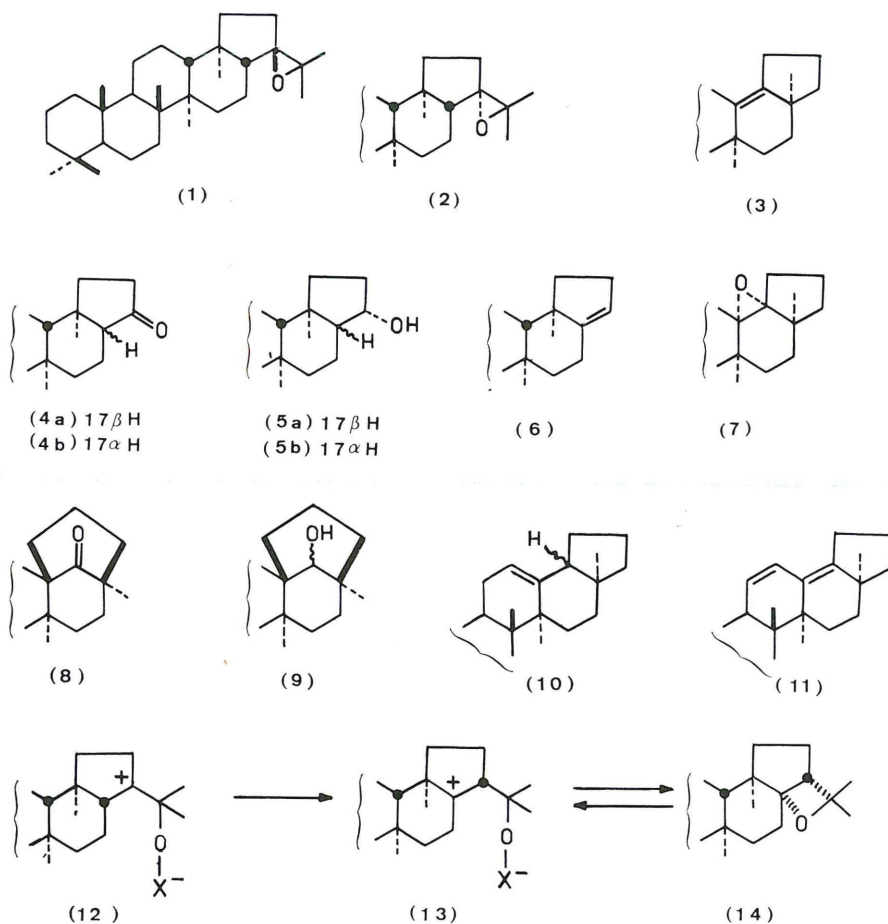
When (1) and (2) were treated with boron trifluoride-ether complex, acetone and a tetrasubstituted olefin were formed. On the basis of the results obtained previously (MORELLI et Al., 1979), the behaviour appeared at first sight anomalous, since the olefin originated in the fragmentation would have had structure (6). Indeed, this latter compound, prepared by treatment of either (5a) or (5b) ⁽¹⁾ with phosphorus oxychloride in pyridine, was easily converted to (3) either by hydrochloric acid or by boron trifluoride-ether complex.

A further proof of the structure of (3) was obtained as follows. Epoxide (7) ⁽²⁾, obtained by treatment of (3) with *m*-chloroperben-

(1) These two compounds were obtained by reduction with lithium aluminium hydride of 21-oxo-22, 29, 30-trisnor-(17 β H)-A'-neogammacerane (4a) (bisnoradiantone) (BERTI et Al., 1963) and its 17 α H-epimer (4b) (isobisnoradiantone) (BERTI et Al., 1963) respectively. The hydroxyl group at C21 in both (5a) and (5b) was shown to have an α -configuration, by using Horeau's method (HOREAU and KAGAN, 1964). This means that hydride attack at C21 of either (4a) or (4b) occurs on the β -side, the α -side being sterically hindered by the methyl groups at C14 and C18.

(2) The structure and configuration of this epoxide, as well as those of compounds (8), (9), (10), and (11), were assigned both on the basis of their spectroscopic characteristics (Experimental) and by analogy with the results obtained previously from 13,18 α -epoxy-B':A'-neogammacerane (hopene-II oxide) (BERTI et Al., 1971).

zoic acid, was transformed by boron trifluoride-ether complex into the bicyclononanone (8); this compound was reduced by lithium aluminium hydride to the mixture of epimeric alcohols (9), which gave the trisubstituted olefin (10) on treatment with phosphorus oxychloride in pyridine. Brief treatment of (10) with hydrochloric acid in chloroform gave (3). The action of hydrochloric acid in ethanol on epoxide (7) led to diene (11).



As already discussed in our previous paper (MORELLI et Al., 1979), the first step of the fragmentation reaction should be attack of the reagent (BF_3) on oxygen of (1) and (2), fission of C21-O bond,

and formation of carbocation (12). Subsequently, hydride shift from C17 to C21 would lead to carbocation (13), whose stereochemistry at C21 should be determined by the hydride shift, which occurs by the same face of the molecule: therefore, the same cation is formed both from (1) and from (2). Cation (13) could undergo fragmentation directly, before formation of oxetane (14). However, it is not unlikely that (13) and (14) may be in equilibrium, as indicated. Indeed, an oxetane such as (14) may be considered the ring tautomeric equivalent of (13).

It is indeed well known that hindered oxetanes undergo fragmentation into ketones and alkenes when treated with acids (SEARLES Jr., 1964).

An oxetane has been shown to arise from 3-(1-methylethylidene)- Δ -A-norcholestane oxide, by the action of alumina (I. MORELLI et AL., 1979), and other cases of oxetane formation in the treatment of epoxides with Lewis' acids have been described (COXON et AL., 1969; GUEST and MARPLES, 1970).

EXPERIMENTAL

M.ps were determined with a Kofler apparatus; I.R. spectra were recorded for Nujol mulls with a Perkin-Elmer 137 spectrophotometer; U.V. spectra were determined for solutions in cyclohexane with a Beckman D.U. spectrophotometer; N.M.R. spectra were recorded for solutions in deuteriochloroform with a JEOL C-60 HL spectrometer (Me_4Si as internal standard); specific rotations were measured for 1% solutions in chloroform at 25° with a Perkin-Elmer 141 photoelectric polarimeter; G.L.C. analyses were performed with a Carlo Erba Fractovap 2300 gas-chromatograph (column: 3% OV 17 silicone rubber on Gas-Chrom. Q. 80-100 mesh, temp. 220°, injection block temp. 270°, carrier gas N_2 , flow rate 50 ml/min). The organic solutions were dried with magnesium sulphate. Light petroleum refers to the fraction of b.p. 40-60°.

22, 29, 30-Trisnor-B':A'-neogammacer-13 (18)-ene (3). - A solution of *21-22-epoxy-A'-neogammaceranes* (1) and (2) (0.5 g) in dry chloroform (25 ml), treated with boron trifluoride-ether complex (2.5 ml), was left 1 min at room temp., washed with aqueous sodium carbonate, dried and evaporated. The product, dissolved in light petroleum, was chromatographed over neutral alumina. The light

petroleum eluate gave (3) (0,35 g), m.p. 172-175° (from acetone) $[\alpha]_D + 12.7^\circ$, none olefinic protons (Found: C, 88.3; H, 12.5. $C_{27}H_{44}$ requires C, 88.0; H, 12.0). Further elution with ether gave no product. When the reaction mixture was treated with aqueous sodium carbonate and steam-distilled into 2,4-dinitrophenylhydrazine solution, acetone-2,4-dinitrophenylhydrazone was obtained, m.p. 124-126° (from ethanol).

21 α -Hydroxy-22, 29, 30-trisnor-(17 β H)-A'-neogammacerane (5a). - *Bisnoradiantone (4a)* (80 mg) in dry ether (40 ml) was refluxed 1 h with lithium aluminium hydride (60 mg). Treatment with water, filtration, evaporation, and crystallisation from acetone gave (5a), m.p. 197-200°, $[\alpha]_D + 41.9^\circ$ (Found: C, 83.5; H, 12.15. $C_{27}H_{46}O$ requires C, 83.9; H, 12.0). This compound (30 mg) was treated with a 0.33 M solution of 2-phenylbutyric anhydride in pyridine (0.8 ml) and left at room temp. for 15 h. After addition of water (2 drops) and heating on a steam bath for 30 min, water (2 ml), excess 1N sodium hydroxide and benzene (3 ml) were added and the solution was extracted two times with benzene. The aqueous layer was acidified with 1N hydrochloric acid and extracted with benzene; the organic layer, when concentrated to 2 ml, had $\alpha_D + 0.010^\circ \pm 0.002$.

21 α -Hydroxy-22, 29, 30-trisnor-(17 α H)-A'-neogammacerane (5b). - *Iso-bisnoradiantone (4b)* (70 mg), reduced with lithium aluminium hydride as described for bisnoradiantone, gave (5b), m.p. 207-210° (from chloroform-methanol), $[\alpha]_D + 30.5^\circ$ (Found: C, 84.0; H, 11.9. $C_{27}H_{46}O$ requires C, 83.9; H, 12.0). The configuration at C21 was determined by Horeau's method as described for (5a). The α_D obtained from 30 mg of alcohol was $+ 0.015^\circ \pm 0.002$.

22, 29, 30-Trisnor-A'-neogammacer-(17)21-ene (6). - A solution of (5a) or (5b) (30 mg) in pyridine (3 ml) was treated with phosphorus oxychloride (0.3 ml) and heated 1 h on a steam bath. Usual work-up, followed by filtration of a light petroleum solution of the product through alumina, gave (6), m.p. 145-147° (from acetone), $[\alpha]_D + 47.1^\circ$, δ 5.8 (1H, m) (Found: C, 88.15; H, 11.9. $C_{27}H_{44}$ requires C, 88.0; H, 12.0).

Rearrangement of (6) with acids. - a) Olefin (6) (50 mg) in chloroform (5 ml) was treated with boron trifluoride-ether complex (0.5 ml). After 1 min at room temp., usual work-up gave (3) (35 mg). b) Olefin (6) (30 mg) was refluxed with 5% ethanolic hydrochloric acid (30 ml) for 1 h. Usual work-up afforded pure (3) (20 mg).

22, 29, 30-Trisnor-13, 18 α -epoxy-B':A'-neogammacerane (7). - Olefin (3) (200 mg) and 75% *m*-chloroperbenzoic acid (120 mg) in chloroform (10 ml) were stored at 5° for 20 h, then washed with aqueous sodium carbonate, water, dried, and evaporated. Epoxide (7), crystallised from acetone, had m.p. 158-160°, $[\alpha]_D + 23.2^\circ$ (Found: C, 83.95; H, 11.8. C₂₇H₄₄O requires C, 84.3; H, 11.55).

18-Oxo-22, 29, 30-trisnor-19(18 \rightarrow 13)abeo-B':A'-neogammacerane (8). - Epoxide (7) (100 mg) in dry chloroform (10 ml) was treated with boron trifluoride-ether complex (1 ml). After 30 min at room temp. the solution was washed with aqueous sodium carbonate, water, dried, and evaporated. The product, dissolved in light petroleum, was chromatographed over neutral alumina. Light petroleum eluted no products; ether eluted (8) (80 mg), m.p. 195-198° (from acetone-methanol), $[\alpha]_D + 21.5^\circ$, $\nu_{\max} 1.705 \text{ cm}^{-1}$ (CO) (Found: C, 84.05; H, 11.75. C₂₇H₄₄O requires C, 84.3; H, 11.55).

18 ξ -Hydroxy-22, 29, 30-trisnor(18 \rightarrow 13)abeo-B':A'-neogammacerane (9). - A solution of (8) (110 mg) in dry ether (45 ml) was refluxed for 2 h with lithium aluminium hydride (80 mg). Usual work-up gave (9) (90 mg), m.p. 204-209° (from acetone), $[\alpha]_D + 10.8^\circ$ (Found: C, 83.6; H, 12.05. C₂₇H₄₆O requires C, 83.9; H, 12.05).

22, 29, 30-Trisnor-B':A'-neogammacer-12-ene (10). - Alcohol (9) (70 mg) in pyridine (4 ml) was treated with phosphorus oxychloride (0.4 ml) and heated for 2 h on a steam bath. Usual work-up afforded (10) (50 mg), m.p. 160-163° (from acetone), $[\alpha]_D + 49.0$, δ 5.33 (1H, m) (Found: C, 87.7; H, 12.2. C₂₇H₄₄ requires C, 88.0; H, 12.0).

Conversion of (10) into (3). - A solution of (10) (30 mg) in chloroform (30 ml), saturated with hydrogen chloride, was stored at room temp. for 7 h and evaporated. The product, dissolved in light petroleum, was filtered over alumina. The eluate gave (3) (20 mg).

22, 29, 30-Trisnor-B':A'-neogammacera-11, 13(18)-diene (11). - A solution of (7) (100 mg) in ethanol (50 ml) and conc. hydrochloric acid (5 ml) was refluxed for 2 h. Dilution with water, usual work-up and crystallisation from acetone gave (11) (65 mg), m.p. 177-180°, $[\alpha]_D + 54.3^\circ$, λ_{\max} 246 (ϵ 23,700), 255 (27,000), 265 nm (17,500), 2 olefinic H (AB part of an ABX system centered at δ 5.8 ppm, J_{AB} 10.0 Hz) (Found: C, 88.0; H, 11.85. C₂₇H₄₂ requires C, 88.45; H, 11.55).

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