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DIADDUCTS FROM METHYL DIAZOACETATE AND NORBORNADIENE

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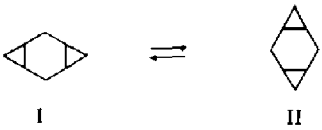
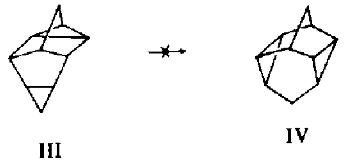
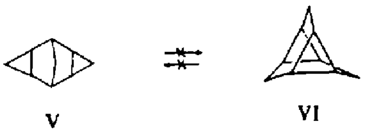
Abstract—Structural assignments given to the two isomeric diadducts arising from reaction of norbornadiene and methyl diazoacetate have been reinvestigated. The results are interpreted to indicate that the two isomers have unrearranged, tetracyclo[3.3.1.$0^{2,4}$.$0^{6,8}$]nonane, structures IX and XVIII and do not undergo facile thermal valence isomerization to tetracyclo[3.3.1.$0^{2,8}$.$0^{4,6}$]nonanes.

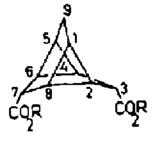
In a recent communication Schleyer[1] has drawn attention to the fact that thermal automerizations of the type (I) ⇄ (II) are formally forbidden by Hoffmann–Woodward rules. In line with these predictions, Schleyer found that the pentacyclodecane (III) was stable below 550° and failed to isomerize to "tetradehydroadamantane" (IV). Reference was also made to unpublished results of Doering and of Musso which lend further support to the predictions: isomerization of the *exo–exo* and *endo–exo* stereoisomers of the tetracyclononane (V) to triasterane (VI), and the reverse reaction, failed to occur on heating.



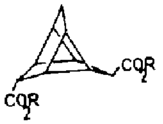




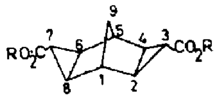
One further example has been reported by Baylouny and Jaret,[2] and the conclusions reached in this case are in contrast to the previous examples. The two diadducts arising from copper catalysed reaction of methyl diazoacetate with norbornadiene were assigned structures VIIa and VIIIa. These products presumably arise via facile thermally induced valence isomerization (of the type I $\rightleftarrows$ II) of the initially formed adducts (IXa and Xa). In view of the examples cited earlier it is difficult to visualize how in these substituted tetracyclononanes (IXa and Xa) the isomerization becomes energetically more favourable. There would appear to be very little support for the idea that the additional activation arises from steric factors since the carbomethoxy substituents as represented are free of pertinent nonbonded interactions. Moreover, on electronic grounds one would not expect substituents at C-atoms 7 and 3 to dramatically influence bond breaking and bond forming processes occurring at C-atoms 2, 4, 6 and 8 (structures IX and X).



VII



VIII



IX

X

a: R = Me; b: R = H

At the time Baylouny's report came to our notice, we were exploring the potential of the reaction between norbornadiene and diazoacetic ester as a source of tetracyclo-$[3.3.1.0^{2,4}.0^{6,8}]$nonanes, (IX and X). Our results, reported below, suggest that the products have the structures IX and XVIII and that these compounds are thermally stable.

RESULTS AND DISCUSSION

Copper catalysed reaction of methyldiazoacetate with norbornadiene according to the procedure of Baylouny and Jaret* gave two isomeric diesters: Isomer A (m.p. 135–136°) and Isomer B (m.p. 115–116·5°). Mainly on the basis of PMR spectra, these authors assigned structure VIIa to Isomer A and structure VIIIa to Isomer B. The PMR spectra are shown in Fig. 1.

Recapitulating the arguments used by Baylouny, the symmetrical nature of the spectrum of Isomer A, suggests a structure such as VIIa or IXa. The high field signal at τ 9·52 (2 protons) implies absorption by two equivalent cyclopropyl protons. Both structures VIIa and IXa contain a set of two such protons, however only in structure VIIa would these two protons, H_1 and H_5, be expected to resonate at high field since in the alternate structure IXa, the relevant protons, H_3 and H_7, would be deshielded by the contiguous carbomethoxy substituents. Accordingly, in terms of Baylouny's preferred structure VIIa, the remaining signals were assigned as follows: τ 8·34 (4 protons, H_2, H_4, H_6 and H_8), τ 8·08 (2 protons, triplet, $J = 2{\cdot}5$ Hz, H_3 and H_7), τ 7·46 (2 protons, $2 \times H_9$) and τ 6·42 (6 protons, $2 \times$ MeO). The clean triplet nature of the signal at τ 8·08 practically necessitates assignment to the two carbomethoxy methine protons, H_3 and H_7.

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* We wish to express our gratitude to Dr Baylouny for providing us with his experimental details.

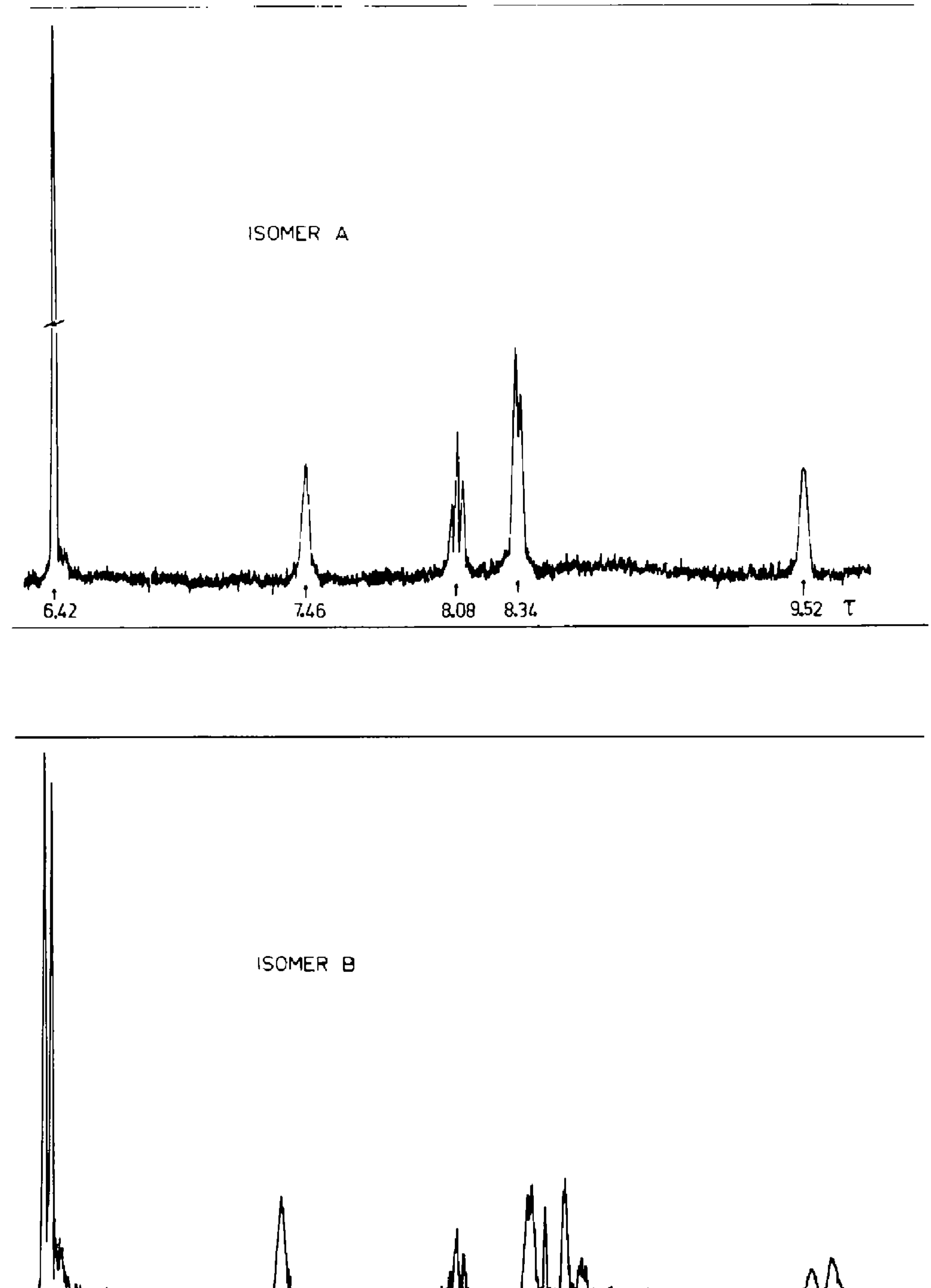


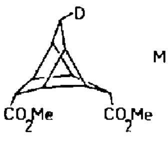
FIG. 1 100 MHz spectra of Isomer A and Isomer B in $CDCl_3$ solution.

Upon further scrutiny of Baylouny's assignment we noted an anomalous relationship between the chemical shifts of the two equivalent H_9 protons and the two equivalent carbomethoxy methine protons, H_3 and H_7. In the absence of the carbomethoxy substituents these two sets of protons would be equivalent. Introduction of the two carbomethoxy substituents would be expected to cause H_3 and H_7 to resonate downfield from the two H_9 protons and not upfield as in the above assignments. Reversal of the assignments of these two sets of proton would appear to remove this anomaly, however another difficulty arises. Triasterane (VI), the parent hydrocarbon corresponding to structure VIIa, gives a PMR spectrum in which the methylene signals occur at τ 7·73.[3] The deshielding of H_3 and H_7 (0·27 ppm) is then consistent with structure VIIa for Isomer A but the concomitant shielding (0·35 ppm) of the two H_9 protons is difficult to rationalize.

An alternative explanation would appear to be that the thermal valence isomerization, IXa → VIIa, had not occurred and indeed that isomer A can best be represented by structure IXa. If one assumes that the highfield signal at τ 9·52 is due, not to cyclopropane protons, but to the bridge methylene protons H_9 (in structure IXa) which are shielded by the proximate cyclopropane rings,[*] then the remaining signals may be assigned quite unambiguously in terms of structure IXa. The four proton signal at τ 8·34 may be assigned to H_2, H_4, H_6 and H_8; the two proton triplet at τ 8·08 to H_3 and H_7 ($J = 2{\cdot}5$ Hz, *trans* vicinal cyclopropane coupling[6]); and the two proton signal at τ 7·46 to the bridgehead protons H_1 and H_5. It is therefore apparent that the foregoing PMR data still allows for some ambiguity in assignment of structure to isomer A.

In order to resolve this ambiguity we reacted 7-monodeuterionorbornadiene (XI) with excess methyl diazoacetate. If isomer A has structure VIIa the monodeuterio-analogue (XII) would show integration for one less proton in τ 7·7 region; if on the other hand isomer A has structure IXa the monodeuterio-analogue (XIII) should integrate for one less proton in the τ 9·52 signal. The monodeuterio-analogue was found to integrate for 1·05 protons in the highfield signal. This result can be rationalized in terms of structure IXa only.

XI



XII

XIII

PMR double resonance experiments yielded results also consistent with structure IXa. Irradiation of the signal at τ 9·52 caused a 20% increase in the relative intensity of the two proton triplet at τ 8·10. The occurrence of this intramolecular nuclear Overhauser effect confirms the fixed, proximate spatial relationship between H_3 (H_7) and H_9.[7]

The relative reactivity of isomer A towards bases also suggests structure IXa. When treated with sodium methoxide in methanol-O-d at 70° for 3 days, isomer A

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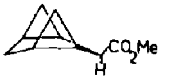
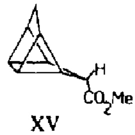
[*] This assumption is not without some support. One of the bridge methylene protons in the *exo*-epoxide of norbornene resonates at τ 9·3.[4] Compounds with related structural features show highfield absorption (τ 9·4) ascribable to bridge protons.[5]

failed to show evidence of epimerization and of deuterium incorporation. The α-hydrogen of ethyl cyclopropanecarboxylate is known to be inert towards bases.[8] In contrast, compounds with structures closely related to VII and VIII equilibrate and/or exchange under similar conditions. For example, the *syn*-epimer of 2-carbomethoxy-*endo*-tricyclo[5.1.0.0^{3,5}]octane[9] (XIV) incorporates deuterium ($t_{\frac{1}{2}}$ ca. 11 hr) when treated with 0·08M sodium methoxide in methanol-0-d at 25° and equilibrates in 0·13M sodium methoxide-methanol at 50° with a half life of about 2·5 hr.[10] Prinzbach[11] has shown that the α-hydrogen of the tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octane derivative (XV) is reactive towards sodium methoxide-methanol.



XIV

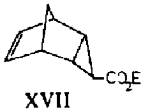


XV

Isomer A was stable up to 350° (maximum temp tried). Saponification with potassium hydroxide-methanol gave the corresponding diacid (IXb). Despite considerable experimentation this diacid could not be converted to an intramolecular anhydride as originally claimed by Baylouny.[2] Only polymeric anhydrides resulted.

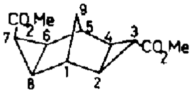
Isomer B displays a PMR spectrum (Fig. 1) which may be interpreted also in terms of a rearranged structure (such as VIIIa) or an unrearranged structure (such as Xa). The spectrum of this isomer shows significant differences from that of isomer A. The carbomethoxy groups are nonequivalent as are the two highfield protons. Furthermore, the carbomethoxy methine triplet at τ 8·07 accounts for only one proton; the other carbomethoxy methine signal is included in the 8·30 to 8·65 multiplet which integrates for five protons. Using arguments similar to those used for isomer A, isomer B was shown to have the unrearranged skeleton since the corresponding d$_1$-isomer B prepared from 7-d$_1$-norbornadiene integrated for one less proton in the τ 9·5 to 9·7 region. Isomer B was stable up to 350°.

XVI



XVII

Since the monoadducts arising from the addition of carboethoxy carbene to norbornadiene are considered to have structures XVI and XVII[6d] we therefore tentatively (and incorrectly) concluded that isomer B had structure Xa. However, on treatment with sodium methoxide in methanol, isomer B was converted quantitatively to isomer A. Using methanol-0-d in this reaction gave isomer A which was shown by PMR spectroscopy to contain 0·83 atoms of deuterium at position 3 (or 7), i.e. the triplet at τ 8·08 integrated for 1·16 protons. It therefore appears that isomer A and isomer B are epimeric at one C atom and that epimerization of isomer B (thermodynamically less stable isomer) proceeds under basic conditions by initial hydrogen abstraction rather than, say, cyclopropane ring opening followed by ring closure. Accordingly, isomer B was assigned structure XVIII. The observation that isomer B forms isomer A under base catalysed equilibrating conditions and that isomer B contains a relatively acidic proton may be accounted for in terms of this structure. Then *endo* carbomethoxy substituent at C-7 would be under steric compression and would transform under basic conditions to the *exo* position with relative ease. This same compression would, at least in part, be responsible for the relative acidity of the C-7 hydrogen although the accessibility of this H atom towards attacking base could undoubtedly contribute. This situation is closely analogous to that of 6-carbomethoxybicyclo[3.1.0]hexane[12] and 7-phenylbicyclo[4.1.0]heptane.[13]



XVIII

As might be expected, saponification of isomer B gave a mixture of diacids. The components of this mixture were not separated, however re-esterification with diazomethane and VPC analysis of the mixture of diesters showed three components: isomer B (10%), isomer A (68%) and an unknown component (22%). Insufficient material prevented an investigation of this unknown component but in terms of structure XVIII it is highly probable that products arising from nucleophilic ring-opening addition[14] could be formed during saponification.[15,]*

EXPERIMENTAL

All m.ps and b.ps were uncorrected. Microanalyses were performed at the Australian Microanalytical Service, Melbourne. Preparative and analytical VPC were carried out using an Aerograph 700 Autoprep with the following conditions. (a) Column ¼" O.D., 10 ft, 15% Apiezon L on non acid washed Chromosorb W 60/80 at 250° (injector 260°). (b) Column ¼" O.D., 10 ft, 15% Ucon 50-HB-2000 on non acid washed Chromosorb W 60/80 at 55° (injector 80°). PMR spectra refer to CCl_4 solns and were recorded using a Varian A-60 or HA-100 spectrometer. Chemical shifts were measured on the τ-scale relative to internal TMS. Relative areas of signals are shown in brackets.

Reaction of norbornadiene with excess methyl diazoacetate. Methyl diazoacetate was reacted with norbornadiene according to the procedure of Baylouny and Jaret.[2] Isolation and purification gave two isomeric, crystalline diadducts. Isomer A, (IXa), after crystallization from MeOH gave m.p. 135–136° (reported[2] 137–139°). Found: C 66·48, H 6·95. Calc. for $C_{13}H_{16}O_4$: C 66·08, H 6·83%; PMR: 9·52, s,* $W_{\frac{1}{2}h}$ = 4 Hz (1·97); 8·34, d, $J = 2·5$ Hz (3·94); 8·08, tr, $J = 2·5$ Hz (1·97); 7·46, s, $W_{\frac{1}{2}h}$ = 3 Hz (1·97); 6·42, sharp, s (6·06).

Isomer B, (XVIII), after crystallization from MeOH gave m.p. 115–116·5° (reported[2] 119·5–120°). Found: C 66·30, H 6·89, Calc for $C_{13}H_{16}O_4$: C 66·08, H 6·83%; PMR: 9·5 to 9·7, two overlapping broad s's, (1·95); 8·3 to 8·65, m (5·10); 8·07, tr, $J = 2·5$ Hz (0·99); 7·35, s, $W_{\frac{1}{2}h}$ = 3 Hz (2·00); 6·39 and 6·37, sharp s's, (5·97).

Both isomers were unchanged (as gauged by PMR) after heating at 350° for 3 hr in sealed evacuated ampoules. Further, both isomers were stable to VPC conditions with injector and column temps of up to 260 and 250°, respectively.

Reaction of 7-monodeuterionorbornadiene with excess methyl diazoacetate. 7-Monodeuterionorbornadiene (>95% monodeuterated) was reacted with methyl diazoacetate under conditions identical to the above. The products were isolated by preparative VPC (conditions a). d_1-Isomer A, (XIII), gave m.p. 135·5–136·5°; PMR: 9·52, broad s, (1·02); 8·34 d, (3·90); 8·08, tr, $J = 2·5$ Hz (2·00); 7·46 s, (2·07); 6·42, s, (6·06). d_1-Isomer B, 9-monodeuterio-*exo*-*endo*-3,7-dicarbomethoxy-*exo*-*exo*-tetracyclo[$3.3.1.0^{2,4}.0^{6,8}$]nonane, gave m.p. 115·5–116·5°; PMR: 9·5 to 9·7, two overlapping broad s's, (1·03); 8·3 to 8·65 m, (4·88); 8·07, tr, $J = 2·5$ Hz (1·06); 7·35, s, (2·03); 6·39 and 6·36, s's, (6·0).

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* Meinwald and Crandall[15] discuss a pertinent example which to our knowledge is the only case of a cyclopropane containing one electron attracting substituent and yet sufficiently activated to undergo nucleophilic ring-opening addition. This additional activation is apparently derived from structural strain.

* s = singlet, d = doublet, tr = triplet, etc.

Attempted deuterium exchange on isomer A. A soln of isomer A (40 mg) in 0·5 M NaOMe in MeOD-0-d[16] (8 ml; 98% deuterium) was sealed in an ampoule and kept at 70° for 3 days. The mixture was then poured into water (50 ml) and the product extracted into ether (2 × 40 ml). The ethereal soln was washed with water (2 × 40 ml) and dried (Na_2SO_4). Evaporation of the solvent left a crystalline residue (35 mg) which after crystallization (once) from aqueous MeOH gave m.p. 135–136°, undepressed on admixture with isomer A. The PMR spectrum of this product was identical with that of isomer A. VPC analysis (conditions a) of the crude product showed only isomer A (>99%).

Saponification of isomer A. Isomer A (10 g) was dissolved in 10% KOH aq in MeOH (300 ml) and the mixture stirred overnight at room temp. The reaction mixture was diluted with water (3 l.), acidified with dil HCl and then continuously extracted with ether (2 × 1 l.). The combined ether extracts were washed with water (2 × 300 ml), dried ($MgSO_4$) and the solvent evaporated to yield a solid (8·4 g; 96% yield). Vacuum sublimation (once) of a portion of this solid gave an analytically pure sample of the diacid, m.p. >280°. (Found: C 63·68, H 5·95. Calc. for $C_{11}H_{12}O_4$: C 63·45, H 5·81%).

A sample of the crude diacid was esterified with an ethereal solution of diazomethane. Analytical VPC (conditions a) of the crude dimethyl ester showed only one component (>99%) with retention time identical to that of isomer A. After crystallization (once) from aqueous MeOH the product gave m.p. 135–136°, undepressed on admixture with isomer A.

Reaction of isomer B with sodium methoxide-methanol. A soln of isomer B (22 mg) in 0·5M NaOMe in MeOH (5 ml) was sealed in an ampoule and kept at 70° for 20 hr. The mixture was then poured into water (50 ml) and the product extracted into ether (3 × 60 ml). The ethereal soln was washed with water (1 × 50 ml) and dried (Na_2SO_4). Evaporation of the solvent gave a crystalline residue (20 mg) which consisted of one component (>99%) by analytical VPC (conditions a). The retention time was identical to that of isomer A. After crystallization (once) from aqueous MeOH the product gave m.p. 135–136° which was undepressed on admixture with isomer A.

The above reaction was repeated using MeOD-0-d (>98% deuterium) and the product crystallized (once) from aqueous MeOH. The PMR spectrum of this product was almost identical to that of isomer A except the triplet at τ 8·10 integrated for 1·16 ± 0·03 protons relative to each of the remaining four signals.

Saponification of isomer B. Isomer B (85 mg) was saponified using conditions similar to those used for the saponification of isomer A, to give the crude diacid (73 mg; 98% yield). A portion of this product was sublimed (once) under vacuum to give an analytical sample, m.p. >280°. (Found: C 63·09, H 5·89. Calc. for $C_{11}H_{12}O_4$: C 63·45, H 5·81%). The remaining crude diacid was esterified with an ethereal soln of diazomethane. Analytical VPC (conditions a) showed the presence of three components: isomer B (10%; identified by retention time only), isomer A (68%; identified by retention time only) and an unknown (22%).

Preparation of 7-chloronorbornadiene. 7-t-Butoxynorbornadiene[17] (28·7 g) was dissolved in Na-dried ether (150 ml) and dry HCl was bubbled through the soln at room temp for 12 hr. The solvent was evaporated under reduced press at 15 to 20° and the residue diluted with fresh ether (300 ml, Na-dried). The dark phase which developed, was separated from the clear ethereal phase. The ethereal phase was dried ($CaCl_2$) and then evaporated under reduced press at 15 to 20° to give 7-chloronorbornadiene (16 g; 72%) of >95% purity as gauged by PMR.

The product was used, without further purification, in the following step.

Preparation of 7-deuterionorbornadiene. Dry 7-chloronorbornadiene (16 g) was dissolved in a mixture of THF (160 ml) and t-butanol-0-d[18] (22 g; >95% monodeuterated). Finely cut Na (11 g) was added and the mixture stirred under reflux for 9 hr. Unreacted Na was removed by filtration and the filtrate diluted with water (1500 ml). The aqueous mixture was extracted with ether (3 × 150 ml). The ethereal soln was washed with water (5 × 50 ml), dried ($MgSO_4$) and evaporated under reduced press to yield a mixture of 7-deuterionorbornadiene and THF. Preparative VPC (conditions b) gave the monodeuterated olefin; PMR: 8·03 (tr, $J = 2$ Hz, rel. area 1·01); 6·49 (m, rel. area 1·96); 3·35 (tr, $J = 2$ Hz, rel. area 4·03).

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