Tetrahedron, 1965, Vol. 21, pp. 2907 to 2912. Pergamon Press Ltd. Printed in Northern Ireland

CARBONIUM ION REACTIONS OF NORBORNENYLCARBINYL SYSTEMS

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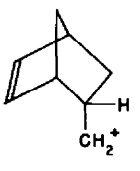
(*Received* 26 *April* 1965; *in revised form* 17 *May* 1965)

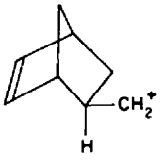
Abstract—Carbonium ion reactions of 5-norbornenylcarbinyl systems have been investigated. The major kinetically controlled product of reactions of the *endo*-system is *exo*-bicyclo(3.2.1)oct-2-en-3-ol. The *exo*-system yields chiefly *endo*-tricyclo (2.2.2.$O^{2,6}$)octan-3-ol, with essentially no crossover products in either case.

INTRODUCTION

FOR some time we have been interested in ring expansion reactions of bi- and tricyclic ring systems.[1] As an outgrowth of this and because of a general interest in carbonium ion reactions of bicyclic systems, we initiated a study of reactions designed to produce carbonium ion intermediates (I and II). We were particularly intrigued by the possibility of generating the tricyclic cation (III) from the *endo*-system by the "π-route."[2]



I



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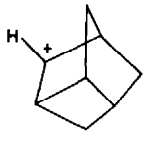


III

RESULTS

The cations in question were generated in two different ways, amine deamination and arenesulfonate solvolysis. The requisite starting materials were the two amines IVa and Va and the *p*-bromobenzenesulfonates IVb and Vb. They were prepared by unexceptional means and were submitted to treatment with nitrous acid and buffered acetic acid conditions, respectively.

The major product of the reactions of the *endo*-systems was the rearranged system, *exo*-bicyclo(3.2.1)oct-2-en-3-ol (VI), first prepared by Wildman and Saunders.[3] Essentially no tricyclic products were found. Structure proof was based on comparison

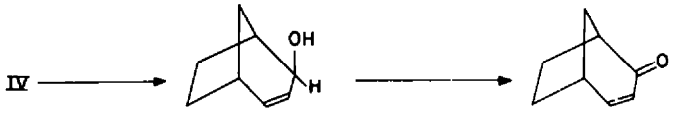
[1] [a] R. R. Sauers and J. A. Beisler, *Tetrahedron Letters No* 32, 2181 (1964); [b] R. R. Sauers and J. A. Beisler, *J. Org. Chem.* 29, 210 (1964); [c] R. R. Sauers and R. J. Tucker, *Ibid.* 28, 876 (1963); [d] R. R. Sauers, *Tetrahedron Letters* 146 (1961); [e] R. A. Parent, R. R. Sauers and H. M. How, *Abstracts of Papers, 148th Meeting of the Amer. Chem. Soc.* p. 58S. Chicago (1964).

[2] S. W. Winstein and P. Carter, *J. Amer. Chem. Soc.* 83, 4485 (1961). This ion, if formed, would be expected to be stable to the reaction conditions, see R. R. Sauers and R. A. Parent, *J. Org. Chem.* 28, 605 (1963).

[3] W. C. Wildman and D. R. Saunders, *J. Amer. Chem. Soc.* 76, 946 (1954).

IV a X = NH_2
b X = OBs

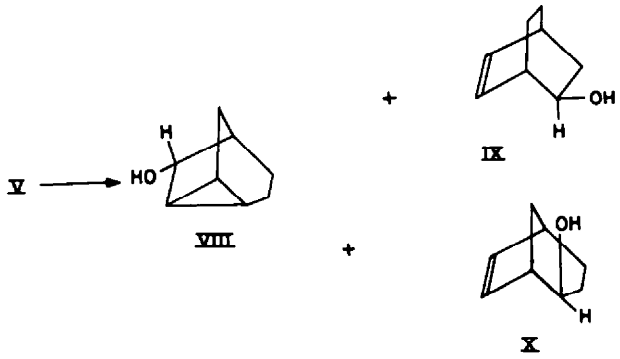
V a X = NH_2
b X = OBs



VI VII

of physical data and conversion of alcohol VI to the α,β-unsaturated ketone (VII) by means of manganese dioxide.[4]

Deamination of the *exo*-amine (Va) with nitrous acid led to a complex mixture of products. The major product (ca. 70%) was shown to be *endo*-tricyclo(2.2.2.$0^{2,6}$)-octan-3-ol (VIII) by comparison with an authentic sample.[5] Minor amounts of *exo*-bicyclo(2.2.2)oct-2-en-5-ol (IX) and *exo*-bicyclo(3.2.1)oct-6-en-2-ol (X) were also found. Again, absence of crossover products was indicated by the absence of VI from this reaction product. The acetolysis results led to similar products but in markedly



VIII IX X

differing ratios. Subsequently, it was found that the reaction conditions were sufficient to cause isomerization of VIII and hence the observed products were probably not the result of kinetic product control.

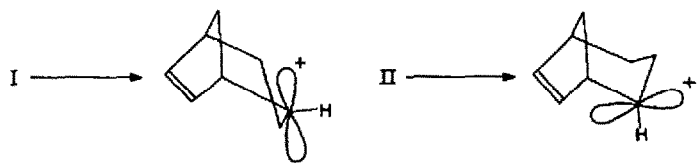
DISCUSSION

Rationalization of these results is relatively straightforward by a combination of the studies of related systems. The results of Berson *et al.* are particularly significant

[4] The correct stereochemistry of VI was simultaneously assigned by us[1d] and by H. L. Goering, R. W. Greiner and M. F. Sloan *J. Amer. Chem. Soc.* **83**, 1391 (1961).

[5] We are deeply indebted to Prof. N. A. LeBel for samples and spectra of several of these materials.

in this respect.[6] These workers studied the saturated analogues and found that there was little crossover between the two ionic systems generated from the *exo*- and *endo*-norbornylcarbinyl derivatives. In other words, subsequent reactions of the ions initially produced were faster than interconversion of them. In the case at hand then, it seems reasonably to postulate that I and II lead mainly to XI and XII respectively, by direct ring expansion.[7] Models show that the p-orbital on C-2 in XI is not suitably



XI XII

oriented with respect to the π-orbital of the double bond for effective overlap. As in the saturated analogue, the C_1–C_8 bond is nearly parallel with the long axis of this orbital and hence migration of this bond is energetically more favorable.[6] The rearranged ion (XIII) is allylic and presumably is attacked by solvent at either end to give VI.[1d,3,4]

XIII

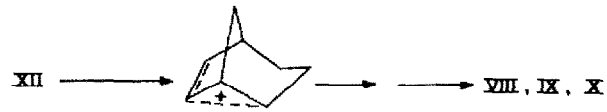
In contrast, effective overlap between the empty p-orbital and the π-bond is possible in XII and migration of the C_1–C_8 bond is stereoelectronically unfavorable.[6] The result is that a new series of products is formed which strongly resemble those obtained by LeBel and Huber in their study of the *exo*-bicyclo(2.2.2)oct-5-en-2-ol system.[8] Thus, XIII could be transformed into the observed products *via* collapse of XIV with solvent. Since the rearranged products predominate in both series, it would seem that these reactions are highly concerted or involve non-classical ions.

[6] J. A. Berson and P. Reynolds-Warnhoff, *J. Amer. Chem. Soc.* **86**, 595 (1964) and J. A. Berson and D. Willner, *Ibid.* **86**, 609 (1964).

[7] Ring expansion in the other direction would not be expected for I[6] but could be expected to occur to the extent of ca. 18% in the *exo* series. This alternative cannot be excluded since not all of the products have been identified. Unfortunately such products, if produced, have not yet been prepared by unambiguous routes.

A referee has suggested the possibility of isomerization of Vb to the nortricyclylcarbinyl system as a possible source of some of the unidentified products. This can be only a minor competing pathway since essentially none of the expected major products of solvolysis of that system were found.

[8] N. A. LeBel and J. E. Huber, *J. Amer. Chem. Soc.* **85**, 3193 (1963); see also R. R. Fraser and S. O'Farrell, *Tetrahedron Letters* 1143 (1962). This ionic system has been entered in a third manner by J. A. Berson and J. J. Gajewski, *J. Amer. Chem. Soc.* **86**, 5020 (1964).



XIV

EXPERIMENTAL

All gas-liquid chromatography was done isothermally on an Aerograph, Model A-90-P, gas chromatograph, using 15–20% stationary phase on firebrick and column diameters are stated as outer diameters. All NMR spectra were taken on a Varian Model A-60 analytical NMR spectrometer, and all recorded chemical shifts are relative to tetramethylsilane (internal standard). CCl_4 was used as solvent unless otherwise specified. IR spectra were run on a Perkin–Elmer Model 21 IR spectrophotometer unless otherwise specified. M.ps were taken on a Mel-Temp capillary apparatus and are uncorrected.

endo- *and* exo-5-*Cyanobicyclo*[2.2.1]*heptene*-2. The synthesis of 5-cyanobicyclo[2.2.1]heptene-2 was carried out according to Alder *et al.*[9] The *endo* and *exo* nitriles were then separated by distillation on a 3′ × 1″ Todd column packed with stainless steel perforated saddles using a reflux ratio of 10:1. The distillation was monitored by gas chromatography using a 6′ × ¼″ tricresyl phosphate column at 100°. Distillation of 576·7 g nitrile resulted in 146·0 g pure *exo* isomer (b.p. 78·1°/12·2 mm, n_D^{25} 1·485; lit.[9] b.p. 80·5°/12 mm, n_D^{20} 1·4862), 163·0 g of a 1:1·33 *exo-endo* mixture, and 171·8 g pure *endo* isomer (b.p. 88·6–90·1°/12·5 mm, n_D^{25} 1·4867; lit.[9], b.p. 88·0°/12 mm) representing an 83·5% recovery from the distillation.

exo-5-Cyanobicyclo[2.2.1]heptene-2 had strong IR absorptions (CCl_4) at 2950 cm^{-1}, 2185 cm^{-1} and 702 cm^{-1}, while the *endo* isomer showed absorptions at 2960 cm^{-1} and 710 cm^{-1}. The NMR spectra of these isomers showed complex multiplets centered at 3·8, 6·8 and 8·2 τ for the *exo* nitrile, and an octet centered at 3·7, and complex multiplets centered at 7·0, 7·8 and 8·6 τ for the *endo* compound. Relative proton areas were consistent with the assigned structures.

endo-5-*Aminomethylbicyclo*[2.2.1]*heptene*-2 (IVa). A solution of *endo*-5-cyanobicyclo[2.2.1]heptene-2 (23·8 g, 0·20 mole) in 150 ml dry ether was added dropwise to a stirred suspension of LAH (8·6 g, 0·23 mole) in 400 ml dry ether at a rate such that the ether was maintained at reflux. The reaction mixture was heated under reflux for 1 hr, at which point the excess LAH was decomposed with wet ether followed by water. The solids were filtered and washed with ether. The combined ether solutions were then dried overnight over KOH, filtered, and distilled, affording 21·67 g (88·1%) *endo*-5-aminomethylbicyclo[2.2.1]heptene-2 (b.p. 57°/4·5 mm). This amine picked up CO_2 very rapidly and thus presented difficulty in its handling (Found: N, 11·20. $C_8H_{13}N$ requires: N, 11·37.)

endo-5-Aminomethylbicyclo[2.2.1]heptene-2 has strong IR absorption (film) at 3300 cm^{-1}, 3400 cm^{-1} and 717 cm^{-1}, and has a NMR spectrum consisting of a multiplet centered at 3·9 τ and a series of complex multiplets centered at 8·3 τ.

The phenylurea derivative was prepared and had m.p. 178·5–180·0° after crystallization from EtOH. (Found: 74·07; H, 7·44; N, 11·47. $C_{15}H_{19}N_2O$ requires; 74·38; H, 7·44; N, 11·57.)

The phenylthiourea derivative was prepared and had m.p. 117·0–117·5° after crystallization from EtOH. (Found: C, 69·59; H, 7·16; N, 10·72. $C_{15}H_{18}N_2S$ requires: C, 69·59; H, 6·98; N, 10·85.)

The *p*-nitrobenzoate derivative was prepared and had m.p. 143·0–143·5° after purification by chromatography over alumina and crystallization from CCl_4. (Found: C, 66·13; H, 6·18; N, 10·34. $C_{16}H_{16}N_2O_4$ requires: C, 66·18; H, 5·88; N, 10·29.)

Reaction of endo-5-*aminomethylbicyclo*[2.2.1]*heptene*-2 *with nitrous acid. endo*-5-Aminomethylbicyclo[2.2.1]heptene-2 (12·3 g, 0·1 mole) was added to 300 ml cold acetic acid containing one drop of conc H_2SO_4. N_2 was bubbled in and the mixture allowed to come to room temp at which point $NaNO_2$ (69 g, 1·0 mole) was added in portions over a 2 hr period, keeping the reaction mixture below 30°. The reaction was stirred overnight under N_2 and was then poured into 600 ml ice cold 20% NaOH aq. Pentane extraction (four 200-ml portions) of the alkaline solution afforded 5·4 g crude mixture while further ether extraction gave an additional 5·05 g product, bringing the yield of crude mixture to 10·45 g (63%). A considerable amount of what appeared to be polymerization product was noted, and most of this could not be extracted with either pentane or ether. Gas chromatography

[9] K. Alder, K. Heimbach and R. Reubke, *Chem. Ber.* **91**, 1516 (1958)

of the crude mixture under various conditions showed that one product dominated (ca. 85%) in the resulting acetates. This was collected by preparative GLC (5′ × ¼″ S.E. 30 silicone oil column at 185°) and identified as *exo*-bicyclo-[3.2.1]oct-3-en-2-yl acetate by comparison of IR and NMR resonance spectra and by comparison of gas chromatographic retention times on several columns (i.e., 5′ × ¼″ S.E. 30 silicone oil at 185°, 10 × ¼″ Castorwax at 185°, 6′ × ¼″ Craig succinate at 155°).

exo-5-*Aminomethylbicyclo*[2.2.1]*heptene*-2 (Va). *exo*-5-Cyanobicyclo[2.2.1]heptene-2 was reduced and worked up in the same manner as the *endo*-nitrile. Distillation of the product from KOH (b.p. 54°/4·5 mm) afforded 87·8% *exo*-5-aminomethylbicyclo(2.2.1)heptene-2. (Found: C, 77·96; H, 10·82; N, 11·20. $C_8H_{13}N$ requires: C, 78·00; H, 10·55; N, 11·37%.)

exo-5-Aminomethylbicyclo[2.2.1]heptene-2 has strong IR absorption (film) at 3350 cm^{-1}, 3425 cm^{-1}, and 702 cm^{-1}, and has a NMR spectrum consisting of a triplet centered at 3·9 τ, and a series of three complex multiplets between 7 and 9 τ.

The phenylthiourea derivative had m.p. 145° after purification by elution from an alumina column and crystallization from benzene–hexane. (Found: C, 69·65; H, 7·03; N, 10·86. $C_{16}H_{18}N_2S$ requires: C, 69·77; H, 6·98; N, 10·85.)

The *p*-nitrobenzoate derivative had m.p. 165° after crystallization from CCl_4. (Found: C, 65·91; H, 5·88; N, 10·20. $C_{15}H_{16}N_2O_5$ requires: C, 66·18; H, 5·88; N, 10·29.)

Deamination of exo-5-*aminomethylbicyclo*[2.2.1]*heptene*-2. *exo*-5-Aminomethylbicyclo[2.2.1]heptene (23·0 g, 0·19 mole) was added to 91 ml water and the mixture cooled in ice. Acetic acid (36·4 ml) and then conc. HCl aq (16·3 ml, 0·19 mole) were added while the temp was maintained below 15°. The reaction mixture was further cooled to 0° and was maintained below 5° during a 1 hr addition of a solution of $NaNO_2$ (25·3 g, 0·37 mole) in water (55 ml). The mixture was allowed to warm to room temp overnight and was then heated on a steam bath for 2 hr at which point it was poured on an equal volume of ice and extracted with three 100-ml portions ether. The combined ether extracts were washed with $NaHCO_3$ aq, then with brine, dried over $MgSO_4$, and reduced directly by stirring with an excess LAH in anhydrous ether. After the usual workup procedure, evaporation of the ether resulted in 7·0 g (21·9% based on hydroxylic products) of crude products. Gas chromatography [7′ × ¼″ γ-nitro-γ-methylpimelonitrile (20% on 35/80 mesh firebrick)] of these products at 100° indicated one major component (70%) and three partially resolved minor ones (30%). The major component has a retention time and IR spectrum identical with that of *endo*-tricyclo[2.2.2.$0^{2,6}$]octan-3-ol (VIII) while two of the minor components have retention times identical with *exo*-bicyclo-(2.2.2)oct-2-en-5-ol (IX) and *axial*-bicyclo(3.2.1)oct-6-en-2-ol (X).[5] Essentially no *exo*-bicyclo(3.2.1)oct-2-en-3-ol was found.

exo-5-*Hydroxymethylbicyclo*(2.2.1)*hept-2-ene* p-*bromobenzenesulfonate* (VI b). *p*-Brombenzenesulfonyl chloride (10·3 g, 0·03 mole) was added portionwise to a cooled solution of *exo*-5-hydroxymethylbicyclo(2.2.1)hept-2-ene[10] (3·1 g, 0·025 mole) in dry pyridine (7 ml). Pyridine hydrochloride precipitated immediately. After 2 hr at room temp and overnight in the refrigerator, the reaction was poured on a mixture of cracked ice (75 g) and conc HCl aq (10 ml). The mixture was extracted with four 50 ml portions of ether and the combined extracts were washed successively with 10% $NaHCO_3$aq, water, and brine. After drying ($CaSO_4$) the extracts were evaporated to give a solid which was crystallized from MeOH to yield 7·3 g (85%) ester, m.p. 55°. (Found: C, 48·70; H, 4·32. $C_{14}H_{15}O_3SBr$ requires: C, 48·98; H, 4·40.)

Acetolysis of exo-5-*hydroxymethylbicyclo*[2.2.1]*hept-2-ene*, p-*bromobenzenesulfonate* (IV b). The *exo*-brosylate (3·4 g, 0·01 mole) was added to a mixture of glacial acetic acid (18·8 ml), a few drops acetic anhydride and NaOAc (0·84 g, 0·012 mole). The reaction was heated in an oil bath at 100° for 4 days, cooled to room temp and poured over crushed ice (45 g) containing sufficient Na_2CO_3 to neutralize the acetic acid. The aqueous mixture was extracted with four 30-ml portions of ether and the combined ether extracts were washed 3 times with 5 ml water and dried over $MgSO_4$. The ethereal solution was concentrated to 10 ml and used directly in the next step.

Lithium aluminum hydride reduction of acetolysis product. The ethereal concentrate from the previous experiment was added dropwise to a stirred suspension of LAH (0·8 g, 0·02 mole) in anhydrous ether (50 ml) at such a rate as to maintain gentle reflux. The reaction mixture was then refluxed for an additional hr, at which point water (20 ml) was added followed by dil. HCl aq.

The ether layer was separated and the aqueous layer was extracted with four 50-ml portions of

[10] J. A. Berson, J. S. Walia, Allen Remanick, S. Suzuki, P. Reynolds-Warnhoff and D. Willner, *J. Amer. Chem. Soc.* **83**, 3986 (1961).

ether; the combined ethereal solutions were washed successively with 10% NaOH aq and brine, dried over $MgSO_4$ and evaporated leaving 0·5 g (40·3%) solids which were initially purified by sublimation.

Acetolysis product analysis. The product analysis was performed on a 7′ × ¼″ copper γ-nitro-γ-methylpimelonitrile column (20% on 35/80 mesh firebrick). Peak areas were determined by weighing the traces on an analytical balance. Identification was accomplished by comparison of retention time with authentic samples and comparison of IR spectra in the cases of *exo*-5-hydroxybicyclo[2.2.2]-oct-2-ene and *exo*-7-hydroxybicyclo[3.2.1]oct-2-ene.[5] A typical analysis is as follows: Unknowns (8 and 15%); *exo*-bicyclo(3.2.1)oct-6-en-2-ol (9%); *exo*-5-hydroxybicyclo(2.2.2)oct-2-ene (30%); *exo*-7-hydroxybicyclo(3.2.1)oct-2-ene (28% max.); *endo*-tricyclo(2.2.2.$0^{3,6}$)octan-3-ol (3%); *exo*-tricyclo(2.2.2.$0^{3,6}$)octan-3-ol (6%). The NMR and IR of the product assigned the structure *exo*-7-hydroxybicyclo(3.2.1)oct-2-ene were very similar to those of an authentic sample[16] but not identical, and hence this structure is only tentative.

Control experiment. A solution of 0·62 g of *endo*-tricyclo(2.2.2.$O^{3,6}$)octan-3-ol in 9·4 ml glacial acetic acid which contained 0·42 g NaAc was heated at ca. 95° for 3 days. Isolation of the products was effected as above and the resulting acetates were reduced with LAH. There was obtained 0·26 g brown residue which consisted of mainly *exo*-bicyclo(2.2.2)oct-2-en-5-ol and smaller amounts of starting material and bicyclo(3.2.1)oct-6-en-2-ol.

endo-5-*Hydroxymethylbicyclo*(2.2.1)*hept*-2-*ene* p-*bromobenzenesulfonate* (V b). This ester was prepared as above and had m.p. 78–79° (lit.[10] m.p. 80–81°). Acetolysis was conducted as above and the crude product was reduced with LAH to yield 0·25 g (40%) of alcohols. Gas chromatography on the NMP column indicated that this material was identical with the major product of acetolysis of the *p*-toluenesulfonate prepared below. A second component (27%) appeared on gas chromatography on a 150′ capillary column (UCON 50 HB2000). No tricyclo(3.2.1.$0^{3,6}$)octanol[3] and no tricyclo(2.2.2.$0^{3,6}$) octanol was found.

The structure of the major product of the acetolysis of the *endo*-system was determined by work-up of a large-scale run on the *endo*-*p*-toluenesulfonate derivative. This material was prepared in a manner analogous to the brosylates but the starting alcohol was the commercially available *endo-exo* mixture[11] (ca. 4:1). The tosylate obtained was an oil and was solvolyzed directly at 100° for 36 hr. From 110 g of tosylate there was obtained 34 g of a mixture of acetate esters boiling in the range 98° (23 mm) to 106° (26 mm). This material was re-fractionated to give a forerun of 5 g and 3 fractions totaling 27 g which boiled as follows: 9·5 g, 83–85° (9 mm); 6·5 g, 86° (11 mm) to 87° (10·5 mm); and 11 g 88·5°–89° (11 mm). The early fractions were about 70% pure as shown by GC on a 5′ Carbowax 20M column. The last fraction appeared to be ca. 90% pure and was used in subsequent experiments. This material had the correct analysis for bicyclo(3.2.1)oct-3-en-2-yl acetate. (Found: C, 72·49; H, 8·59. $C_{10}H_{14}O_2$ requires: C, 72·26; H, 8·49.)

Cleavage of the ester with LAH gave essentially a quantitative yield of alcohol (VI) which melted at 78–83° after sublimation (lit.[4], m.p. 102–108°, 87·2–88·2°). The IR spectrum agreed with that reported.[4] The *p*-nitrobenzoate had m.p. 86–87° (lit., m.p. 81–81·5°[3], 86·2–86·6°). The phenylurethan had m.p. 125–127° (lit.,[3] 126–126·5°).

Bicyclo(3.2.1)*oct*-3-*en*-2-*one*. was prepared by treatment of 1·0 g alcohol with 5 g freshly prepared MnO_2[12] in 55 ml pentane at room temp for 3 days. The crude product (0·7 g) showed weak hydroxyl absorption in the IR spectrum. After distillation at 98·5–99·5° (20 mm) (lit.,[4] b.p. 76°/7 mm) the product had n_D^{21} 1·5126 (lit.,[4] n_D^{25} 1·5123) λ_{max} (ETOH) 227 mμ (log e 3·9). (lit., λ_{max} 227, log e, 3·9;[3] λ_{max} 227, log e, 3·98[4]). The IR spectrum was in agreement with that reported by Goering *et al*[4]. The 2,4-dinitrophenylhydrazone had m.p. 140–142° after crystallization from EtOH (lit.,[4] m.p. 140·4–141·5°). (Found: C, 55·31; H, 5·23; N, 18·96. Calc. for $C_{14}H_{14}N_4O_4$: C, 55·62; H, 4·67; N, 18·54.)

Acknowledgement—We wish to thank the following agencies for financial support of this work: National Institutes of Health (GM-08701) and the American Cyanamid Co. for a Junior Fellowship award to R.A.P.

[11] We are grateful to the Interchemical Corp. for a generous gift of this material.

[12] O. Mancera, G. Rosenkranz and F. Sondheimer, *J. Chem. Soc.* 2189 (1953).