Bis(bicyclo[3.2.0]heptadienyl) Dications. Synthesis of the Precursors and Chemical Behavior

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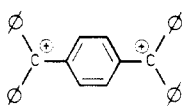
A number of bis(bicyclo[3.2.0]heptanediols), **11–14**, have been synthesized from the corresponding diketones **8** and **9**, which in turn have been prepared by coupling of the bicyclic ketones **6** and **7**, respectively. The reactions of the alcohols **11–14** with FSO_3H/SO_2ClF at low temperatures have been studied by ^1H and ^{13}C NMR spectroscopy. Definite structural assignments for the dications could not be derived from the complex spectra, with the exception of dication **17**.

Relatively few studies concerning carbodications have been reported if compared to those on monocations. In the earliest examples of the dications stabilization was provided by delocalization of the positive charges in aromatic rings,[2,3] e.g., **1**; more recent studies deal with cyclic



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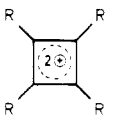

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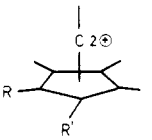

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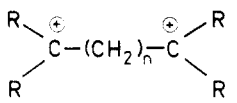
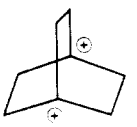
dications, which find their stabilization by being Hückeloid $(4n + 2)\pi$ electron systems,[4-8] an example being the cyclobutadiene dication **2**.[4] The pyramidal dications **3**[9-11] are also examples of resonance-stabilized dications. A series of acyclic alkyl/aryl substituted dications (**4**) was



4, $n \geq 2$



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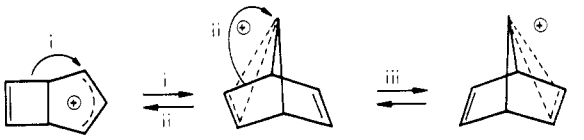
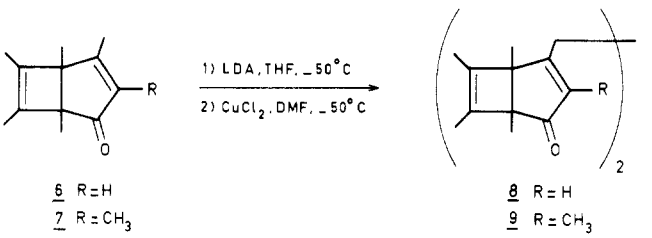
reported by Olah and co-workers,[12] and analogous static dications were found in rigid polycyclic systems[13-16] (e.g., **5**[13]). All these examples represent dications which undergo no rearrangements.

Scheme I



Scheme II



6 R=H
7 R=CH_3

8 R=H
9 R=CH_3

The effect of substituents upon rearrangements of monocations has been (and still is) intensively studied, but to our knowledge no information is available concerning the influence of a second positive charge upon such rearrangements. Such an attempt has been made now in the case of the polymethyl substituted bicyclo[3.2.0]heptadienyl cations.[17] The strategy we followed to this end was to couple two precursor molecules, thus forming dimeric species, which upon ionization in superacid would afford bis(bicyclo[3.2.0]heptadienyl) dications. The rearrangements of the bicyclo[3.2.0]heptadienyl monocations mainly involve 1,2 Wagner–Meerwein shifts, interconverting [3.2.0] and [2.2.1] skeletons (i and ii), and the bridge flip (iii) in the [2.2.1] isomers[17,18] (Scheme I).

In this paper we report the synthesis of the dimeric alcohols that served as precursors for the bisbicyclo[3.2.0]heptadienyl dications and the reactions of these alcohols with FSO_3H at low temperatures. The ^1H and ^{13}C NMR spectroscopic results[19] proved to be too complicated for a detailed analysis, however, except in the case of alcohol **12**.

Synthesis of Cation Precursors

(A) Coupling of Bicyclic Ketones. A useful method for carbon–carbon bond formation is the transition-metal-promoted oxidative dimerization of carbanions; e.g., dimerizations of carbanions, stabilized by sulfonyl, phos-

(1) To whom correspondence should be addressed.
(2) Hart, H.; Sulzberg, T.; Rajos, R. R. *J. Am. Chem. Soc.* **1963**, *85*, 1800.
(3) Volz, H.; Volz de Leica, H. J. *Tetrahedron Lett.* **1964**, 1871.
(4) Olah, G. A.; Staral, J. S. *J. Am. Chem. Soc.* **1976**, *98*, 6290.
(5) Olah, G. A.; Staral, J. S.; Liang, G.; Paquette, L. A.; Melega, W. P.; Carmody, M. J. *J. Am. Chem. Soc.* **1977**, *99*, 3349.
(6) Olah, G. A.; Liang, G. *J. Am. Chem. Soc.* **1976**, *98*, 3033.
(7) Olah, G. A.; Liang, G. *J. Am. Chem. Soc.* **1977**, *99*, 6045.
(8) Oth, J. F. M.; Smith, D. H.; Prange, V.; Schroder, G. *Angew. Chem.* **1973**, *85*, 352.
(9) Hogeveen, H.; Kwant, P. W. *Acc. Chem. Res.* **1975**, *8*, 413.
(10) Giordano, C.; Heldeweg, R. F.; Hogeveen, H. *J. Am. Chem. Soc.* **1977**, *99*, 5851.
(11) Hogeveen, H.; van Kruchten, E. M. G. A. *J. Org. Chem.* **1981**, *46*, 1350.
(12) (a) Bollinger, J. M.; Cupas, C. A.; Friday, K. J.; Woolfe, M. L.; Olah, G. A. *J. Am. Chem. Soc.* **1967**, *89*, 156. (b) Olah, G. A.; Grant, J. L.; Spear, R. J.; Bollinger, J. M.; Serianz, A.; Sipos, G. *J. Am. Chem. Soc.* **1976**, *98*, 2501.
(13) Olah, G. A.; Liang, G.; Schleyer, P. v. R.; Engler, E. M.; Dewar, M. J. S.; Bingham, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6829.
(14) Olah, G. A.; Liang, G.; Schleyer, P. v. R.; Parker, W.; Watt, C. I. F. *J. Am. Chem. Soc.* **1977**, *99*, 966.
(15) Olah, G. A. *Top. Curr. Chem.* **1979**, *80*, 21.
(16) Olah, G. A.; Surya Prakash, G. K.; Rawdah, T. N. *J. Am. Chem. Soc.* **1980**, *102*, 6127.
(17) (a) Hogeveen, H.; van Kruchten, E. M. G. A. *Recl. Trav. Chim. Pays-Bas* **1977**, *96*, 61. (b) Hogeveen, H.; van Kruchten, E. M. G. A. *J. Org. Chem.* **1977**, *42*, 1472. (c) Hogeveen, H.; van Kruchten, E. M. G. A. *Top. Curr. Chem.* **1979**, *80*, 89.
(18) Lustgarten, R. K.; Brookhart, M.; Winstein, S. *J. Am. Chem. Soc.* **1972**, *94*, 2347.
(19) Relevant NMR spectroscopic data are found in ref 17c and the references cited therein.

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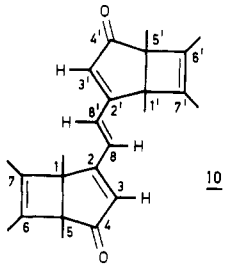
phoryl, imidoyl,[20,21] and alkoxycarbonyl[22] groups in the presence of copper salts are well established. In 1977 Saegusa[23] reported the oxidative coupling of ketone enolates with $CuCl_2$ in DMF to yield 1,4-diketones, and this method proved to be convenient to dehydrodimerize the bicyclic ketones 6[24] and 7.[25] The dimeric ketones 8 and 9[26] were obtained in yields of 39% and 44%, respectively (Scheme II). Under some circumstances a byproduct, 10,



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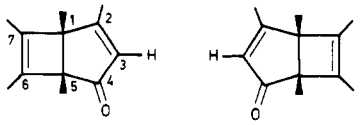
was obtained in the coupling reaction, of ketone 6. In a separate experiment it was found that the initial coupling product 8 can be transformed into 10 under the coupling reaction conditions. The structural assignment of the bright yellow product 10 is based on the mode of formation and on spectral data (these include both ^1H and ^{13}C NMR, mass, and UV[27] spectroscopy; see Experimental Section). Molecular models of dimer 10 show that the *Z* configuration of the central double bond is unfavorable.

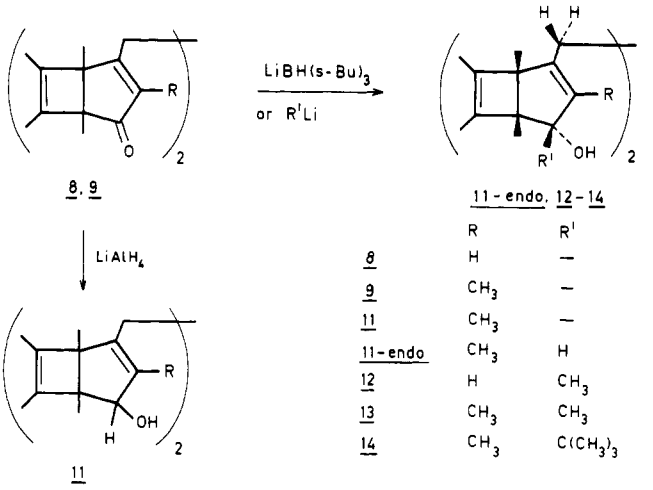
(B) Stereochemical Aspects of the Coupling Products. The starting materials for the coupling reaction, ketones 6 and 7, exist both as a racemic mixture of enantiomers A (1*R*,5*R*) and B (1*S*,5*S*). Consequently, the



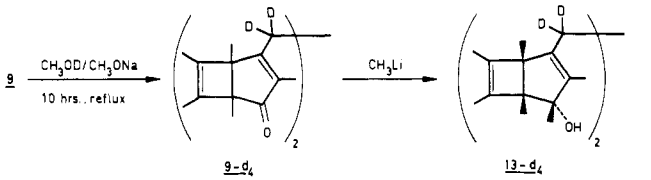
A (1R,5R) B (1S,5S)

coupling reaction can in principle result in three products,

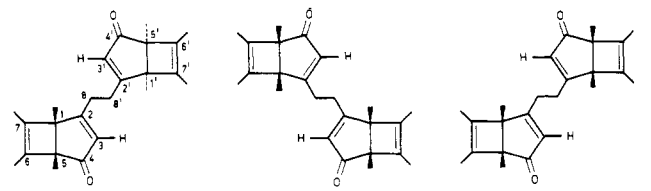
Scheme III



Scheme IV



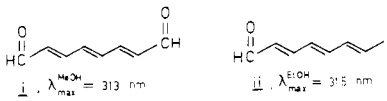
viz., the pair of enantiomers A–A and B–B and the meso dimer A–B. Surprisingly, sharp melting points were ob-



A-B B-B A-A

served for both dimers 8 and 9. Also the NMR spectra of compounds 8 and 9 suggested the presence of only one of both diastereomers; no double signals were observed, neither in the ^1H nor in the ^{13}C NMR spectra. Paramagnetic shift reagents[32,33] [$Eu(tfc)_3$, $Eu(fod)_3$] were applied in the case of the ^1H NMR spectra of 8; however, it was unsuccessful in showing the presence of the two expected diastereomers. The formation of the dimer 10 as a byproduct in the conversion of 6 into 8 turned out to be a fortunate circumstance, in the sense that with this compound the existence of two diastereomers (meso and *dl* pair) could be established. Inspection of the ^{13}C NMR spectrum of compound 10 shows that for one hydrogen-substituted sp^2 carbon atom of 10 [either C-8(8′) or C-3(3′)] two peaks of nearly equal intensities at δ 131.0 and 130.8 are present.[34] The presence of two diastereomers of 10 was further confirmed by the use of $Eu(fod)_3$. In the ^1H NMR spectrum three signals [C-1(1′) methyls, C-3(3′) hydrogens, C-6(6′) methyls] were each split into two signals of equal intensities, showing the presence of the meso and *dl* stereoisomers in a 1.0:1.0 ratio. Because of the presence of two stereoisomers of the dimer 10, the dimer 8 (the precursor of 10) can also safely be assumed to consist of

(20) Kauffmann, T.; Berger, D. *Chem. Ber.* **1968**, *101*, 3022.
(21) Maryanoff, C. A.; Maryanoff, B. E.; Tang, R.; Mislow, K. *J. Am. Chem. Soc.* **1975**, *97*, 2912.
(22) Rathke, M. W.; Lindert, A. *J. Am. Chem. Soc.* **1971**, *93*, 4605.
(23) Ito, Y.; Konoiko, T.; Harada, T.; Saegusa, T. *J. Am. Chem. Soc.* **1977**, *99*, 1487.
(24) Junker, H.-N.; Schäfer, W.; Niedenbrück, H. *Chem. Ber.* **1967**, *100*, 2508.
(25) Hart, H.; Nitta, M. *Tetrahedron Lett.* **1974**, 2109.
(26) Diketone 9 has also been reported by Hart (Hart, H.; Willer, R. Tetrahedron *Lett.* **1977**, 2307), using Br_2 as the coupling reagent for the enolate anion of 7. However, no detailed experimental conditions and spectroscopic data were given, except for its melting point, which agrees with that obtained by us.
(27) The experimentally found λ_{max} of compound 10 (332 nm) agrees well with the value calculated by using Woodward's rules[28] (341 nm). Using these rules, one should bear in mind that in conjugated systems terminated by two oxygen atoms, only one of the carbonyl functions takes part in the spectral conjugation.[29] This is nicely demonstrated by the mono- and dicarbonyl compounds i[30] and ii,[31] which are related to dimer 10.



i, λ_{max}^{MeOH} = 313 nm ii, λ_{max}^{EtOH} = 315 nm

(28) See: Williams, D. H.; Fleming, I. In "Spectroscopic Methods in Organic Chemistry", 2nd ed.; McGraw-Hill: London, 1973; p 18.
(29) Braude, E. A. In "Determination of Organic Structures by Physical Methods"; Braude, E. A., Nachod, F. C., Eds.; Academic Press: New York, 1955; p 148.
(30) Anet, R. *Tetrahedron Lett.* **1961**, 720.
(31) Blout, E. R.; Fields, H. *J. Am. Chem. Soc.* **1948**, *70*, 189.
(32) See: Sievers, R. E., Ed. "Nuclear Magnetic Resonance Shift Reagents" Academic Press: New York, London, 1973.
(33) McCreary, M. D.; Lewis, D. W.; Wernick, D. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 1038.
(34) Very recently, the meso and *dl* diastereoisomers of several disubstituted succinic acids have been shown to give different ^{13}C NMR chemical shifts: Hasan, M. *Org. Magn. Reson.* **1980**, *14*, 309.

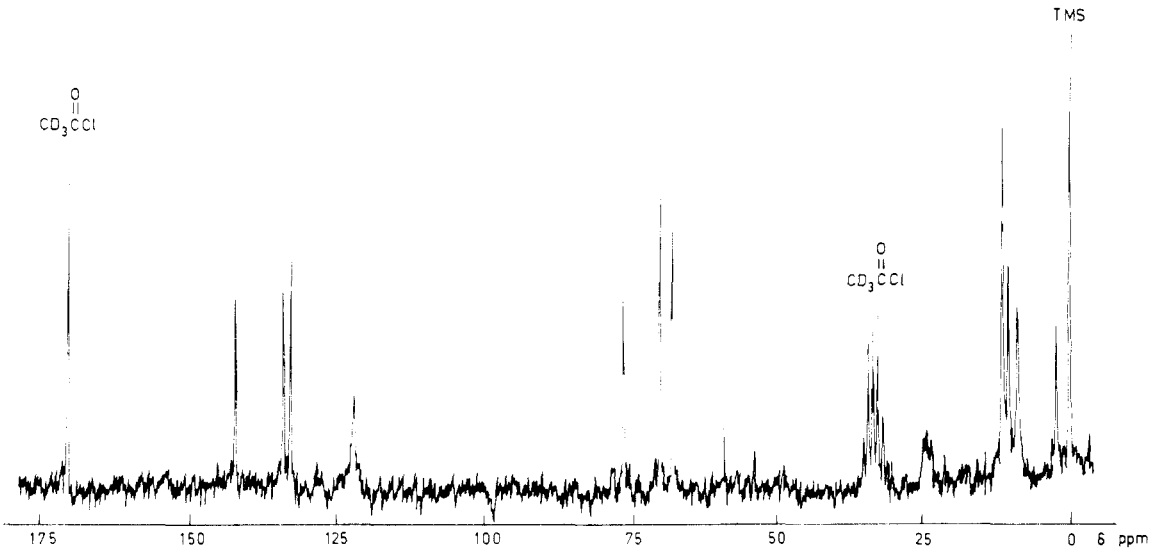


Figure 1. 25.16-MHz ^{13}C NMR spectrum of alcohol **12** in FSO_3H/SO_2ClF at −112 °C.

a mixture of the meso isomer (A–B) and the *dl* pair (A–A and B–B). It is tacitly supposed that the same holds for the dimer **9**.

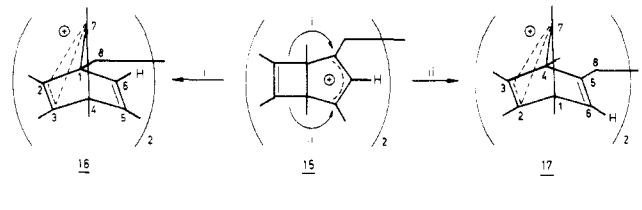
(C) Synthesis of Alcohols. The alcohols, that served as precursors for the dications, were prepared as presented in Scheme III. The secondary alcohol **11** was obtained as a mixture of the diastereomeric endo and exo alcohols[35] upon treatment of dimer **9** with $LiAlH_4$ at −10 °C.[36] The tertiary endo alcohols[17,18,38] **12–14** were obtained upon treatment of the corresponding ketones with the appropriate alkyllithium reagents. Similar to the monomeric alcohols,[17] the dimeric tertiary alcohols showed a tendency for dehydration under rather mild conditions. The labeled alcohol **13**-d_4 was prepared as shown in Scheme IV.

Results and Discussion

Reactions with FSO_3H. It is important to mention that in the following discussion two assumptions will be made.[39] First, the stereochemistry of the dications will be ignored, supposing that diastereomeric dications are not observed to be separated by NMR spectroscopy; this is reasonable, because it holds for both the neutral precursors (**8, 9**) and the first dication to be discussed (**17**; see below). Second, only the symmetrically rearranged cations will be considered, these cations being formed by the same rearrangement in each monomeric part of the original dication.

(A) Alcohol 12. Upon dissolution of alcohol **12** in FSO_3H/SO_2ClF at −125 °C a cation was obtained, having a [2.2.1] skeleton with a hydrogen atom at the "unbound" double bond (^1H NMR, δ 5.82[17,18]). Starting from alcohol **12**, on can envisage two different [2.2.1] structures for this cation, viz., **16** and **17**, which both arise from the initially formed ion **15** (Scheme V). Evidence for the dication to have either the structure **16** or **17** is provided by both the

Scheme V



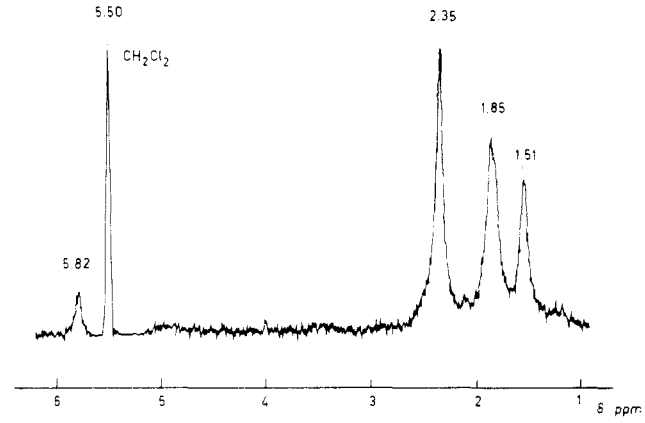


Figure 2. 60-MHz ^1H NMR spectrum of alcohol **12** in FSO_3H/SO_2ClF at −85 °C.

^1H and ^{13}C NMR spectra. At −112 °C, the ^{13}C NMR spectrum, depicted in Figure 1, was obtained, with the following peaks: δ 143.2 (C–5), 134.9 and 133.6 (C-2,3), 122.8 (d, $J \approx 180$ Hz, C-6), 76.5 (C-7), 70.3 and 68.0 (C-1,5), 11.4, 11.4, 10.4, and 8.8 (q, $J \approx 135$ Hz, methyl carbons), 2.2 (q, $J \approx 135$ Hz, C-7 methyl carbon); the broad signal around δ 24.4 may belong (partly) to C-8. In these dicationic systems it was, in general, impossible to observe unambiguously the triplet signal belonging to the dimethylene chain (see below). On the basis of the ^{13}C NMR data, one cannot distinguish between structures **16** and **17**; however, the ^1H NMR spectral data (Figure 2) give rise to a strong preference for structure **17**: δ 5.82 (C-6 hydrogen), 2.35 (C-2,3 methyls and C-8 hydrogens), 1.85 (C-1,4 methyls), 1.51 (C-7 methyl). These assignments are based upon comparison with the spectra of the corresponding monocations.[17] The alternative structure **16** should show a different ^1H NMR spectrum, viz., a chemical shift difference of about 0.2 ppm should certainly have been found for the signals of the methyls at C-4 and C-5, rather than the observed single absorption at δ 1.85. The

(35) Story, R. R.; Fahrenholtz, S. R. F. *J. Am. Chem. Soc.* **1965**, *87*, 1623.

(36) A powerful reagent for the stereoselective reduction of (bi)cyclic ketones is L-Selectride (lithium tri-*sec*-butylborohydride), which possesses an almost enzymelike selectivity.[37] The reduction of dimer **9** with L-Selectride afforded the 11-endo alcohol (according to ^1H NMR >95% of one isomer), due to attack of the reducing agent from the less hindered exoside.

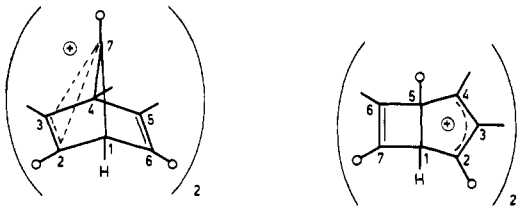
(37) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1972**, *94*, 7159.

(38) Hoffmann, R. W.; Schüttler, R.; Loof, I. H. *Chem. Ber.* **1977**, *110*, 3410.

(39) Without these assumptions "mixed" dimeric cations with both a [3.2.0] and a [2.2.1] structural part have also to be considered, making the discussion even more complicated.

preference for pathway ii over i agrees with the Baker–Nathan order:[40] a CH_3 group having a larger stabilizing effect than a CH_2 group in the transition state of the rearrangement.[17,41,42]

Warming the solution of **17** caused rearrangements to new dications, as shown by ^1H and ^{13}C NMR spectra.[43] At −65 °C at least one new [2.2.1] isomer appeared, while at still higher temperatures (−50 °C) [3.2.0]isomers were observed. In the ^{13}C NMR spectrum at −50 °C typical peaks of the allylic skeleton carbon atoms are found at δ 238.2, 236.0, 234.5 (C-2,4), and 155.0 (C-3), as well as the terminal allylic methyl groups at δ 24.2 and 22.9. Unfortunately, on the basis of the spectral data no definite structural assignments could be made. Inspired by the rearrangements of the related monomeric cations,[17] we propose the formation of any of the four [2.2.1] isomeric dications **16** and **18** at −65 °C and of the three [3.2.0] isomers **19** at −50 °C.

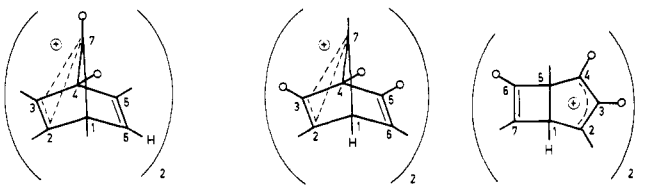


18 **19**

○— ≡ -CH_2.CH_3 (2x)

Finally, the mass spectrum of the product(s) obtained on quenching the ^{13}C NMR sample at −60 °C (kept below −30 °C during 1–2 days) with excess CH_3ONa/CH_3OH indicates the dimeric nature of these ions, a M^+ peak being found at m/e 346 ($C_{26}H_{34}$). The mass spectrum resembles that of the precursor alcohol **12**, except for some higher molecular weight peaks.

(B) Alcohol 11. Ionization of alcohol **11** in FSO_3H/SO_2ClF at −125 °C afforded a reaction mixture, the ^{13}C NMR spectrum of which at −102 °C shows the presence of only [2.2.1] isomers.[43] On the basis of the rearrangements discussed previously,[17] the two isomers **20** and the three isomers **21** can arise by starting from alcohol **11**.

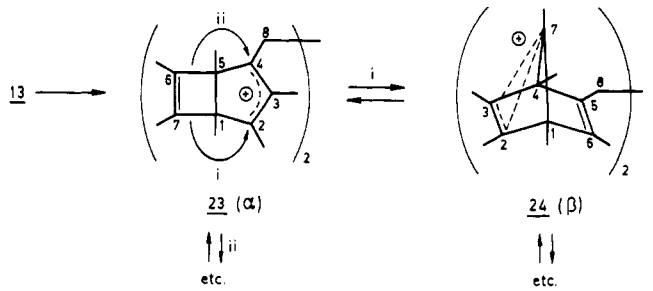


20 **21** **22**

○— ≡ -CH_2.CH_3 ○— ≡ -CH_2.CH_3 (2x)

Warming this mixture of [2.2.1] isomers to −65 °C[43] resulted in a single new dication with a [3.2.0] skeleton with hydrogen substituted in the bridgehead position. Rearrangements of the various [2.2.1] isomers can in principle afford the three [3.2.0] isomers **22**. The structure with the dimethylene chain in terminal allylic position is rejected, because both ^1H and ^{13}C NMR spectra show the presence of two terminal allylic methyl groups (^1H, δ 3.13 and 3.03;

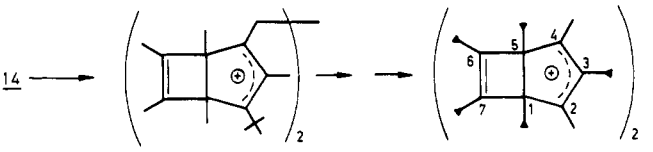
Scheme VI



23 (α) **24** (β)

etc. etc.

Scheme VII



25 **26** → : CH_2, t-Bu and three CH_3

^{13}C, δ 24.0 and 22.7). At even higher temperatures (−35 °C) other [3.2.0] isomers were also produced.

(C) Alcohol 13. The permethyl substituted dimer **13** showed, when dissolved in FSO_3H/SO_2ClF, no NMR spectral changes due to rearrangements of the resulting dications between −100 and −45 °C. Both ^1H and ^{13}C NMR spectra[43] indicate the presence of at least two [3.2.0] isomers and one [2.2.1] isomer. In Scheme VI are depicted two of the possible isomers, viz., **23** and **24**. Evidence for more than one [3.2.0] isomer is found in the number of ^{13}C NMR peaks in the terminal allylic region. In order to obtain more information concerning the possible isomers, we treated the labeled alcohol **13**-d_4 with FSO_3H/SO_2ClF at low temperature, but unfortunately no reduced intensity for any certain signal was found in the ^1H NMR spectrum. A tentative conclusion that can be drawn from this experiment is that the dimethylene chain is situated in several positions of the [2.2.1] and [3.2.0] isomers, an assertion that is strengthened by the fact that above −45 °C a reversible line broadening was observed in the ^1H NMR spectra of the dications derived from alcohol **13**. The latter two experiments are in agreement with the scrambling found in the permethyl-substituted monomeric cations.[17]

(D) Alcohol 14. The ^1H NMR spectra of the *tert*-butyl-substituted alcohol **14** in FSO_3H/SO_2ClF, measured below −75 °C, are too badly resolved to be able to afford information concerning the structure of the cation(s). Above −75 °C the resonances become better resolved and show the presence of at least two [3.2.0] isomers. The spectra (both ^1H and ^{13}C NMR[43]) indicated that the first-generated cation **25** is not present but rather rearranged isomers (**26**, Scheme VII). The rearrangement of **25** into **26** is indicated by the intensity of the ^1H NMR signal of the terminal allylic methyl groups at δ 3.20 and the presence of two ^{13}C NMR signals at δ 24.6 and 22.3, belonging to those methyl groups. The presence of at least two isomers **26** is shown by broad ^1H NMR signals, a double ^1H NMR peak for the *tert*-butyl group (δ 1.45 and 1.41), and the number of ^{13}C NMR peaks.

(E) Concluding Remarks. As shown above it has proven difficult if not impossible to distinguish on basis of NMR spectroscopy isomers that are structurally so closely related as in the examples discussed. This is connected with, among other things, the difficulty in locating in most cases the position of the dimethylene chain in the dimeric cations. This was due to the circumstance that in the proton-coupled ^{13}C NMR spectra no difference in

(40) (a) Baker, J. W.; Nathan, W. S. *J. Chem. Soc.* **1935**, 1844. (b) Baker, J. W. In "Hyperconjugation", Oxford University Press: New York, 1952.

(41) Brouwer, D. M.; Hogeveen, H. *Prog. Phys. Org. Chem.* **1972**, *9*, 179.

(42) Saunders, M.; Vogel, P.; Hagen, E. L.; Rosenfeld, J. *Acc. Chem. Res.* **1973**, *6*, 53.

(43) Detailed spectroscopic data is presented in the Supplementary Material.

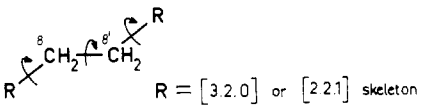


Figure 3.

the long-range coupling pattern of the skeleton carbon atoms, with either a methyl or a methylene group, was observed. Moreover, the ^{13}C NMR signals of the methylene carbons (C-8) were barley visible in most cases. The latter phenomenon may originate from (a combination of) different sources. First, the effect of the presence of different isomeric cations, as discussed above, will be larger on the methylene carbons than on the other carbons, because the former experience the influence of both bicyclic fragments of the molecule. This will introduce (relatively small) chemical shift differences for C-8 in the various isomers and consequently a broadened ^{13}C NMR signal. Second, an internal barrier(s) to rotation due to the bulky groups, as presented in Figure 3, may cause a brodening of the C-8 signals, although it is not self-evident why the C-8 peaks should show such a broadening.[44] In order to obtain more information concerning this problem, we have recorded ^{13}C NMR spectra (at -7, -41, -57, and -73 °C) of the neutral dimer **9** in acetone-d_6, which show a temperature-dependent line broadening. At −73 °C no methylene signal was observed, while broadened signals (10–12 Hz) for the methyl groups and sharp signals for the skeleton atoms were found. At −57 °C a very broad (~25 Hz) methylene signal appeared that became sharper upon further warming: ~12 Hz at −41 °C and ~6 Hz at −7 °C (the natural line width if compared to the other signals). This indicates that a rotational process(es) occurs in the neutral compound. By extrapolation one might assume a restricted rotation(s) to be the origin (at least in part) of the problems that we encountered with the ^{13}C NMR absorptions of C-8 in the dications.

Experimental Section

General Methods. The IR spectra were taken on a Perkin-Elmer 257 spectrophotometer (Nujol). UV spectra were recorded on a Beckman DB-G photospectrometer. Mass spectra were obtained on a AEI MS-902 by Mr. A. Kiewiet. Proton magnetic resonance spectra were recorded by using 60-MHz JEOL C-60 HL or Hitachi Perkin-Elmer R-24B spectrometers, the first equipped with a variable-temperature probe, and tetramethylsilane (δ 0.00) as an internal standard for the neutral compounds. For the cations, Me_4Si in CD_3COCl was used as an external reference (δ 0.00). Chemical shifts are denoted in parts per million downfield from Me_4Si. A Varian XL-100 was used for the 100-MHz proton spectra and for the 25.2-MHz natural-abundance carbon-13 magnetic resonance spectra. The latter were recorded by using a Fourier transform and were proton-noise decoupled unless otherwise stated. All solvents were purified by common methods. The superacids and the SO_2ClF used were purchased from Cationics Inc.

Dimer 8. A solution of diisopropylamine (1 mL; 7 mmol) in dry THF (10 mL, freshly distilled from $LiAlH_4$) was treated under N_2 with 5 mL (8 mmol) of *n*-butyllithium (as a 15% solution in *n*-hexane, Merck) at −50 °C. After 15 min, 1 g (5.7 mmol) of ketone **6**[24] in 10 mL of anhydrous THF was added dropwise to the resulting solution of lithium diisopropylamine (LDA). After 15 min of magnetical stirring, anhydrous $CuCl_2$ (1 g, 7.5 mmol) dissolved in 15 mL of DMF was added at once to the THF solution of the lithium enolate at −50 °C. The dark green solution was stirred for an additional 30 min and then allowed to reach room temperature. The reaction mixture became dark brown and was treated with 3% aqueous HCl, resulting in a light green solution which, was extracted twice with ether (35 mL). The ether extract was washed twice with 3% aqueous HCl and with water. A certain amount of the dimeric reaction product was insoluble, as shown by a yellow precipitate. Addition of chloroform made the solution homogeneous, and this solution was dried over $MgSO_4$ and filtered, and the solvent was evaporated in vacuo to afford a quanitative yield of a mixture of starting material **6** and dimeric product **8**. Washing the organic material with *n*-pentane yielded 370 mg (1.1 mmol, 39%) of dimer **8**, which was pure enough (>95% according to NMR) for further conversions. Analytically pure **8** (mp 255.4–256.6 °C) was obtained upon crystallization from ethyl acetate: IR 1690 and 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.64 (C-3 hydrogens), 2.59 (C-8 hydrogens), 1.62 (C-7 methyl), 1.57 (C-6 methyl), 1.22 (C-1 methyl), and 1.16 (C-5 methyl); ^{13}C NMR ($CDCl_3$) δ 208.2 (C-4), 181.1 (C-2), 144.5 and 140.5 (C-6 and C-7), 124.8 (C-3, d, J = 160 Hz), 60.2 and 58.6 (C-1 and C-5), 27.1 (C-8, t, J = 130 Hz), 12.9, 11.3, 10.1, and 8.8 (C-1, C-5, C-6, and C-7 methyls, q, J = 130 Hz); mass spectrum, m/e 350 (M^+). Anal. Calcd for $C_{24}H_{30}O_2$ (mol wt 350): C, 82.24; H, 8.63. Found: C, 82.17; H, 8.61.

Dimer 9. Ketone **7**[25] was dimerized as described above for ketone **6**. Coupling of 500 mg (2.6 mmol) of ketone **7** afforded after crystallization (ethyl acetate) 220 mg (0.5 mmol, 44%) of dimer **9**: mp 190.3–190.8 °C (lit.[26] mp 195–198 °C); IR 1680 and 1630 cm^{-1}; UV (ethanol) λ_{max} 245 nm (log ε 4.22); ^1H NMR (CCl_4) δ 2.38 (C-8 hydrogens), 1.67 (C-3 methyl), 1.59 (C-7 methyl), 1.53 (C-6 methyl), 1.25 (C-1 methyl), 1.11 (C-5 methyl); ^{13}C NMR ($CDCl_3$) δ 207.8 (C-4), 171.8 (C-3), 145.1, 139.8, and 133.8 (C-2, C-6, and C-7), 59.0 and 57.1 (C-1 and C-5), 26.4 (C-8, t, J = 130 Hz), 13.2, 11.6, 10.6, 8.6, and 8.1 (C-1, C-3, C-5, C-6, and C-7 methyls, q, J = 130 Hz); mass spectrum, m/e 378 (M^+). Anal. Calcd for $C_{26}H_{34}O_2$ (mol wt 378): C, 82.49; H, 9.05. Found: C, 82.13; H, 9.07.

Compound 9-d_4. Dimer **9** was treated with CH_3OD/CH_3ONa as described for the monomeric ketones,[17] yielding 100% of labeled dimer **9**-d_4, the ^1H NMR (CCl_4) spectrum of which differed from that of **9** by lacking the signal at δ 2.38 (C-8 hydrogens).

Compound 10. Treatment of the dimeric ketone **8** with LDA and $CuCl_2$ as described above for the coupling reaction afforded in quantitative yields a mixture of **8** and **10**, with various amounts of product **10** (60–90%). Variations in reaction time and amount of base (1–4 equiv) did not change the conversion dramatically. A 20–50% conversion of **8** into **10** was found in reactions lacking $CuCl_2$. To obtain pure **10**, we again subjected a mixture of **8** and **10** to the reaction conditions. For example, 40 mg (0.1 mmol) of a 2:3 mixture of **8** and **10** in 5 mL of dry THF was treated at −50 °C with 3 mL of an LDA solution (ca. 0.8 mmol) prepared from 0.5 mL (3.5 mmol) of $HN(i\text{-}Pr)_2$ and 2.5 mL (4 mmol) of *n*-BuLi solution in 10 mL of dry THF. After the addition of 50 mg (0.4 mmol) of $CuCl_2$ in 2 mL of DMF and the normal workup procedure, including crystallization from ethyl acetate, 10 mg (25%) of product **10** was obtained: mp 259.6–260.2 °C; IR 1680 and 1580 cm^{-1}; UV (ethanol) λ_{max} 332 nm (log ε 4.33); ^1H NMR ($CDCl_3$) δ 6.96 (C-8 hydrogens), 6.03 (C-3 hydrogens), 1.71 (C-7 methyl), 1.62 (C-6 methyl), 1.40 (C-1 methyl), 1.25 (C-5 methyl); ^{13}C NMR ($CDCl_3$) δ 208.1 (C-4), 172.1 (C-2), 144.2 and 140.9 (C-6 and C-7), 131.0 and 130.8 (diastereomeric C-8 or C-3 of *meso*- and *dl*-**17**, d, J = 155 Hz), 128.7 (C-3 or C-8, d, J = 170 Hz), 61.4 and 57.2 (C-1 and C-5), 14.1, 11.9, 10.5, and 8.9 (C-1, C-5, C-6, and C-7 methyls, q, J = 130 Hz); exact mass calcd at m/e 348.209 (M^+) found m/e 348.211. Anal. Calcd for $C_{24}H_{28}O_2$ (mol wt 348): C, 82.72; H, 8.10. Found: C, 82.06; H, 8.04.

Diol *endo*-11. To a cold solution (−18 °C, ice/salt mixture) of 100 mg (0.26 mmol) of diketone **8** in dry THF (freshly distilled from $LiAlH_4$) was added dropwise 1 mL of L-Selectride solution (1 mmol, 1 M solution in THF, Aldrich) under magnetic stirring. The solution was allowed to warm to room temperature, and stirring was continued for 3 h. Subsequently, 0.4 mL of water, 1.5 mL of ethanol, 2 mL of 10% aqueous NaOH, and 1.5 mL of 30% H_2O_2 were added dropwise and carefully. After being stirred for 2 h, the resulting mixture was extracted twice with ether (20 mL). The combined organic layers were washed with water (2 × 25 mL), dried over $CaCl_2$, and filtered, and the solvent was evaporated in vacuo. The resulting solid was washed with *n*-pentane, affording 64 mg (0.17 mmol, 64%) of alcohol *endo*-**11**:

(44) A similar phenomenon will be reported in the case of a dimeric σ-$AlCl_3$–cyclobutadiene complex: Kok, D. M. Ph.D. Thesis, University of Groningen, 1981.

^{1}H NMR ($CDCl_3$) δ 4.05 (C-4 hydrogens), 2.04 (C-8 hydrogens), 1.66 (C-3 methyl), 1.60 (C-6 and C-7 methyls), 1.14 and 1.02 (C-1 and C-5 methyls).

Diols 11, 12, 13, 13-d_4 and 14. Analogously to the synthesis of the corresponding monomeric alcohols, as described in the literature,[17] the secondary alcohol **11** and the tertiary alcohols **12–14** were prepared from the corresponding diketones. The crude products were obtained in nearly quantitative yields (95–100%) and were in principle pure enough for the generation of the dications.

Compound 11 (Mixture of Diastereomers). After recrystallization from *n*-hexane (–30 °C) 179 mg (0.47 mmol, 88%) of diol **11** was obtained by starting from 200 mg (0.53 mmol) of ketone **16**: IR 3440 cm^{-1} (br); ^{1}H NMR (CCl_4) in addition to the signals reported above the *endo*-**11** additional peaks for the exoisomer are found at δ 3.90, 1.69, 1.52, and 1.08; mass spectrum, *m/e* 346 ($M^+ - 2H_2O$).

Compound 12. Crystallization from *n*-hexane (–30 °C) afforded 232 mg (0.61 mmol, 71%) of diol **12** from 300 mg (0.86 mmol) of diketone **8**: mp 136–138 °C; IR 3350 cm^{-1} (br); ^{1}H NMR ($CDCl_3$) δ 5.01 (C-3 hydrogens), 2.13 (C-8 hydrogens), 1.59 (C-6 and C-7 methyls), 1.22, 1.07, and 0.95 (C-1, C-4, and C-5 methyls); exact mass calcd *m/e* 346.266 ($M^+ - 2H_2O$), found *m/e* 346.267.

Compound 13. Crystallization from *n*-hexane (–30 °C) afforded 265 mg (0.65 mmol, 81%) of diol **13** from 300 mg (0.8 mmol) of diketone **9**: mp 140–142 °C; IR 3560 cm^{-1} (br); ^{1}H NMR ($CDCl_3$) δ 2.00 (C-8 hydrogens), 1.61 (C-3, C-6, and C-7 methyls), 1.19, 1.09, and 1.02 (C-1, C-4, and C-5 methyls); exact mass calcd *m/e* 374.297 ($M^+ - 2H_2O$), found *m/e* 374.297.

Compound 13-d_4. A 145-mg (0.35 mmol, 90%) sample of crude product **13-d_4** was obtained by starting from 150 mg (0.39 mmol) of labeled diketone **9-d_4**. The ^{1}H NMR ($CDCl_3$) was identical with that for **13** except that it lacked the signal at δ 2.00 (C-8 hydrogens).

Compound 14. From 200 mg (0.53 mmol) of diketone **9** was obtained 265 mg (0.53 mmol, 100%) of crude diol **14**. Diol **14** was crystallized from ethyl acetate (–30 °C): IR 3600 cm^{-1} (br); ^{1}H NMR ($CDCl_3$) δ 2.10 and 2.05 (diastereomeric hydrogens at C-8), 1.63 (C-3 methyl), 1.58 (C-6 and C-7 methyls), 1.34 (C-5 methyl), 1.04 (C-1 methyl and *t*-Bu); exact mass calcd *m/e* 458.391 ($M^+ - 2H_2O$), found *m/e* 458.390.

Generation of Cations. The ionization of the diols with FSO_3H/SO_2ClF to the corresponding dications was performed analogously to the generation of the cations described previously.[17]

Quenching of Cations. After the ^{13}C NMR measurements the samples were in several cases quenched with excess CH_3ONa/CH_3OH. No interpretable ^{1}H NMR spectra were obtained (very broad signals in the δ 1.0–2.5 region) from the unattractive reaction mixtures; however, mass spectra indicated the presence of dimeric products. The mass spectra of the products of the quenching reaction of solutions of **12** and **13** in FSO_3H/SO_2ClF gave M^+ peaks at *m/e* 346 ($C_{26}H_{34}$) and 374 ($C_{28}H_{38}$), respectively, the latter one showing a very low intensity.

Registry No. **6**, 78592-55-9; **7**, 78592-56-0; *meso*-**8**, 78592-57-1; *dl*-**8**, 78655-21-7; *meso*-**9**, 78655-97-7; *dl*-**9**, 78655-22-8; *meso*-**9-d_4**, 78592-58-2; *dl*-**9-d_4**, 78655-23-9; *meso*-**10**, 78655-98-8; *dl*-**10**, 78592-59-3; **11** (isomer 1), 78592-60-6; **11** (isomer 2), 78655-24-0; **12**, 78592-61-7; **13**, 78592-62-8; **13-d_4**, 78592-63-9; **14**, 78609-78-6.

Supplementary Material Available: Spectral data for the alcohols **11–14** in FSO_3H/SO_2ClF at low temperatures (7 pages). Ordering information is given on any current masthead page.

Structure and Properties of a Stable Isoindole. The Dimethyl Acetylenedicarboxylate–1-(Ethylthio)-2-*n*-propylisoindole Substitution Product

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The reactions of 1-(alkylthio)-2-*n*-propylisoindoles with various dienophiles were investigated. Reactions with dimethyl acetylenedicarboxylate (DMAC) yielded stable 1:1 adducts which are dark red, α-substituted isoindoles with a fumarate side chain. The crystalline 1:1 adduct **6**, formed from 1-(ethylthio)-2-*n*-propylisoindole and DMAC was found to exist as a sterically congested, intramolecular charge-transfer complex. This steric crowding undoubtedly contributes to the stability of the isoindole and forces the plane of the fumarate side chain to be approximately perpendicular to the isoindole ring. These structural conclusions were confirmed by an X-ray structure determination of **6**, which also represents the first X-ray structure determination of an isoindole. In addition, these studies unambiguously identify isoindoles as the products of the reaction of *o*-phthalaldehyde and thiols with primary amines. The formation of a fumarate-substituted isoindole is analogous to the reactions of DMAC with pyrrole. However, spectroscopic and X-ray structural data show that the substituted isoindole **6** possesses considerable aromatic character and is not simply a 1,3-butadiene-annulated pyrrole. These results are discussed in terms of the hitherto unresolved questions regarding the structure and reactivity of isoindoles in general.

Questions regarding stability and reactivity have permeated almost all studies of isoindoles. The preparation of the first isoindole in 1951[1] and the unsubstituted, parent isoindole (**1**) in 1972[2] demonstrated that the ring system was stable enough for isolation. However, the questions of whether isoindoles were aromatic, as suggested by their 10-π-electron structure, and why they are so reactive remained unanswered. Because of the relative instability of isoindoles, most attempts to resolve these questions have involved comparisons of isoindole and pyrrole reactivity in Diels–Alder reactions and predictions of the molecular

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(1) Wittig, G.; Tenhaeff, H.; Schoch, W.; Koenig, G. *Justus Liebigs Ann. Chem.* **1951**, *572*, 1–22.
(2) Bonnett, R.; Brown, R. F. C. *J. Chem. Soc., Chem. Commun.* **1972**, 393–395.

0022-3263/81/1946-4739$01.25/0