Stereoselectivity Due to Electrostatic Repulsion in the Polar Cycloaddition of the Acridizinium Ion

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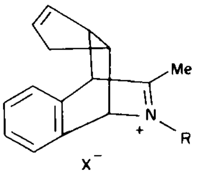
It was recently (1) proposed that the extreme stereoselectivity observed in the cycloaddition of cyclopentadiene and alkyl vinyl ethers (2) with the 2,3-dimethylisoquinolinium ion originates from the difference in the electrostatic replusion encountered in the alternative transition states leading to the second stage in the reaction. In the case of the cyclopentadiene adduct **1**, but not in the case of the alkyl vinyl ether adducts **2**, the observed (*syn*) orientation may appear to be explicable by the rule of Alder and Stein (3) concerning the maximum accumulation of double bonds. Since the acridizinium-(benzo[*b*]quinolizinium) ion is sufficiently symmetrical to make the application of the rule of Alder and Stein problematical, it seemed important to reexamine the cycloaddition products obtained from it.



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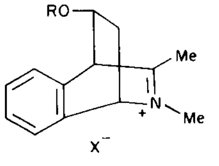

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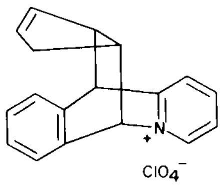
Although Fields *et al.* (4) described the 1,4-cycloaddition of cyclopentadiene with the acridizinium ion, they appear to have been unaware that the product **3** was a single geometrical isomer. In our hands, the reaction proved extremely stereoselective, for a crude, unrecrystallized sample of the adduct (96% yield) gave nmr evidence for the presence of but a single racemate. In Table I a comparison is made between protons of types common to both the acridizinium **3** and the dimethylisoquinolinium cyclopentaidene adducts (**1**). Assignment of the resonances to the specific protons shown in the formula were made by means of spin-spin decoupling experiments. The correspondence between the resonances observed for comparable protons in compounds **3** and **1** is quite remarkable both in regard to coupling pattern and chemical shift. With the understandable exception of the bridgehead proton (H_b) adjacent to the quaternary nitrogen atom, the differences in chemical shift amount to less than 0.22 ppm, leaving little doubt concerning the similarity in stereochemistry of **3** and **1**, or that **3** is *syn* with respect to the phenylene ring.

As a further test of the validity of the charge separation rule, the stereochemistry of the adduct (**4**), (5), from the reaction of methyl vinyl ether with acridizinium perchlorate was determined. Nmr spectra of the unrecrystallized adduct **4** revealed the presence of only a single geometrical isomer. Comparison of the nmr spectrum (Table II) of **4** with that of the adduct **2** of known structure (3) obtained by reaction of methyl vinyl ether with 2,3-dimethylisoquinolinium iodide, shows a remarkable similarity in the multiplicity and sequence of the signals consistent only with the assumption that the two compounds have similar stereochemistry.

From the generalization concerning stereoselectivity due to electrostatic repulsions, it should follow that less dramatic examples of such selectivity would be observed when the intermediate carbonium ion is less stabilized by resonance than it is in the allylic type of the cyclopentenyl adducts or carbonium-oxonium type of the vinyl ethers. It is probably significant that the norbornadiene-acridizinium adduct **5**, which would be formed from an intermediate carbonium ion stabilized by homoconjugation, should show only a 73%:27% preference for



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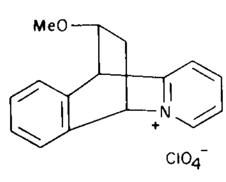

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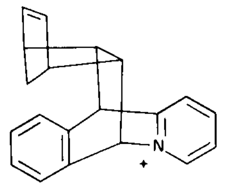

5 (*Syn* 73%)

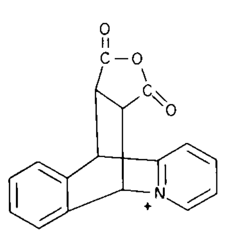

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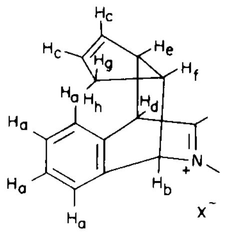
TABLE I

Comparison of Chemical Shifts (δ) of Related Protons in Adducts of Cyclopentadiene With the Acridizinium Ion and the 2,3-Dimethylisoquinolinium Ion

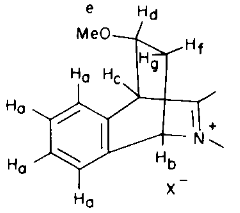


Protons	Acridizinium Adduct, **3**, X=ClO$_4$ Chem. Shift, δ (a)	Multiplicity	Di-Me-Isoquinolinium Adduct, **1**, R=Me, X=I Chem. Shift, δ	Multiplicity	Difference between Chem. Shifts, ppm.
a	7.48	m	7.44	m	0.04
b	6.17	d	5.50	d	0.67
c	5.43	s	5.30	s	0.13
d	5.08	d	4.87	d	0.21
e	3.62	m	3.62	m	0.00
f	3.32	m	3.38	m	-0.06
g	2.65	m	2.48	m	0.17
h	2.07	m	1.87	m	0.20

(a) All spectra were determined in trifluoroacetic acid.

TABLE II

Comparison of Chemical Shifts (δ) of Related Protons in Adducts of Methyl Vinyl Ether With the Acridizinium Ion and the 2,3-Dimethylisoquinolinium Ion



Proton(s)	Acridizinium Adduct, **4** Chem. Shift, δ (a)	Multiplicity	Di-Me-Isoquinolinium Adduct, **2**, R=Me, X=I Chem. Shift, δ	Multiplicity	Difference in Chem. Shifts, ppm
a	7.64	m	7.58	m	0.06
b	6.49	m	5.75	m	0.74
c	5.63	d	5.38	d	0.25
d	4.48	m	4.57	m	-0.09
e	3.72	s	3.60	s	0.12
f	3.00	m	3.00	m	0.00
g	2.22	m	1.78	m	0.44

(a) All spectra were determined in trifluoroacetic acid.

the *syn* configuration (6). Finally, the adduct **6** obtained in good yield (7) by the reaction of maleic anhydride with the acridizinium ion has been shown (8) to be in the *anti* configuration (6). It would not be expected that the intermediate carbonium ion would be stabilized by charge delocalization in the way that is possible in the examples previously cited and one might predict that approximately equal quantities of the two geometrical isomers would be formed. That the orientation is predominantly *anti* is possibly a result of charge transfer complex formation. More important, it is clear that the reaction product of maleic anhydride with the acridizinium ion is of opposite stereochemistry from that obtained by the reaction of cyclopentadiene with the same cation, indicating that any effort to apply the rule of Alder and Stein to *polar* cycloaddition is probably meaningless.

EXPERIMENTAL

The elemental analyses were carried out by M-H-W Laboratories, Garden City, Michigan. Melting points were determined in capillaries using a Thomas-Hoover melting point apparatus and are uncorrected. Proton magnetic resonance spectra were obtained at 60 MHz on Varian A-60 and T-60 Spectrometers using tetramethylsilane as an internal standard. Spin-spin decoupling experiments were performed using a Varian T-60 or Brucker HF-X-10 Spectrometer.

Adduct **3** of Acridizinium Perchlorate with Cyclopentadiene.

Freshly cracked cyclopentadiene (10 ml.) was added to a solution of 4.5 g. of acridizinium perchlorate in 120 ml. of acetonitrile. After 12 hours at room temperature all volatiles were removed under reduced pressure and most of the cyclopentadiene dimer was removed by trituration of the residue with petroleum ether (30-60°). The crude adduct, 5.3 g. (96%), m.p. 210-220° had a pmr spectrum suggesting the presence of only a single geometrical isomer. Crystallization from acetonitrile-ether afforded a colorless microcrystalline solid, m.p. 241-245° (lit. (4) m.p. 246°).

syn-12-Methoxy-6,11-dihydro-6,11-ethanoacridizinium Perchlorate (**4**).

A solution of acridizinium perchlorate in 25 ml. of acetonitrile was cooled to 0° and 0.6 g. of methyl vinyl ether, cooled to -10° was added along with a small amount of *p*-methoxyphenol. After allowing 4 hours for reaction in a stoppered flask at room temperature, an additional 0.5 g. of methyl vinyl ether was added and an additional 12 hours allowed for reaction. All volatiles were removed under reduced pressure and a sample of the crude residue dissolved in trifluoroacetic acid. Pmr examination of the spectrum indicated that conversion was quantitative to a single geometrical isomer. Recrystallization from acetonitrile-methanol gave a colorless microcrystalline solid, m.p. 96-98°.

Anal. Calcd. for $C_{16}H_{16}ClNO_5$: C, 56.90; H, 4.78; N, 4.15. Found: C, 56.66; H, 4.71; N, 3.87.

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