Stereochemistry of Cationic Polar Cycloaddition[1]

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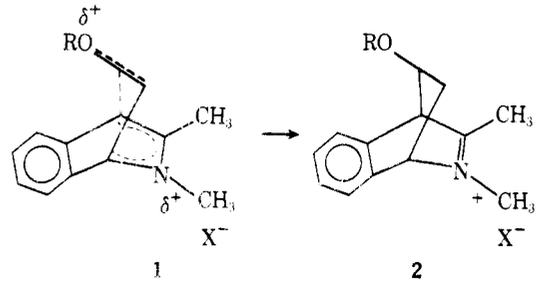
By new application of ^{1}H NMR it has been possible to determine the syn/anti ratio of adducts obtained by the reaction of the acridizinium (benzo[*b*]quinolizinium) cation, or its derivatives, with polarizable alkenes. Study of 24 such adducts shows that nearly all are formed with significant stereoselectivity, which may be rationalized in terms of electrostatic effects (repulsion or attraction) at or enroute to the transition state.

Along with the principle of maintenance of stereochemical integrity of the dienophile,[2] Alder's endo addition rule[3] is frequently invoked in discussion of the stereochemistry of classical Diels–Alder cycloadditions. The observed endo stereoselectivity has been attributed[4,5] to symmetry-controlled secondary orbital interactions which are sufficiently weak to be overridden at times by steric factors[6] ("steric approach control"), as in the exo addition of dienes to norbornene derivatives.[3]

In cycloadditions involving quaternary salts neither secondary orbital interactions nor steric effects appear to account adequately for the stereoselectivity observed. Instead electrostatic interactions[7-10] are believed to be the determining factor, since electrostatic effects are operative over larger distances than are nonbonded interactions and should assume precedence.

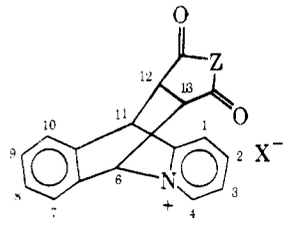
Illustrating this point most effectively, the addition of vinyl ethers to both the 2,3-dimethylisoquinolinium[10] (see adduct **2**) and the acridizinium[9] (benzo[*b*]quinolizinium) ions has been demonstrated to occur with 100% stereoselectivity. This selectivity is consistent with the concept of a concerted but nonsynchronous process in which the electrostatic interactions develop early in the reaction. The orientation of the alkoxyl group, demonstrated in the case of **2** by single crystal X-ray analysis[10] to be syn[11] with respect to the phenylene ring, is consistent with the maximum separation of like charges in the transition state **1** which must resemble a charge-transfer complex.[12]



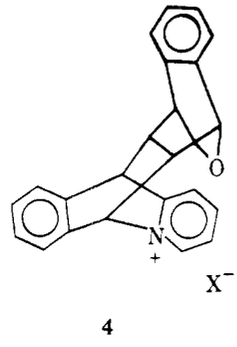
1 **2**

The stereospecific additions and identical orientation of cyclopentadiene in cycloadditions with both isoquinolinium[8] and acridizinium[9] systems have indicated that this high stereoselectivity is not an isolated phenomenon of vinyl ethers. Consequently, a stereoselectivity rule governing polar cycloadditions has been advanced:[8] "... if two geometrical isomers are possible ... and if the transition states ... differ in the distances between the centers of receding and developing positive charge, then the geometrical isomer formed in the larger amount will be that with the greater distance between the charge centers in the transition state."

Another type of stereoselectivity which appears to have a polar basis has been observed in the cycloaddition of maleic anhydride[13] and aryl maleimides[14] to the acridizinium ion. In contrast to the stereospecific formation of syn adducts with vinyl ethers and cyclopentadiene, maleic anhydride yields selectively the anti isomer **3**. The anti orientation has been explained[15,16] in terms of a preferential interaction in the charge-transfer complex, more exactly, the unshared pair of the heteroatom in either the maleic anhydride or the imide ring being attracted to the positively charged pyridinium ring. Further evidence in support of this concept has been provided[15] by the exclusively anti addition of 1,4-dihydronaphthalene 1,4-*endo*-oxide to yield adduct **4**. Since maleic anhydride



3, Z = O, NR



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and 1,4-dihydronaphthalene 1,4-*endo*-oxide exhibit distinctly different relative reactivities[15] their identical stereospecific orientations are most likely derived from the lone pairs of electrons available at oxygen in both olefins.

From the NMR spectra of a large number of adducts obtained from the acridizinium ion, Fields et al.[17] concluded that both syn and anti addition had occurred in every case. There is no doubt but that the majority of addends, particularly those of low nucleophilicity, do afford mixtures of geometrical isomers. A reasonable test of our thesis that in polar cycloaddition polar influences not only control regiochemistry[18] but also have a major influence on stereochemistry appeared to be an examination of the composition of some of these mixtures of geometrical isomers for signs of polar influence.

Determination of Syn/Anti Ratios. Although the cycloaddition of styrene with the acridizinium ion has been investigated previously in two laboratories,[13,19] the distribution of the syn and anti forms in the product had never been determined, and neither of the diastereomers had been obtained as a pure racemate. We have now found that the syn and anti forms can be separated by fractional crystallization of the styrene adduct (12-phenyl-6,11-dihydro-6,11-ethanoacridizinium perchlorate, **5** and **6**) from 1-butanol. The major stereoisomer, which also proved to be the least soluble, was the syn isomer (**5**), as shown by methods to be described. Separation of the syn and anti forms by fractional crystallization is not usually a very useful analytical method for the estimation of the proportion of each racemate present in the original product mixture and therefore priority was placed upon the development of methods for the estimation of the ratio of the stereoisomers present in the mixture.

In the NMR spectra of both of the pure racemates (**5** and **6**), signals for two aromatic protons appeared at an unusually high field, δ 6.5–6.8. In agreement with an earlier assignment[19] these shielded aromatic protons were attributed to the phenyl

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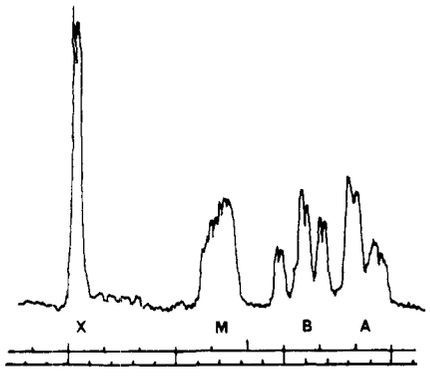


Figure 1. The ABMX Portion of the ^1H NMR spectrum of the syn isomer (**5**). The Y portion of this ABMXY spin system was obscured by overlapping aromatic signals.

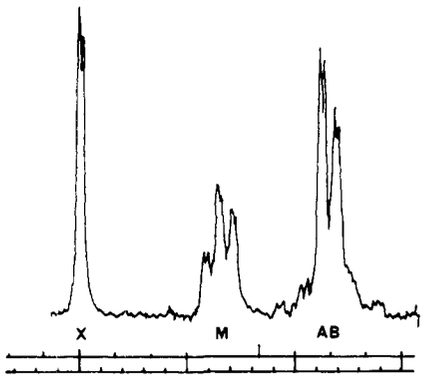
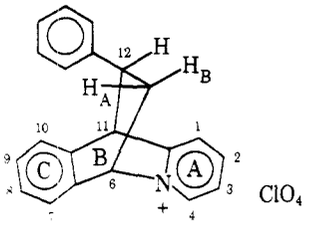
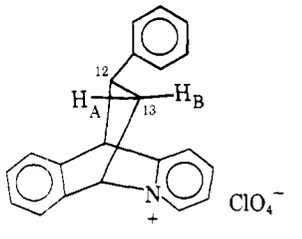


Figure 2. The ABMX portion of the ^1H NMR spectrum of the anti isomer (**6**). As in Figure 1 the Y portion of this ABMXY spin system was obscured by overlapping aromatic signals.



5, syn isomer, mp 245–247 °C



6, anti isomer, mp 203–204 °C

group at position 12 atop the bridge and result from the two ortho hydrogens sweeping through the Π cloud of the phenylene or pyridinium ring. Since the adduct mixture can be selectively hydrogenated[15] in the pyridinium ring, the anti isomer (**6**) can be deprived of this type of shielding with the result that the ortho hydrogens give signals in the usual aromatic range. In contrast, selective hydrogenation of the higher melting isomer had little effect upon the NMR signals generated by the ortho hydrogens, forming a basis for the assignment of this isomer as the syn isomer (**5**).

The assignments made for the two isomers were also consistent with those made using other portions of the ^1H NMR spectra. Although in each case the nonaromatic protons comprised an ABMXY spin system, several distinct differences were exhibited in the spectra of the two isomers. As may be seen in Figures 1 and 2, the syn adduct possessed a greater line separation in the AB portion than did the anti isomer.

The respective patterns of the isomers may be explained in terms of through-space proximity effects of the pyridinium ring as well as of the phenyl group located at C-12. In the syn isomer (**5**) a small shielding contribution from the phenyl group at C-12 is directed on 13a, the bridge hydrogen cis to the ring. At the same time bridge proton 13b, nearest the pyridinium ring, is being deshielded by the charge of the quaternary nitrogen, resulting in a wide spacing of the AB protons (Figure 1). In the anti isomer, however, the opposing effects of the shielding by the bridge phenyl group and deshielding by the cationic charge operate on the same proton, 13b. The result of these offsetting effects is a close spacing of the AB protons (Figure 2). The deshielding effect of the quaternary nitrogen is significant for in the adduct obtained from the reaction of 1,1-diphenylethylene with the acridizinium ion, the patterns for protons 13a and 13b are separated by δ 0.43 in the ^1H NMR spectrum.

Likewise, the near equivalence of the 13a and 13b protons in the anti adduct of styrene is reflected in the multiplicity of the C-12 proton, which appears (Figure 2) essentially as a triplet with minor splitting from the C-11 bridgehead hydrogen. In the syn isomer (Figure 1) the C-12 signal appears as a complex multiplet.

Another signal useful for distinguishing between the stereoisomers is the C-4 signal which occurs farthest downfield, and is easily identified and measured. When the C-12 phenyl group is positioned correctly to shield the 13b proton as in the anti isomer (**6**) the deshielding edge of the phenyl ring is directed toward the pyridinium ring. Apparently this contribution is significant in that the C-4 hydrogen in the anti isomer is centered at δ 9.20, whereas the corresponding syn absorbance occurs at δ 9.07. Since the value for the C-4 hydrogen of the syn isomer agrees closely with that found in adducts lacking a bridge phenyl group, it appears reasonable to conclude that a syn phenyl at position 12 does not perturb the C-4 resonance.

Some of these differences in the ^1H NMR spectra have been utilized in determining the isomeric composition of unseparated mixtures. For example, a partial separation of the syn and anti forms of the *p*-methoxystyreneacridizinium ion adduct revealed that in the ^1H NMR the methoxyl signals of the stereoisomers occur at slightly different field values. By comparison with the known styrene adducts these syn and anti adducts have been identified easily on the basis of their ABMXY spin patterns, making it possible to assign to the anti isomer the methoxyl signal occurring at the lower field. A similar analysis of the stereoisomeric adducts obtained from *p*-methylstyrene and the acridizinium ion revealed that the methyl group at lower field was that of the anti isomer. For the methoxystyrene and methylstyrene adducts the relative intensities of the methyl signals can be used to estimate the stereoisomer ratio. A similar estimate of isomer ratio can be based upon the relative intensity of the C-4 proton signals.

A more complex but more general method is based upon the selective reduction of the pyridinium ring of the adducts, a procedure discussed earlier. Recall that the catalytic reduction of the pyridinium ring deprived the anti isomer but not the syn isomer of two shielded aromatic (ortho) protons. A simple algebraic equation permits the calculation of the isomer ratio from the relative areas of the shielded vs. the normal aromatic ^1H NMR resonances.

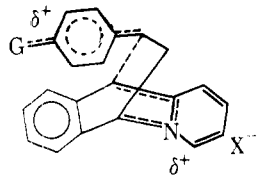
The limitations of the reduction method of analysis are that there must be a phenyl group (or substituted phenyl group having at least one ortho hydrogen) at position 12 of the ad-

Table I. Determination of the Percent Syn Isomer in Adducts Obtained by Reaction of Acridizinium Ion with Para Substituted Styrenes at 80 °C

para substituent	% syn isomer obtained by reduction	C-4H	CH_3
H	67		
Me	64	65	70
MeO		73	76

duct and that the system not be substituted in such a way that the signals from the ortho hydrogens are no longer clearly separated from those of the other aromatic hydrogens. The limitation of the accuracy of the methods used is the error in the ^1H NMR integration which in our case is estimated at 5–7%.[20] A comparison of results obtained by the three independent methods may be seen in Table I. In the case of the sterioisomerism of the *p*-methylstyrene adduct for which measurements by all three methods are available, the results deviate less than 5% from the simple average of 66% syn isomer in the crude adduct.

Table I also reveals that in every instance the formation of the syn product is favored. Assuming that the positive charge is delocalized into the styryl ring in the transition state (cf., **7**), the observed predominance of the syn adduct is consistent



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with the coulombic repulsion stereoselectivity rule[8] for cationic polar cycloadditions. Since the amount of coulombic repulsion must depend upon the intensity of the secondary positive charge developed in the charge transfer type transition state [12] (as well as its distance from the ethylene axis), it does not seem surprising that *p*-methoxystyrene would afford a higher yield of syn adduct than would the unsubstituted styrene. If the aryl group attached to the ethylene is incapable of stabilizing a positive charge it would be predicted that the stereoselectivity would be less pronounced, and indeed when 2-vinylpyridine is the addend, equal quantities of the syn and anti racemates appear to be formed.

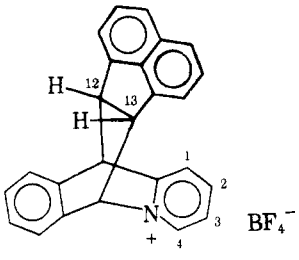
Since only those reaction mixtures which are produced by a kinetically controlled process provide useful mechanistic information, the possibility of thermodynamic control in the styrene–acridizinium addition was examined. The purified syn styrene adduct (**5**) was subjected to the conditions of the cycloaddition reaction and found unchanged after 36 h. Since the isomeric mixtures analyzed in Table I were isolated almost quantitatively after 12 h, and isomer ratios do not appreciably change on further heating, it is safe to conclude that the observed ratio of isomers is not the result of a thermodynamic equilibrium.

As a kinetically controlled reaction, the differences in isomer distribution must be explained by differences in the energy of the transition states. For a 70:30 mixture formed at 80 °C an energy difference in the transition states of only 0.6 kcal/mol would be required.

In the significant work of Cristol and Linn[21] it was suggested that there was a correlation between the stereochemistry observed in the Diels–Alder synthesis of certain substituted janusenes and the ability of the substituted benzenoid ring to attract an unsubstituted ring by a Π base–Π acid interaction. Clearly such an influence is not usually the dominant one in polar cycloaddition for if it were the addition of styrenes to the acridizinium ion would be largely anti (**6**) as a result of the attraction of the pyridinium ring (a Π acid) for the phenyl group of the styrenes.

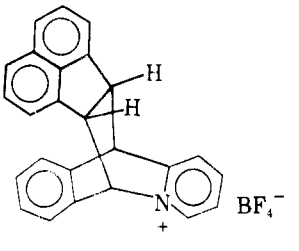
To determine whether substitution on the phenylene ring of the acridizinium nucleus would bring about significant changes in the stereochemistry of addition, the syn and anti ratios have been determined for the addition of styrene to 9-methylacridizinium and to 8,9-dichloro-11-methylacridizinium tetrafluoroborates. Even though the electronic nature of ring C was modified considerably between these two examples, nearly identical syn to anti ratios of 69:31 and 74:27 have been calculated for the 9-methyl and dichloro examples, respectively. This would indicate that changes in the Π acid–base character of the phenylene ring are not the major influence on stereochemistry in this cycloaddition.

Acenaphthylene also forms an adduct which contains both stereoisomers (**8** and **9**) and these may be separated by fractional crystallization. Assignment of the lower melting isomer as the anti isomer was made by the observation that the C-4 proton signal appeared at δ 8.35 indicating that it was strongly shielded (viz., **8**) whereas the high-melting isomer had an al-



8

45 ± 5% mp 272–274 °C

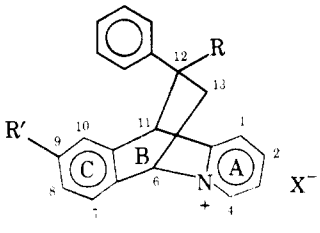


9

55 ± 5% mp 304–304.5 °C

most unperturbed value for the C-4 proton, δ 9.13. The validity of these assignments has been reenforced by the observation that the bridge protons at C-12 and C-13 are more nearly equivalent in the anti isomer than in the syn since this is in agreement with an earlier observation.[15] Analysis of the original mixture of stereoisomers was effected by comparison of the integration of the syn C-4 signal versus that of a bridgehead resonance common to both isomers. That the ratio of syn to anti isomers is only 55:45 (±5%) was somewhat surprising, but suggests that a simple Lewis acid–Lewis base interaction might be observed if an aryl group were at position 13 with none at position 12.

The methyl group of α-methylstyrene has little influence on the orientation of cycloaddition, but in the adduct provides useful information concerning the stereochemistry of addition. If the C-12 methyl is above the pyridinium ring (e.g., **10**) its



10, R′ = H; R = Me
11, R′ = Me; R = H

signal appears at a lower field than that of the stereoisomer in which the methyl group is over a phenylene ring. Integration of the signals shows that 64% of the α-methylstyrene adduct has the phenyl group in the syn position (**10**).

The Use of a Methyl Group on the Acridizinium Nucleus as a Stereochemical Indicator. When the adduct of

Table II. The ^{1}H NMR Chemical Shifts[a] for the 9-Methyl Group in Acridizinium Adducts and the Isomeric Compositions Derived from the Data

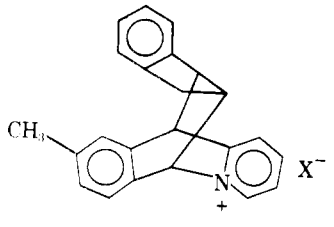
alkene addend	*anti*-9-Me	*syn*-9-Me	% syn
9-vinylcarbazole		2.06	100[b]
indene	2.45	2.10	80
styrene	2.46	2.32	72
2-vinylpyridine	2.52	2.45	50
acenaphthylene	2.42	1.92	48

[a] Chemical shifts are expressed in δ units and were taken in TFA. [b] Cycloaddition was performed at 25 °C in 1:1 (v/v) methanol–acetonitrile; all other values are for additions run at 80 °C in acetronitrile

styrene with 9-methylacridizinium ion was examined by NMR spectroscopy, two distinct methyl resonances were observed. The one of higher intensity, also found at the higher field, was easily identifiable as due to the syn isomer (**11**), since this is the stereoisomer which can produce maximum shielding. A more elegant example of such shielding is to be found in the work of Wieland and McCarty[22] on the adduct of benzocyclobutadiene with 2,7-dimethylanthracene. The use of acridizinium derivatives with methyl groups in ring C has proved a convenient means for the determination of the orientation of an aryl group at position 12 of an adduct. A summary of five such determinations with 9-methylacridizinium tetrafluoroborate is shown in Table II.

Since in the *anti*-9-methylacridizinium adducts the effect of shielding by the aryl group at position 12 would be minimized, it is not surprising that in that isomer signals from the 9-methyl group are all nearly the same. In marked contrast the *syn*-methyl resonances varied dramatically, but in an understandable pattern. Specifically, the evidence of shielding increases as the size and the expected electron richness of the π system are increased. Furthermore the shielding is magnified when the aryl group is constrained in a rigid configuration as in the case of the acenaphthylene adduct which must focus the π cloud continuously on the methyl substituent. The similarity in isomer ratios to those determined by the methods used for the unsubstituted acridizinium ion suggest that the steric influence of the 9-methyl group on orientation is relatively minor.

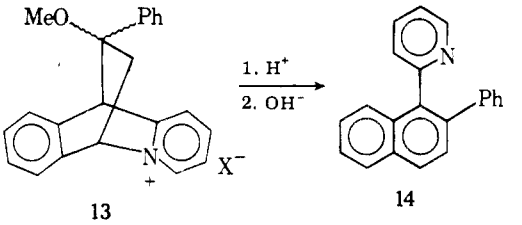
Table II also reveals that addition of 9-vinylcarbazole to 9-methylacridizinium ion is stereospecific. Like vinyl ethers and cyclopentadiene[9] 9-vinylcarbazole is highly reactive toward the acridizinium ion and is likewise polarizable. It is known[18] that the regiochemistry of the addition of indene to the acridizinium ion resembles that of styrene. The *stereochemistry* of the addition of indene to 9-methylacridizinium ion bears a similar resemblance to that of styrene in that the predominant product (**12**) has the two phenylene groups opposed (syn).



12

It has already been demonstrated[9] that a methoxyl group attached to an ethylenic bond (as in methyl vinyl ether) will orient 100% syn when added to the acridizinium nucleus, in other words, it is more strongly syn directing than the phenyl group of styrene. As a competition experiment between the directive powers of the phenyl and methoxyl groups the orientation of the adduct of 9-methylacridizinium ion with α-methoxystyrene was examined. Despite the indications from model experiments that the methoxyl group should predominate in syn orientation, the reaction mixture consisted of almost equal parts syn and anti products. A possible clue to the lack of the effectiveness of the methoxyl group is provided by ^{13}C NMR studies carried out by Hatada et al.[23] which showed that introduction of an α-alkyl group into vinyl ethers resulted in steric inhibition of resonance. It seems likely that an α-phenyl group would have a similar effect on resonance involving the methoxyl group of α-methoxystyrene.

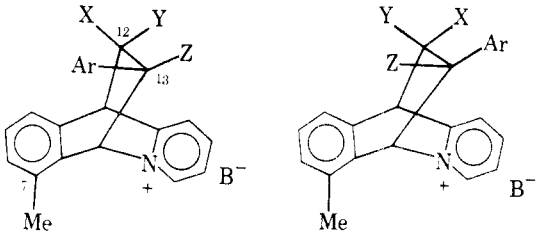
When the α-methoxystyrene adduct (**13**) was dissolved in trifluoroacetic acid there was a slow rearrangement of the Fields[19] type which could be easily followed by changes in the ^{1}H NMR spectrum, affording 1-(2-pyridyl)-2-phenylnaphthalene (**14**), identical with an authentic sample.[24] Although



13 **14**

13 is an ether of the benzyl type, the ease with which it undergoes cleavage is remarkable.

The success met with in using a methyl group at position 9 of the acridizinium nucleus as a probe for the stereochemistry of adducts having an aryl group at position 12 of the ethano bridge invited the question whether a methyl at position 7 might not play a similar diagnostic role in the study of adducts having an aryl group on the ethano bridge at position 13 (**15** and **16**).



15 **16**

An aryl group at position 13, if in the syn configuration (**15**), would shield the methyl group at position 7, while in the anti position (**16**) shielding effects would be minimal. If the stereochemistry of the alkene addend is known and if group Z is not aryl it is possible to describe precisely the stereochemistry of the racemate **15** or **16** obtained. As mentioned earlier,[18] *cis*-β-methoxystyrene adds regiospecifically with the phenyl ring at carbon 13. Selective reduction of the pyridinium ring and NMR of the product revealed that the phenyl group was 96% syn. When the same cycloaddition was carried out using 7-methylacridizinium tetrafluoroborate the NMR results (Table III) showed that 93% of the adduct had the syn configuration (**15**, X = OMe; Y = Z = H).

The 7-methylacridizinium ion proved a useful substrate for studying the stereochemistry of addition of *trans*-stilbenes. Results obtained with two *trans*-stilbenes suggest that the tendency to add in the 12-anti-13-syn mode is predominant, reflecting an unexplained pattern observed earlier[13,25] in the addition of diethyl fumarate to the acridizinium ion.

It appears that the optimum system for observing the aryl shielding effect, and hence the stereochemistry at C-12, would be the 10-methylacridizinium ion. Unfortunately this mono-

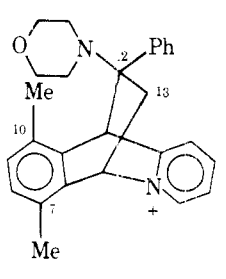
Table III. The ^{1}H NMR Chemical Shifts for the 7-Methyl Group in Several Acridizinium Adducts and the Isomeric Compositions Estimated from the Data

alkene addend	chemical shifts,[a] ppm *anti*-7-Me	*syn*-7-Me[b]	% syn[b]
cis-β-methoxystyrene[c]	2.62	2.19	93
trans-stilbene	2.68	1.96	64
trans-4,4′-dimethoxystilbene	2.69	2.13	55

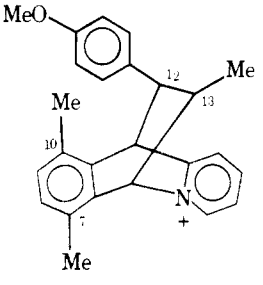
[a] Chemical shifts were measured in CF_3COOH. [b] Syn refers to the C-13 aryl function and the phenylene ring, the orientation **15**. [c] While the purity of the *cis*-β-methoxystyrene was evidenced by its ^{1}H NMR spectrum the presence of a small quantity of trans isomer cannot be excluded. Likewise the possibility of a small amount of cis–trans rearrangement was not rigidly excluded.

substituted aromatic cation is not easily available from the usual synthetic routes[25] to the acridizinium nucleus. Since for adducts of 7-methylacridizinium the effect of an aryl group at the remote (C-12) bridgehead position was demonstrated to be negligible, the known[26] 7,10-dimethylacridizinium ion offered a substitute for the 10-methyl analogue. The principal application of this new stereochemical probe has been in determining the stereochemistry of addition of 1-morpholino-1-phenylethylene to the acridizinium nucleus. Although the addition to the parent cation had been carried out earlier[19] it was not noted that only a single racemate is formed in the reaction. The addition to 9-methylacridizinium is likewise stereounique but in the absence of an isomer for comparison purposes it was difficult to decide whether or not the NMR chemical shift observed for the protons of the methyl group reflected shielding by the phenyl ring.

When the adduct of 7,10-dimethylacridizinium ions was examined by NMR the two methyl signals at δ 2.52 and 2.46 were too close together for the phenyl group to have been syn and therefore the correct assignment is as the *anti*-phenyl isomer (17), the isomer which would have been expected to



17, 100%



18, 79%

predominate from the coulombic repulsion rule. In order to demonstrate that the 10-methyl group will respond to aryl shielding, the anethole adduct was prepared. The expected major product (18) having the aryl group syn (79% yield) showed a highly shielded methyl signal at δ 1.85 whereas the stereoisomer showed an "unperturbed" methyl signal at δ 2.63.

Cycloaddition of Dienes. The observed[8,9] stereospecificity of the cycloaddition of cyclopentadiene to aromatic quaternary salts has implied the importance of conjugative effects. In terms of a nonsynchronous mechanism, the delocalization of incipient positive charge in the alkene through conjugative or participatory effects should lower the energy of the activated complex. Furthermore according to the coulombic repulsion rule the greater degree of delocalization available in alkenes capable of conjugation or participation should be manifested in the high stereoselectivity of their reactions with aromatic cations.

In the present work it was first assumed that the stereochemistry of the cycloaddition of 1,3-cyclohexadiene to aromatic cations might be solely syn as seen earlier in the addition of cyclopentadiene. While the major product (2:1) of cycloaddition with the acridizinium ion was indeed that predicted by the coulombic repulsion rule the reaction was no longer stereounique. The differences in the cycloaddition behavior between cyclopentadiene and 1,3-cyclohexadiene in their cycloaddition behavior must originate in their relative ground state geometries. These have been compared[27] recently. In contrast to the planar configuration of double bonds in cyclopentadiene, one ethylene group in 1,3-cyclohexadiene is rotated with respect to the other about the C-2–C-3 bond by 17.5°. The importance of this difference in the interplanar angle between the vinyl groups in cyclopentadiene and in 1,3-hexadiene has already been demonstrated[28] in the difference in the course of reaction with benzyne.

Additional support for the view that the double bonds are not acting independently has been supplied by a comparison of the relative ease of cycloaddition of cyclohexene[15] and 1,3-cyclohexadiene with the acridizinium nucleus. The reaction with cyclohexene requires a temperature of 120 °C while that with cyclohexadiene proceeds satisfactorily at room temperature. Similarly cyclopentadiene has been reported[29] to add more readily and be more than five times more diastereoselective than cyclopentene in polar cycloadditions with the amidomethylenium ion. In summary any mechanism proposed must account for the favorable effects of conjugation in the 2π component in polar cycloadditions involving aromatic cations.

Nonconjugated cyclic dienes in which the double bonds are for some reason constrained to lie parallel are known to undergo transannular chemical reactions in the presence of electrophiles, the reaction of norbornadiene with bromine to afford 3,5-dibromonortricyclene (3,5-dibromotricyclo-[2.2.1.0^{2,6}]heptane)[30] being a classical example. While it appears that no nortricyclene derivative is formed in the cycloaddition of norbornadiene with the acridizinium ion there is a 73:27 preference for the syn isomer,[15] a selectivity made less remarkable by the observation that norbornene, with only a single double bond, gives a 60:40 preference for the syn configuration.

1,5-Cyclooctadiene exists in a "tub" conformation with its double bonds parallel and transannular π participation is a well-documented pathway for its reactions.[32] Similar participation in the polar cycloaddition would facilitate dispersion of positive character in the charge transfer complex which must be along the reduction pathway. In any case cycloaddition of 1,5-cyclooctadiene with the acridizinium ion gave only a single geometrical isomer. The adduct melted sharply and the melting point did not change on recrystallization. The ^{1}H NMR of the adduct gave no evidence that more than one isomer was present. Selective reduction of the pyridinium ring produced only a minimal shift in the vinyl proton signals indicating that the sole product was indeed the syn isomer, the product favored by the coulombic repulsion rule. Cyclooctene is less reactive toward the acridizinium ion than 1,5-cyclooctadiene and the adduct appears to be a mixture of racemates. Although the examples are extremely limited these initial results indicate the importance of further investigations into polar cycloadditions involving 2π components capable of participation.

The proposal[12] that the transition state in polar cycloaddition is or closely resembles a charge-transfer complex gains support from the numerous examples of stereoselectivity explicable in terms of polar effects.

Experimental Section

The elemental analyses were performed by M-H-W Laboratories, Garden City, Mich. Melting points were determined in capillary tubes

Table IV. Adducts Obtained by Reaction with Acridizinium Tetrafluoroborates in Refluxing Acetonitrile

adduct no.	acridizinium substituents	addend	time, h	yield,[a] %	mp of samples for analysis, °C NMR	mp of samples for analysis, °C elemental[b]
5, 6	c	styrene[d-f]	12	96	180–218	222–230
	g	1,1-diphenylethylene	4[h]	97	162–167[i]	217–218[j]
		p-methoxystyrene[d,f]	12	99	132–145	132–145
		p-methylstyrene[d,f]	10	97	189–197	197–205
		2-vinylpyridine	24	98	190–195	197–201
8, 9		acenaphthylene	48	100	*k*	288–293
		α-methylstyrene	13	>90	*k*	203–204[l]
11	9-Me[m]	styrene	6	99	*k*	198–202
	8,9-dichloro-11-methyl[n]	styrene	12	96	*k*	294–296
	9-Me	9-vinylcarbazole	69[p]	92	203–205[q]	203–204[r]
12	9-Me	1,1,3-trideuterioindene	12	97	178–204	213–214[s]
	9-Me	2-vinylpyridine	24	99	145–170	168–182[t]
	9-Me	acenaphthylene	48	100	238–260	290–291[u]
13	9-Me	α-methoxystyrene[v]	100[w]	100	193–210	214–215
	7 Me[x]	*cis*-β-methoxystyrene	106[y]	96	*k*	178–180
	7-Me	*trans*-stilbene	72[y]	95	173–200	198–203
	7-Me	4,4′-dimethoxystilbene	68	100	*k*	142–154[z]
17	9-Me	1-morpholino-1-phenylethylene	0.5[w]	94	165–167[q]	165–167[r]
	7,10-$(Me)_2$	1-morpholino-1-phenylethylene	0.1[w]	93	*q*	121–123[r,aa]
18	7,10-$(Me)_2$	anethole[bb]	52	93	143–156	150–153
		1,3-cyclohexadiene	3.5	100	226–231	231–232.5[cc]
		1,5-cyclooctadiene	36	95	303–305[q]	303–304[cc]
		cyclooctene	54	100	247–260	263–267[cc]

[a] Yield of crude cycloaddition product used for NMR analysis. Except as noted, this product, where possible, consists of a mixture of racemates. [b] Elemental analyses were carried out on recrystallized samples although usually still mixtures of racemates would contain less of the more soluble racemate. The Editor has been supplied with analyses (C,H,N) for each of the products included. [c] Reference 24. [d] Cycloaddition of the bromide salt with the addend has been reported previously. [e] Reference 17. [f] Reference 13. [g] Cycloaddition using the bromide salt. [h] In refluxing acetic acid. [i] The perchlorate salt, prepared by addition of 35% perchloric acid to a solution of the adduct. [j] Bromide salt. [k] Melting point of crude product not recorded. [l] Appears to be pure syn isomer. [m] The tetrafluoroborate salt, mp 193–195 °C, was prepared from the known (ref 33) bromide. [n] The perchlorate salt (ref 32) was used in the cycloaddition. [o] Crystallized from acetronitrile. [p] Reaction carried out at room temperature in 1:1 (v/v) methanol–acetonitrile. Under reflux a large portion of the 9-methylacridizinium salt was recovered. [q] Single racemate. [r] Recrystallized by addition of anhydrous ether to a concentrated solution made by dissolving the adduct in acetronitrile at room temperature. [s] Recrystallized from acetonitrile. [t] Elemental analysis suggests that the substance crystallizes from 95% ethanol as a hemihydrate. [u] Pure syn isomer obtained by recrystallization of adduct from 1-butanol. [v] Reference 34. [w] Reaction at room temperature. [x] The tetrafluoroborate (mp 213–214 °C) was prepared from the known (ref 33) bromide. [y] Cycloaddition in refluxing 1-butanol. [z] Recrystallized from acetronitrile–ether. [aa] Elemental analysis indicates the analytical sample to be a difluoroborate salt, $C_{27}H_{30}B_2F_8N_2O$. [bb] 1-(*p*-Methoxyphenyl)-1-propene. [cc] Crystallized from acetonitrile.

with a Thomas-Hoover melting point apparatus and are uncorrected. All proton magnetic resonance spectra were made using tetramethylsilane as a standard; the instruments used were: 60 MHz, Varian T-60; 90 MHz, Brucker HF X-10; 100 MHz, JEOL-JNM-MH-100.

Preparation of Acridizinium Adducts for Determination of Stereoisomer Ratios. The methods used in carrying out the cycloadditions have already been described.[13,17] The acridizinium tetrafluoroborate was refluxed in acetronitrile usually with 2–3 molar equiv of the alkene until examination of the UV spectrum showed that the long wavelength maximum due to the acridizinium ion has disappeared. Usually at least part of the solvent was removed under vacuum and ether or ethyl acetate or ethyl acetate–ligroin added to precipitate the adduct. This crude product was used in NMR studies of stereoisomer ratios, but elemental analyses were performed only after recrystallization, ethanol being the usual solvent. The results are summarized in Table IV.

***syn*-12-Phenyl-6,11-dihydro-6,11-ethanoacridizinium Perchlorate (5).** A water solution of the known[17,13] bromide (a mixture of racemates) was treated with 35% perchloric acid to afford the perchlorate, mp 208–220 °C. The mixture of stereoisomers was digested with boiling 1-butanol and filtered hot. The undissolved fraction was fractionally crystallized from 95% ethanol: mp 245–247 °C; ^{1}H NMR (CF_3COOH) δ 2.08–3.18 (m, 2, C-13), 3.48–3.82 (m, 1, C-12), 4.97 (d, 1, J = 2.5 Hz, C-11), 6.47–6.80 (m, 3, C-6, *o*-phenyl), 7.06–8.52 (m, 10), and 9.07 (d, 1, J = 6 Hz, C-4).

Anal. Calcd for $C_{21}H_{18}ClNO_4$: C, 65.71; H, 4.73; N, 3.65. Found: C, 65.85; H, 4.92; N, 3.40.

***anti*-12-Phenyl-6,11-dihydro-6,11-ethanoacridizinium Perchlorate (6).** The hot 1-butanol extract (preceding experiment) still contained some of the syn isomer which was removed by fractional crystallization from 1-butanol, followed by recrystallization of the more soluble isomer as colorless platelets from ethanol: mp 203–204 °C; ^{1}H NMR (CF_3COOH) δ 2.50–2.72 (m, 2, C-13), 3.48–3.82 (m, 1, C-12), 4.95 (d, 1, J = 2 Hz, C-11), 6.47–6.87 (m, 3, C-6, *o*-phenyl), 7.05–8.70 (m, 7), and 9.20 (d, 1, J = 6 Hz, C-4).

Anal. Calcd for $C_{21}H_{18}ClNO_4$: C, 65.71; H, 4.73; N, 3.65. Found: C, 65.51; H, 4.81; N, 3.57.

Reduction of 12-Phenyl-6,11-dihydro-6,11-ethanoacridizinium Tetrafluoroborate. A sample of the styrene adduct (5 and 6) was hydrogenated for 24 h at 40 psi using a platinum oxide catalyst. After removal of the catalyst by filtration the solvent was removed under reduced pressure. A portion of the residue was dissolved in trifluoroacetic acid for NMR analysis. The other portion was converted to the free base and treated in ether with an excess of methyl iodide. The resulting methiodide was converted to the **methoperchlorate** by addition of 35% perchloric acid to an aqueous solution: mp 269–270 °C; ^{1}H NMR (CF_3COOH) δ 1.13–2.20 (m, 7), 2.77–4.07 (m, 9, with Me peak at δ 3.41), 4.68 (broad s, 1, C-6), and 6.47–7.71 (m, 9).

Anal. Calcd for $C_{22}H_{26}ClNO_4$: C, 65.42; H, 6.49; N, 3.47. Found: C, 65.32; H, 6.55; N, 3.37.

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Supplementary Material Available: ^{1}H NMR and other experimental data for the adducts listed in Table IV (6 pages). Ordering information is given on any current masthead page.

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Trimethylsilylketene. Cycloadditions of Ketenes and Aldehydes

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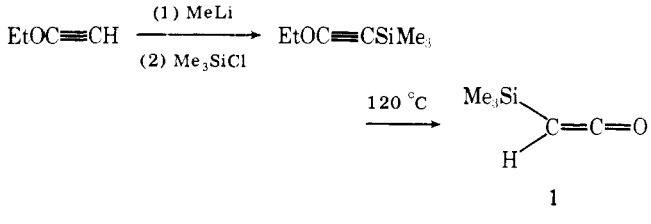
The cycloaddition of trimethylsilylketene with saturated aldehydes in the presence of a catalytic amount of BF_3·Et_2O resulted in the formation of the *cis*- and *trans*-2-oxetanones. Trimethylsilylketene reacted with α,β-unsaturated aldehydes, cinnamaldehyde, crotonaldehyde, furfural, and α-methylcinnamaldehyde, in the presence of BF_3·Et_2O, to yield trimethylsilyl dienoate esters. These esters are derived from the 2-oxetanones which underwent a silicon migration from carbon to oxygen accompanied by a ring-opening reaction. Dichloroketene and diphenylketene reacted with cinnamaldehyde to yield the corresponding 2-oxetanones, which readily decarboxylated to the substituted 1,3-butadienes.

Trimethylsilylketene (**1**) was first reported in 1965 and was prepared by the pyrolysis of (trimethylsilyl)ethoxyacetylene.[1] The effect of the trimethylsilyl substituent on the properties and chemistry of this ketene is truly remarkable. This ketene is a colorless liquid which boils at 82 °C, is very stable (and yet an aldoketene, which is most unusual), does not dimerize upon heating, and can be stored for long periods of time.[2] Numerous efforts to effect cycloaddition of **1** with a variety of unsaturated compounds have been mostly unsuccessful.[2] Cycloaddition of **1** with dimethyl- and diethylketene acetals under rather vigorous conditions for a ketene cycloaddition has been reported.[3] Also, the cycloaddition of **1** with benzaldehyde gave *cis*- and *trans*-2-oxetanones, which decarboxylated upon distillation to yield both *cis*- and *trans*-trimethylsilylstyrenes.[4]



1

Me_3Si = trimethylsilyl

There are numerous reports in the literature on the cycloaddition of ketenes and carbonyl compounds to yield 2-oxetanones.[5] The cycloaddition of ketene with α,β-unsaturated carbonyl compounds has received considerable attention, primarily in the patent literature, but there is little to be found on the cycloaddition of other ketenes with these unsaturated compounds.

This report describes the cycloaddition of trimethylsilylketene with both saturated and α,β-unsaturated aldehydes. Also, we describe the cycloaddition of dichloroketene and diphenylketene with some α,β-unsaturated aldehydes and the reaction of trimethylsilylketene with ketene bis(trimethylsilyl) acetal.

Trimethylsilylketene was prepared by the pyrolysis of (trimethylsilyl)ethoxyacetylene and by the dehydrochlorination of (trimethylsilyl)acetyl chloride.[2,6] The former method gives a much better yield and was the method most often used.

The addition of equimolar quantities of **1** and simple aldehydes containing a few drops of BF_3·Et_2O at 0 °C under a nitrogen atmosphere afforded the corresponding 2-oxetanones in 50–60% yields. The 2-oxetanones revealed the carbonyl band in the IR at 1805–1810 cm^{-1}. The cis and trans isomers were distinguished on the basis of the cis and trans coupling constants for the methinyl hydrogens in the NMR spectrum. The NMR spectrum of 4-ethyl-3-(trimethylsilyl)-2-oxetanones (**2a** and **2b**) revealed a doublet at δ 2.8 and a multiplet at δ 4.0 (J = 4 Hz) and a doublet at δ 3.2 and a multiplet at δ 4.3 (J = 6 Hz). The larger coupling constant was assigned to the cis isomer. The ratio of cis (**2a**)/trans (**2b**) was 55:45 based on the NMR and VPC data.

The 2-oxetanones did not undergo thermal decarboxylation

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