gram exhibited two peaks, retention times 1.2 and 4.4 min, corresponding to the solvents and the hydrogenation product, respectively. The peak at 4.4 min was collected and rechromatographed to yield a small amount of a colorless liquid. This liquid had an infrared spectra ($CHCl_3$) identical with that of previously prepared ethyl N-methyl adipamate (**12**).

Registry No.—**1**, 19519-85-8; **3**, 19519-86-9; **4**, 19519-87-0; **5**, 19519-88-1; **7**, 19519-89-2; **8**, 19519-90-5; **10**, 19519-91-6; **11**, 19519-92-7; **12**, 19519-93-8.

Acknowledgment.—The authors wish to thank Dr. Sungzong Kang for his help and the use of his program in the calculation of the kinetic data.

Addition of Dienophiles to the Acridizinium Ion. III.[1] Evidence for a Two-Step Reaction

C. K. Bradsher and J. A. Stone[2]

Department of Chemistry, Duke University, Durham, North Carolina 27706

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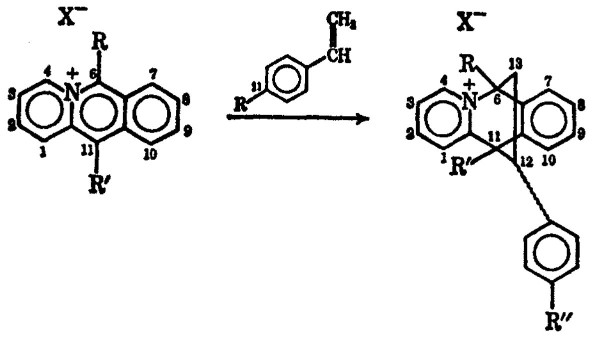
The introduction of a methyl group into the two *meso* positions of the acridizinium ion has opposite effects, at position 6 *decreasing* and at position 11 *increasing* the rate of reaction. Even in the presence of sodium acetate (hence in the absence of any traces of perchloric acid) diethyl maleate adds to acridizinium ion to give a rearranged (*anti, syn*) product (**12**). It is believed that these observations can best be explained in terms of a two-step mechanism.

The discovery several years ago[3] that the acridizinium (benzo[*b*]quinolizinium) ion (**1**) will undergo 1,4 cycloaddition with some common dienophiles was rationalized by the recent evidence[4,5] that the reaction is an example of what Sauer and Wiest have designated as a Diels–Alder reaction with inverse electron demand (Scheme I).[6] The great ease with which acridizinium derivatives can be prepared[7-9] makes the system of unique promise in the study of the factors affecting the Sauer and Wiest type of cycloaddition.

Scheme I



1, R = R′ = H
2, R = CH_3; R′ = H
3, R = H; R′ = CH_3
4, R = R′ = CH_3
5, R = R′ = H
6, R = CH_3; R′ = H
7, R = H; R′ = CH_3
8, R = R′ = CH_3

For the classical Diels–Alder reaction, it has been reported that introduction of methyl groups into the *meso* (9,10) positions of anthracene results in a very significant enhancement of the reaction rate.[10] Difficulty in assessing the relative importance of steric and electronic factors might have made prediction of the net effect of *meso* substitution difficult, but the observed rate enhancement is readily understood in terms of the predominant effect of the electron release of the methyl groups.

If one introduces one or two methyl groups into the *meso* (6, 11) positions of the acridizinium ion, it would appear, at least at first glance, that both steric and electronic effects would cooperate to reduce the speed of the reaction. With 6-methylacridizinium (**2**) perchlorate, the rate of addition of styrene to form adduct **6**, as measured by the disappearance of the long-wavelength absorption of the 6-methylacridizinium ion, is in fact about one-half the rate at which the acridizinium ion undergoes the same reaction (Table I). The nmr of styrene adduct **6** showed the signal for the C-11 proton as a doublet, indicating that the phenyl group was at the 12 rather than the 13 position. The adducts from the reaction of 6-methylacridizinium ion with the *substituted* styrenes were not isolated, but it was observed that the effect of the *para* substituent in the styrene ring on the rate parallels that observed[5] earlier for the acridizinium ion.

If the methyl group is introduced at position 11 instead of position 6 there is no decrease in the observed rate of addition to styrene, but instead a 13-fold *increase* in reaction rate over that for the unsubstituted acridizinium ion. A similar but smaller increase in rate was observed when methyl groups were introduced in both the 6 and 11 positions of the acridizinium ion. The adducts of styrene with 11-methyl- and 6,11-dimethylacridizinium ion (**7** and **8**) cannot be characterized as 12-phenyl (rather than 13-phenyl) derivatives with the same certainty as the adduct which possesses a hydrogen at position 11[11]; however, all indirect

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(1) For the preceding papers of this series, see ref 3 and 5.

(2) NASA Trainee. This work was supported in part by Public Health Grant No. HE-02170 of the National Heart Institute of the National Institutes of Health.

(3) C. K. Bradsher and T. W. G. Solomons, *J. Amer. Chem. Soc.*, **80**, 933 (1958).

(4) D. L. Fields, T. H. Regan, and J. C. Dignan, *J. Org. Chem*, **33**, 390 (1968).

(5) C. K. Bradsher and J. A. Stone, *ibid.*, **33**, 519 (1968).

(6) J. Sauer and H. Wiest, *Angew. Chem.*, **74**, 353 (1962).

(7) C. K. Bradsher and L. E. Beavers, *J. Amer. Chem. Soc.*, **77**, 4812 (1955).

(8) C. K. Bradsher and J. C. Parham, *J. Org. Chem.*, **28**, 83 (1963).

(9) C. K. Bradsher and J. C. Parham, *J. Heterocycl. Chem.*, **1**, 121 (1964).

(10) Preparative experiments carried out by W. E. Bachmann and M. C. Kloetzel [*J. Amer. Chem. Soc.*, **60**, 481 (1938)] indicated that 9,10-dimethylanthracene might react as much as 90 times as fast as anthracene.

(11) Even in the cases in which there is a hydrogen at position 6, it is so strongly deshielded by the adjacent positive charge that the signal from it becomes indistinguishable from the signals from the aromatic protons.

TABLE I

RATE OF CYCLOADDITION OF *para*-SUBSTITUTED STYRENES WITH ACRIDIZINIUM PERCHLORATE AT 65°

meso substituent		Rate[a] k, min^{-1} × 10^{-3}			
R (6)[b]	R′ (11)[b]	R″=CH$_3$O	R″=CH$_3$	R″=H	R″=NO$_2$
H	H	18 ± 1	8.1 ± 0.2	5.0 ± 0.1	2.3 ± 0.3
CH$_3$	H	5.7 ± 0.2	3.2 ± 0.2	2.5 ± 0.2	1.8 ± 0.3
H	CH$_3$	180 ± 10	94 ± 2	68 ± 3	36 ± 5
CH$_3$	CH$_3$	93 ± 6	57 ± 4	43 ± 1	30 ± 2

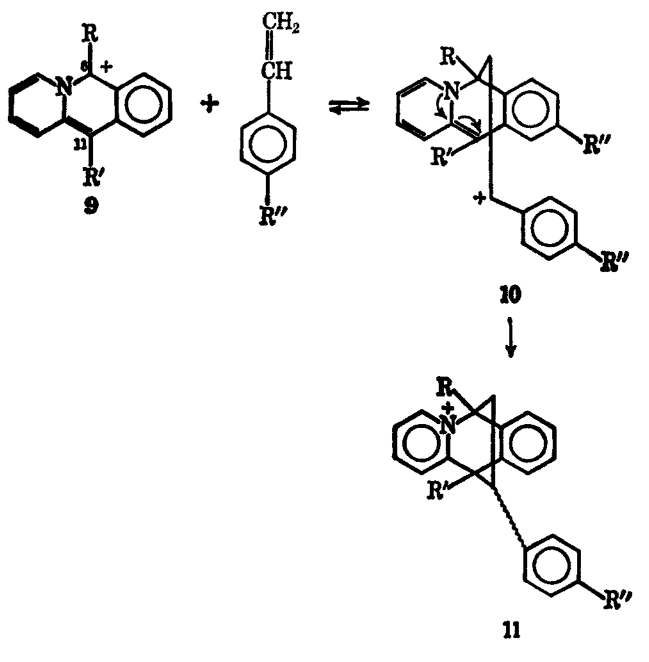
[a] A tenfold excess of the styrenes was used in order to obtain pseudo-first-order kinetics. [b] 6 and 11 position.

evidence such as similarities in ir and nmr spectra point to the assigned structures. The rates of disappearance of 11-methyl- (**3**) and 6,11-dimethylacridizinium ion (**4**) with substituted styrenes parallels the inverse electron demand pattern seen with the parent compound (**1**) and its 6-methyl derivative (**2**).

It appears that the reaction rate studies can best be rationalized by the assumption that the reaction of the acridizinium ion with substituted olefins occurs through a regiospecific[12] two-step reaction.

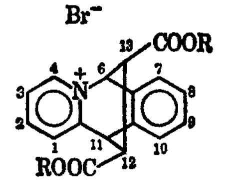
It has been shown[13] that in reaction with nucleophiles the acridizinium ion is attacked at position 6, suggesting that the resonance hybrid can react as the carbonium ion **9**. If such an ion reacts with styrene to form the most stable (benzylic) carbonium ion (**10**), this could then cyclize by attack of the electrons at position 11 (Scheme II). The divergent effects of the substitution of methyl groups at the two *meso* positions is understandable in terms of this mechanism. A methyl group at position 6 for steric[14] and electronic reasons should adversely affect the concentration of intermediate **10** at equilibrium and hence the observed rate. A methyl group at position 11 could make electrons more readily available at that position and increase the tendency of the benzylic carbonium ion (**10**) to undergo cyclization. In each case it is the second step in the reaction which must be rate determining.

SCHEME II



In the preceding publication of this series an effort was made to rationalize the reaction of diethylmaleate with acridizinium bromide to yield *anti,syn*-12,13-dicarboethoxy-6,11-dihydro-6,11-ethanoacridizinium ion **12**.

diethyl maleate + acridizinium bromide ⟶



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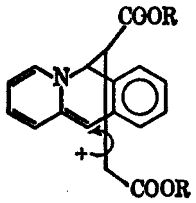
It was demonstrated that hydrogen bromide was formed during the reaction and that the excess ester, recovered after 7.5 hr, was essentially pure diethyl fumarate. The evidence which we have discussed in the preceding paragraphs made it important to establish whether the diethyl maleate reaction could be taking place by a two-step process. A preliminary test showed that the reaction of diethylmaleate with acridizinium perchlorate would take place in acetic acid in the presence of 2 equiv (excess) of anhydrous sodium acetate. The excess ester recovered from such a reaction was *unrearranged* diethylmaleate. Although a lower yield was obtained in the presence of excess sodium acetate, the only adduct obtained (41% yield) was the *anti,syn* product (**12**, R = C_2H_5).

It now appears most likely that the addition of maleate esters can likewise take place as a two-step reaction and that the carbonium ion first formed (**13**) rotates through 180° before cyclization. In harmony with this theory is the observation made earlier[5] that the addition of dimethyl maleate to acridizinium perchlorate yielded a mixture containing chiefly the *syn,syn* sterioisomer (to be expected if there had been no rotation about the C-12–C-13 bond in **13**) and the *anti,syn* isomer (to be expected if rotation about the bond occurred).



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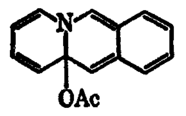

14

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[12] A. Hassner [*J. Amer. Chem. Soc.*, **90**, 216 (1968)] has introduced the useful term regiospecific to describe orientation in the addition to multiple bonds.

[13] C. K. Bradsher and J. P. Sherer, *J. Org. Chem.*, **32**, 733 (1967).

[14] Under the conditions used for the reaction of 6-methylacridizinium, the 6-propylacridizinium ion[9] had a rate constant of 1.0 ± 0.2 min^{-1} × 10^{-3} with styrene.

Table II

Reaction Rates[a] of Acridizinium Perchlorate with Maleate and Fumarate Esters at 100°

Ester	Medium	k, min^{-1} × 10^{-4}
Dimethyl maleate	$MeNO_2$	1.1 ± 0.1
Dimethyl fumarate	$MeNO_2$	8.9 ± 0.1
Diethyl maleate	$MeNO_2$	1.7 ± 0.0[b]
Diethyl maleate	HOAc	1.6 ± 0.0[b]
Diethyl maleate	HOAc + NaOAc[c]	1.5 ± 0.1[b,d]
Diethyl fumarate	$MeNO_2$	13 ± 1[b]
Diethyl fumarate	HOAc	12 ± 0.5
Diethyl fumarate	HOAc + NaOAc[c]	9.6 ± 0.8[d]

[a] Except as noted all values are the average of at least three determinations. [b] Average of only two values. [c] Sodium acetate (2 equiv) added. [d] Darkening of solution prevented measurements after 10 hr.

Rates for the reaction of maleate and fumarate esters are shown in Table II. As in the case of the classical Diels–Alder reaction,[15] the rate of addition of fumarate esters exceeds that of the maleate isomers. This difference in rate would appear to be a steric rather than an electronic effect, otherwise the order of reactivity should be reversed in going from a classical to an inverse electron demand type of 1,4-cycloaddition. The reaction rate of methyl esters seems to be slightly less than that of the ethyl homologs. No very great rate difference was observed in going from acetic acid to nitromethane as a reaction medium nor was the rate change observed when sodium acetate was added to the acetic acid used as a solvent great enough to suggest that the nature of the reaction was significantly altered. It is now clear that acetic acid does not participate in the addition reaction and that an uncharged molecule such as **14** cannot be an intermediate in the cycloaddition reaction.

Experimental Section[16]

6-Methyl-12-phenyl-6,11-dihydro-6,11-ethanoacridizinium (6) Perchlorate.—A solution containing 0.6 g of 6-methylacridizinium (**2**) perchlorate[9] and 1 ml of styrene in 50 ml of acetonitrile was refluxed for 16 hr. The volume of the solution was reduced to about 25 ml and poured into 100 ml of cold anhydrous ether. The resulting precipitate was recrystallized from ethanol affording 0.4 g of a colorless powder, mp 238–240°. The analytical sample consisted of colorless prisms: mp 264–266°; uv λ_{max} 272 mμ (log ε = 3.76), 265 sh (3.74); nmr[17] (CF_3COOH) τ 7.5–8.0 (m, 2, CH_2), 7.39 (s, 3, 6-Me), 6.60–6.11 (m, 1, C-12 proton); 5.06 (d, 1, J = 2 Hz, C-11 proton).

Anal. Calcd for $C_{22}H_{20}ClNO_4$: C, 66.33; H, 5.03; N, 3.52. Found: C, 66.21; H, 5.11; N, 3.50.

11-Methyl-12-phenyl-6,11-dihydro-6,11-ethanoacridizinium (7) Perchlorate.—Starting with 1.5 g of 11-methylacridizinium perchlorate and following the procedure used in the preparation of isomer **6**, 1.7 g (84%) of colorless needles were obtained: mp 235–237°; uv λ_{max} 270 mμ (log ε 3.73), 266 sh (3.71); nmr (CF_3COOH) τ 8.25 (s, 3, CH_3), 8.13–6.76 (m, 3, C-12 and C-13 protons).

Anal. Calcd for $C_{22}H_{20}ClNO_4$: C, 66.33; H, 5.03; N, 3.52. Found: C, 66.17; H, 5.17; N, 3.52.

6,11-Dimethyl-12-phenyl-6,11-dihydro-6,11-ethanoacridizinium (8) Perchlorate.—Following the procedure used in the preparation of lower homologs **6** and **7**, except that the starting material was 6,11-dimethylacridizinium (**4**) perchlorate, the title compound (**8**) was obtained in 55% yield and crystallized from acetone as colorless needles: mp 223–224°; uv λ_{max} 273 mμ (log ε 3.74), 266 sh (3.71); nmr (CF_3COOH) τ 8.25 (s, 3, 11-CH_3), 7.47 (s, 3, 6-CH_3); 8.08–6.03 (complex, 3, CH_2, CH).

Anal. Calcd for $C_{23}H_{22}ClNO_4$: C, 66.99; H, 5.34; N, 3.40. Found: C, 66.93; H, 5.65; N, 3.11.

Reaction Rates for Cycloaddition Reactions of Acridizinium Derivatives.—The reaction rates in Table I were determined exactly as described in ref 5 except that pure dimethyl sulfoxide rather than a mixture with acetic acid was used as the solvent, and that for each substituted acridizinium salt the progress of the reaction was followed by measuring the absorption at the long wavelength maximum (corresponding to 397 mμ for the acridizinium ion).

The measurements described in Table II likewise were carried out as in ref 5 except that pure solvents rather than a mixture of acetic acid and dimethyl sulfoxide were used, and water rather than methanol was used in the vapor bath.

Reaction of Acridizinium Perchlorate with Diethyl Maleate in the Presence of Sodium Acetate.—A solution of 0.6 g (0.00215 mol) of acridizinium (**1**) perchlorate, 0.35 g (0.0043 mol) of sodium acetate and 1.5 ml (0.0093 mol) of diethyl maleate in 15 ml of acetic acid was heated on the steam bath for 3 days and the cooled mixture poured into cold anhydrous ether. The precipitate crystallized from ethanol as colorless needles: mp 182–183°, yield 0.4 g (41%). This material was shown by ir to be *anti,syn*-12,13-dicarbethoxy-6,11-dihydro-6,11-ethanoacridizinium (**5**) perchlorate.

If the reaction was interrupted after 6 hr, poured into water and the excess ester recovered by ether extraction, it was found by vapor phase chromatography[5] that no isomerization to diethyl fumarate had occurred. In a similar experiment *without* sodium acetate, it had been shown[5] that nearly complete isomerization of the excess ester had occurred.

Registry No.—**1** perchlorate, 18507-95-4; **6** perchlorate, 19190-65-9; **7** perchlorate, 19202-63-2; **8** perchlorate, 19190-66-0; **12** (R = C_2H_5), perchlorate, 15259-87-7.

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[15] J. Sauer, H. Wiest, and M. Mielert, *Z. Naturforsch.*, *B*, **17**, 203 (1962); J. Sauer, D. Lang, and H. Wiest, *ibid.*, *B*, **17**, 206 (1962).

[16] General details concerning the experimental technique will be found in the first paragraph of the Experimental Section of ref 5.

[17] In this and in subsequent nmr reports signals in the aromatic proton region have been omitted.