aqueous $NaHCO_3$, the benzene layer dried ($MgSO_4$), and the solvent removed *in vacuo*, thus yielding 0.88 g (4.83 mmol, 94% yield) of benzophenone, mp 46–48°. The alkaline aqueous extracts were brought up to pH 1 (6 *N* HCl) and in turn extracted with benzene, and the benzene extract was dried ($MgSO_4$) and, after solvent removal, gave 0.61 g (5.0 mmol, 96% yield) of benzoic acid, mp 120–122°. To determine the ketone yields by glpc (Table I), stoichiometric amounts (usually *ca.* 2 mmol) of diazoalkane and peracid were allowed to react in the given solvent containing a known amount of a suitable internal standard, thereafter following the known analytical procedure;[27] glpc data were obtained on a Varian-Aerograph 1520 gas chromatograph using a 7 ft × 0.25 in. 5% SE-30 on Chromosorb W (60–80 mesh) column and a 6 ft × 1/8 in. 10% Carbowax 20M-TPA on Chromosorb W (60–80 mesh) column, tc detector, He carrier gas at *ca.* 30 ml/min.

Kinetics.—Kinetic data were obtained according to standard spectrophotometric techniques.[3a] The change of absorbance with time at the wavelength of maximum absorption in the visible for each diazoalkane (where PBA and reaction products are essentially transparent) was monitored by using a Gilford 2400 recording spectrophotometer equipped with a thermostatic cell holder. Temperature control was better than ±0.5°. Rate constants were obtained from pseudo-first-order integrated plots on the basis of the following equation.

$$-\log (A_t - A_\infty) = (k_1/2.3)t - \log (A_0 - A_\infty)$$

(27) H. M. McNair and E. J. Bonelli, "Basic Gas Chromatography," 5th ed, Varian-Aerograph, Walnut Creek, Calif., 1969, p 150.

Rate constants reported in Tables II and III are average values from at least two independent experiments whose results of which agree within the limits of experimental errors (±4%). The rate constants obeyed the Arrhenius equation and the activation parameters were evaluated by standard methods;[3a] precision in the estimation of $\Delta H^{\pm}$ is better than ±0.8 kcal mol^{-1} and better than ±3 cal deg^{-1} mol^{-1} for $\Delta S^{\pm}$.

Registry No.—$C_6H_5C(=N_2)C_6H_5$, 883-40-9; $C_6H_5C(=N_2)C_6H_4$-*p*-OCH_3, 20359-74-4; $C_6H_5C(=N_2)C_6H_4$-*p*-Cl, 1140-33-6; $C_6H_5C(=N_2)C_6H_4$-*m*-NO_2, 1218-71-9; $C_6H_5C(=N_2)C_6H_4$-*p*-NO_2, 13271-32-4; 1-diazo-1-phenylethane, 22293-10-3; *p*-nitroperoxybenzoic acid, 943-39-5; benzhydryl isopropyl ether, 5670-79-1; PBA, 93-59-4; PBA-d_1, 31657-65-5.

Acknowledgments.—Generous support of this work by the Italian National Research Council (CNR) is gratefully acknowledged. We wish to thank Professor G. Modena (this CNR Centre) and Professor J. O. Edwards (Brown University, Providence, R. I.) for many helpful discussions; thanks are also due to the International Division of FMC Corporation for a gift of a 98% hydrogen peroxide sample.

Stereochemistry of the Addition of *N*-Arylmaleimides to the Acridizinium Ion[1]

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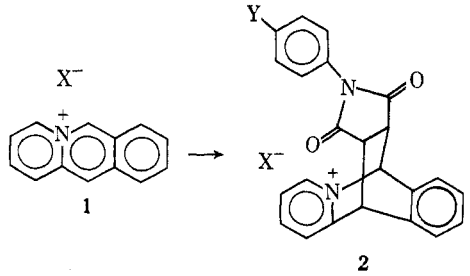
The cycloaddition of *N*-arylmaleimides to the acridizinium nucleus occurs stereospecifically anti with regard to the benzenoid nucleus. In strong acid *cis*-12,13-dicarboxy-6,11-dihydro-6,11-ethanoacridizinium salts undergo rearrangement affording a trans structure. Pyrolysis of the acridizinium arylmaleimide addition products affords derivatives of *N*-aryl-1-(2-pyridyl)naphthalene-2,3-dicarboximide.

The acridizinium ion (**1**) was the first positively charged alkenophile found to undergo a 4 + 2 cycloaddition reaction.[2] Although recently there has been a large increase in the number of examples of such cycloadditions,[3-6] for only five of the adducts is the *stereochemistry* known. It is already clear that despite the stereoselectivity shown in the cationic addition reaction the presence of the positive charge makes it impossible to apply without modification the rules[7] which have proved so useful in understanding the classical Diels–Alder reaction, and indeed, there exists some evidence that the cationic cycloaddition may not be concerted.[5,8]



1 **2**

The purpose of the present study was to determine whether the stereochemistry of the cycloaddition of *N*-arylmaleimides to the acridizinium ion was altered by changes in polarity of the *N*-aryl group and to learn something about the chemistry of the products. Two general procedures were used for the preparation of the adducts. Either the salt **1** was suspended in acetic acid and heated with the maleimide at 100°, or a melt was formed by heating the reactants at 160–170° without solvents. The high-temperature reaction had the advantage of being quite rapid and giving clean reaction products although the yields were slightly lower. Both reaction conditions led to the isolation of the same product, which seemed to consist of a single stereoisomer. As may be seen from Table I all adducts possessed carbonyl absorptions at 1704–1715 and 1783–1790 cm^{-1}. As would be expected from known imide spectra,[9] the lower frequency absorptions (asymmetric carbonyl stretch) were significantly the weaker of the two.

The nmr showed the expected doublets at approximately δ 5.7 for the bridgehead proton at C-11 and δ

(1) This research was supported by Public Health Service Grants No. HE-2170 of the National Heart Institute and No. CA-05509 of the National Cancer Institute.

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

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

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

(5) C. K. Bradsher and J. A. Stone, *ibid.*, **34**, 1700 (1969).

(6) D. L. Fields and J. B. Miller, *J. Heterocycl. Chem.*, **7**, 91 (1970).

(7) *E.g.*, J. A. Norton, *Chem. Rev.*, **31**, 319 (1942).

(8) C. K. Bradsher and I. J. Westerman, *J. Org. Chem.*, **36**, 969 (1971).

(9) R. T. Conley, "Infrared Spectroscopy," Allyn and Bacon, Boston, Mass., 1966.

Table I.—Cycloaddition Products 2 of Acridizinium Salts with *N*-Arylmaleimides

2

X	Y	Prepn method[a] (yield, %)	Registry no.	Mp,[b] °C	Formula[c]	Ir, carbonyl, cm^{-1}	Nmr (multiplicity)[d] C-6	C-11	C-12	C-16	Other
ClO_4	H	A (95)	32120-19-7	354–356	$C_{23}H_{17}ClN_2O_6$	1709, 1786	7.07 (d)	5.75 (d)	4.27 (q)	4.73 (q)	
Br	H	A (90), B (75)	32120-20-0	>380	$C_{23}H_{17}BrN_2O_2$						
ClO_4	Me	A (85)	32120-21-1	343–345	$C_{24}H_{19}ClN_2O_6$	1704, 1783	7.00 (d)	5.77 (d)	4.20 (q)	4.60 (q)	2.34 (s)
Br	Me	B (70)	32120-22-2	>380	$C_{24}H_{19}BrN_2O_2$						
ClO_4	Cl	A (90)	32120-86-8	311–313	$C_{23}H_{16}Cl_2N_2O_6$	1711, 1786	7.00 (d)	5.77 (d)	4.22 (q)	4.60 (q)	
Br	Cl	A (90), B (75)	32120-87-9	>380	$C_{23}H_{16}BrClN_2O_2$						
ClO_4	OMe	A (90)	32120-88-0	314–315	$C_{24}H_{19}ClN_2O_7$	1709, 1784	7.0[e]	5.74 (d)	4.18 (q)	4.55 (q)	3.88
Br	OMe	A (90), B (80)	32120-89-1	362–363	$C_{24}H_{19}BrN_2O_3$						
ClO_4[f]	$N(Me)_2$	A (60)	32120-90-4	327–329	$C_{25}H_{25}Cl_2N_3O_{10}$	1715, 1790	7.0[e]	5.70 (d)	4.20 (q)	4.60 (q)	3.66

[a] In method A the acridizinium salt was heated in acetic acid suspension at 100° with an excess of the maleimide, the time being about 20 hr for perchlorates and 2 hr for bromides. In method B the molten reactants were heated at 160–170° for ~15 min. See Experimental Section. [b] All occurred with decomposition. [c] Satisfactory analytical data was presented for all compounds in this table: Ed. [d] Signals due to aromatic protons have been omitted. Protons listed under *other* showed expected integration. [e] Overlapped signal. [f] Both counterions are perchlorate.

7.0 for the more strongly deshielded proton at C-6. Homonuclear spin decoupling studies with the *N*-(*p*-tolyl) derivative (Y = Me) showed that irradiation of the signal at δ 7.0 caused the quartet at δ 4.6 to collapse to a doublet, while irradiation of the signal at δ 5.7 caused the quartet at δ 4.2 to collapse to a doublet. This allowed assignment of the signal at δ 4.2 to be that of the proton at C-12 spin coupled to C-11 (J = 3.5 Hz) and to C-16 (J = 7 Hz). The signal at δ 4.6 must arise from the C-16 proton, spin coupled to the protons at C-6 and C-12.

It had been shown earlier[2] that the selective reduction of a cycloaddition product derived from an acridizinium salt could be effected in such a way that the pyridinium ring is saturated while the benzenoid ring is left intact. When hydrogenated under these conditions the *N*-phenylmaleimide adduct (**2**, Y = H) yielded **3**, which

3

had an nmr which was useful in making a tentative stereochemical assignment. Although the reduction produced dramatic changes in certain parts of the spectrum the signals due to the hydrogens at C-12 and C-16 remained virtually unchanged, suggesting that they were over the intact benzene ring as represented in **3** rather than over the reduced pyridine ring.

It had been hoped that unequivocal evidence for the stereochemical structure of maleimide adducts could be obtained by relating them to the known *anti,anti*- (**4b**) and *syn,syn*- (**5b**) 12,13-dicarbomethoxy-6,11-dihydro-6,11-ethanoacridizinium perchlorates. The imides **2** proved resistant to hydrolysis except in strong acid solutions and in 48% hydrobromic afforded neither of the known cis dicarboxylic acids (**4a** or **5a**) but a trans diacid (**6a**) characterized as its dimethyl ester (**6b**). In order to learn something more about this interesting rearrangement, the action of 48% hydro-

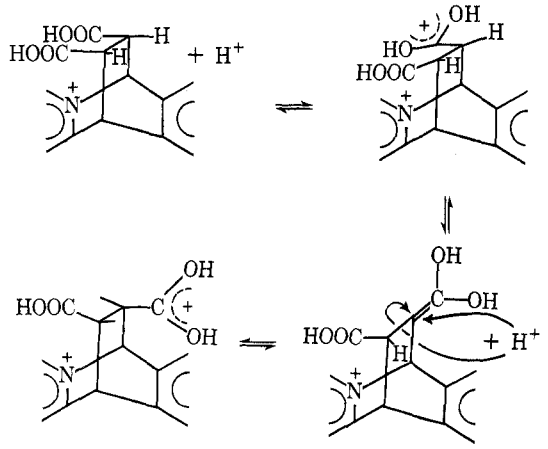
a, R = H
b, R = Me

bromic acid on the known cis dimethyl esters (**4b** and **5b**) was studied. Both were found to undergo hydrolysis and rearrangement to the same trans dicarboxylic

acid, making it clear that rearrangement involved the possibility of inversion of configuration at both of the ethano bridge carbon atoms (C-12 and C-13).

To explain this rearrangement it is postulated that the carboxyl groups are protonated followed by loss of the α hydrogen to give an enediol which may be protonated from either direction giving either inversion or retention of configuration. Scheme I shows the

SCHEME I
MECHANISM SHOWING INVERSION AT C-13



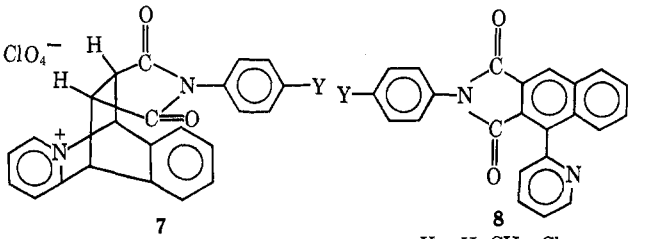
steps involved in the inversion at C-13, which is similar to what must happen at C-12. The structure of the trans product of the reaction is explicable in that the positively charged protonated carboxyl groups are at a maximum distance from each other without either group being in the immediate proximity of the positively charged nitrogen atom.

Support for this mechanism was obtained by carrying out the hydrolysis in 20% DCl in D_2O at reflux temperature. The diacid formed showed the C-6 and C-11 protons as singlets rather than doublets, while the signals for the C-12 and C-13 protons were very weak, together integrating for less than one-third of a proton, indicating almost complete exchange of the C-12 and C-13 hydrogens as would be predicted by the mechanism.

Proof of the stereochemistry of our maleimide cycloaddition products was obtained by synthesizing them from *anti,anti*-12,13-dicarboxy-6,11-dihydro-6,11-ethanoacridizinium perchlorate (**4a**) by refluxing it in acetonitrile with the appropriate arylamine. For the three imides synthesized (2, Y = H, Me, OMe) all physical properties were in complete agreement with those obtained from the cycloaddition products.

In order to compare the physical properties of some examples stereoisomeric with **2** but in which the imide ring was syn rather than anti with respect to the benzene ring, the syn,syn dicarboxylic acid (**5a**, available by an improved method) was heated with three arylamines, affording products (**7**) which were distinctly different from the anti isomers. It would be predicted that there might be an observable difference in the ir spectrum between the carbonyl absorptions of the stereoisomer with an imide ring over a quaternary nitrogen atom and the one in which the imide ring is over an uncharged benzenoid ring. All the maleimide cycloaddition products (2) in Table I show a pair of carbonyl absorption bands in the 1700–1800 region, the difference between them being 76 ± 3 cm^{-1}. It is probably ignificant that the corresponding difference observed for the three syn stereoisomers (**7**) synthesized was 63 ± 4 cm^{-1}. On the basis of the correlation it is probably safe to conclude that all of the maleimide addition products have the anti configuration.

The maleimide adducts (**2**) were found to lose hydrogen bromide on heating and although thin layer chromatography showed that several products were formed in each decomposition, only one type, an arylimide (**7**) derived from 1-(2-pyridyl)naphthalene-2,3-



7 **8**

Y = H, CH_3, Cl

dicarboxylic acid, was isolated. The structure is supported by spectroscopic evidence and by analogy to earlier work by Fields, *et al.*, on the ring opening of acridizinium cycloaddition products.[3,10] The uv absorption spectrum resembled that of 1-(2-pyridylnaphthalene) and the ir showed the characteristic double carbonyl absorption of imides as well as an absorption at 910 cm^{-1} corresponding to the C–H out-of-plane vibrations for a pentasubstituted benzene ring. The nmr of the parent compound (**8**, Y = H) showed no aliphatic hydrogens. The mass spectrum suggested an aromatic structure in that there were only four ions of any significant abundance. These corresponded to the molecular ion, the M − 1 ion, the M − ArNCO ion, and the M − ArN − C_2O_2 ion. The formation of the wholly aromatic structure in the pyrolysis must arise from disproportionation or some other mode of dehydrogenation.

Experimental Section

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Ir spectra were determined with a Perkin-Elmer 137 spectrometer as potassium bromide pellets. All uv spectra were measured in 95% ethanol with a Beckman DBG spectrometer. The nmr spectra were determined with a Varian T-60 spectrometer and unless otherwise indicated trifluoroacetic was the solvent. Elemental analyses were by M-H-W Laboratories, Garden City, Mich.

***N*-(*p*-Trimethylammonium phenylperchlorate)maleimide.**—*N*-(*p*-Dimethylaminophenyl)maleimide[11] (3 g) was quaternized by refluxing for 3 hr with 12 g of methyl iodide in 50 ml of acetone. The product was crystallized from methanol–ethyl acetate and then dissolved in a minimum quantity of hot water, and 35% perchloric acid was added. The precipitate was crystallized from methanol–ethyl acetate, affording silvery plates, mp 275–277°, yield 46%.

Anal. Calcd for $C_{13}H_{15}ClN_2O_6$: C, 47.27; H, 4.54; N, 8.48. Found: C, 46.96; H, 4.54; N, 8.43.

Cycloaddition Reactions. Method A.—A suspension of 1.2 g of acridizinium perchlorate and 2–3.5 molar equiv of the *N*-arylmaleimide in 20 ml of glacial acetic acid was heated at 100° and stirred until there was a disappearance of the uv absorption at 399 mμ. This required 20 hr or more for the perchlorates and only about 2 hr for the more soluble bromides. The perchlorate salts were isolated by pouring the suspension into dry ether, collecting the precipitate, and crystallizing from acetonitrile–

(10) D. L. Fields and T. N. Regan, *J. Org. Chem.*, **35**, 1870 (1970).
(11) W. R. Roderick and P. L. Bhatia, *ibid.*, **28**, 2018 (1963).

ethyl acetate. The bromide salts were isolated simply by cooling the reaction mixture, collecting the product, and recrystallizing from methanol–ethyl acetate. Results of these reactions are reported in Table I.

Method B.—Acridizinium bromide was ground in a mortar with 2–3.5 molar equiv of the *N*-arylmaleimide. The mixture was heated in an oil bath at 160–170°. A clear melt was first formed, but after about 15 min a precipitate appeared. The hot suspension was poured into hot glacial acetic acid and the hot solution was filtered. The colorless product which crystallized on cooling was almost pure, but could be recrystallized from methanol–ethyl acetate.

***syn,syn*-12,13-Dicarbomethoxy-6,11-dihydro-6,11-ethanoacridizinium Perchlorate (4).**—The following procedure is superior to that described earlier.[4] Acridizinium perchlorate (3 g) and dimethyl maleate (8 g) were heated (safety shield!) at 150–160° for 15–20 min. The precipitate (2.0 g, 44%) which had formed during the heating was collected by filtering the hot solution. The solid was colorless, mp 299–300° (lit[4] 298–299°), and identical (ir, nmr) with an authentic sample. This material was hydrolyzed to the corresponding dicarboxylic acid by heating with 4% hydrobromic acid.[4]

Acid-Catalyzed Rearrangement of 12,13-Dicarboxy-6,11-dihydro-6,11-ethanoacridizinium Derivatives.—The following procedure for the hydrolysis–rearrangement of the *N*-phenylmaleimide adduct (**2**, Y = H), (as the perchlorate) will serve as an example of the general procedure used for all 12,13-dicarboxy derivatives. The adduct (1.0 g) in 35 ml of 48% hydrobromic acid was refluxed for about 20 hr. The volume of hydrobromic acid was reduced to 5 ml by vacuum evaporation and while the solution was still hot a small quantity of perchloric acid was added. Upon cooling colorless needles formed, mp 264–266°, which were probably the *anti,syn*-dicarboxylic acid although the melting point was higher than previously reported (lit.[4] 244–246°). The ir was identical with that found previously and the dimethyl ester formed by refluxing the diacid for 4 hr in a 5% methanolic solution of hydrogen chloride was identical in melting point, ir, and nmr with known *anti-syn*-12,13-dicarbomethoxy-6,11-dihydro-6,11-ethanoacridizinium perchlorate (**6a**).

Hydrogenation of the *N*-Phenylimide Adduct (2, X = ClO_4, Y = H).—The perchlorate salt of the named compound (2 g) was dissolved in 200 ml of 50% aqueous methanol. Platinum oxide (0.4 g) was added and the mixture was hydrogenated at atmospheric pressure and room temperature. After 2 hr, 3 molar equiv of hydrogen had been absorbed and absorption of hydrogen had virtually ceased. The solution was filtered and concentrated, and 35% perchloric acid added to precipitate the product. The analytical sample crystallized from methanol as off-white needles, mp 227–229°.

Anal. Calcd for $C_{23}H_{23}ClN_2O_6$: C, 60.21; H, 5.02; N, 6.11; Cl, 7.74. Found: C, 60.36; H, 5.24; N, 5.98; Cl, 7.70.

Synthesis of *N*-Aryl-13,15-dioxo-6,11,12,13,15,16-hexahydro-[6,11-*c*]pyrroloacridizinium Perchlorates.—The procedure is illustrated for the *syn*-*N*-*p*-tolyl derivative (**7**, Y = Me). The syn dicarboxylic acid perchlorate (**5a**, 0.75 g) was refluxed in 25 ml of acetonitrile for 2 hr with 1.5 g of *p*-toluidine. The solution was concentrated and ethyl acetate was added. Acetonitrile–ethyl acetate was used for recrystallization of the colorless product, mp 328–330° dec, ir 1724 and 1783 cm^{-1} (C=O).

Anal. Calcd for $C_{24}H_{19}ClN_2O_6$: C, 61.74; H, 4.07; N, 6.00. Found: C, 61.78; H, 4.12; N, 5.77.

The *syn*-*N*-phenyl analog (7, Y = H) was prepared by use of aniline in place of *p*-toluidine, mp 303–304° dec, ir 1715 and 1780 cm^{-1} (C=O).

Anal. Calcd for $C_{23}H_{17}ClN_2O_6$: C, 61.00; H, 3.76; N, 6.19. Found: C, 61.35; H, 3.80; N, 6.00.

The *syn*-*N*-(*p*-anisyl) analog (7, Y = OMe) was prepared by use of *p*-anisidine in place of *p*-toluidine, mp 325–327° dec, ir 1721 and 1786 cm^{-1} (C=O).

Anal. Calcd for $C_{24}H_{19}ClN_2O_7$: C, 59.69; H, 3.94; N, 5.80. Found: C, 60.01; H, 3.92; N, 5.73.

The anti analogs (2, X = ClO_4, Y = H, Me, OMe) were prepared in similar fashion except that the anti, anti dicarboxylic acid[4] (**4a**) was used in place of **5a**. In each case the product was identical (melting point, ir) with the cycloaddition product **2** obtained by reaction of the appropriate *N*-arylmaleimide with acridizinium perchlorate.

***N*-Aryl-1-(2-pyridyl)naphthalene-2,3-dicarboximides (8) by Pyrolysis of Adducts (2).**—This procedure was that used in pyrolysis of the *N*-phenylmaleimide adduct (**2**, X = Br, Y = H) to **8**, Y = H. The salt (2 g) was sublimed at 350° under a pressure of 0.2 mm. The sublimate was dissolved in ethanol and precipitated by addition of water, affording 0.5 g of an orange solid. The product was obtained as yellow needles: mp 229° from methanol; uv max 268 mμ (ε 11,200); ir 1704, and 1761 cm^{-1} (C=O); mass spectrum *m/e* (rel intensity) 350 (80), 349 (100), 231 (10), 203 (10).

Anal. Calcd for $C_{23}H_{14}N_2O_4$: C, 78.86; H, 4.00; N, 8.00. Found: C, 78.97; H, 4.00; N, 7.97.

***N*-*p*-Tolyl Analog (8, Y = CH_3).**—This had mp 242–243°; uv max 262 mμ (ε 62,300); ir 1724 and 1773 cm^{-1} (C=O); mass spectrum *m/e* (rel intensity) 364 (80), 363 (100), 231 (10), 203 (15).

Anal. Calcd for $C_{24}H_{16}N_2O_2$: C, 79.12; H, 4.40; N 7.69. Found: C, 79.44; H, 4.56; N, 7.79.

***N*-*p*-Chlorophenyl Analog (8, Y = Cl).**—This had mp 217–218°; uv max 263 mμ (ε 79,600); ir 1730 and 1775 cm^{-1} (C=O); mass spectrum *m/e* (rel intensity) 384 (80), 383 (100), 231 (10), 203 (10).

Anal. Calcd for $C_{23}H_{13}ClN_2O_2$: C, 71.87; H, 3.38; N, 7.28. Found: C, 71.59; H, 3.52; N, 7.17.

Registry No.—**1**, 260-62-8; **3**, 32207-36-6; **4**, 15314-08-6; **7** (Y = H), 32207-37-7; **7** (Y = OMe), 32120-85-7; **7** (Y = Me), 32207-38-8; **8** (Y = H), 32111-05-0; **8** (Y = Cl), 32111-06-1; **8** (Y = Me), 32111-07-2; *N*-(*p*-trimethylammonium phenylperchlorate)maleimide, 32111-08-3.