Synthesis and Diels−Alder Reactions of Butadienylpyridinium Bromides

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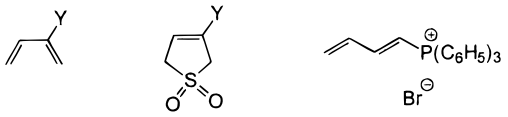
1-(3-Sulfolen-3-yl)pyridinium bromide (**5**) and 1-(3-methyl-2-sulfolen-4-yl)pyridinium bromide (**35)** have been prepared and served as the stable precursors for the cation-substituted dienes **6a** and **32a**, respectively. Compounds **6a** and **32a** are reactive dienes in the Diels−Alder reactions with a number of electron-poor dienophiles. Some [4 + 2] cycloadditions of **6a** and **32a** can take place in water.

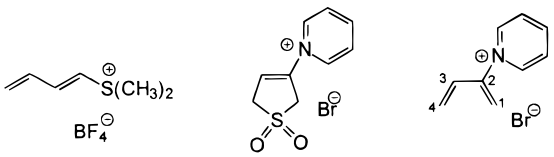
Introduction

3-Sulfolenes have been widely used as stable precursors for synthetically useful 1,3-dienes.[1] Electron-poor dienes such as 2-(methoxycarbonyl)- (**1a**),[1b] 2-nitro- (**1b**),[1c] 2-(arylsulfonyl)- (**1c**),[1d,e] and 2-cyano- **(1d)**[1f] 1,3-butadienes may be generated in situ by thermolysis of the corresponding 3-sulfolenes **2a**−**d**, and their [4 + 2] cycloaddition reactions with electron-deficient dienophiles have been successful.[1] These electron-poor dienes are also dienophilic, so they dimerize in a [4 + 2] cycloaddition manner in the absence of a dienophile. The introduction of a positively charged substituent at the 2-position of 1,3-butadienes would make them more electron-deficient and could influence both the reactivity and the mode of cycloaddition reactions. However, the cycloaddition reactions of 1,3-butadienes bearing a cationic substituent are hardly known. It was reported that butadienylphosphonium salts **3** do not undergo cycloaddition reactions with maleic anhydride or tetracyanoethylene,[2] but they react well with ketone enolates. The cycloadducts were formed via a conjugate addition and intramolecular Wittig reaction sequence.[3] Butadienylsulfonium salts **4** are known to react with enolates to produce dihydroarene oxides via a nonconcerted mechanism.[4] In this paper, we report the details of the preparation of 1-(3-sulfolen-3-yl)pyridinium bromide (**5**) and 1-(3-methyl-2-sulfolen-4-yl)pyridinium bromide (**35)** as the stable precursors for the positively charged dienes **6a** and **32a** and the success of their Diels−Alder reactions.[5]



1 **2** **3**

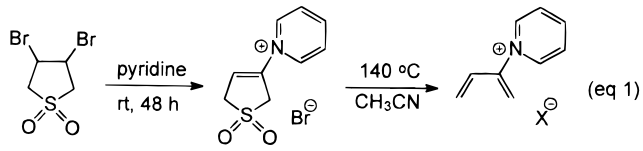
a: Y = CO_2Me
b: Y = NO_2
c: Y = SO_2Ar
d: Y = CN



4 **5** **6a**

Results and Discussion

Treatment of the known 3,4-dibromosulfolane with pyridine at ambient temperature gave compound **5** in 40% yield.[6] Thermolysis of compound **5** in acetonitrile at 140 °C for 1 h caused SO_2 extrusion and gave **6a** in quantitative yield (eq 1). Diene **6a** is a reasonably stable



5 **6a** X = Br **6b** X = PF_6

compound which can be stored at room temperature for over 1 month without appreciable decomposition. Despite its stability, an analytically pure sample of bromide salt **6a** could not be obtained due to its oiliness. The diene **6a** was thus treated with aqueous $NaPF_6$ for counterion exchange so that it could be purified and characterized more easily by recrystallization.

Since there is a strong electron-withdrawing pyridinium attached at the 2-position, the reactions of compound **6a** with electron-rich dienophiles were first tested. However, treatment of **6a** with ethyl vinyl ether in acetonitrile at 100 °C for 3 h resulted in no reaction, whereas the reaction with ethyl vinyl ether or dihydrofuran in acetonitrile at 140 °C for 1 h gave no cycloadducts but did yield complex mixtures. Apparently, inverse electron demand Diels−Alder reactions[7] of **6a** did not take place.

On the other hand, reactions of the cationic species **6a** with a number of electron-deficient alkenes in acetonitrile or water proceeded smoothly to give [4 + 2] cycloadducts (Scheme 1 and Table 1). The cycloadducts were also treated with aqueous $NaPF_6$ for counterion exchange to

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(1) (a) Chou, T. S.; Tso, H. H. *Org. Prep. Proc. Int.* **1989**, *21*, 257. (b) McIntosh, J. M.; Sieler, R. A. *J. Org. Chem.* **1978**, *43*, 4431. (c) Berestovitskaya, V. M.; Speranskii, E. M.; Perekalin, V. V. *Zh. Org. Khim.* **1979**, *15*, 185. (d) Chou, T. S.; Hung, S. C.; Tso, H. H. *J. Org. Chem.* **1987**, *52*, 3394. (e) Chou, T. S.; Hung, S. C. *J. Org. Chem.* **1988**, *53*, 3020. (f) Baraldi, P. G.; Barco, A.; Benetti, S.; Manfredini, S.; Pollini, G. P.; Simoni, D.; Zanirato, V. *Tetrahedron* **1988**, *44*, 6451.

(2) Ford, J. A.; Wilson, C. V. *J. Org. Chem.* **1961**, *26*, 1433.

(3) (a) Fuchs, P. L. *Tetrahedron Lett.* **1974**, 4055. (b) Buchi, G.; Pawlak, M. *J. Org. Chem.* **1975**, *40*, 100.

(4) Garst, M. E. *J. Org. Chem.* **1979**, *44*, 1578.

(5) The preliminary results of this approach have been published as a communication, see: Lee, S. J.; Chien, C. J.; Peng, C. J.; Chao, I.; Chou, T. S. *J. Org. Chem.* **1994**, *59*, 4367.

(6) (a) Bailey, W. J.; Cummins, E. W. *J. Am. Chem. Soc.* **1954**, *76*, 1932. (b) Ellis, F.; Sammes, P. G.; Hursthouse, M. B.; Neidle, S. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1560.

(7) Sauer, J. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 16.

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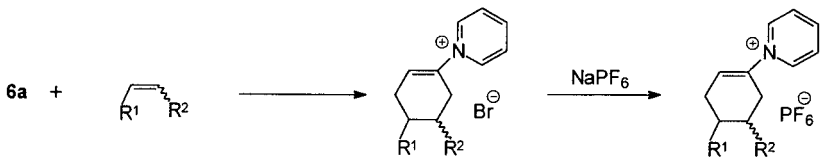
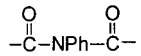
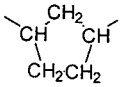
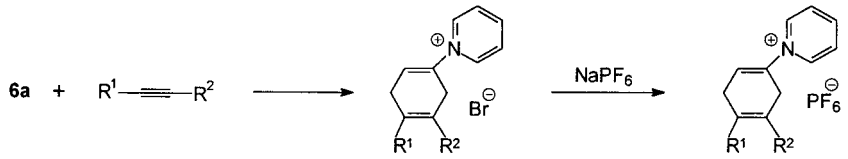
Scheme 1



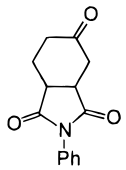
$R^1, R^2 =$ 	**7a**	**7b**
$R^1 = R^2 = CO_2Me$ (*trans*)	**8a**	**8b**
$R^1 = R^2 = CO_2Me$ (*cis*)	**9a**	**9b**
$R^1, R^2 =$ 	**10a**	**10b**
R^1 or R^2 = H or CO_2Me	**11a**: $R^1 = CO_2Me$, R^2 = H **12a**: R^1 = H, $R^2 = CO_2Me$	**11b**: $R^1 = CO_2Me$, R^2 = H **12b**: R^1 = H, $R^2 = CO_2Me$
R^1 or R^2 = H or COMe	**13a**: R^1 = COMe, R^2 = H **14a**: R^1 = H, R^2 = COMe	**13b**: R^1 = COMe, R^2 = H **14b**: R^1 = H, R^2 = COMe
$R^1 = R^2 = CO_2H$ (*trans*)	**15a**	**15b**
$R^1 = R^2 = CO_2H$ (*cis*)	**16a**	**16b**
$R^1 = R^2 = CN$ (*trans*)	**17a**	**17b**
R^1 or R^2 = H or CO_2H	**18a**: $R^1 = CO_2H$, R^2 = H **19a**: R^1 = H, $R^2 = CO_2H$	**18b**: $R^1 = CO_2H$, R^2 = H **19b**: R^1 = H, $R^2 = CO_2H$



R^1 or R^2 = H or CO_2H	**20a**: $R^1 = CO_2H$, R^2 = H **21a**: R^1 = H, $R^2 = CO_2H$	**20b**: $R^1 = CO_2H$, R^2 = H **21b**: R^1 = H, $R^2 = CO_2H$
$R^1 = R^2 = CO_2H$	**20a**: $R^1 = CO_2H$, R^2 = H **21a**: R^1 = H, $R^2 = CO_2H$	**20b**: $R^1 = CO_2H$, R^2 = H **21b**: R^1 = H, $R^2 = CO_2H$

facilitate their purification and characterization by recrystallization. The cycloadditions with *N*-phenylmaleimide, dimethyl fumarate, and methyl vinyl ketone (e.g. entries 1, 4, and 8 of Table 1) were completed in acetonitrile at 140 °C in 1 h. In fact, the reactions can be performed at even lower temperatures. For example, reaction of **6a** with *N*-phenylmaleimide at room temperature for 6 h or at 70 °C for 2 h produced **7a** in almost quantitative yield. It is especially interesting that the cycloaddition reaction of **6a** with the water-soluble dienophiles including fumaric acid, maleic acid, fumaronitrile, acrylic acid, propiolic acid, and acetylenedicarboxylic acid took place smoothly in water as well (entries 9−14 of Table 1). Although there are some examples of water-catalyzed Diels−Alder reactions,[8] our results illustrate that water can sometimes serve as a good solvent for "organic" Diels−Alder reactions.

In addition to spectral analysis, the structure of the vinylpyridinium-containing cycloadduct **7a** was further confirmed by chemical transformations. When **7a** was treated with sodium borohydride at 0 °C[9] followed by hydrolysis,[10] the pyridinium functionality was transformed into the substituted cyclohexanone **22**, presumably via a dihydropyridine intermediate. Therefore, compound **6a** may be considered as a water-soluble version of 2-alkoxy-1,3-butadiene in aqueous Diels−Alder reactions.



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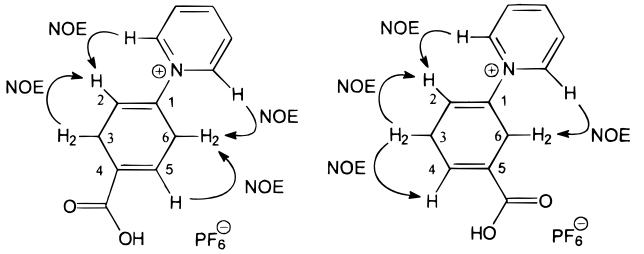
(8) (a) Lubineau, A.; Auge, J.; Queneau, Y. *Synthesis* **1994**, 741. (b) Li, C. J. *Chem. Rev.* **1993**, *93*, 2023. (c) Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 159. (d) Rideout, D. C.; Breslow, R. *J. Am. Chem. Soc.* **1980**, *102*, 7816. (e) Breslow, R.; Maitra, U.; Rideout, D. *Tetrahedron Lett.* **1983**, *24*, 1901. (f) Grieco, P. A.; Garner, P.; He, Z. *Tetrahedron Lett.* **1983**, *24*, 1897.

(9) Schenker, K.; Druey, J. *Helv. Chim. Acta* **1959**, *42*, 1960.

(10) Stamhuis, E. J.; Cook, A. G. In *Enamines: Synthesis, Structure, and Reactions*; Cook, A. G., Ed.; Marcel Dekker: New York, 1988; Chapter 3.

Two regioisomers were obtained (*para*:*meta* = 2:1) when **6a** was reacted with unsymmetric alkenes (entries 7, 8, and 12 of Table 1). The ratios of these two isomers were determined by ^{1}H NMR spectral analyses. Counterion exchange ($NaPF_6$) and recrystallization of any of the mixtures **11b**/**12b**, **13b**/**14b**, or **18b**/**19b** gave the major regioisomer as a white crystal. The structures of the major isomers were subjected to 2D NMR COSY experiments. The cross-peaks corresponding to the C_3 methylene hydrogens with the C_2 vinyl hydrogen and the C_4 methine hydrogen in the spectra indicated that these major isomers **11b**, **13b**, and **18b** are all "*para*".[11] The structure of **18b** was also unambiguously established by X-ray crystallographic analysis.

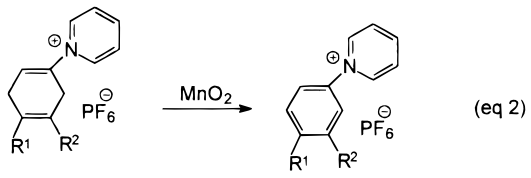
The regiochemical assignments of **20b** and **21b** were supported by their 2D NMR NOESY experiments. For compound **20b**, the NOE correlations between (1) the C_2 vinyl hydrogen and the C_3 methylene hydrogens, (2) the C_2 vinyl hydrogen and the *ortho*-hydrogens of the pyridinium, (3) the C_6 methylene hydrogens and the C_5 vinyl hydrogen, and (4) the C_6 methylene hydrogens and the *ortho*-hydrogens of the pyridinium were observed, indicating their close proximity. Whereas for **21b**, NOE



NOESY correlations observed on **20b** NOESY correlations observed on **21b**

correlations between (1) the C_3 methylene hydrogens and the C_2 and C_4 vinyl hydrogens and (2) *ortho*-hydrogens of the pyridinium and the C_6 methylene hydrogens and the C_2 vinyl hydrogen were observed.

Analytically pure samples of the cyclohexadienes **20b** and **21b** could not be obtained due to their instability. Therefore, the dienes were aromatized oxidatively with MnO_2 to **23** and **24,** respectively, of which purification and characterization were achieved.



(eq 2)

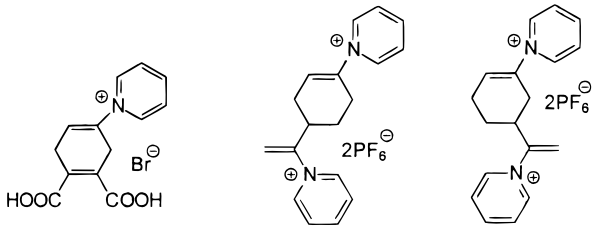
20b: $R^1 = CO_2H$, $R^2 = H$ **23**: $R^1 = CO_2H$, $R^2 = H$
21b: $R^1 = H$, $R^2 = CO_2H$ **24**: $R^1 = H$, $R^2 = CO_2H$

Somewhat unexpectedly, two regioisomers, **20a** and **21a**, were obtained (*para*:*meta* = 4:3) when **6a** was reacted with acetylenedicarboxylic acid (entry 14 of Table 1). The anticipated cycloadduct **25** was not detected. Their structures were confirmed by comparing with the products obtained from the reaction of **6a** with propiolic acid. This result is consistent with a report in the literature in which acetylenedicarboxylic acid loses CO_2 readily upon heating in H_2O to give propiolic acid.[12] Under the reaction condition, acetylenedicarboxylic acid was first converted to propiolic acid, which then participated in the cycloaddition reaction with **6a** to give **20a** and **21a**.

Table 1. Diels−Alder Reactions of Diene 6a

entry	dienophile (equiv)	conditions (solvent)	product (ratio)	PF_6^- salt (% yield[a])
1	*N*-phenylmaleimide (10)	140 °C, 1 h (CH_3CN)	**7a**	**7b** (88)
2	*N*-phenylmaleimide (10)	rt, 6 h (CH_3CN)	**7a**[b]	
3	*N*-phenylmaleimide (10)	70 °C, 2 h (CH_3CN)	**7a**[b]	
4	dimethyl fumarate (10)	140 °C, 1 h (CH_3CN)	**8a**	**8b** (86)
5	dimethyl maleate (10)	140 °C, 3 h (CH_3CN)	**9a**	**9b** (79)
6	norbornene (10)	140 °C, 1.5 h (CH_3CN)	**10a**	**10b** (92)
7	methyl acrylate (10)	140 °C, 1.5 h (CH_3CN)	**11a** + **12a** (2:1)[c]	**11b** (55)[d]
8	methyl vinyl ketone (10)	140 °C, 1 h (CH_3CN)	**13a** + **14a** (2:1)[c]	**13b** (57)[d]
9	fumaric acid (2)	110 °C, 4 h (H_2O)	**15a**	**15b** (68)
10	maleic acid (2)	110 °C, 22 h (H_2O)	**16a**	**16b** (62)
11	fumaronitrile (10)	100 °C, 45 h (H_2O)	**17a**	**17b** (64)
12	acrylic acid (2)	100 °C, 9 h (H_2O)	**18a** + **19a** (1.6:1)[c]	**18b** (33), **19b** (19)
13	propiolic acid (10)	100 °C, 24 h (H_2O)	**20a** + **21a** (5:4)[c]	**20b** (33), **21b** (32)
14	acetylenedicarboxylic acid (10)	100 °C, 24 h (H_2O)	**20a** + **21a** (4:3)[c]	**20b** (35), **21b** (33)

[a] These are isolated yields of the hexafluorophosphate salts after recrystallization. [b] Compound **7a** was obtained in nearly quantitative yield. The ^{1}H NMR spectrum of which indicates the purity to be better than 95%. [c] The ratio of these two regioisomers was determined by ^{1}H NMR spectral analysis. [d] Although **11b** and **13b** could be isolated in pure state by fractional crystallization, we were unable to get a pure sample of **12b** (or **14b**) uncontaminated by **11b** (or **13b**) by this method.



25 **26** **27**

Since substituted vinylpyridinium salts are very reactive dienophiles,[13] it was at first anticipated that **6a** might be a good dienophile to react only with electron-rich dienes. However, when the thermal extrusion of SO_2 from **5** was performed above a certain concentration,[14] [4 + 2] dimerization of the primary product **6a** would take place to give **26** and **27**, to some extent indicating that compound **6a** is also a dienophile which can react with electron-deficient dienes. Unlike the dimerization reactions of **1a**−**d**, the C_1−C_2 double bond of **6a** is less reactive as a dienophile than the C_3−C_4 double bond. The

(11) Although **11b** and **13b** could be isolated in pure state by fractional crystallization, we were unable to get a pure sample of **12b** (or **14b**), uncontaminated by **11b** (or **13b**), by this method.

(12) Bandrowski, E. *Chem. Ber.* **1879**, *12*, 2212.

(13) (a) Jung, M. E.; Buszek, K. R. *J. Org. Chem.* **1985**, *50*, 5441. (b) Jung, W. E.; Buszek, K. R. *Tetrahedron Lett.* **1986**, *27*, 6165.

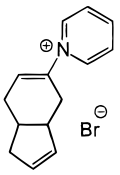
(14) Lee, S. J.; Tzeng, C. B.; Lin, S. C.; Chao, I.; Lu, H. F.; Chou, T. S. *J. Org. Chem.* **1996**, *61*, 9293.

unusual site-selectivity of **6a** in its dienophilic behavior seems to originate from the steric effect of the pyridinium ring.

When **6a** was reacted with cyclopentadiene at lower temperatures (under 100 °C), mixtures containing the cycloadduct **28** from the reaction of **6a** as the diene with cyclopentadiene as the dienophile and **29** from the reaction of cyclopentadiene as the diene with **6a** as the dienophile were obtained.[14] The major cycloadduct **29** could be converted completely to the cycloadduct **28** by a sigmatropic rearrangement process at 140 °C. Similar to the dimerization reaction of **6a**, it is the C_3-C_4 double bond of **6a** which reacted as the dienophile in the crossed Diels–Alder reaction with cyclopentadiene.

Competitive Diels–Alder reactions were carried out by treating **6a** with mixtures of dienophiles to examine their relative dienophilicity. The reaction of **6a** with a mixture of equal molar equivalents of *N*-phenylmaleimide and norbornene in acetonitrile at 140 °C for 1 h produced **7a** as the only cycloadduct. The reaction of **6a** with a mixture of equal molar equivalents of *N*-phenylmaleimide and dimethyl fumarate gave a mixture of **7a** and **8a** in a 2:1 ratio. The ratio was easily determined by ^{1}H NMR spectral analysis since the vinyl proton of **7a** (δ 6.42) exhibits lower chemical shift than that of **8a** (δ 6.18). The results of these competitive studies indicate that *N*-phenylmaleimide is more dienophilic than dimethyl fumarate, even more so than norbornene toward compound **6a**. This trend is consistent with the results of the Diels–Alder reactions of other electron-rich dienes.[15] It thus appears that **6a** behaves as a normal diene despite its electron-deficient nature.

Treatment of an equimolar of **6a** and another diene (2,3-dimethyl-1,3-butadiene or isoprene) with *N*-phenylmaleimide at room temperature for 1 h led to the formation of cycloadduct **7a** as the only product with no indication of the formation of **30** or **31**. This result indicates that the dienic reactivity of **6a** is substantially higher than that of 2,3-dimethyl-1,3-butadiene and isoprene.



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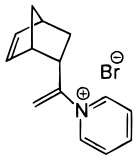

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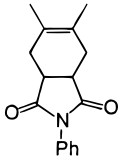

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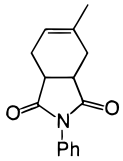

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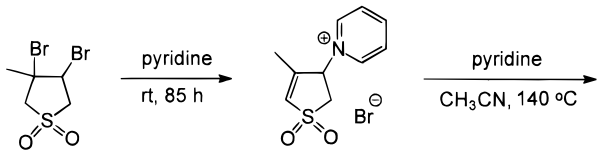
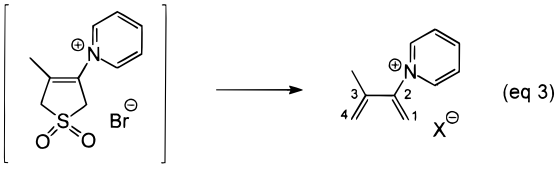
We were interested in comparing the methylated pyridinium diene **32a** with **6a** on the basis of their dienic reactivities and the regioselectivity of their cycloaddition reactions. On the basis of the same idea that inspired the preparation of diene **6a**, the desired diene **32a** was synthesized via the corresponding 3-sulfolene **33**. Bromination of the commercially available 3-methyl-3-sulfolene afforded 3,4-dibromo-3-methylsulfolane (**34**),[16] which was treated with pyridine at ambient temperature to give compound **35** in 52% yield. Isomerization of **35** to the 3-sulfolene **33** could not be accomplished under any of the various conditions attempted. Fortunately, compound **35** could be thermolyzed directly at 140 °C in the presence of pyridine to give the diene **32a** (eq 3). A base-



34 **35**



33

32a X = Br
32b X = PF_6

catalyzed isomerization did take place to give **33** as the intermediate under the reaction conditions. The subsequent extrusion of SO_2 from **33** to produce **32a** was essentially irreversible since the SO_2 could be trapped by pyridine.

Compound **32a**, similar to compound **6a**, was also found to be a reactive diene in [4 + 2] cycloaddition reactions with electron-deficient dienophiles (Scheme 2 and Table 2), but not with electron-rich dienophiles. However, higher reaction temperatures and/or longer reaction times are required for the completion of the cycloaddition reactions. For example, the cycloaddition reaction of **32a** with norbornene (16 equiv), at 200 °C took 4 h to complete. The results indicate the lower dienic reactivity of **32a** than **6a**. The difference in dienic reactivity between **6a** and **32a** may be associated with their conformational natures. It is obvious that **32a** has more difficulties than **6a** adopting the *s-cis* conformation necessary for [4 + 2] cycloaddition to take place. On the other hand, the difference in dienophilic reactivity of these two dienes is more distinct. Unlike compound **6a**, compound **32a** neither dimerizes nor reacts as a dienophile toward dienes. Conceivably, both steric and electronic effects of the methyl substituent disfavor the dienophilicity of the C_3-C_4 bond of **32a**. Therefore, replacement of the C_3-hydrogen of **6a** with a methyl group has significant influences on the chemical properties in Diels–Alder reactions.

Two regioisomers were obtained (**40a**:**41a** = 2:1 and **42a**:**43a** = 4:3) when **32a** was treated with unsymmetric alkenes (entries 5 and 6 of Table 2). The ratios of these two isomers were determined by ^{1}H NMR spectral analyses. Counterion exchange ($NaPF_6$) of the mixtures allowed easy separation of the isomers by silica gel column chromatography. The slower moving isomers on silica gel column were the major isomers **40b** and **42b**.

To establish the regiochemistry of these isomers, the 2D NMR COSY (^{1}H–^{1}H and ^{1}H–^{13}C) and NOESY experiments were carried out. In the ^{1}H–^{1}H COSY spectra of **40b** or **42b**, there are cross-peaks between (1) the C_3 methylene hydrogens and the C_4 methine hydrogen and (2) the C_2 methyl hydrogens and the C_6 methylene hydrogens. In addition, the NMR NOESY experiments of both **40b** and **42b** showed that (1) the C_3 methylene hydrogens are in proximity to the C_2 methyl hydrogens and the C_4 methine hydrogen and (2) the C_6 methylene hydrogens are in proximity to the *ortho*-hydrogens of the pyridinium ring. These results indicated that the meth-

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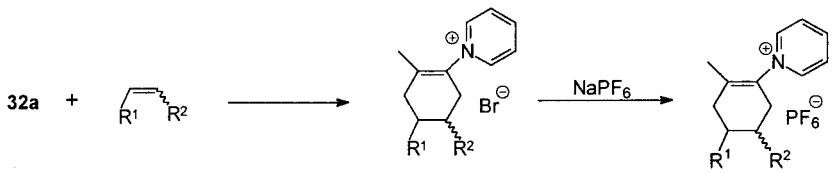
(16) Krug, R. C.; Yen, T. F. *J. Org. Chem.* **1956**, *21*, 1441.

Scheme 2



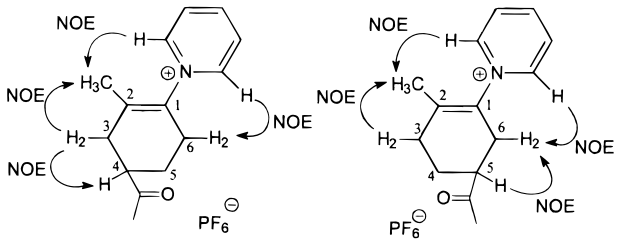
R^1, R^2 = –C(=O)–NPh–C(=O)–	**36a**	**36b**
$R^1 = R^2 = CO_2Me$ (*trans*)	**37a**	**37b**
$R^1 = R^2 = CO_2Me$ (*cis*)	**38a**	**38b**
R^1, R^2 = –CH=CH–CH$_2$–CH$_2$–	**39a**	**39b**
R^1 or $R^2 = CO_2Me$ or H	**40a**: $R^1 = CO_2Me$, R^2 = H **41a**: R^1 = H, $R^2 = CO_2Me$	**40b**: $R^1 = CO_2Me$, R^2 = H **41b**: R^1 = H, $R^2 = CO_2Me$
R^1 or R^2 = COMe or H	**42a**: R^1 = COMe, R^2 = H **43a**: R^1 = H, R^2 = COMe	**42b**: R^1 = COMe, R^2 = H **43b**: R^1 = H, R^2 = COMe
$R^1 = R^2 = CO_2H$ (*trans*)	**44a**	**44b**
$R^1 = R^2 = CO_2H$ (*cis*)	**45a**	**45b**

Table 2. Diels–Alder Reactions of Diene 32a

entry	dienophile (equiv)	conditions (solvent)	product (ratio)	PF_6^- salt (% yield)[a]
1	*N*-phenylmaleimide (5)	140 °C, 6 h (CH_3CN)	**36a**	**36b** (81)
2	dimethyl fumarate (5)	140 °C, 5 h (CH_3CN)	**37a**	**37b** (72)
3	dimethyl maleate (10)	140 °C, 15 h (CH_3CN)	**38a**	**38b** (62)
4	norbornene (16)	200 °C, 4 h (CH_3CN)	**39a**	**39b** (56)
5	methyl acrylate (5)	140 °C, 6 h (CH_3CN)	**40a** + **41a** (2:1)[b]	**40b** (40), **41b** (18)
6	methyl vinyl ketone (10)	140 °C, 10 h (CH_3CN)	**42a** + **43a** (4:3)[b]	**42b** (35), **43b** (21)
7	fumaric acid (2.5)	110 °C, 19 h (H_2O)	**44a**	**44b** (75)
8	maleic acid (2.5)	110 °C, 120 h (H_2O)	**45a**	**45b** (49)

[a] These are isolated yields of the hexafluorophosphate salts after recrystallization or purification by silica gel column chromatography. [b] The ratio of these two regioisomers was determined by ^{1}H NMR spectral analysis.

oxycarbonyl group of **40b** and the acetyl group of **42b** are "*para*" to the pyridinium ring. Using the same technique, the methoxycarbonyl group of **41b** and the acetyl group of **43b** were found to be "*para*" to the methyl group.



NOESY correlations observed on **42b** NOESY correlations observed on **43b**

In summary, we have demonstrated a very easy entry to **6a** and **32a**, which are stable 1,3-butadienes bearing a positively charged substituent, by way of the corresponding 3-sulfolenes. The success of the Diels–Alder reactions of these two dienes is noteworthy. Their dienic reactivity toward electron-deficient alkenes and their inability to undergo inverse electron demand Diels–Alder reactions are especially interesting observations. In addition, our study of the aqueous reactions of water-soluble dienophiles with **6a** and **32a** should broaden the scope of the long-popular Diels–Alder reaction.

Experimental Section

General Procedure for the Diels–Alder Reaction of Compound 6a in CH_3CN. A sealed tube containing a CH_3CN (10 mL) solution of **6a** (180 mg, 0.85 mmol) and a dienophile (10 equiv) was heated for the period of time shown in Table 1. After removal of the solvent, the residue was dissolved in water and then was washed with ethyl acetate to remove the excess dienophile. $NaPF_6$ (2 equiv) was added to the aqueous layer, and the resulting mixture was stirred at room temperature overnight. The crude hexafluorophosphate salt which precipitated was recrystallized from hot water to give the pure product **7b**–**10b**, **11b**, or **13b**. The yields of Diels–Alder reactions are summarized in Table 1. The room temperature or 70 °C Diels–Alder reactions were carried out by stirring the reaction mixtures under nitrogen and were worked up as described above.

1-(1,3-Dioxo-2-phenyl-1,3,3a,4,7,7a-hexahydroisoindol-5-yl)pyridinium hexafluorophosphate (7b): white solid, mp 233–234 °C; ^{1}H NMR (D_2O, 200 MHz) δ 2.76–2.86 (m, 2H), 3.13 (d, 2H, J = 5.1 Hz), 3.51–3.63 (m, 1H), 3.74–3.85 (m, 1H), 6.62 (t, 1H, J = 5.2 Hz), 7.13–7.19 (m, 2H), 7.40–7.48 (m, 3H), 8.09 (t, 2H, J = 7.4 Hz), 8.58 (t, 1H, J = 7.8 Hz), 8.81 (d, 2H, J = 5.5 Hz); IR (KBr) 3131, 3048, 1700, 1472, 1381, 1198 cm^{-1}; FABMS (m/z) calcd for $C_{19}H_{17}N_2O_2$ 305, found 305; calcd for PF_6 145, found 145. Anal. Calcd for $C_{19}H_{17}F_6N_2O_2P$: C, 50.68; H, 3.81; N, 6.22. Found: C, 50.41; H, 3.46; N, 5.98.

1-[*trans*-4,5-Bis(methoxycarbonyl)-1-cyclohexen-1-yl]-pyridinium hexafluorophosphate (8b): white solid, mp 128–130 °C; ^{1}H NMR (D_2O, 300 MHz) δ 2.48–2.62 (m, 1H), 2.65–2.78 (m, 1H), 2.87–2.94 (m, 2H), 3.08–3.19 (m, 1H),

3.26−3.37 (m, 1H), 3.72 (s, 6H), 6.34 (br s, 1H), 8.07 (t, 2H, J = 7.1 Hz), 8.57 (t, 1H, J = 7.7 Hz), 8.81 (d, 2H, J = 6.0 Hz); IR (KBr) 3154, 3085, 2956, 1724, 1434, 1304, 1175 cm^{-1}; FABMS (m/z) calcd for $C_{15}H_{18}NO_4$ 276, found 276; calcd for PF_6 145, found 145. Anal. Calcd for $C_{15}H_{18}F_6NO_4P$: C, 42.77; H, 4.31; N, 3.32. Found: C, 42.49; H, 3.90; N, 3.00.

1-[*cis*-4,5-Bis(methoxycarbonyl)-1-cyclohexen-1-yl]pyridinium hexafluorophosphate (9b): white solid, mp 85−86 °C; ^1H NMR (D_2O, 200 MHz) δ 2.56−2.67 (m, 2H), 2.85−2.96 (m, 2H), 3.23−3.34 (m, 1H), 3.38−3.50 (m, 1H), 3.64 (s, 6H), 6.21−6.27 (m, 1H), 7.97 (t, 2H, J = 7.9 Hz), 8.49 (dt, 1H, J = 1.0, 7.7 Hz), 8.73 (d, 2H, J = 6.5 Hz); IR (KBr) 3141, 2956, 1724, 1433, 1207 cm^{-1}; FABMS (m/z) calcd for $C_{15}H_{18}NO_4$ 276, found 276; calcd for PF_6 145, found 145. Anal. Calcd for $C_{15}H_{18}F_6NO_4P$: C, 42.77; H, 4.31; N, 3.32. Found: C, 42.37; H, 3.86; N,3.00.

1-(1,2,3,4,4a,5,8,8a-Octahydro-1,4-methanonaphthalen-6-yl)pyridinium hexafluorophosphate (10b): white solid, mp 152−153 °C; ^1H NMR (D_2O, 300 MHz) δ 1.08 (d, 1H, J = 10.3 Hz), 1.19 (d, 2H, J = 7.0 Hz), 1.52 (d, 2H, J = 8.1 Hz), 1.64 (dd, 1H, J = 10.3, 1.7 Hz), 1.68−1.82 (m, 2H), 1.88−1.98 (m, 1H), 2.00−2.05 (m, 2H), 2.21−2.35 (m, 1H), 2.50−2.60 (m, 1H), 2.67 (dd, 1H, J = 15.8, 8.0 Hz), 6.36−6.44 (m, 1H), 8.01 (t, 2H, J = 7.5 Hz), 8.50 (t, 1H, J = 7.8 Hz), 8.76 (d, 2H, J = 5.5 Hz); IR (KBr) 3139, 2949, 2868, 1629, 1472 cm^{-1}; FABMS (m/z) calcd for $C_{16}H_{20}N$ 226, found 226; calcd for PF_6 145, found 145. Anal. Calcd for $C_{16}H_{20}F_6NP$: C, 51.76; H, 5.43; N, 3.77. Found: C, 51.47; H, 5.50; N, 3.53.

1-[4-(Methoxycarbonyl)-1-cyclohexen-1-yl]pyridinium hexafluorophosphate (11b): white solid, mp 138−139 °C; ^1H NMR (D_2O, 500 MHz) δ 1.75−1.85 (m, 1H), 1.98−2.06 (m, 1H), 2.28−2.36 (m, 1H), 2.36−2.45 (m, 2H), 2.46−2.56 (m, 1H), 2.62−2.70 (m, 1H), 3.50 (s, 3H), 6.10 (br s, 1H), 7.85 (t, 2H, J = 7.2 Hz), 8.35 (t, 1H, J = 7.8 Hz), 8.62 (dd, 2H, J = 5.6, 1.3 Hz); ^{13}C NMR (D_2O, 50.3 MHz) δ 25.8, 27.8, 28.1, 54.1, 129.2, 129.6, 142.8, 144.5, 147.9, 179.2; IR (KBr) 3140, 1724, 1618, 1469, 1192 cm^{-1}; FABMS (m/z) calcd for $C_{13}H_{16}NO_2$ 218, found 218; calcd for PF_6 145, found 145. Anal. Calcd for $C_{13}H_{16}F_6NO_2P$: C, 42.97; H, 4.44; N, 3.86. Found: C, 43.00; H, 4.15; N, 3.57.

1-(4-Acetyl-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (13b): white solid, mp 124−125 °C; ^1H NMR (D_2O, 500 MHz) δ 1.68−1.76 (m, 1H), 2.01−2.07 (m, 1H), 2.08 (s, 3H), 2.19−2.27 (m, 1H), 2.29−2.41 (m, 2H), 2.47−2.57 (m, 1H), 2.75−2.81 (m, 1H), 6.11 (br s, 1H), 7.85 (t, 2H, J = 7.5 Hz), 8.32−8.35 (m, 1H), 8.61 (dd, 2H, J = 5.6, 1.3 Hz); ^{13}C NMR (D_2O, 75.4 MHz) δ 25.3, 27.0, 28.2, 29.2, 46.5, 129.4, 129.5, 142.5, 144.3, 147.8, 217.8; IR (KBr) 3120, 3080, 2923, 1690, 1620, 1418, 1350 cm^{-1}; FABMS (m/z) calcd for $C_{13}H_{16}NO$ 202, found 202; calcd for PF_6 145, found 145. Anal. Calcd for $C_{13}H_{16}F_6NOP$: C, 44.97; H, 4.64; N, 4.03. Found: C, 44.76; H, 4.24; N, 3.79.

General Procedure for the Diels−Alder Reaction of Compound 6a in H_2O. A sealed tube containing **6a** (70 mg, 0.33 mmol) and a suitable amount of dienophile in H_2O (10 mL) was heated for the period of time as shown in Table 1. To the reaction mixture was then added $NaPF_6$ (2 equiv) and the mixture stirred at room temperature overnight. After removal of the precipitate by filtration, the filtrate was concentrated under reduced pressure. The residue was recrystallized from hot water to give the pure hexafluorophosphate salt **15b**−**17b**. Regioisomers (**18b**/**19b** and **20b**/**21b**) were separated individually by fractional crystallization from hot water. Compounds **18b** and **21b** were the isomers obtained first from the fractional crystallization method.

1-(*trans*-4,5-Dicarboxy-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (15b): white solid, mp 167−168 °C; ^1H NMR (D_2O, 300 MHz) δ 2.35−2.50 (m, 1H), 2.55−2.68 (m, 1H), 2.73−2.82 (m, 2H), 2.88−3.0 (m, 1H), 3.04−3.15 (m, 1H), 6.22 (br s, 1H), 7.94 (t, 2H, J = 7.1 Hz), 8.44 (t, 1H, J = 7.9 Hz), 8.70 (d, 2H, J = 6.4 Hz); IR (KBr) 3134, 3085, 1696, 1632, 1474 cm^{-1}; FABMS (m/z) calcd for $C_{13}H_{14}NO_4$ 248, found 248. Anal. Calcd for $C_{13}H_{14}F_6NO_4P$: C, 39.71; H, 3.59; N, 3.56. Found: C, 39.76; H, 3.82; N, 3.30.

1-(*cis*-4,5-Dicarboxy-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (16b): white solid, mp 183−185 °C; ^1H NMR (D_2O, 300 MHz) δ 2.56−2.65 (m, 2H), 2.85−2.92 (m, 2H), 3.13−3.23 (m, 1H), 3.28−3.38 (m, 1H), 6.20 (br s, 1H), 7.95 (t, 2H, J = 7.0 Hz), 8.45 (t, 1H, J = 7.6 Hz), 8.78 (d, 2H, J = 6.1 Hz); IR (KBr) 3433, 3134, 3084, 1745, 1705, 1475, 1158 cm^{-1}; FABMS (m/z) calcd for $C_{13}H_{14}NO_4$ 248, found 248. Anal. Calcd for $C_{13}H_{14}F_6NO_4P$: C, 39.71; H, 3.59; N, 3.56. Found: C, 39.78; H, 3.53; N, 3.46.

1-(*trans*-4,5-Dicyano-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (17b): yellow solid, mp 155−157 °C; ^1H NMR (D_2O, 300 MHz) δ 2.70−2.86 (m, 2H), 2.92−3.15 (m, 2H), 3.48−3.58 (m, 1H), 3.66−3.76 (m, 1H), 6.31 (br s, 1H), 7.97 (t, 2H, J = 7.2 Hz), 8.47 (t, 1H, J = 7.8 Hz), 8.74 (d, 2H, J = 5.7 Hz); IR (KBr) 3139, 3089, 2251, 1633, 1478 cm^{-1}; FABMS (m/z) calcd for $C_{13}H_{12}N_3$ 210, found 210. Anal. Calcd for $C_{13}H_{12}F_6N_3P$: C, 43.96; H, 3.40; N, 11.83. Found: C, 43.48; H, 3.45; N, 11.45.

1-(4-Carboxy-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (18b): white solid, mp 191−193 °C; ^1H NMR (D_2O, 500 MHz) δ 1.92−2.03 (m, 1H), 2.10−2.20 (m, 1H), 2.41−2.50 (m, 1H), 2.50−2.60 (m, 2H), 2.60−2.71 (m, 1H), 2.72−2.82 (m, 1H), 6.26 (s, 1H), 8.01 (t, 2H, J = 7.0 Hz), 8.50 (t, 1H, J = 7.8 Hz), 8.77 (d, 2H, J = 6.3 Hz); ^{13}C NMR (MeOH-d_4, 50.3 MHz) δ 26.0, 28.0, 28.1, 38.6, 129.3, 129.4, 143.0, 144.6, 147.6, 177.8; IR (KBr) 3145, 3084, 1710, 1629, 1475, 1436, 1328, 1265, 1211 cm^{-1}; FABMS (m/z) calcd for $C_{12}H_{14}NO_2$ 204, found 204. Anal. Calcd for $C_{12}H_{14}F_6NO_2P$: C, 41.27; H, 4.04; N, 4.01. Found: C, 41.0; H, 4.16; N, 3.91.

X-ray Structure Analysis of Compound 18b. Crystal data: $C_{12}H_{14}F_6NO_2P$, molecular weight 349.21; monoclinic system, space group $P2_1/c$; a = 7.162(2), b = 16.815(7), c = 12.605(4) Å, β = 98.00(2)°; V=1503.3(9) Å^3, Z = 4, F(000) = 704, D_{calc} = 1.543 mg m^{-3}, μ = 2.53 cm^{-1}. Of the 1966 reflections collected ($2\theta_{max}$ = 45), 1043 unique reflections were considered observed ($I > 2\sigma(I)$) after Lorentz polarization and empirical absorption corrections. The reliability factors converged to R_1 = 0.099.[17]

1-(5-Carboxy-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (19b): white solid, mp 124−126 °C; ^1H NMR (MeOH-d_4, 500 MHz) δ 1.88−1.98 (m, 1H), 2.072.15 (m, 1H), 2.40−2.50 (m, 2H), 2.73−2.88 (m, 2H), 2.88−2.98 (m, 1H), 6.37 (s, 1H), 8.16 (t, 2H, J = 7.0 Hz), 8.66 (t, 1H, J = 7.8 Hz), 9.01 (d, 2H, J = 5.6 Hz); ^{13}C NMR (MeOH-d_4, 75.4 MHz) δ 24.4, 24.7, 31.1, 40.0, 129.4, 130.5, 142.1, 144.8, 147.7, 177.3; IR (KBr) 3136, 3083, 1714, 1632, 1473, 1331, 1266, 1213 cm^{-1}; FABMS (m/z) calcd for $C_{12}H_{14}NO_2$ 204, found 204. Anal. Calcd for $C_{12}H_{14}F_6NO_2P$: C, 41.27; H, 4.04; N, 4.01. Found: C, 41.10; H, 4.07; N, 3.99.

1-(4-Carboxy-1,4-cyclohexdien-1-yl)pyridinium hexafluorophosphate (20b): white solid, mp 186−188 °C; ^1H NMR (D_2O+acetone-d_6, 300 MHz) δ 3.15−3.25 (m, 2H), 3.48−3.58 (m, 2H), 6.40 (s, 1H), 6.98 (s, 1H), 8.10 (t, 2H, J = 7.1 Hz), 8.60 (t, 1H, J = 7.8 Hz), 8.89 (d, 2H, J = 6.0 Hz); ^{13}C NMR (MeOH-d_4, 75.4 MHz) δ 27.5, 30.6, 128.1, 128.4, 129.5, 134.8, 139.7, 144.8, 148.0, 169.0; IR (KBr) 1708, 1690, 1632, 1472, 1264, 1198 cm^{-1}; FABMS (m/z) calcd for $C_{12}H_{12}NO_2$ 202, found 202.

1-(5-Carboxy-1,4-cyclohexdien-1-yl)pyridinium hexafluorophosphate (21b): white solid, mp 181−183 °C; ^1H NMR (D_2O+acetone-d_6, 300 MHz) δ 3.15−3.30 (m, 2H), 3.38−3.48 (m, 2H), 6.34 (s, 1H), 6.99 (s, 1H), 8.12 (t, 2H, J = 7.1 Hz), 8.60 (t, 1H, J = 7.8 Hz), 8.92 (d, 2H, J = 5.6 Hz); ^{13}C NMR (MeOH-d_4, 75.4 MHz) δ 29.0, 29.2, 126.7, 128.1, 129.5, 135.7, 141.2, 144.9, 148.0, 168.7; IR (KBr) 1683, 1642, 1479, 1423, 1295 cm^{-1}; FABMS (m/z) calcd for $C_{12}H_{12}NO_2$ 202, found 202.

1-(4-Carboxyphenyl)pyridinium hexafluorophosphate (23): A mixture of **20b** (17.7 mg, 0.05 mmol) and MnO_2 (20 mg, 0.23 mmol) in H_2O (5 mL) was refluxed at 100 °C for 3 h. The resulting mixture was filtered and the filtrate was concentrated under reduced pressure to give a solid residue. The residue was then recrystallized from acetone to give compound **23** as white crystal in 62% yield: mp 193−195 °C;

(17) The authors has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

^{1}H NMR (D_2O+acetone-d_6, 300 MHz) δ 7.61 (d, 2H, J = 6.8 Hz), 7.94 (d, 2H, J = 6.8 Hz), 8.10 (t, 2H, J = 6.8 Hz), 8.60 (t, 1H, J = 6.4 Hz), 9.00 (d, 2H, J = 5.5 Hz); ^{13}C NMR (MeOH-d_4, 75.4 MHz) δ 125.4, 129.4, 132.4, 137.0, 145.3, 146.2, 148.1, 171.4; IR (KBr) 3429, 1712, 1629, 1470, 1257 cm^{-1}; FABMS (m/z) calcd for $C_{12}H_{10}NO_2$ 200, found 200. Anal. Calcd for $C_{12}H_{10}F_6NO_2P$: C, 41.76; H, 2.92; N, 4.06. Found: C, 41.45; H, 3.05; N, 4.31.

1-(3-Carboxyphenyl)pyridinium hexafluorophosphate (24): This compound was obtained from the oxidation of **21b** by MnO_2 in 82% yield by the same procedure used for **23** as a white solid: mp 174−176 °C; ^{1}H NMR (D_2O+acetone-d_6, 300 MHz) δ 7.68−7.78 (m, 1H), 7.80−7.88 (m, 1H), 8.12−8.18 (m, 2H), 8.25 (t, 2H, J = 6.8 Hz), 8.73 (t, 1H, J = 7.9 Hz), 9.12 (d, 2H, J = 6.3 Hz); ^{13}C NMR (MeOH-d_4, 75.4 MHz) δ 126.8, 129.6, 129.8, 132.1, 133.6, 135.0, 144.6, 146.3, 148.3, 167.5; IR (KBr) 3405, 1707, 1634, 1619, 1421, 1314 cm^{-1}; FABMS (m/z) calcd for $C_{12}H_{10}NO_2$ 200, found 200. Anal. Calcd for $C_{12}H_{10}F_6NO_2P$: C, 41.76; H, 2.92; N, 4.06. Found: C, 42.01; H, 2.99; N, 3.83.

2-Phenyl-hexahydroisoindoline-1,3,5-trione (22). To a solution of compound **7a** (330 mg, 0.86 mmol) in CH_3CN (10 mL) was added $NaBH_4$ (38.9 mg, 1.03 mmol) and MeOH (0.8 mL). The resulting mixture was stirred at room temperature for 20 min and then quenched with water. The mixture was extracted with CH_2Cl_2 and the combined organic layers were concentrated under reduced pressure. To a solution of the crude residue in THF (5 mL) was added 2% HCl aqueous solution (5 mL). The resulting mixture was stirred at room temperature for 2 h. The mixture was extracted with CH_2Cl_2 and the combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. The crude material was purified by HPLC (1:5 *n*-hexane/EtOAc) to give compound **22** (107 mg, 52%) as a white solid: mp 138−140 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.22−2.50 (m, 4H), 2.75−2.92 (m, 2H), 3.28−3.36 (m, 1H), 3.40−3.50 (m, 1H), 7.25−7.32 (m, 2H), 7.38−7.55 (m, 3H); IR (KBr) 3219, 1704, 1494, 1385, 1188 cm^{-1}; MS (m/z) 293 (M^+, 100), 202, 188, 173, 119, 96, 68, 54. Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 68.81; H, 5.38; N, 5.70.

3,4-Dibromo-3-methylsulfolane (34). This compound was obtained from the bromination of 3-methyl-3-sulfolene in $CHCl_3$[16] as a white solid: mp 127−128 °C (lit.[16] 126−127 °C); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.17 (s, 3H), 3.64 (dd, 1H, J = 3.4, 14.3 Hz), 3.73 (s, 2H), 4.25 (dd, 1H, J = 6.2, 14.4 Hz), 4.94 (dd, 1H, J = 3.4, 6.4 Hz); IR (KBr) 3000, 2932, 1400, 1306, 1294, 1237, 1182, 1139 cm^{-1}; MS (m/z) 293 (M^+), 291, 289, 213, 211 149, 147, 67 (100). Anal. Calcd for $C_5H_8BrO_2S$: C, 20.57; H, 2.76. Found: C, 20.57; H, 2.70.

1-(3-Methyl-2-sulfolen-4-yl)pyridinium bromide (35): A mixture of **34** (5.1 g, 17.12 mmol) and dry pyridine (45 mL) was stirred at room temperature for 85 h. The yellow precipitate that formed was collected, washed with benzene, and then recrystallized from hot ethanol-methanol (3:2) to give compound **35** in 52% yield[6b] as white needle crystal: mp 215−216 °C; ^{1}H NMR (D_2O, 300 MHz) δ 1.90 (s, 3H), 3.93 (dd, 1H, J = 2.6, 15.5 Hz), 4.31 (dd, 1H, J = 8.8, 15.5 Hz), 6.25 (d, 1H, J = 8.7 Hz), 7.24 (s, 1H), 8.20 (t, 2H, J = 7.1 Hz), 8.69 (t, 1H, J = 7.5 Hz), 8.91 (d, 2H, J = 5.7 Hz); IR (KBr) 3028, 2962, 2897, 1619, 1290, 1264, 1146, 1098 cm^{-1}; FABMS (m/z) calcd for $C_{10}H_{12}NO_2S$ 210, found 210. Anal. Calcd for $C_{10}H_{12}BrNO_2S$: C,41.53; H, 4.19; N, 4.85. Found: C, 41.14; H, 4.09; N, 4.56.

1-(3-Methyl-1,3-butadien-2-yl)pyridinium bromide (32a). A mixture of compound **35** (409 mg, 1.41 mmol) and pyridine (0.55 g, 7 mmol) in CH_3CN (14 mL) was heated in a sealed tube at 140 °C for 4 h. The solvent was then removed under reduced pressure to afford **32a** in nearly quantitative yield as a greenish oil: ^{1}H NMR (D_2O, 200 MHz) δ 1.93 (s, 3H), 4.30 (s, 1H), 5.18 (s, 1H), 5.52 (s, 1H), 5.72 (s, 1H), 7.98 (t, 2H, J = 7.1 Hz), 8.52 (t, 1H, J = 7.8 Hz), 8.69 (d, 2H, J = 6.7 Hz). ^{13}C NMR (MeOH-d_4, 50.3 MHz) δ 20.0, 117.8, 118.8, 129.5, 139.7, 146.4, 148.5, 151.1.

1-(3-Methyl-1,3-butadien-2-yl)pyridinium hexafluorophosphate (32b): A solution of **32a** (283 mg, 1.25 mmol) and $NaPF_6$ (419 mg, 2.5 mmol) in H_2O (12 mL) was stirred at room temperature for 14 h. The resulting precipitate was collected by filtration, and the filtrate was extracted with CH_2Cl_2. The organic layers were concentrated under reduced pressure to give a solid residue. The combined solids were then recrystallized from hot water to give **32b** in 64% yield as pale greenish needle crystal: mp 128−129 °C. ^{1}H NMR (acetone-d_6, 200 MHz) δ 2.16 (s, 3H), 4.58 (s, 1H), 5.41 (s, 1H), 5.97 (s, 1H), 6.04 (s, 1H), 8.34 (t, 2H, J = 7.1 Hz), 8.86 (t, 1H, J = 7.8 Hz), 9.04 (d, 2H, J = 5.1 Hz); IR (KBr) 3134, 3079, 1624, 1606, 1467, 1390, 1195 cm^{-1}; FABMS (m/z) calcd for $C_{10}H_{12}N$ 146, found 146. Anal. Calcd for $C_{10}H_{12}F_6NP$: C, 41.25; H, 4.15; N, 4.81. Found: C, 41.45; H, 4.21; N, 4.59.

General Procedure for the Diels−Alder Reaction of Compound 32a in CH_3CN. A sealed tube containing a suitable amount of **32a** and a dienophile in CH_3CN was heated for the period of time as shown in Table 2. After removal of the solvent, the residue was dissolved in water and then was washed with ethyl acetate to remove the excess of dienophile. $NaPF_6$ (2 equiv) was added to the aqueous layer, and the resulting mixture was stirred at room temperature overnight. The resulting crude hexafluorophosphate salt was purified by silica gel column chromatography (CH_2Cl_2/MeOH) to give the pure product **36b**−**39b**. Regioisomers (**40b**/**41b** and **42b**/**43b**) were separated individually by silica gel column chromatography (CH_2Cl_2/MeOH = 9:1). Compounds **40b** and **42b** were the slower moving isomers collected from the silica gel column.

1-(1,3-Dioxo-6-methyl-2-phenyl-1,3,3a,4,7,7a-hexahydroisoindole-5-yl)pyridinium hexafluorophosphate (36b): white solid, mp 246−248 °C. ^{1}H NMR (D_2O + acetone-d_6 , 300 MHz) δ 1.67 (s, 3H), 2.70 (dd, 1H, J = 3.9, 16 Hz), 2.83 (dd, 1H, J = 7.9, 16 Hz), 2.95 (dd, 1H, J = 3.3, 16 Hz), 3.06−3.15 (m, 1H), 3.52−3.60 (m, 1H), 3.65−3.74 (m, 1H), 7.18−7.22 (m, 2H), 7.35−7.48 (m, 3H), 8.18 (t, 2H, J = 7.0 Hz), 8.65 (t, 1H, J = 8.0 Hz), 8.67−8.72 (m, 2H); IR (KBr) 3125, 3082, 1700, 1471, 1381, 1196 cm^{-1}; FABMS (m/z) calcd for $C_{20}H_{19}N_2O_2$ 319, found 319. Anal. Calcd for $C_{20}H_{19}F_6N_2O_2P$: C, 51.73; H, 4.12; N, 6.03. Found: C, 51.43; H, 4.12; N, 5.87.

1-[*trans*-4,5-Bis(methoxycarbonyl)-2-methyl-1-cyclohexen-1-yl]pyridinium hexafluorophosphate (37b): white solid, mp 119−121 °C. ^{1}H NMR (acetone-d_6 + D_2O, 300 MHz) δ 1.43 (s, 3H), 2.40−2.62 (m, 2H), 2.70−2.80 (m, 2H), 3.00−3.10 (m, 1H), 3.14−3.24 (m, 1H), 3.62 (s, 3H), 3.65 (s, 3H), 8.12 (t, 2H, J = 6.8 Hz), 8.60 (t, 1H, J = 7.8 Hz), 8.75 (d, 2H, J = 6.0 Hz); IR (neat) 2959, 1734, 1629, 1475, 1439 cm^{-1}; FABMS (m/z) calcd for $C_{16}H_{20}NO_4$ 290, found 290. Anal. Calcd for $C_{16}H_{20}F_6NO_4P$: C, 44.15; H, 4.63; N, 3.22. Found: C, 44.35; H, 4.51; N, 2.82.

1-[*cis*-4,5-Bis(methoxycarbonyl)-2-methyl-1-cyclohexen-1-yl]pyridinium hexafluorophosphate (38b): yellowish oil; ^{1}H NMR (D_2O, 300 MHz) δ 1.23 (s, 3H), 2.36−2.48(m, 2H), 2.58−2.70 (m, 2H), 3.10−3.18 (m, 1H), 3.24−3.32 (m, 1H), 3.48 (s, 6H), 7.92 (t, 2H, J = 7.0 Hz), 8.40 (t, 1H, J = 7.8 Hz), 8.47 (d, 2H, J = 5.8 Hz); IR (neat) 2953, 1732, 1626, 1473, 1438 cm^{-1}; FABMS (m/z) calcd for $C_{16}H_{20}NO_4$ 290, found 290. Anal. Calcd for $C_{16}H_{20}F_6NO_4P$: C, 44.15; H, 4.63; N, 3.22. Found: C, 44.20; H, 4.48; N, 3.02.

1-(1,2,3,4,4a,5,8,8a-Octahydro-7-methyl-1,4-methanonaphthalen-6-yl)pyridinium hexafluorophosphate (39b): yellowish oil; ^{1}H NMR (MeOH-d_4, 300 MHz) δ 1.13 (d, 1H, J = 10.3 Hz), 1.28 (dd, 2H, J = 7.2, 1.6 Hz), 1.59 (d, 2H, J = 9.0 Hz), 1.64 (s, 3H), 1.76 (d, 1H, J = 10.3 Hz), 1.80−1.92 (m, 1H), 1.94−2.15 (m, 4H), 2.30−2.45 (m, 2H), 2.51 (dd, 1H, J = 15.1, 7.2 Hz), 8.22 (t, 2H, J = 7.0 Hz), 8.67 (t, 1H, J = 7.7 Hz), 8.87 (d, 2H, J = 5.8 Hz); IR (neat) 3116, 2951, 2872, 1625, 1472 cm^{-1}; FABMS (m/z) calcd for $C_{17}H_{22}N$ 240, found 240. FABHRMS calcd for $C_{17}H_{22}N$ 240.1752, found 240.1753.

1-(4-Methoxycarbonyl-2-methyl-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (40b): colorless oil; ^{1}H NMR (MeOH-d_4, 500 MHz) δ 1.52 (s, 3H), 1.98−2.08 (m, 1H), 2.22−2.28 (m, 1H), 2.53−2.61 (m, 3H), 2.62−2.72 (m, 1H), 2.86−2.94 (m, 1H), 3.73 (s, 3H), 8.21 (t, 2H, J = 7.0 Hz), 8.69 (t, 1H, J = 7.8 Hz), 8.90 (d, 2H, J = 6.3 Hz); IR (neat) 3132, 3081, 2956, 1731, 1628, 1474, 1439 cm^{-1}; FABMS (m/z) calcd for $C_{14}H_{18}NO_2$ 232, found 232. FABHRMS calcd for $C_{14}H_{18}NO_2$ 232.1337, found 232.1338.

1-(5-Methoxycarbonyl-2-methyl-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (41b): yellowish oil; ^{1}H NMR (MeOH-d_4, 500 MHz) δ 1.50 (s, 3H), 1.93−2.02 (m, 1H), 2.122.19 (m, 1H), 2.32−2.46 (m 2H), 2.70−2.83 (m, 2H), 2.98−3.05 (m, 1H), 3.74 (s, 3H), 8.22 (t, 2H, J = 7.0 Hz), 8.70 (t, 1H, J = 7.8 Hz), 8.92 (d, 2H, J = 5.4 Hz); IR (neat) 3132, 3081, 2956, 1731, 1628, 1474, 1439 cm^{-1}; FABMS (m/z) calcd for $C_{14}H_{18}NO_2$ 232, found 232. FABHRMS calcd for $C_{14}H_{18}NO_2$ 232.1337, found 232.1339.

1-(4-Acetyl-2-methyl-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (42b): yellowish oil; ^{1}H NMR (MeOH-d_4, 500 MHz) δ 1.52 (s, 3H), 1.86−1.95 (m, 1H), 2.22−2.26 (m, 1H), 2.27 (s, 3H), 2.44−2.48 (m, 2H), 2.50−2.58 (m, 1H), 2.61−2.73 (m, 1H), 2.94−3.01 (m, 1H), 8.19 (t, 2H, J = 7.0 Hz), 8.68 (t, 1H, J = 7.8 Hz), 8.86 (d, 2H, J = 6.0 Hz); ^{13}C NMR (DMSO-d_6, 50.3 MHz) δ 18.0, 24.8, 28.6, 29.6, 31.9, 45.8, 129.1, 133.4, 135.9, 145.6, 147.0, 210.6; IR (neat) 3656, 3131, 2933, 1707, 1629, 1473 cm^{-1}; FABMS (m/z) calcd for $C_{14}H_{18}NO$ 216, found 216.

1-(5-Acetyl-2-methyl-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (43b): yellowish oil; ^{1}H NMR (MeOH-d_4, 500 MHz) δ 1.48 (s, 3H), 1.85−1.93 (m, 1H), 2.17−2.24 (m, 1H), 2.27 (s, 3H), 2.29−2.36 (m 1H), 2.40−2.49 (m, 1H), 2.58−2.65 (m, 1H), 2.692.77 (m, 1H), 3.06−3.13 (m, 1H), 8.21 (t, 2H, J = 7.0 Hz), 8.70 (t, 1H, J = 7.8 Hz), 8.92 (d, 2H, J = 6.0 Hz); ^{13}C NMR (DMSO-d_6, 50.3 MHz) δ 17.7, 24.0, 28.3, 30.0, 31.1, 46.6, 129.1, 134.0, 135.1, 145.6, 147.0, 209.8; IR (neat) 2927, 2853, 1706, 1625, 1473 cm^{-1}; FABMS (m/z) calcd for $C_{14}H_{18}NO$ 216, found 216. Anal. Calcd for $C_{14}H_{18}F_6NOP$: C, 46.55; H, 5.02; N, 3.88. Found: C, 46.94; H, 5.27; N, 3.35.

General Procedure for the Diels−Alder Reaction of Compound 32a in H_2O. A sealed tube containing **32a** (54.4 mg, 0.24 mmol) and a suitable amount of dienophile in H_2O (12 mL) was heated for the period of time as shown in Table 2. After removal of the solvent, the residue was washed with ethyl ether (entry 7) or acetone (entry 8) to remove the excess of dienophile. Then the residue was dissolved in water and $NaPF_6$ (2 equiv) was added to the solution. The resulting mixture was stirred at room temperature for overnight. The mixture was concentrated under reduced pressure. The residue was recrystallized from hot water to give the pure hexafluorophosphate salt **44b** or **45b**.

1-(*trans*-4,5-Dicarboxy-2-methyl-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (44b): white solid, mp 228−230 °C. ^{1}H NMR (acetone-d_6 + D_2O, 300 MHz) δ 1.53 (s, 3H), 2.45−2.70 (m, 2H), 2.70−2.92 (m, 2H), 3.02−3.12 (m, 1H), 3.13−3.26 (m, 1H), 8.23 (t, 2H, J = 7.0 Hz), 8.71 (t, 1H, J = 7.8 Hz), 8.87 (d, 2H, J = 6.0 Hz); ^{13}C NMR (MeOH-d_4, 75.4 MHz) δ 17.7, 32.3, 32.9, 42.0, 42.8, 130.0, 135.1, 135.6, 146.1, 148.0, 177.5, 178.1; IR (KBr) 3493, 2922, 1723, 1678, 1469, 1429 cm^{-1}; FABMS (m/z) calcd for $C_{14}H_{16}NO_4$ 262, found 262. Anal. Calcd for $C_{14}H_{16}F_6NO_4P$: C, 41.29; H, 3.96; N, 3.44. Found: C, 41.65; H, 4.37; N, 3.34.

1-(*cis*-4,5-Dicarboxy-2-methyl-1-cyclohexen-1-yl)pyridinium hexafluorophosphate (45b): white solid, mp 230−232 °C. ^{1}H NMR (D_2O, 300 MHz) δ 1.35 (s, 3H), 2.50−2.57 (m, 2H), 2.76 (br s, 2H), 3.15−3.24 (m, 1H), 3.26−3.35 (m, 1H), 8.01 (t, 2H, J = 7.0 Hz), 8.49 (t, 1H, J = 7.9 Hz), 8.60 (d, 2H, J = 6.0 Hz); IR (KBr) 3500, 2911, 1725, 1676, 1469, 1430 cm^{-1}; FABMS calcd for $C_{14}H_{16}NO_4$ 262.1079, found 262.1083.

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Supporting Information Available: ^{1}H NMR spectra of all new compounds; ^{13}C NMR spectra of **18b**−**21b**, **23**, **24**, and **42b**−**44b**; ^{1}H−^{1}H COSY spectra of **18b**−**21b**, and **40b**−**43b**; NOESY spectra of **20b**, **21b**, and **40b**−**43b**; and the ORTEP drawing of **18b** (57 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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