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ALKENYLIMMONIUM SALTS AS DIENOPHILES IN DIELS-ALDER CYCLOADDITIONS WITH HIGH REACTIVITY AND STEREOSELECTIVITY[1]

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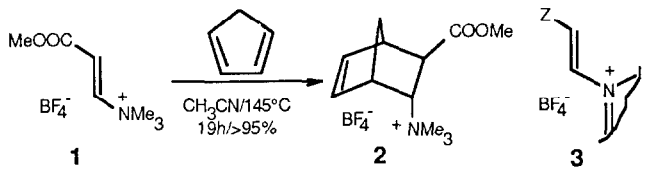
Abstract: Alkenylimmonium salts, such as the substituted vinylpyridinium salts, **6**, **7**, **12**, and **16**, are easily prepared and are very reactive dienophiles in Diels-Alder cycloadditions.

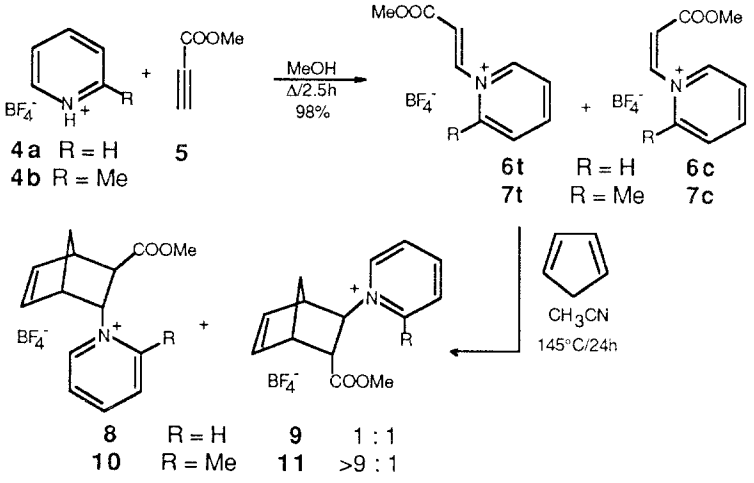
Recently we reported that alkenyltrialkylammonium salts such as **1** underwent Diels-Alder reactions with dienes such as cyclopentadiene to afford the endo adducts **2** as the sole products.[3] One potential drawback to the general utility of this cycloaddition process was that high temperatures were generally required to produce high yields of adducts in a reasonable period of time, due presumably to the great steric hindrance associated with the trialkyl ammonium groups. We now report that the readily prepared alkenylimmonium salts such as **3** are much more reactive than the corresponding salts **1** and do not require additional electron-withdrawing groups to give complete reaction at room temperature. We also have determined the reasons for the high endo stereoselectivity observed with both sets of salts.



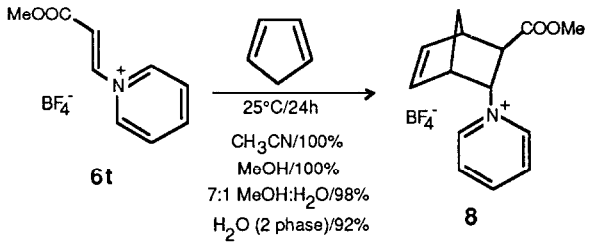
1 **2** **3**

As discussed in our earlier paper,[3] the high endo selectivity of the cycloadditions of salts such as **1** could be due to either of two factors: 1) a purely steric interaction between the very large trimethylammonium group and the methylene group of cyclopentadiene which would disfavor the exo transition state; 2) an attractive charge-dipole interaction between the charged ammonium group and the polarized diene which would favor the endo transition state. To test which of these two factors is more important, we chose to react a less hindered salt with

the same electronic properties, namely an immonium salt such as **3** (sp^2 N vs sp^3 N). Thus reaction of pyridinium tetrafluoroborate **4a** and methyl propiolate **5** (methanol, 65°C, 2.5h, 98%) produced a 44:56 mixture of the trans and cis N-(2-carbomethoxyvinyl)pyridinium tetrafluoroborate **6tc**, which could be separated by fractional crystallization.[4,5] Cycloaddition of the trans isomer **6t** with cyclopentadiene under identical reaction conditions as for **1** (CH_3CN, 145°C, 24h) afforded an approximately 1:1 mixture of stereoisomeric adducts **8** and **9** in 65% yield.[6] Thus it seems clear that it is the steric factor which favors endo selectivity, since the sterically much smaller pyridinium group can now occupy the exo position.[7] A confirmation of this hypothesis was the result of the reaction of the 2-methyl analogue of **6t**, namely **7t**,[8] with cyclopentadiene under identical conditions which gave a >9:1 mixture of **10:11**. Thus as the steric bulk of the immonium group increases, the amount of endo isomer increases.

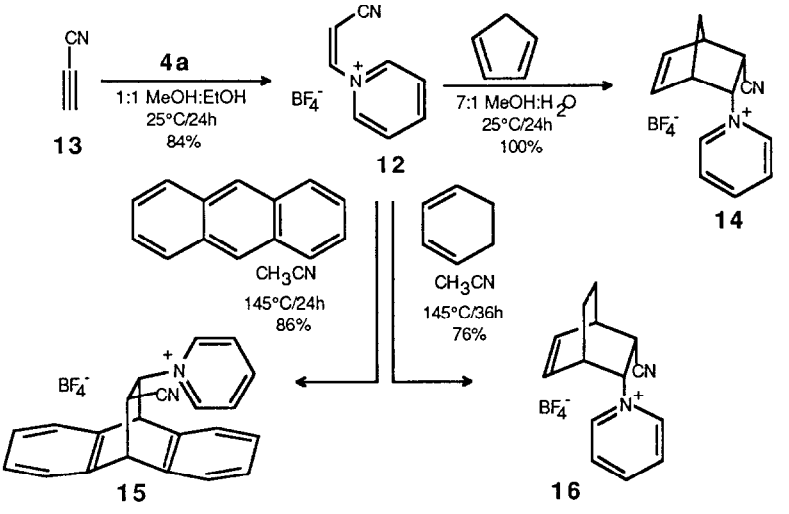


More important for synthetic use was the demonstration that the much less-hindered pyridinium salts had predictably much higher reactivity. Thus the cycloaddition of **6t** and cyclopentadiene could be carried out at room temperature in any of several solvent systems as shown, all in nearly quantitative yield to furnish the endo isomer **8** as the sole product. Presumably at lower temperatures, the more sterically hindered transition state with the immonium group exo is disfavored. In like fashion cis N-(2-cyanovinyl)pyridinium tetrafluoroborate **12**, prepared in 84% yield by reaction of **4a** with propionitrile **13** (1:1 MeOH:EtOH, 25°C, 24h), gave only the endo isomer **14** when reacted with cyclopentadiene at room temperature (7:1 MeOH:H_20, 25°C, 24h, 100%). The less hindered diene, anthracene, also reacts with **12** to produce the Diels-Alder adduct **15** in 86% yield. The less

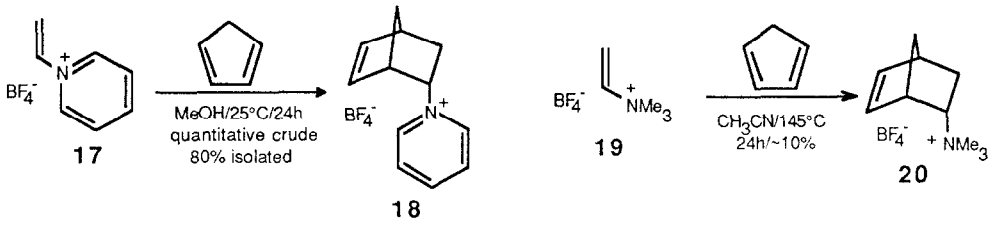


reactive diene, cyclohexadiene, also reacted cleanly with **12** to produce **16** the endo adduct in 76% yield.

However the best indication of the very heightened reactivity of the immonium salts vs. the ammonium salts is



the cycloaddition of the unsubstituted N-vinylpyridinium tetrafluoroborate **17**, prepared from 1,2-dibromoethane and pyridine in 2 steps,[9] with cyclopentadiene in methanol at 25°C for 24h to give only the endo adduct **18** in quantitative crude yield (80% purified). Thus the activation provided by an immonium group is sufficient by itself to convert ethylene into a very reactive dienophile. For a direct comparison, the cycloaddition of the corresponding trimethylvinylammonium tetrafluoroborate (neurine tetrafluoroborate, prepared by ion exchange of commercially available neurine bromide) **19** with cyclopentadiene at 145°C for 24h produced only 10% the corresponding endo cycloadduct **20**. Further applications of the cycloadditions of alkenylimmonium salts, especially for asymmetric induction, are currently under investigation.



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References and Notes

1. Presented at the 192nd American Chemical Society National Meeting, Anaheim, CA, Sept. 1986.
2. UCLA Gold Shield Faculty Awardee, 1986-8.
3. Jung, M. E.; Buszek, K. R. *J. Org. Chem.* **1985**, *50*, 5440-5441.
4. All new compounds exhibited spectroscopic data (500 MHz ^{1}H and 125 MHz ^{13}C NMR, IR, FAB-MS and/or elemental analysis) in full accord with their assigned structures.
5. Although **6t** could be isolated in pure state by fractional crystallization, we were unable to get a pure sample of **6c**, uncontaminated by **6t**, by this method and therefore have not investigated the cycloadditions of **6c**. We have shown separately that **6t** and **6c** are thermally stable under these reaction conditions.
6. Separate experiments show that **8** and **9** do not equilibrate under these reaction conditions and thus the 1:1 ratio is a kinetic one. In fact, no isomerization of any of the cycloadducts - **8-11**, **14-16**, **18**, **20** - under these thermal conditions has been observed.
7. We assume that the electronic interaction of a trimethylammonium group and the pyridinium group with the diene would be essentially identical.
8. The 2-methylpyridinium salt **7t** could not be prepared by the route used for **6t** due to steric hindrance of attack of the nitrogen on the propiolate. The following modification was used for **7t** and other hindered pyridinium salts: reaction of 1 eq of the 2-methylpyridinium chloride (corresponding to **4b**), 3 eq of the propiolate, and 0.5-1 eq of 2-methylpyridine in methanol for 1h gave a 1:1.2 mixture of the trans and cis chlorides which were separated by fractional crystallization and converted into **7t** and **7c** by ion exchange.
9. Katritzky, A. R.; Rubio, O. *J. Org. Chem.* **1983**, *48*, 4017-4021.

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