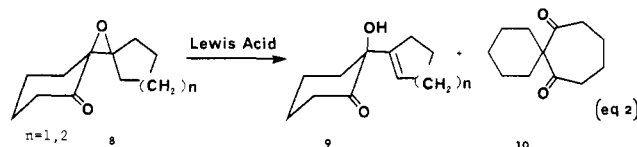


carbonyl π -bond is ideally poised to overlap with the developing empty carbon p orbital at C₆ early on the reaction coordinate as depicted in 1a. Rotation about the C₄-C₅ bond allows the π_{CO} bond to become parallel to the C₅-C₆ bond axis.^{4f} As the 1,2-migration proceeds the partially empty p orbital on oxygen, resulting from reverse polarization of the carbonyl π -bond, is able to mix with the Walsh orbitals of the developing cyclopropyloxonium ion^{4d-f} and effectively disperse the positive charge arising from C-O bond cleavage (1b). Essentially quantitative acyl migration was observed at -78 °C in about 2 h; at room temperature the rearrangement is complete in less than 1 min. In general, one can anticipate facile acyl migration when a transition state resembling 1b can be attained without undue bond angle deformation or steric interactions. However molecular models suggest that attempted ring expansion of a cyclohexanone derivative such as 8 will move the carbonyl carbon away from the migration terminus unless the internal bond angles of the ring are compressed. Consequently, the transition state cannot be effectively stabilized by nonclassical stabilization as in 1b and an E₁ elimination occurs affording allylic alcohol 9 as the major product with both BF₃·Et₂O and Mg(ClO₄)₂ (eq 2). Carbonyl migration in 8 (*n* = 1) has been noted with



SbCl₅ in SO₂ solvent^{3b,3f} but the formation of a chlorohydrin intermediate^{4d} preceding carbonyl migration remains a distinct possibility. We observe the formation of a fluorohydrin intermediate that precedes carbonyl migration in the formation of 6 and 7.

In summary, the overall reaction sequence in Scheme I provides a practical route to a variety of 1,3-diketospiranes and clearly demonstrates the synthetic utility of rearrangements involving carbonyl migration. In all cases (Table I), acyl migration with attendant *ring expansion* proceeded with no detectable competing alkyl migration. The geometric requirements for formation of a uniquely stabilized transition state resembling 1b provides a qualitative rationale for both rate differences and the different product distribution observed upon treatment of α,β -epoxyketones with Lewis acids.^{4d} The unusually mild reaction conditions required for introducing the spiro center should provide a convergent synthesis of more highly functionalized natural products comprising β -vetivone and related compounds.

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Robert D. Bach,* Russell C. Klix

Department of Chemistry
Wayne State University
Detroit, Michigan 48202

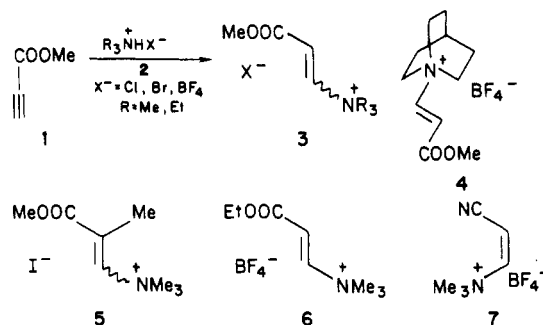
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Alkenyltrialkylammonium Salts as Dienophiles in Diels-Alder Reactions: Preparation, Cycloadditions, and Further Reactions. β -(Dimethylamino)acrylonitrile Equivalent in Cycloadditions¹

Summary: Diels-Alder cycloadditions of a new class of dienophiles, alkenylammonium salts, can be carried out in acetonitrile, giving the desired cycloadducts in excellent yield.

Sir: Although the Diels-Alder reaction is one of the most powerful constructive methods available to synthetic chemists today, there is still a need for further improvements and innovations. One particular drawback is the inability to use dienophiles containing dialkylamino substituents in cycloadditions, a process with significant potential for alkaloid synthesis.² We now report a method for accomplishing this transformation which involves the first cycloadditions of alkenylammonium salts, a potentially quite useful class of electron-deficient olefins.

Treatment of methyl propiolate (1) with trialkylammonium halides 2 produces (90%) mainly the *trans*-carboxymethoxyvinyl trialkylammonium salts 3 (t:c = 90:10).³



Exchange of halide for BF₄⁻ via ion exchange chromatography gives the corresponding BF₄⁻ salts, which can be prepared more easily (89%) by adding the corresponding BF₄⁻ salts to 1 (t:c = 55:45, separable by fractional crystallization).⁴ The quinuclidinium salt 4 was prepared by addition of the free base quinuclidine to 1 to give the betaine (80%) followed by carboxylate salt methylation with dimethyl sulfate (95%) and ion exchange. The salt 5 was prepared by a method developed for cyclic derivatives, namely, thiophenylation of methyl β -(dimethylamino)- α -methylpropionate (LDA, PhSSPh, 80%) followed by selective N-methylation (excess MeI, 100%), oxidation (MCPBA, 95%) and thermal elimination (80 °C, PhH, 84%).⁵ Finally the *trans* ethyl acrylate derivative 6 and the *cis* acrylonitrile derivative 7 were prepared analogously from ethyl propiolate and propiolonitrile, respectively. In the case of 7, the *cis* isomer preferentially crystallizes from solution.

Seldom have salts been used as dienophiles in cycloadditions.⁶ We hoped that the electron-withdrawing

(1) Presented at the 5th International Conference on Organic Synthesis, Freiburg, Germany, Aug 1984.

(2) Although enamines can be used in reverse-electron demand Diels-Alder reactions, the corresponding β -(dialkylamino)acrylates, -acrylonitriles, etc., cannot.

(3) (a) Herkes, F. E.; Simmons, H. E. *J. Org. Chem.* 1973, 38, 2845. (b) McCulloch, A. W.; McInnes, A. G. *Can. J. Chem.* 1974, 52, 3569.

(4) All new compounds possessed spectroscopic data (high field NMR, IR, FAB MS, and/or elemental analysis) in full accord with their assigned structure.

(5) This reaction was carried out by Dr. G. S. Arora and gives a 4:1 mixture of 5 (one isomer, stereochemistry unknown) and methyl α -(trimethylammoniummethyl)acrylate.

Table I. Cycloadditions of Alkenylammonium Tetrafluoroborate Salts

dienophile	diene	temp (°C)	time	yield	product
3, R = Me (E)	Cp	145	1-2 days	92%	8 (R = Me; R' = Me)
3, R = Me (E)	Cp	190	1 h	90%	8 (R = Me; R' = Me)
4	Cp	140	19 h	82%	8 (R ₃ = quinuclidine; R' = Me)
3, R = Et (E)	Cp	145	49 h	85%	8 (R = Et; R' = Me)
6	Cp	145	49 h	85%	8 (R = Me; R' = Et)
7	Cp	145	1 h	100%	9
7	Cp	53	24 h	78%	9
3, R = Me (E)	isoprene	145	72 h	80%	10ab
18	Cp	145	21 h	60%	19

power of the ammonium salt would offset its considerable steric hindrance (comparable to a *tert*-butyl group) and allow the cycloaddition to proceed. This was indeed the case, as is shown in Table I. The BF_4^- salts are advantageous for two reasons: (1) increased solubility in aprotic organic solvents (e.g., CH_3CN) and (2) the halide salts suffer thermal *N*-dealkylation.³ The reactions were carried out in acetonitrile solutions in sealed tubes heated in pipe ovens.

The stereochemistry of the reaction was determined with cyclopentadiene (Cp), the adducts 8-9 having the trialkylammonium group completely in the endo position.⁷ This result is presumably due to the large steric bulk of the trialkylammonium group which causes the transition state with the ammonium group exo to be sterically disfavored, although there may also be some stabilizing overlap of the diene π -system with the charged ammonium group in the endo position. The regiochemistry was de-

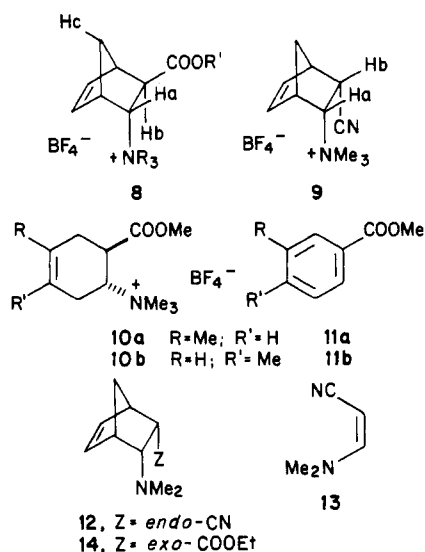
termined by reaction of 3 (R = Me) with isoprene which gave a 65:35 mixture of 10a:10b in good yield. The regiochemical assignment of this mixture was made by conversion into the methyl toluates 11ab by β -elimination ($\text{NaOMe}/\text{MeOH}/65^\circ\text{C}/14\text{ h}/41\%$) followed by oxidation ($\text{DDQ}/\text{PhH}/25^\circ\text{C}/18\text{ h}/71\%$). This ratio of *m*- to *p*-toluates was approximately 65:35, thereby indicating that the trimethylammonium group is a stronger directing group in cycloadditions than an ester.

The high reactivity of the nitrile 7 is worth noting. It required only 1 h at 140 °C to completely react with Cp. In addition, the reactions can be run at much lower temperatures. For example, reaction of 7 with Cp at 53 °C for 24 h produced a 78% yield of 9, while reactions at room temperature in acetonitrile or water occurred but at a

much slower rate (20% and 10% after 24 h, respectively). However, the use of the mixed solvent system 7:1 $\text{MeOH}/\text{H}_2\text{O}$, in which neither component is completely soluble, allowed the cycloaddition of 7 and Cp to be carried out conveniently at 25 °C, giving 9 in 60% yield after 24 h. Thus, by proper choice of reaction solvent, one can perform the reaction at normal temperatures.

The second step in the two-step process for the overall addition of methyl β -(dimethylamino)acrylonitrile (13) involves demethylation of the salt 9 to give 12, the formal adduct of Cp and 13. This was easily accomplished by simple hydride reduction (NaBH_4 , Me_2SO , 65 °C)⁸ to give 12 in 90-100% yield. Treatment of the ester 8 (R = Me; R' = Et) with DABCO in refluxing DMF for 1 h⁹ gave the ester 14 in 88% yield.

Finally, the reaction can also be done intramolecularly. For example, the diene-amine 16, prepared in 93% yield from pyrrolidine and the dienyl tosylate 15,¹⁰ reacted with



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methyl *trans*- β -chloroacrylate 17 to give an excellent yield of the *trans*-carbomethoxyalkenylammonium salt 18, after ion exchange. Thermolysis of 18 in acetonitrile at 145 °C for 21 h gave an approximately 60% yield of the adduct 19 as a mixture of isomers.

Thus alkenylammonium salts are readily available, react stereospecifically and regioselectively with typical dienes, and can be easily converted to the formal adducts of β -(dialkylamino)acrylates and -propiolates. Further investigations, including the possibility of asymmetric induction by using optically active amines in compounds such as 3, are underway.

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(9) Ho, T.-L. *Synthesis* 1972, 702.

(10) Prepared from sorbic acid in three steps—deconjugation, reduction, and tosylation.

Michael E. Jung,* Keith R. Buszek

Department of Chemistry and Biochemistry
University of California
Los Angeles, California 90024

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(7) For example, in 8 (R = Me; R' = Et) Ha appears as a dd ($J = 3, 5\text{ Hz}$) while there is W coupling between Hb and Hc. In 9, Ha appears as a dd ($J = 3, 9\text{ Hz}$) while Hb is a dd ($J = 4, 9\text{ Hz}$).