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MILD AND PRACTICAL CYCLOADDITION REACTIONS OF FURANS WITH PHENYL VINYL SULFONATE

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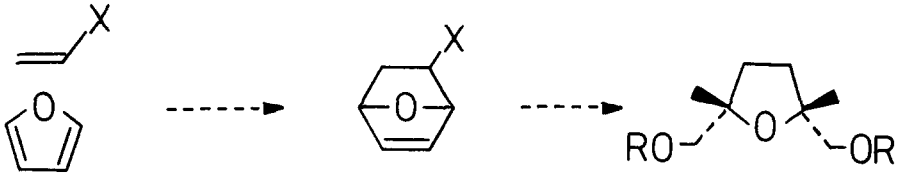
Abstract: Phenyl vinyl sulfonate reacts with various alkyl furan derivatives under mild conditions to produce excellent yields of the corresponding cycloadducts.

The usefulness of the intermolecular cycloaddition reaction of furan dienes in synthesis has been limited by several factors. The modest reactivity of furan requires an extremely reactive dienophile, and the reversible nature of this reaction often leads to an equilibrium mixture predominating in the furan starting material.[1] Attempts to solve these problems have involved the use of Lewis acids,[2a] doubly activated dienophiles,[2b] or high pressure conditions.[2c] Yet even in these cases, yields of products have not been consistantly high, most particularly in the case of 2,5-disubstituted furan dienes.

Recently, we have been involved in the preparation and utilization of highly substituted furan cycloadducts for natural product synthesis.[3] We required a dienophile whose reactivity would lead to practical amounts of cycloadduct and whose activating group could be easily removed (Scheme 1). Although sulfonyl activated dienophiles[4] would seem to satisfy these

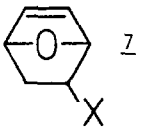
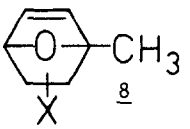
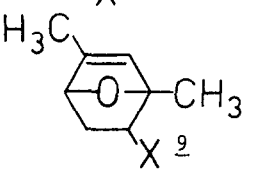
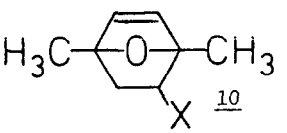
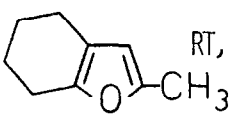
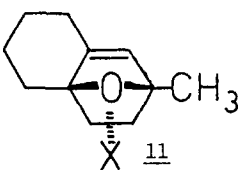
Scheme 1



criteria, no account of a successful cycloaddition of these derivatives with furan has appeared.[5] Therefore, we report here that phenyl vinyl sulfonate is, thus far, one of the most effective dienophiles for a mild and high yield preparation of various 7-oxabicyclo[2.2.1.]heptene systems.

Few reports concerning the use of vinyl sulfonate esters as dienophiles have appeared in the last twenty years in spite of preliminary indications of their high reactivity. Although both the alkyl and aryl sulfonates have been shown to be powerful dienophiles, phenyl vinyl sulfonate **1** was chosen for our studies due to its ease of preparation and greater stability.[6,7] This crystalline compound is prepared in 85% yield by reacting β-chloroethanesulfonyl chloride with phenol in the presence of sodium hydroxide.[8] It is stable for all routine manipulations and can be stored indefinitely at 0°C.

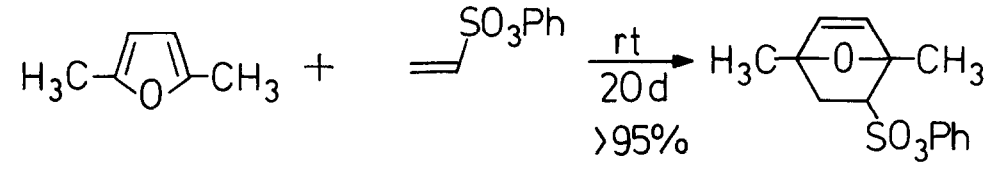
TABLE

Entry	Diene	Conditions	Product[a]	Yield[b]	Exo/Endo[c]
			X = SO_3PH		
1	Furan 2	RT, 20 days	 7	>95% (84%)	1/2.6
2	2	70°C, 4 days[d]	7	50% (48%)	5/1
3	2-Methylfuran 3	RT, 20 days	 8	>95% (35%)	2/5[e]
4	2,4-Dimethylfuran 4	RT, 20 days	 9	90% (88%)	1/2.6[f]
5	2,5-Dimethylfuran 5	RT, 20 days	 10	>95% (87%)	1/5.4
6	5	70°C, 4 days[d]	10	50% (48%)	1/2
7	 6	RT, 20 days	 11	>95% (90%)	Endo[g] only
8	6	70°C, 4 days[d]	11	>95% (88%)	1/1

[a]Satisfactory ^1H NMR, ^{13}C NMR, and IR data was obtained for all products. [b]Numbers in parentheses refer to isolated yields following chromatographic purification. [c]Measured by ^1H NMR or isolated weights. [d]Reactions were run in a sealed tube. [e]Regioisomers: Vicinal-endo:Vicinal-exo:Distal-endo:Distal-exo, 3:1:2:1. [f]Only vicinal regioisomers could be seen. [g]Regioisomers were not separated.

When this sulfonate was stirred neat with 2,5-dimethylfuran (1.1 eq.) at room temperature for twenty days, a near-quantitative yield of cycloadduct **10** was obtained (Scheme 2). Since the reaction was devoid of any sideproducts, the workup involved simply evaporating the excess

Scheme 2



furan. The cycloaddition of **1** with furan, 2-methylfuran, and 2,4-dimethylfuran gave similar excellent results (Table). In the case of the more highly substituted tetrahydrobenzofuran **6**,[9] the cycloadduct with **1** crystallized out of the reaction mixture, thus producing a quantitative yield after only five hours.

When the known phenyl vinyl sulfone[4c] was stirred at room temperature with 2,5-dimethylfuran, an equilibrium mixture containing not more than 50% of the desired cycloadduct was produced. Heating this sulfone or **1** with 2,5-dimethylfuran (excess) in a sealed tube also led to approximately equal amounts of starting dienophile and product. In all cases, the major isomer produced at 25°C had the endo stereochemistry while the exo isomer was the predominant product isolated from the heated reaction mixtures. For entries 3 and 4, regioisomers are distinguishable, and the major isomer has the phenoxysulfonyl group vicinal to the bridgehead methyl group. This selectivity has been seen in other cases.[2b]

The mild conditions, high yields, and potential of the sulfonate group for further functionalization, provide this method with many advantages. Methods for the removal of the sulfonate group and for further elaboration of these cycloadducts are presently under investigation.

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10. Data
11. 7-endo: ^{1}H NMR ($CDCl_3$): δ 1.68 (1H, dd, 12Hz, 4.4Hz), 2.34 (1H, ABX, 12Hz, 9.1Hz, 4.4Hz), 3.96 (1H, ABX, 4.4Hz, 4.4Hz, 9.1Hz), 5.13 (1H, d, 3.1Hz), 5.27 (1H, 3.1Hz), 6.43 (1H, dd, 5.8Hz, 1.5Hz), 6.58 (1H, dd, 5.8Hz, 1.76Hz), 7.23 - 7.46 (5H, complex); ^{13}C NMR ($CDCl^3$): δ 29.3, 57.7, 77.8, 78.9, 121.9, 127.3, 129.9, 131.6, 137.6, 149.9.

7-exo: ^{1}H NMR ($CDCl_3$): δ 1.78 (1H, dd, 8.1Hz, 12.1Hz), 2.34 (1H, dt, 4.7Hz, 4.7Hz, 12.1HZ), 3.30 (1H, dd, 8.1Hz, 4.2Hz), 5.21 (1H, d, 4.7Hz), 5.45 (1H, dd, 0.9Hz, 1.8Hz), 6.38 (1H, dd, 1.8Hz, 5.8Hz), 6.50 (1H, dd, 5.8Hz, 1.6Hz), 7.43 - 7.24 (5H, complex); ^{13}C NMR ($CDCl_3$): δ 28.6, 59.5, 78.1, 79.4, 122.0, 127.2, 129.9, 134.0, 138.5, 149.2.

8a-endo: ^{1}H NMR ($CDCl_3$): δ 1.80 (3H,s), 1.80 (1H, dd, 12Hz, 4.2Hz), 2.44 (1H, ABX, 12Hz, 9.1Hz, 4.8Hz), 3.58 (1H, dd, 4.2Hz, 9.1Hz), 4.97 (1H, dd, 4.6Hz, 1.7Hz), 6.28 (1H, d, 5.7Hz), 6.51 (1H, dd, 1.7Hz, 5.7Hz), 7.19 - 7.42 (5H, complex); ^{13}C NMR ($CDCl_3$): δ 18.1, 32.7 62.7, 77.8, 87.4, 121.9, 127.2, 129.9, 134.9, 137.7, 148.9.

8a-exo: ^{1}H NMR ($CDCl_3$): δ 1.92, (3H, s), 1.86 (1H, dd, 8.4Hz, 12.1Hz), 2.51 (1H, dt, 12.1Hz, 4.6Hz, 4.4Hz), 3.36 (1H, 8.4Hz, 4.4Hz), 5.35 (1H, 4.6Hz, 1.8Hz), 6.32 (1H, d, 5.8Hz), 6.40 (1H, dd, 5.8Hz, 1.8Hz), 7.24 - 7.39 (5H, complex); ^{13}C NMR ($CDCl_3$): δ 16.5, 32.1, 61.6, 77.3, 87.4, 121.9, 127.0, 129.8, 138.0, 138.8, 149.1.

8b-endo: ^{1}H NMR ($CDCl_3$): δ 1.63 (3H, s), 1.79 (1H, dd, 11.9Hz, 4.2Hz), 2.02 (1H, dd, 11.9Hz, 9Hz), 4.07 (1H, complex), 5.17 (1H, d, 3.6Hz), 6.39 (2H, s), 7.19 - 7.44 (5H, complex); ^{13}C NMR ($CDCl_3$): δ 18.3, 35.3, 60.2, 78.5, 87.9, 121.9, 127.3, 129.9, 132.2, 140.5, 148.9.

8b-exo: ^{1}H NMR ($CDCl_3$): δ 1.66 (3H, s), 1.80 (1H, dd, 12.1Hz, 8.2Hz), 2.03 (1H, 12.1Hz, 4.4Hz), 3.34 (1H, dd, 8.21Hz, 4.4Hz), 5.31 (1H, d, 1.7Hz), 6.27 (1H, d, 5.8Hz), 6.35 (1H, d, 5.7Hz, 1.3Hz), 7.19 - 7.38 (5H, complex); ^{13}C NMR ($CDCl_3$): δ 18.0, 34.3, 62.4, 79.4, 86.5, 122.1, 127.1, 129.9, 134.6, 141.6, 149.2.

9-endo: ^{1}H NMR ($CDCl_3$): δ 1.74 (3H, s), 1.77 (1H, dd, 4.4Hz, 12.0Hz), 1.84 (3H, d, 1.7Hz), 2.42 (1H, ABX, 4.6Hz, 4.4Hz, 12.0Hz), 3.62 (1H, dd, 4.4Hz, 9.0Hz), 4.7 (1H, d, 4.6Hz), 5.8 (1H, d, 1.7Hz), 7.19 - 7.42 (5H, complex); ^{13}C NMR ($CDCl_3$): δ 12.1, 18.0, 31.8, 64.6, 81.2, 87.9, 121.7, 126.8, 128.0, 129.6, 147.8, 148.7.

9-exo: ^{1}H NMR ($CDCl_3$): δ 1.76 (3H, dd, 1.6Hz), 1.82 (3H, s), 1.92 (1H, dd, 8.2Hz, 12.0Hz), 2.41 (1H, dt, 4.4Hz, 4.4Hz, 12.0Hz), 3.28 (1H, dd, 4.4Hz, 8.2Hz), 4.72 (1H, d, 4.4Hz), 5.62 (1H, d, 1.6Hz), 7.20 - 7.38 (5H, complex): ^{13}C NMR ($CDCl_3$): δ 12.1, 18.0, 31.8, 64.6, 81.2, 87.9, 121.7, 121.9, 126.8, 129.6, 147.8, 148.7.

10-endo: ^{1}H NMR ($CDCl_3$): δ 1.58 (3H, s), 1.77 (3H, s), 1.92 (1H, dd, 4.2Hz, 12.0Hz), 2.16 (1H, dd, 9Hz, 12.0Hz), 3.74 (1H, dd, 4.2Hz, 9Hz), 6.26 (1H, d, 5.6Hz), 6.33 (1H, d, 5.6Hz), 7.2 - 7.45 (5H, complex); ^{13}C NMR ($CDCl_3$): δ 18.3, 18.5, 38.6, 65.3, 86.4, 87.3, 121.9, 127.2, 129.2, 129.8, 135.4, 140.5, 149.5.

10-exo: ^{1}H NMR ($CDCl_3$): δ 1.64 (3H, s), 1.85 (3H, s), 2.02 (1H, dd, 8.1Hz, 12.2Hz), 2.19 (1H, dd, 4.8Hz, 12.2Hz), 3.33 (1H, dd, 4.8Hz, 8.1Hz), 6.12 (1H, d, 5.6Hz), 6.26 (1H, d, 5.6Hz), 7.19 - 7.40 (5H, complex); ^{13}C NMR ($CDCl_3$): δ 16.7, 18.3, 37.9, 64.6, 85.4, 87.3, 122.0, 127.0, 129.8, 138.7, 141.8, 149.3.

11: ^{1}H NMR ($CDCl_3$): δ 1.75 - 2.14 (12H, complex), 2.58 (1H, broad doublet, 16.4Hz), 3.78 (1H, dd, 5.2Hz, 7.8Hz), 5.80 (1H, d, 2.6Hz), 7.20 - 7.44 (5H, complex); ^{13}C NMR ($CDCl_3$): δ 18.4, 22.9, 24.5, 25.0, 31.0, 36.7, 67.5, 86.3, 86.8, 121.9, 126.0, 127.1, 129.9, 149.0, 149.7.

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