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DIASTEREOSELECTIVE DIELS-ALDER REACTIONS WITH CHIRAL SULFINYL DERIVATIVES AS DIENOPHILES UNDER HIGH PRESSURE

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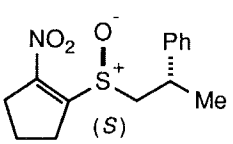
Abstract: Using the high pressure technique, asymmetric Diels-Alder reaction utilizing chiral 2-nitro-1-sulfinylolefins and dienes proceeded smoothly to give highly functionalized cyclohexene derivatives with satisfactory chemical yield and high diastereomeric excess.

Aliphatic conjugated nitroolefins bearing sulfonyl or sulfinyl groups are electron deficient compounds and potentially useful synthons in synthetic organic transformations. Their versatilities have been well documented by many groups.[1] Further advantage is the possibility of asymmetric induction, when the chiral tricoordinate sulfur atom transfers its chirality to the product. On the basis of this idea, we recently reported an enantioselective nitroolefination of lactams *via* an addition-elimination reaction.[2] The asymmetric Diels-Alder reaction utilizing optically active sulfinyl nitroalkenes and Danishefsky's diene was also of current interest.[3] This dienophile provided high enantioselectivity in certain cases, but was totally inert toward the ordinary dienes such as butadiene and cyclopentadiene under ambient conditions. However it is well known that the reactions having large negative activation volumes[4] ($\Delta V^{\ddagger}$) can be accelerated by employing the high-pressure technique[5] and therefore this technique is extremely effective for the [4+2]cycloaddition[6] involving relatively inert dienes,[7] although there are only a few reports on the Diels-Alder reactions carried out in an asymmetric manner.[8] As an extension of our investigations into asymmetric Diels-Alder cycloadditions, we wish to describe the high pressure [4+2]cycloaddition of chiral 2-nitro-1-sulfinylolefins with non-activated conventional dienes.



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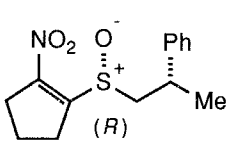

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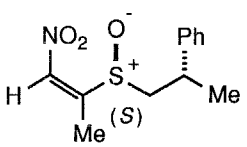

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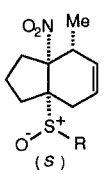
Table I. High Pressure Diels-Alder Cycloaddition[a] of Chiral 2-Nitro-1-sulfinylalkenes **1-3** with Dienes.

Entry	Dienophile	Diene	Adduct[b]	Yield (%)[c]
1	**1**	1,3-pentadiene	**4**	80
2[f]	**1**	1,3-pentadiene	--	0
3	**1**	2,3-dimethyl-1,3-butadiene	**5**	77
4[d]	**1**	cyclopentadiene	**6** **7**[e]	39 61
5[f]	**1**	cyclopentadiene	**6** **7**	14 32
6	**2**	2,3-dimethyl-1,3-butadiene	**8**	68
7	**2**	cyclopentadiene	**9** **10**	41 59
8[f]	**2**	cyclopentadiene	**9** **10**	19 32
9	**3**	1,3-pentadiene	**11**	81
10	**3**	2,3-dimethyl-1,3-butadiene	**12**	71
11	**3**	isoprene	**13,14** (5:1)[g]	64

a) The reaction conditions were not optimized.
b)



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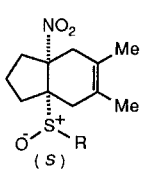

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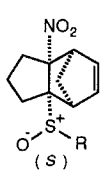

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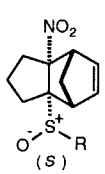

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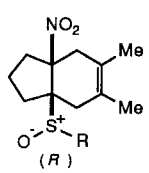

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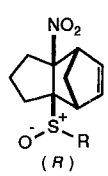

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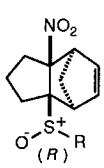

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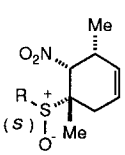

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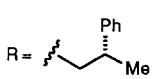
12; $R^1 = R^2 = Me$

13; $R^1 = H$, $R^2 = Me$

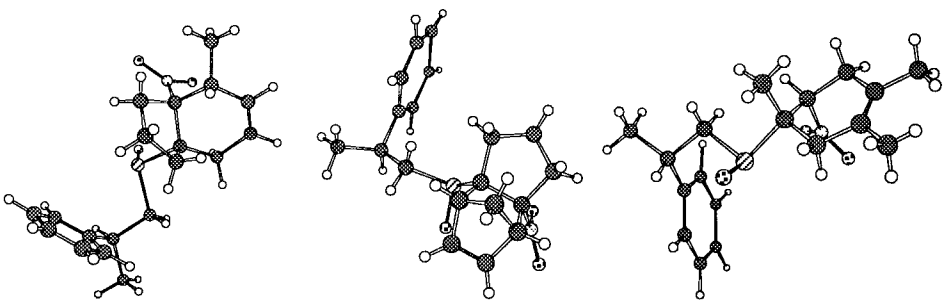
14; $R^1 = Me$, $R^2 = H$



c) Isolated yield. d) THF was used as a solvent. e) 92% de by ^1H NMR analysis.
f) Cycloaddition was carried out under 1 atm for 11 days at room temperature.
g) The ratio was determined by ^1H NMR.

Using three kinds of optically active 2-nitro-1-sulfinylolefins **1-3**,[2,3] the cycloadditions were carried out in methylene chloride for 5 days in the high-pressure reactor[9] under 8 kbar pressure at room temperature. Results are summarized in Table I.[10] In sharp contrast to the Diels-Alder reaction conducted at the elevated temperature, where elimination or aromatization often occurs owing to the good leaving ability of the sulfinyl group,[1a-c] the cycloaddition proceeded smoothly in a satisfactory yield without any side reactions (entries 1, 3, 6, 9, 10 and 11). When 1,3-pentadiene was employed for the cycloaddition, complete endo selectivity was observed (entries 1 and 9), whereas poor selectivity was observed with cyclopentadiene (entries 4 and 7). A similar preferred tendency in the regioselectivity was revealed with 1,3-pentadiene (entries 1 and 9) compared with isoprene (entry 11). The absolute stereochemistries of **4**, **7** and **12** were unambiguously determined by X-ray analysis and their perspective views are shown in Figure 1, in which the absolute configuration of the carbon α to nitro group in the adducts is *R*.

Figure 1. Perspective Views of Cycloadducts **4**, **7** and **12**.



4 **7** **12**

These diastereoselectivities could be well explained on the base of the s-trans conformation of the dienophiles in the same way as reported previously.[3] The attack of the diene occurs preferentially from the less hindered side with the lone pair electrons on the sulfur atom.

The present study reveals the effectiveness of the high-pressure technique for the asymmetric Diels-Alder cycloaddition, in which the reaction smoothly proceeds at room temperature in highly diastereoselective fashion with no subsequent eliminative side reactions. Since the cycloadducts formed are highly functionalized optically active cyclohexenes, they are very useful for the synthesis of biologically interesting compounds.

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9) In a typical experiment, a solution of **1** (42 mg, 0.15 mmol), 1,3-pentadiene (0.5 ml, 5.0 mmol) and hydroquinone (1.0 mg, 0.01 mmol) in methylene chloride (1.0 ml) in a Teflon capsule was allowed to stand at a pressure of 8 kbar at room temperature for 5 days. Concentration of the mixture gave a residue, which was subjected to column chromatography on silica gel with hexane-ethyl acetate (1:1) to afford **4** (42 mg) in 80% yield.
10) All new compounds were fully characterized spectroscopically and by combustion and /or high-resolution mass spectral analyses.