α,β-Unsaturated Oxazolines, a Powerful Tool in Asymmetric Diels-Alder Cycloadditions

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Abstract: α,β-Unsaturated oxazolines **10**, **12**, and **16**, activated with trifluoroacetic anhydride, proved to be very powerful dienophiles toward various dienes such as **17**–**23** including Danishefsky type diene. The reactions were performed generally between −100 and −20 °C and the diastereoselectivity is usually better than 90%.

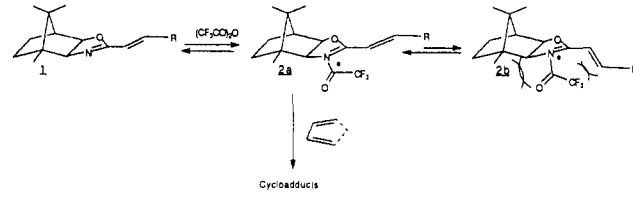
Recently, considerable progress has been achieved in asymmetric Diels-Alder cycloadditions.[1] High stereochemical control has been secured by the use of chiral dienophiles,[2] chiral dienes,[3] or chiral catalysts.[4] However, this good selectivity, which in the case of chiral dienophiles is generally[5] due to the use of Lewis acids as catalysts increasing both reactivity and chelation-controlled stereoselectivity, is often limited to nonfunctionalized dienes such as cyclopentadiene, butadiene, or isoprene. The relatively low reactivity of such chiral dienophiles is obviously a limitation for their synthetic use in cycloaddition reactions.

Increased reactivity has been observed in the case of cationic Diels-Alder reactions[6] in which an allylic cation adds to 1,3-dienes at low temperature. Related cycloadditions using acetylenic alkoxy imminium salts had been reported in 1976 by Baum and Viehe[7] and in two recent publications Jung[8a] and Ghosez[8b] described the use of optically active vinyl (trimethylsilyl)oxy imminium salts in several asymmetric Diels-Alder cycloadditions.

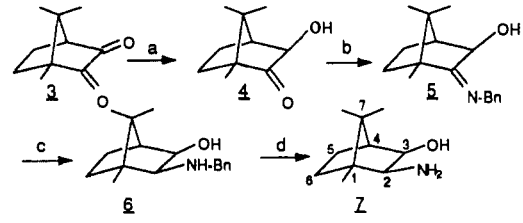
A few years ago we anticipated that α,β-unsaturated oxazolines,[9] which can be easily prepared as achiral and chiral dienophiles, could afford, after activation by N-acylation, very reactive intermediates in [2 + 4] cycloadditions.[10] We report in the present paper a full account of our studies directed toward the development of these chiral dienophiles in the Diels-Alder process.

In general, optically active oxazolines were prepared from chiral β-amino alcohols resulting from the reduction of the corresponding amino acids. In the Meyers' methodology[11] in which the chiral oxazolines act as nucleophiles, the stereochemical control was secured by chelation of the lithium cation with a side chain in the azaenolate intermediate. Inasmuch as we wished to develop a process in which the oxazolines were considered as electrophilic reagents, the stereochemical control could not be obtained by a chelated intermediate, but rather by the geometry of the oxazoline itself. Hence we anticipated that camphor-derived oxazoline[12] of general formula **1** should secure the stereochemical control during the [2 + 4] cycloaddition process (Scheme I). Thus such derivatives after treatment with an acyl halide or an anhydride should give rise to a very reactive acyl imminium salt intermediate of general formula **2** in which the s-trans conformation **2a** is clearly the more stable conformation on the basis of an examination of molecule models.

Scheme I

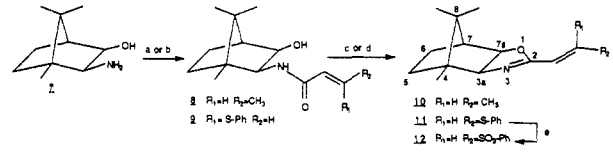


Scheme II[a]



[a] Reagents: (a) L-Selectride, THF, −78 °C, 5 min; (b) $BnNH_2$ (2 equiv), THF, 4-Å molecular sieves, 20 °C, 48 h; (c) $NaBH_4$, MeOH, 20 °C; (d) H_2, Pd–C, MeOH, 24 h.

Scheme III[a]



[a] Reagents: (a) CH_3CH=CHCOCl (*E*) (1.1 equiv), Na_2CO_3 (1.2 equiv), CH_2Cl_2, H_2O, 20 °C, 45 min; (b) PhSCH=CHCOCl (*Z*) (1.1 equiv), Na_2CO_3 (2 equiv), CH_2Cl_2, H_2O, 20 °C, 2 h; (c) **8**, $POCl_3$ (4 equiv), $PhCH_3$, 100 °C, 10 min; (d) **9**, $POCl_3$ (8 equiv), $PhCH_3$, 100 °C, 1 h; (e) *m*CPBA (2.2 equiv), CH_2Cl_2, 20 °C, 5 h.

(1) For recent reviews on the asymmetric Diels–Alder reaction, see: (a) Paquette, L. A. *Asymmetric Synthesis*; Morrison, J. D. Ed.; Academic Press: New York, 1984; Vol. 3, Chapter 7, p 455. (b) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876. (c) Helmchen, G.; Kargue, P.; Weetman, J. *Modern Synthetic Methods*; Sheffold, R. Ed.; Springer Verlag: Berlin, Heidelberg, 1986; Vol. 4, p 26.

(2) See inter alia: (a) Oppolzer, W.; Dupuis, D.; Poli, G.; Raynham, T. M.; Bernardielli, S. *Tetrahedron Lett.* **1988**, *29*, 5885. (b) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238. (c) Helmchen, G.; Ihrig, K.; Schindler, H. *Tetrahedron Lett.* **1987**, *28*, 183.

(3) (a) Mehmandoust, M.; Marazano, C.; Singh, R.; Gillet, B.; Cesario, M.; Fourrey, J.-L.; Das, B. C. *Tetrahedron Lett.* **1988**, *29*, 4423. (b) Tripathy, R.; Franck, R. W.; Onan, K. D. *J. Am. Chem. Soc.* **1988**, *110*, 3257. (c) Lubineau, A.; Queneau, J. *J. Org. Chem.* **1987**, *52*, 1001 and references therein.

(4) For asymmetric catalyst in the Diels–Alder cycloaddition see: Furuta, K.; Miwa, Y.; Iwanaga, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 6254 and references therein.

(5) For uncatalyzed asymmetric Diels–Alder reaction see: (a) Mulzer, J.; Kappert, M.; Huttner, G.; Jibril, I. *Tetrahedron Lett.* **1985**, *26*, 1631. (b) Feringa, B. L.; de Jong, J. C. *J. Org. Chem.* **1988**, *53*, 1125.

(6) (a) Gassman, P. G.; Chavan, S. P. *J. Org. Chem.* **1988**, *53*, 2392. (b) Roush, W. R.; Gillis, H. R.; Essenfeld, A. P. *J. Org. Chem.* **1984**, *49*, 4674. (c) Harirchian, B.; Bauld, N. L. *Tetrahedron Lett.* **1987**, *28*, 927.

(7) Baum, J. S.; Viehe, H. G. *J. Org. Chem.* **1976**, *41*, 183.

(8) (a) Jung, M. E.; Vaccaro, W. D.; Buszek, K. R. *Tetrahedron Lett.* **1989**, *30*, 1893. (b) Lamy-Schelkens, H.; Ghosez, L. *Tetrahedron Lett.* **1989**, *30*, 5891.

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(10) (a) Pouilhès, A.; Kouklovsky, C.; Langlois, N.; Langlois, Y. *Tetrahedron Lett.* **1987**, *28*, 6183. (b) Pouilhès, A.; Uriarte, E.; Kouklovsky, C.; Langlois, N.; Langlois, Y.; Chiaroni, A.; Riche, C. *Tetrahedron Lett.* **1989**, *30*, 1395.

(11) For a recent paper concerning the Meyers' methodology, see: Meyers, A. I.; Roth, G. P.; Hoyer, D.; Barner, B. A.; Laucher, D. *J. Am. Chem. Soc.* **1988**, *110*, 4611.

(12) For the use of camphor derivatives in asymmetric synthesis, see: Oppolzer, W. *Tetrahedron* **1987**, *43*, 1969.

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Table I. Diels–Alder Reaction with Substituted α,β-Unsaturated Oxazolines **10** and **12** and Various Acylating Reagents

entry	oxazoline	diene (equiv)	reagent (equiv)	adduct	react temp [°C] (time, h)	yield % (endo %)	ds[a]
1	**10**	**17** (20)	$(CF_3CO)_2O$ (1.5)	**24**	−78 (4)	76 (100)	94
2	**10**	**17**	$(CH_3CO)_2O$ (1)	**24**	−78 (1) then 20 (24)	20 (100)	>90
3	**10**	**17**	$ClCO_2CH_3$ (1)	**24**	−78 (2) then 20 (24)	45 (100)	>90
4	**10**	**18**	$(CF_3CO)_2O$ (3.5)	**25**	0 (6)	47 (100)	>90
5	**10**	**19** (40)	$(CF_3CO)_2O$ (4)	**26**	18 (24)	50	92
6	**12**	**17** (5)	$(CF_3CO)_2O$ (2)	**27a** + **27b**	−100 (4)	76 (50)	>90

[a] Degree of selectivity.

The preferred s-trans conformation **2a** in this intermediate could be due to several steric factors: the occurrence of a steric hindrance between the methyl group on carbon 4 and the acyl group on nitrogen could induce a further steric hindrance between this acyl group and the ethylenic side chain in s-cis conformer **2b** shifting the equilibrium toward the s-trans conformer **2a**.

Thus a good diastereofacial differentiation in this model could be the result of two factors: a highly favored perpendicular attack of the dienes by the α-face of the dienophile and a good control of the equilibrium between conformers **2a** and **2b** in favor of the former. These two facts should ensure a high degree of selectivity during the Diels–Alder reaction.

Preparation of Amino Alcohol 7

The cornerstone amino alcohol **7** was prepared in four steps from camphorquinone (**3**)[13] in 55% overall yield. Regio- and stereoselective reduction of camphorquinone (**3**) with L-Selectride afforded the known cetol **4**[14] (79%). Condensation of the latter with benzylamine in the presence of 4-Å molecular sieves gave rise to the imine **5** (70%) which after reduction with sodium borohydride afforded the benzylamine **6** (100%). Hydrogenolysis of **6** led to the target amino alcohol **7**[15] (100%) (Scheme II).

Preparation of the α,β-Unsaturated Oxazolines 10, 12, and 16

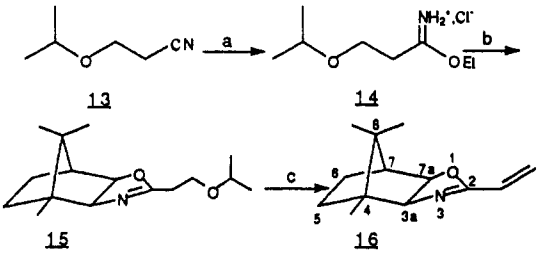
The substituted α,β-unsaturated oxazolines **10** and **11** were prepared in a two-step sequence. N-Acylation of amino alcohol **7** under Schotten–Baumann conditions either with (*E*)-2-butenoyl chloride or with (*Z*)-3-(phenylthio)-2-propenoyl chloride afforded quantitatively the corresponding amides **8** and **9**. Cyclizations into oxazolines **10** and **11** were performed in the presence of phosphorus oxychloride in 76% and 73% yield, respectively (Scheme III). A concomitant isomerization of the *Z* double bond of amide **9** occurred during this cyclization step. Final oxidation of oxazoline **11** afforded the corresponding oxazoline sulfone **12** (Scheme III).

It appeared rapidly that this sequence was completely inefficient for the preparation of vinylic oxazolines. After numerous attempts, we decided to generate the vinylic unit after formation of the oxazoline ring. Thus 3-(isopropyloxy)propionitrile (**13**) treated with anhydrous ethanolic hydrochloric acid afforded the corresponding imino ether salt **14** (99%). This salt smoothly condensed with the amino alcohol **7**, giving rise to the oxazoline **15** (97%). The target vinylic oxazoline **16** was in turn cleanly generated by a β-elimination, promoted with potassium *tert*-butoxide in the presence of a catalytic amount of 18-crown-6 ether (yield of 86%)[16] (Scheme IV).

Preparation of the Dienes 21 and 22

4-*tert*-Butoxy-3-butene-2-one was prepared according to Danishefsky[17] in 93% yield. Deprotonation of this ketone with lithium diisopropylamide followed by a slow addition of diphenylphosphoryl chloride afforded the diene **21** in 70% yield. 2-Cyclopentenone was deprotonated in THF–HMPA at −78 °C and treated for 15 min at this temperature with diphenylphosphoryl chloride. After usual treatment the diene **22a** was isolated in 57% yield along with 14% of its regioisomer **22b** (Scheme V). 1-Phenylthiobutadiene (**18**)[18] and *N*-carbomethoxy-1,2-dihydropyridine **23**[19] were prepared according to the literature procedures.

Scheme IV[a]



[a] Reagents: (a) HCl gas, EtOH; (b) **7**, Et_3N, CH_2Cl_2, 25 °C; (c) *t*BuOK (1.3 equiv), 18-crown-6 ether (0.05 equiv), THF, 0 °C, 15 min.

Scheme V

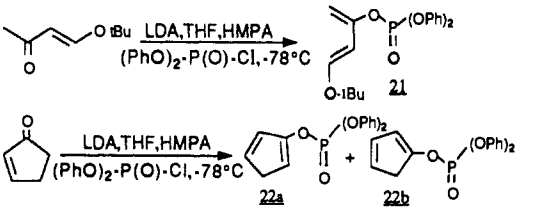


Table II. Diels–Alder Reaction with Vinylic Oxazoline **16** and Trifluoroacetic Anhydride (3 equiv)

entry	diene (equiv)	adduct	react temp [°C] (time, min)	yield % (endo %)	ds[a]
1	**17** (20)	**28**	−78 (4)	70 (100)	>99
2	**18** (4)	**29**	−20 (20)	47 (95)	95
3	**19** (10)	**30**	−15 (25)	66	68
4	**20** (10)	**31**	−15 (30)	82 (100)	>99
5	**21** (4)	**32**	−40 (20)	63 (99)	99
6	**22a** (4)	**33**	−78 (120)	66 (99)	92
7	**23** (4)	**34**	−78 (60)	60 (99)	88

[a] Degree of selectivity.

Cycloadditions of α,β-Unsaturated Oxazolines 10, 12, and 16

In a typical procedure, oxazolines **10**, **12**, or **16** in anhydrous dichloromethane solution in the presence of 4–20 equiv of diene and 4–5 equiv of anhydrous calcium carbonate were treated under

(13) Rupe, H.; di Vignano, A. T. *Helv. Chim. Acta* **1937**, *20*, 1078.
(14) Pfrunder, B.; Tamm, C. *Helv. Chim. Acta* **1969**, *52*, 1630.
(15) Daniel, A.; Pavia, A. A. *Bull. Soc. Chim. Fr.* **1971**, 1060.
(16) For an alternative preparation of achiral α,β-unsaturated oxazolines, see: Clinet, J. C.; Balavoine, G. *Tetrahedron Lett.* **1987**, *28*, 5509.
(17) Danishefsky, S.; Bednarski, M.; Izawa, T.; Maring, C. *J. Org. Chem.* **1984**, *49*, 2290.
(18) Evans, D. A.; Bryan, C. A.; Sims, C. L. *J. Am. Chem. Soc.* **1972**, *94*, 2891.
(19) Fowler, F. W. *J. Org. Chem.* **1972**, *37*, 1321.

Table III. Diels–Alder Reactions with Isomeric Oxazolines **40** and **42**

entry	oxazoline	diene (equiv)	$(CF_3CO)_2O$ (equiv)	adduct	react temp [°C] (time, min)	yield % (endo %)	ds[a]
1	**40**	**17** (10)	(1.3)	**35**	−78 (15)	70 (100)	54
2	**40**	**22a**	(1.2)	**36**	−78 (90)	72 (100)	68
3	**42**	**17** (20)	(1.3)	**37**	−78 (90)	61 (100)	28

[a] Degree of selectivity.

Chart I

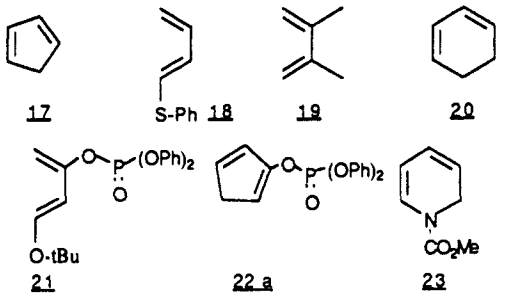
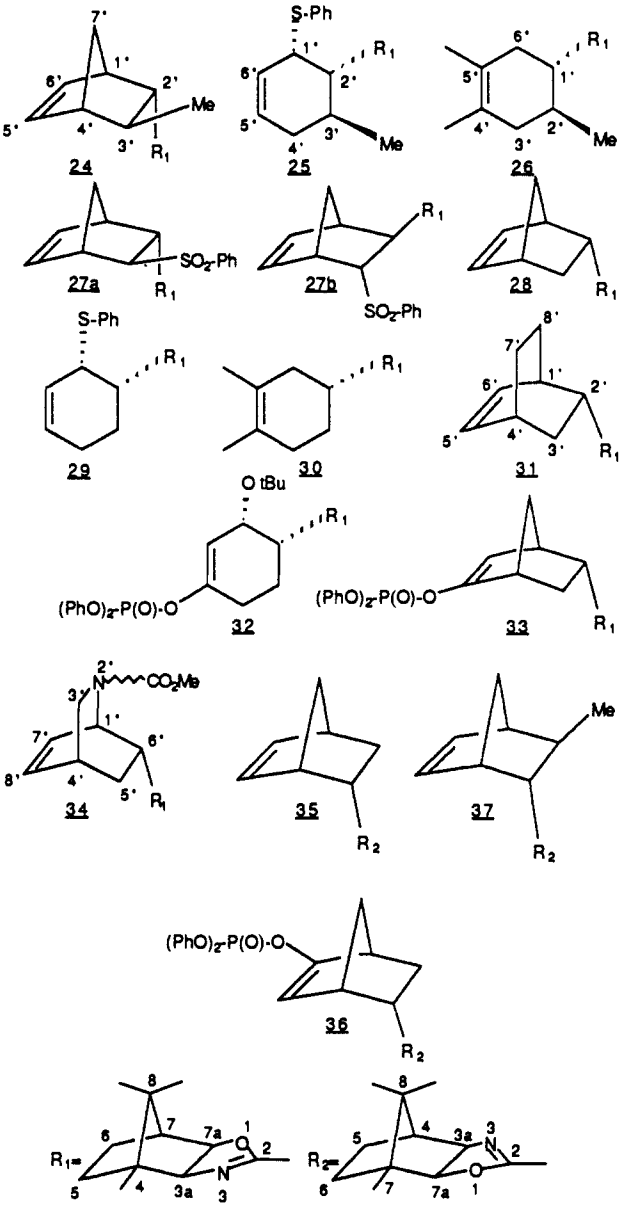


Chart II



an argon atmosphere at the indicated temperature with 3 equiv of freshly distillated trifluoroacetic anhydride. The reactions were monitored by thin-layer chromatography.

The results of these reactions are summarized in Tables I and II. As expected, the cycloadditions of substituted oxazolines **10** and **12** (Table I) occurred at low temperatures with the reactive cyclopentadiene with high degree of stereoselectivity (entries 1 and 6). Trifluoroacetic anhydride appeared to be the reagent of choice for activation of oxazolines. Acetic anhydride and methyl chloroformate were less efficient (entries 2 and 3). Surprisingly, trifluoromethanesulfonic anhydride, even freshly distilled, promoted the polymerization of cyclopentadiene. With less reactive dienes like 1-(phenylthio)butadiene (**18**) and 2,3-dimethylbutadiene (**19**) (entries 4 and 5), cycloadditions required higher temperatures and longer times. The absolute configuration of the adduct **24** was determined by performing an X-ray analysis of a single crystal at the corresponding hydrobromide.[10b]

As expected, vinylic oxazoline **16** proved to be more reactive than its substituted counterpart **10** and **12** and in this case the rate of the cycloadditions was greatly accelerated (Table II). More interestingly, this oxazoline was an efficient dienophile not only with classical dienes such as cyclopentadiene (**17**) (entry 1), dimethylbutadiene (**19**) (entry 3), and cyclohexadiene (**20**) (entry 4) but also with functionalized dienes like 1-(phenylthio)butadiene **18** (entry 2) and the Danishefsky type diene **21** (entry 5) (Chart I).

As far as we know, this is the first example of an asymmetric cycloaddition forming carbon–carbon bonds between a chiral acrylic unit and this type of diene.[20] In this cycloaddition, the classical 3-[(trimethylsilyl)oxy]-1-*tert*-butoxy-1,3-butadiene was not stable in the presence of trifluoroacetic anhydride. The corresponding enol phosphate **21** was the diene of choice in this reaction.[21]

In order to apply this asymmetric Diels–Alder reaction to the synthesis of natural products, two other dienes were tested. Thus the enol phosphate **22a** afforded in the presence of vinylic oxazoline **16** the cycloadduct **33**, a possible precursor in the synthesis of bicyclo[2.2.1]heptane-2,7-dione, an intermediate in the synthesis of milbemycin[22] (entry 6).

Oxazoline **16** was an equally powerful dienophile with 1-carbomethoxy-1,2-dihydropyridine **23**, affording the isoquinuclidine derivative **34**, a model in the enantioselective synthesis of ibogane alkaloids[3a,23] (entry 7).

It is worthy of note that except with 2,3-dimethylbutadiene the diastereoselectivity was generally better than 90%.

All product diastereomer analyses were carried out by capillary gas chromatography coupled with mass spectrometry analysis or by HPLC. The four diastereomers corresponding to the adduct **24** were prepared as comparison samples by cycloaddition of cyclopentadiene (**17**) with acrylic acid and subsequent separation of the endo–exo diastereomers.[2b] The resulting acids were sequentially treated with oxalyl chloride; amino alcohol **7** in the presence of sodium carbonate and phosphorus oxychloride. On

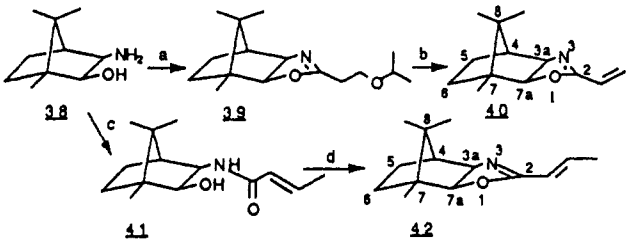
(20) For the use of *O*-hetero asymmetric Diels–Alder reaction with Danishefsky dienes, see: Danishefsky, S. J.; Armistead, D. M.; Wincott, F. E.; Selnick, H. G.; Hungate, R. *J. Am. Chem. Soc.* **1989**, *111*, 2967 and references therein.

(21) During the completion of this work, an independent study concerning the cycloaddition of phosphate dienes appeared in the literature: Calogeropoulou, T.; Wiemer, D. F. *J. Org. Chem.* **1988**, *53*, 2295.

(22) Bac, N. V.; Langlois, Y. *Tetrahedron Lett.* **1988**, *23*, 2819.

(23) For recent synthesis of ibogane alkaloid catharanthine using a Diels–Alder reaction, see: Raucher, S.; Bray, B. L.; Lawrence, R. F. *J. Am. Chem. Soc.* **1987**, *109*, 442.

Scheme VI[a]



[a] Reagents: (a) **14**, Et_3N, CH_2Cl_2, 25 °C; (b) *t*BuOK (1.3 equiv), 18-crown-6 ether (0.05 equiv), THF, 0 °C, 15 min; (c) $CH_3CH{=}CHCOCl$ (1.1 equiv), Na_2CO_3 (5 equiv), CH_2Cl_2, H_2O, 20 °C, 45 min; (d) $POCl_3$, $PhCH_3$, 100 °C, 10 min.

the other hand, the adducts **24**, **28**, **31**, and **37** (Chart II) were transformed into the corresponding acids of known absolute configurations, unequivocally establishing the stereochemistry of cycloadducts (vide infra).

In order to test the influence of the methyl group on carbon 4 in the oxazolines **10** and **16**, the isomeric amino alcohol **38** was prepared according to a known procedure.[24] This compound, after the same sequence of reactions as above, afforded the two isomeric oxazolines **40** and **42** (Scheme VI). These two oxazolines were more reactive but less selective in the Diels–Alder cycloaddition with cyclopentadiene (**17**) and with dienic enol phosphate **22a** (Table III). This observation fully confirmed our initial hypothesis concerning the influence of a methyl group on carbon 4 in the control of the s-cis–s-trans equilibrium in the trifluoroacyl iminium salt intermediate **2** (Scheme I).

Hydrolysis of Oxazoline Adducts

Generally the oxazoline group was hydrolyzed in strong acidic medium and afforded the corresponding carboxylic acid and an amino alcohol.[9] This method proved to be completely inefficient with the adduct **24**. On the other hand, the sequence of reactions described by Weinreb,[25] in the case of adduct **31**, afforded probably a compound resulting from the electrophilic attack of chlorine on the double bond followed by a nucleophilic addition of the oxazoline group.[26]

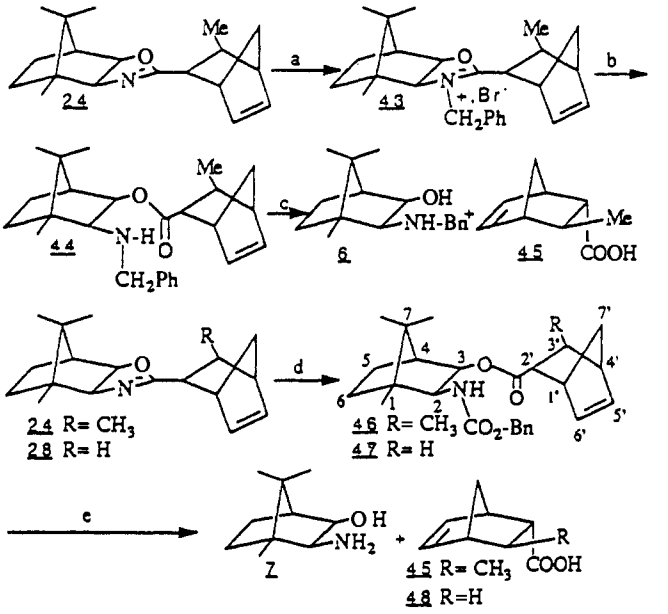
Following those preliminary studies two methods were successively tested. In the first one, the adduct **24** after N-alkylation with benzyl bromide afforded the oxazolinium salt **43**. Addition of sodium hydroxide on this salt gave rise to the amino ester **44** which afforded after further hydrolysis the *N*-benzyl amino alcohol **6** and the carboxylic acid **45** (Scheme VII). However, this method was not fully satisfactory and we suspected that a small amount of isomerization could occur during the alkaline treatment.

As an alternative shorter method, the adduct oxazolines **24** and **28** were treated with benzyl chloroformate in the presence of aqueous sodium carbonate (Schotten–Baumann conditions), affording the carbamates **46** and **47** (respectively, 93% and 82% yield) which in turn were smoothly hydrolyzed to afford the starting amino alcohol **7** (90%) and the carboxylic acid **45** and **48** (respectively, 96% and 89% yield) (Scheme VII). This method was applied successfully to adducts **30**, **31**, and **37**.

The rotatory power of compound **48** is in good accord with the value previously measured.[27a] However, the rotatory power of compound **45** showed a deviation with the literature value[27b] (respectively, +131° versus −151° for the enantiomer).

Thus the enantiomeric purity of this compound has been measured after complexation with tris(tetraphenylimidodiphosphinato)praseodymium in the presence of diisopropylamine by 500-MHz ^1H NMR spectrometry.[28] Within the detection limit

Scheme VII[a]



[a] Reagents: (a) BnBr (1 equiv), 40 °C, 20 h, (b) NaOH (1 N in H_2O, 12 equiv), THF, 60 °C, 5 h; (c) NaOH (1.5 N in H_2O, 40 equiv), CH_3OH, 80 °C, 48 h, (d) $ClCO_2Bn$ (1.1 equiv), CO_3Na_2 (2 equiv), CH_3OH–H_2O (50/50), 20 °C; 6 h, (e) NaOH (2.5 N in H_2O, 12.5 equiv), CH_3OH, 80 °C, 14 h.

of this very recent method, the acid **45** was found to be enantiomerically pure.

In conclusion, we have demonstrated that enantiomerically pure α,β-unsaturated oxazolines easily prepared from (+)-camphor, activated with trifluoroacetic anhydride, are very reactive dienophiles especially useful with functionalized dienes. The diastereoselectivity of these cycloadditions is generally up to 90%. A mild and high yield hydrolysis of the oxazoline adducts allowed the recovery of the starting amino alcohol and of the corresponding carboxylic acid without epimerization. The study of the further scope of these cycloadditions, as well as, their application to natural product synthesis are in development in our laboratory.

Experimental Section

IR spectra (ν (cm^{-1}), $CHCl_3$) were recorded on a Perkin-Elmer 257 spectrophotometer and $[\alpha]_D$ were measured on a Perkin-Elmer 241 in chloroform and the concentrations were given in g/100 mL. ^1H NMR spectra were obtained if not specified on Brucker WM 200 and AC 200 spectrometers (δ = 0 (TMS), $CDCl_3$. Coupling constants, *J*, were given in hertz; s, d, t, dd and m, respectively indicated singlet, doublet, triplet, doublet of doublets, and multiplet. Mass spectra and high-resolution mass spectra were, respectively, measured on a AEI MS 50 spectrometer and on a Kratos MS 80F. GC-MS spectra and chromatograms were recorded on a INCOS 50 mass spectrometer coupled with a Varian 3400 chromatograph (capillary column DB5 (25 M)) and a Finnigan Mat computer. HPLC separations were performed on a Waters chromatograph coupled with a Merck 2500 integrator. Preparative thin-layer chromatographies (preparative TLC) were performed with Kieselgel HF 254 (Merck) and flash column chromatography on Kielselgel 60 (230–400 mesh, Merck).

Usual workup means that the reaction medium was extracted with dichloromethane, washed successively with water and with brine, dried over magnesium sulfate, filtrated, and evaporated under vacuum.

Tetrahydrofuran (THF), toluene, and ether were distilled from sodium metal–benzophenone ketyl. Dichloromethane was distilled from calcium hydride. Trifluoroacetic anhydride was distilled under argon from phosphorus pentoxide just before use.

Preparation of Ketol 4. To a solution of camphorquinone (**3**)[13] (674 mg, 4.1 mmol.) in anhydrous THF (11 mL) was added dropwise a solution of L-Selectride in THF (1 M; 4.5 mmol, 4.5 mL) at −78 °C under argon. The reaction medium was stirred for 5 min at −78 °C and hydrolyzed at the same temperature with a solution of hydrochloric acid in anhydrous methanol (2.8 M; 1.8 mL). After extraction with di-

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chloromethane, the organic solution was washed with an saturated aqueous solution of sodium chloride, dried over magnesium sulfate, filtered, and evaporated under vacuum. The resulting yellow oily product was purified by column chromatography on silica gel (eluant, hexane–ethyl acetate 70:30) and afforded ketol **4**[14] (540 mg, 79%), $[\alpha]_D = +104°$ ($c = 2.02$).

Preparation of Imine 5. To a solution of cetol **4** (259 mg, 1.54 mmol.) in anhydrous THF (5 mL) was added successively benzylamine (0.34 mL, 3.08 mmol) and 4-Å molecular sieves (300 mg). The reaction medium was slowly stirred under argon at 20 °C for 2 days. After filtration through Celite, the resulting solution was extracted with ether and washed with aqueous hydrochloric acid (10%). The acidic aqueous solution was basified with aqueous ammonia and extracted with dichloromethane. After column chromatography (SiO_2, dichloromethane–methanol 95:5) imine **5** was isolated (276 mg, 70%): IR, 3200, 2950, 1680; ^1H NMR 7.23 (m, 5 H, aromatic), 4.77 (2 d, 2 H, $J = 13$, $CH_2C_6H_5$), 4.17 (br s, C_3-H), 3.29 (s, 1 H, OH), 1.82 (1 H, d, $J = 5$, C_4-H), 1.03 (s, 3 H), 1.01 (s, 3 H), 0.90 (s, 3 H); MS m/z 257 ($M^{\cdot+}$), 256, 255, 195, 168, 160 (100), 125, 118, 109, 92; $[\alpha]_D = -46°$ ($c = 1.11$ in $CHCl_3$). Anal. Calcd for $C_{17}H_{23}NO$: C, 79.38; H, 8.95; N, 5.45. Found: 79.60; H, 8.70; N, 5.60.

Preparation of Amino Alcohol 6. An excess of sodium borohydride was added in small portions to a solution of imine **5** (839 mg, 3.26 mmol) in methanol (10 mL) at room temperature. The progress of the reaction was monitored by TLC (dichloromethane–methanol–ammonia 98:2:0.5). The reaction mixture was stirred for 1 h at room temperature, poured into brine solution, and extracted with dichloromethane. After usual treatment amino alcohol **6** was obtained quantitatively (840 mg): IR 3350, 2950; ^1H NMR (80 MHz) 7.25 (br s, 5 H), 3.76 (s, 2 H), 3.58 (d, 1 H, $J = 8$), 3.08 (s, 2 H), 2.66 (d, 1 H, $J = 8$), 1.05 (s, 3 H), 0.86 (s, 3 H), 0.74 (s, 3 H); MS m/z 259 $M^{\cdot+}$, 100), 230, 202, 188, 168, 120, 95, 91; $[\alpha]_D = -52$ ($c = 1.11$). Anal. Calcd for $C_{17}H_{25}NO$: C, 78.76; H, 9.65; N, 5.40. Found: C, 78.73; H, 9.89; N, 5.39.

Preparation of Amino Alcohol 7. A solution of amino alcohol **6** (850 mg, 3.28 mmol) in methanol (10 mL) was stirred under hydrogen in the presence of Pd–C 10% (200 mg) for 48 h. The solution, after filtration on a column of Celite and evaporation, afforded quantitatively amino alcohol **7**:[15] IR 3420, 3400, 3100, 2920, 2880; ^1H NMR (80 MHz) 3.70 (d, 1 H, $J = 7.4$, C_3-H), 2.91 (d, 1 H, $J = 7.4$, C_2-H), 2.46 (br s, 3 H, O*H*, NH_2), 1.11 (s, 3 H), 0.94 (s, 3 H), 0.80 (s, 3 H) ^{13}C NMR (50 MHz) 75.1 (C_3), 62.6 (C_2), 51.1 (C_4), 47.9 and 46.7 (C_1 and C_7), 35.8 (C_5), 23.9 (C_6), 21.8, 20.9, and 11.9 (3 CH_3); MS m/z 169 ($M^{\cdot+}$), 98, 95, 70, 59 (100); $[\alpha]_D = -44$ ($c = 1.62$).

Preparation of Amide 8. To a solution of amino alcohol **7** (1.014 g, 6 mmol) in dichloromethane (20 mL) was added successively a solution of sodium carbonate (760 mg, 7.2 mmol) in water (12 mL) and dropwise butenoyl chloride (630 μL, 6.6 mmol) at room temperature. The mixture was stirred for 45 min. The organic solution was separated, and the aqueous phase was extracted with dichloromethane. Washing of the combined organic solutions with aqueous sodium carbonate (10%) and saturated brine and concentration of the dried ($MgSO_4$) solution under vacuum gave an oil (1.42 g, 100%) which was crystallized in ether: mp 108–11 °C; IR 3350, 2950, 1660, 1620, 1050; ^1H NMR 6.91 (qd, 1 H, $J_{H_B-CH_3} = 7.5$, $J_{HA-HB} = 15$, CH_A–CH_3), 5.98 (1 H, N-*H*), 5.93 (dd, 1 H, $J_{HB-CH_3} = 1.5$, $J_{HB-HA} = 15$, -CH_B=CH_A-), 4.09 (1 H, d, $J = 8$, C_3-H), 4.02 (1 H, d, $J = 8$, C_2-H), 1.90 (dd, 3 H, $J_{HA-CH_3} = 7.5$, $J_{HB-CH_3} = 1.5$, C_{HA}-CH_3), 1.83 (d, 1 H, C_4-H), 1.11 (s, 3 H), 0.88 (s, 3 H), and 0.82 (s, 3 H) C_1-CH_3, C_7-CH_3 and C_7-CH_3; MS m/z 237 ($M^{\cdot+}$), 209, 139, 134, 86, 69 (100); $[\alpha]^{25}_D = -81°$ ($c = 1.94$ in $CHCl_3$). Anal. Calcd for $C_{14}H_{23}NO_2$: C, 70.88; H, 9.77; N, 5.90. Found: C, 70.79; H, 9.76; N, 6.03.

Preparation of Amide 9. To a solution of amino alcohol **7** (366 mg, 2.16 mmol) in dichloromethane (11 mL) was added a solution of sodium carbonate (1.1 g, 10.4 mmol) in water (11 mL) and 3-(phenylthio)-2-propenoyl chloride (477 mg, 2.4 mmol). The reaction medium was stirred for 30 min at room temperature and extracted with dichloromethane. After usual workup amide **9** (717 mg) was isolated quantitatively: IR 3380, 2950, 1640, 1575, 1500; ^1H NMR (80 MHz) 7.33 (m, 5 H), 6.98 (d, 1 H, $J = 10$), 5.81 (d, 1 H, $J = 10$), 1.12 (s, 3 H), 0.92 (s, 3 H), 0.84 (s, 3 H); MS m/z 331 ($M^{\cdot+}$), 303, 302, 233, 180, 163, 109.

Preparation of Oxazoline 10. To a stirred solution of amide **8** (1 g, 4.22 mmol) in toluene (30 mL) under argon was added phosphorus oxychloride (3.92 mL, 42 mmol). The reaction medium was refluxed for 15 min and, after cooling, evaporated under vacuum. The oily residue was dissolved in toluene and again evaporated to dryness. This process was repeated twice, and the final residue was treated with an aqueous solution of sodium bicarbonate (10%) and extracted with dichloromethane. After usual treatment the crude oily product (925 mg) was purified by column chromatography (SiO_2 hexane–ethyl acetate 70:30) and afforded oxazoline **10** (647 mg, 70%): IR 2950, 1665, 1610, 1380, 1050; ^1H NMR 6.54 (qd, 1 H, $J_{HA-CH_3} = 7.5$, $J_{HA-HB} = 15$, CHA–CH_3), 5.95 (qd, 1 H, $J_{HB-CH_3} = 1.5$, $J_{HB-HA} = 15$, CH_B-CH_A), 4.45 (d, 1 H, $J = 8$, C_{7a}-H), 3.88 (d, 1 H, $J = 8$, C_{3a}-H), 2.13, (d, 1 H, $J = 5$, C_4-H), 1.83 (dd, 3 H, $J_{HA-CH_3} = 7.5$, $J_{HB-CH_3} = 1.5$, CH_A-CH_3), 1.05 (s, 3 H), 0.88 (s, 3 H) and 0.85 (s, 3 H) C_4-CH_3, C_8-CH_3, and C_8-CH_3; MS m/z 438, 423, 356, 259, 246, 220, 219 ($M^{\cdot+}$), 191, 135, 95 (100); $[\alpha]^{25}_D = -166$ ($c = 1.19$). Anal. Calcd for $C_{14}H_{21}NO$: C, 76.67; H, 9.65; N, 6.39. Found: C, 76.21; H, 9.95; N, 6.27.

Preparation of Oxazoline 11. Phosphorus oxychloride (10 mL, 107 mmol) was added at room temperature under argon to a solution of amide **9**. The reaction medium was refluxed for 15 min and evaporated under vacuum after cooling. According to the procedure given above for oxazoline **10**, the crude product was purified by column chromatography (dichloromethane–methanol 98:2) and afforded oxazoline **11** (518 mg, 73%): IR 3350, 2950, 1630; ^1H NMR (80 MHz) 7.3 (m, 6 H), 5.77 (d, 1 H, $J = 15$), 4.36 (d, 1 H, $J = 9$), 3.80 (d, 1 H, $J = 9$), 1.02 (s, 3 H), 0.87 (s, 3 H), 0.80 (s, 3 H); MS m/z 313 ($M^{\cdot+}$), 285, 203, 163; $[\alpha]_D = -109°$ ($c = 1.04$ in $CHCl_3$).

Oxidation of Oxazoline 11. A solution of oxazoline **11** (300 mg, 0.96 mmol) in ethyl acetate (7 mL) was treated with 3-chloroperbenzoic acid (365 mg, 2.12 mmol). The solution was stirred at room temperature for 3 h. 3-Chloroperbenzoic acid (83 mg, 0.48 mmol) was added, and the reaction mixture was stirred for additional 3 h. Treatment with aqueous sodium carbonate and extraction with dichloromethane afforded a crude product. After purification by preparative thin-layer chromatography (ethyl acetate–hexane 30:70), oxazoline **12** was isolated (78 mg, 23%): IR 1630, 1600; ^1H NMR (200 MHz) 7.96–7.65 (m, 5 H), 7.12 (d, 1 H, $J = 16$), 7.02 (d, 1 H, $J = 16$), 4.52 (d, 1 H, $J = 9$), 3.97 (d, 1 H, $J = 9$), 1.07 (s, 3 H, CH_3), 0.86 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3); MS m/z 346 (M + 1), 345 ($M^{\cdot+}$), 317, 236, 110, 95; $[\alpha]_D = -130°$ ($c = 1.16$).

Preparation of Nitrile 13. Sodium (640 mg, 20 mmol) was introduced in small pieces into 2-propanol (100 mL) under argon. The mixture was refluxed for 1 h until disappearance of sodium. After cooling, acrylonitrile (13.2 mL, 20 mmol) was added, and the reaction medium was stirred at room temperature overnight. After neutralization with acetic acid (1.14 mL, 20 mmol), 2-propanol in excess was distilled under vacuum, and the viscous residue was dissolved in dichloromethane and washed with water. After usual treatment, the yellow crude liquid (20 g), distilled in vacuum under phosphorus pentoxide (1 g) (Eb_{50}: 70 °C), afforded nitrile **13** (15.6 g, 73%): IR 2950, 2250, 1480, 1380, 1100; ^1H NMR (60 MHz) 3.5 (m, 3 H, $CH(CH_3)_2$ and CH_2O), 2.5 (t, 2 H, $J = 7$, CH_2CN), 1.15 (d, 6 H, 2 CH_3).

Preparation of Imino Ether Hydrochloride 14. Nitrile **13** was dissolved in anhydrous ethanol under argon and cooled at 0 °C. This solution was saturated with a stream of hydrochloric acid and stirred at 0 °C for 3 days. Anhydrous ether (10 mL) was added, and the reaction medium was evaporated under vacuum. After the medium was dried under vacuum, an hygroscopic white solid was obtained (20.6 g, 99%): IR (Nujol) 3400, 2900, 1650, 1480, 1380, 1100; ^1H NMR (60 MHz) 4.6 (q, 2 H, $J = 7$), 3.73 (t, 2 H, $J = 7$), 3.6 (m, 1 H), 2.9 (t, 2 H, $J = 7$), 1.45 (t, 3 H, $J = 7$), 1.1 (d, 6 H, $J = 7$); MS (CI isobutene) m/z 160, 132.

Preparation of Oxazoline 15. The amino alcohol **7** (1 g, 5.9 mmol) and the imino ether hydrochloride **14** (1.16 g, 5.9 mmol) in anhydrous dichloromethane (20 mL) were stirred at room temperature, and a solution of triethylamine (823 μl, 5.9 mmol) in dichloromethane (1 mL) was added dropwise. The reaction medium was stirred for 5 h. After usual treatment, oxazoline **15** (1.33 g, 97%) was isolated as a pale yellow oil: IR 2950, 1665, 1380, 1050; ^1H NMR 4.41 (d, 1 H, $J = 8$, C_{7a}-H), 3.8 (d, 1 H, $J = 8$, C_{3a}-H), 3.67 (t, 2 H, $J = 7$, CH_2–O–), 3.61 (1 H, C*H*-O), 2.41 (t, 2 H, $J = 7$, CH_2–CH_2–O–), 2.08 (d, 1 H, $J = 5$, C_7-H), 1.12 (d, 6 H, $J = 7$, $(CH_3)_2CH$), 1 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3); MS m/z 265 ($M^{\cdot+}$), 250, 237, 222, 208, 156, 95 (100); $[\alpha]^{25}_D = -43°$ ($c = 2.14$). Anal. Calcd for $C_{16}H_{27}NO_2$: C, 72.41; H, 10.25; N, 5.28. Found: C, 72.65; H, 10.08; N, 5.09.

Preparation of Oxazoline 16. To a solution of freshly sublimated potassium *tert*-butoxide (146 mg, 1.3 mmol) and of 18-crown-6 ether (7 mg, 0.05 mmol) in dry THF (8 mL) containing some crystals of phenothiazine was introduced dropwise at 0 °C under argon a solution of oxazoline **15** (265 mg, 1 mmol) in dry THF (2 mL). The orange reaction medium was stirred at 0 °C for 15 min and treated with a saturated aqueous solution of ammonium chloride. The organic layer was extracted with dichloromethane, washed with brine, and dried on magnesium sulfate. After filtration, SiO_2 (230–400 mesh, 1 g) was added to the dichloromethane solution, and the resulting suspension was evaporated under vacuum. The white powder was introduced at the top of a column for chromatography (SiO_2, 230–400 mesh, 5 g) and eluted with pentane–ethyl acetate 75:25. Oxazoline **16** was isolated (176 mg, 86%): IR 2950, 1665, 1600, 1380, 1050; ^1H NMR 6.23 (dd, 1 H, $J_{HA-HB} = 11$, $J_{HA-HC} = 17$, $_{HA}>C=C<^{HC}_{HB}$), 6.0 (dd, 1 H, $J_{HC-HB} = 1$, $J_{HC-HA} = 17$,

H_C), 5.65 (dd, 1 H, J_{HB-HC} = 1, J_{HB-HA} = 11, H_B), 4.47 (d, 1 H, J = 8, C_{7a}-H), 3.93 (d, 1 H, J = 8, C_{3a}-H), 2.1 (d, 1 H, J = 5, C_7-H), 1.06 (s, 3 H, CH_3), 0.86 (s, 3 H, CH_3), 0.80 (s, 3 H, CH_3); ^{13}C NMR (50 MHz) 164.6, 125.7, 125.6, 86.6, 81.2, 48.9, 48.5, 46.9, 34.4, 23.3, 23.2, 18.3, 11.7; MS m/z 206 ($M^{\bullet+}$), 134, 95 (100), 79; $[\alpha]^{25}_D$ = −176° (c = 0.09). Anal. Calcd for $C_{13}H_{19}NO$: C, 76.05; H, 9.33. Found: C, 75.80; H, 8.99.

Preparation of Diene Phosphate 21. Lithium diisopropylamide was prepared by dropwise addition of butyllithium in hexane (1.6 N, 5 mL, 8 mmol) to diisopropylamine (1.2 mL, 8 mmol) in dry THF (20 mL) at 0 °C. After 30 min, the solution was cooled at −78 °C and 4-*tert*-butoxy-3-buten-2-one (1.13 g, 7.9 mmol) in dry THF (1 mL) was then added dropwise. After the solution was stirred at −78 °C for 30 min, HMPA (0.5 mL) was added to the green reaction medium. After an additional 30 min at −78 °C, a solution of diphenyl chlorophosphate (1.8 mL, 8.7 mmol) in THF (2 mL) was added dropwise. The reaction medium became yellow and progressively turned red while the temperature raised to 0 °C in 90 min. The reaction was quenched with a saturated solution of ammonium chloride, diluted with pentane (100 mL), and washed with small quantities of an aqueous solution of sodium carbonate (10%) until the organic layer became clear. After usual treatment, the crude product was purified by column chromatography (6 × 20 cm, hexane–ethyl acetate 85:15). Diene phosphate **21** was obtained as pale yellow oil (2.3 g, 78%) which easily polymerized: IR 2950, 1660, 1600, 1480, 1380, 1300, 1180, 1000; ^1H NMR (80 MHz) 7.23 (10 H, aromatics), 6.66 (d, 1 H, J = 12), 5.41 (dd, 1 H, J = 12, J = 2), 4.77 (dd, 1 H, J = 2), 4.59 (dd, 1 H, J = 2, J = 1), 1.18 (s, 9 H); MS m/z 374 ($M^{\bullet+}$), 327, 326, 319, 318, 251, 250 (100), 225, 175, 170, 144, 94.

Preparation of Diene Phosphates 22a and 22b. To a lithium diisopropylamide (10.2 mmol) in THF (40 mL), prepared as above, was added under argon at −78 °C HMPA (1.2 mL). After 30 min a solution of 2-cyclopenten-1-one (980 mg, 10.2 mmol) in THF (2 mL) was added slowly. The green yellow reaction medium was stirred for 5 min at −78 °C, and a solution of diphenyl chlorophosphate (2.28 mL, 11 mmol) in THF (2 mL) was added. The mixture was stirred for 15 min at −78 °C and treated as above. The crude mixture was purified by column chromatography (pentane–ethyl acetate 88:12) and afforded two products: the less polar diphenyl 1,3-cyclopentadiene-1-yl phosphate (**22b**) (450 mg, 14%) and the more polar regio isomer, diphenyl 1,3-cyclopentadiene-2-yl phosphate (**22a**) (1.78 g, 57%).

Diphenyl 1,3-cyclopentadiene-1-yl phosphate (**22b**): ^1H NMR 7.23 (10 H), 6.33 (dd, 1 H, C_3-H), 6.06 (br s, 1 H, C_2-H), 5.96 (dd, 1 H, C_4-H), 3.00 (s, 2 H, C_5-H_2).

Diphenyl 1,3-cyclopentadiene-2-yl phosphate (**22a**): IR 2950, 1600, 1490, 1380, 1300, 950; ^1H NMR 7.23 (10 H), 6.43 (m, 2 H, C_2-H and C_3-H), 5.96 (dd, 1 H, J = 2, J = 1, C_4-H), 3.00 (s, 2 H, C_5-H_2); MS m/z 314 ($M^{\bullet+}$) 276, 250, 233, 215, 158, 130, 95, 82, 77.

General Procedure for the Diels–Alder Reaction. Diels–Alder Reaction between Cyclopentadiene (17) and Oxazoline 10. Preparation of Compound 24. Trifluoacetic anhydride (413 μL, 2.9 mmol, 1.5 equiv) was added dropwise to a stirred solution of oxazoline **10** (425 mg, 1.94 mmol) and cyclopentadiene (**17**) (3.2 mL, 40 mmol, 20 equiv) in dry dichloromethane (5 mL) containing a suspension of calcium carbonate (600 mg, 6 mmol) at −78 °C under argon. The mixture was stirred for 4 h at the same temperature and warmed to 0 °C in 30 min. The reaction medium was poured in a saturated aqueous solution of sodium hydrogen carbonate, and the organic layer was washed with brine, dried over magnesium sulfate, filtrated, and evaporated under vacuum.

The crude residue, analyzed by gas chromatography–mass spectrometry, showed two products m/z 285 ($M^{\bullet+}$) in a ratio 97:3. Two spots (R_f 0.43 major and 0.5 minor) were detected by thin-layer chromatography (hexane–ethyl acetate 80:20). The crude product after purification by flash column chromatography (20 × 3 cm, hexane–ethyl acetate 85:15) afforded adduct **24** (420 mg, 76%): IR 2950, 1660, 1050; ^1H NMR 6.33 and 6.06 (m, 2 H, C_5-H and C_6-H), 4.37 (d, 1 H, J = 8, C_{7a}-H), 3.77 (d, 1 H, J = 8, C_{3a}-H), 1.1 (d, 3 H, J = 7, C_3-CH_3), 1.03 (s, 3 H, CH_3), 0.87 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3); ^{13}C NMR (50 MHz) 170.9, 137.9, 133.7, 86.5, 80.6, 48.9, 48.0, 47.5, 46.8, 46.6, 46.4, 38.6, 34.3, 23.4, 21.2, 18.7, 11.7; MS m/z 285 ($M^{\bullet+}$, 100), 270, 257, 220, 134, 120, 95; $[\alpha]^{25}_D$ = +81° (c = 0.69 in $CHCl_3$). Anal. Calcd for $C_{19}H_{27}NO$: C, 79.95; H, 9.54; N, 4.91. Found: C, 79.77; H, 9.40; N, 4.85.

Diels–Alder Reaction between 1-(Phenylthio)-1,3-butadiene (18) and Oxazoline 10. Preparation of Compound 25. This compound was prepared from oxazoline **10** (44 mg, 0.2 mmol), diene **18** (162 mg, 1 mmol, 5 equiv), and trifluoracetic anhydride (100 μL, 0.7 mmol, 3.5 equiv) in the presence of calcium carbonate (100 mg, 1 mmol) in dichloromethane (2 mL) at 0 °C for 6 h. Purification by flash chromatography (20 × 1 cm, hexane–ethyl acetate 85:15) produced pure **25** (36 mg, 47%): IR 2950, 1665, 1600, 1190, 1100, 1010; ^1H NMR 7.23 (m, 5 H), 5.80 and 5.72 (2 m, 2 H, C_5-H and C_6-H), 4.26 (m, 1 H, C_1-H), 4.09 (d, 1 H, J = 8, C_{7a}-H), 3.31 (d, 1 H, J = 8, C_{3a}-H), 2.91 (dd, 1 H, $J_{2'-3'}$ = 10, $J_{2'-1'}$ = 4.5, $C_{2'}$-H), 2.09 (d, 1 H, J = 5, C_7-H), 1.05 (d, 3 H, J = 7, $C_{3'}$-CH_3), 1.01 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3); MS m/z 381 ($M^{\bullet+}$), 329, 296, 272, 252, 220, 193, 137 (100), 110. This product was not stable. $[\alpha]_D \cong +18$ (c = 3).

Diels–Alder Reaction between 2,3-Dimethyl-1,3-butadiene (19) and Oxazoline 10. Preparation of Compound 26. This compound was prepared from oxazoline **10** (44 mg, 0.2 mmol), 2,3-dimethyl-1,3-butadiene (**19**) (0.993 mL, 8.8 mmol, 40 equiv), trifluoroacetic anhydride (114 μL, 0.8 mmol, 4 equiv), and calcium carbonate (100 mg, 1 mmol) in dichloromethane (2 mL) at 20 °C for 24 h. Gas chromatography–mass spectrometry showed the presence in the crude residue after extraction of two products m/z 301 ($M^{\bullet+}$) in a ratio 96:4. The crude mixture was purified by flash chromatography (18 × 1 cm, hexane–ethyl acetate 85:15) and afforded compound **26** (30 mg, 50%): IR 2950, 1665, 1050; ^1H NMR 4.5 (d, 1 H, J = 8, C_{7a}-H), 3.83 (d, 1 H, J = 8, C_{3a}-H, 2.35 (m, 1 H, $C_{1'}$-H), 2.1 (d, 1 H, J = 5, C_7-H), 1.6 (m, 6 H, $C_{4'}$-CH_3 and $C_{5'}$-CH_3), 1.07 (s, 3 H, CH_3), 1 (d, 3 H, J = 7, $C_{2'}$-CH_3), 0.9 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3); MS m/z 301 ($M^{\bullet+}$), 286, 219, 85, 57 (100); $[\alpha]^{25}_D$ = +15° (c = 0.78 in $CHCl_3$). Exact mass calcd: 301.2397. Found: 301.2401.

Diels–Alder Reaction between Cyclopentadiene (17) and Oxazoline 12. Preparation of Compounds 27a and 27b. These compounds were prepared from oxazoline **12** (76 mg, 0.22 mmol), cyclopentadiene (**17**) (0.9 mL, 11.2 mmol), and trifluoroacetic anhydride (0.06 mL; 0.44 mmol) in dichloromethane (6 mL) at −100 °C for 4 h. Extraction and purification (preparative TLC eluant, ethyl acetate–hexane 30:70) afforded two products **27a** (34 mg, 38%) and **27b** (34 mg, 38%).

Less polar product **27b**: IR 1670; ^1H NMR 7.93–7.63 (m, 5 H), 6.37 (br s, 2 H), 4.23 (m, 2 H), 3.6 (d, J = 8, 1 H), 0.95 (s, 3 H, CH_3), 0.83 (s, 6 H, 2 CH_3); ^{13}C NMR 168, 140, 136.6, 134.7, 133.4, 129, 128.5, 87.7, 80.6, 68.8, 53.5, 48.6, 46.9, 44.9, 48.1, 47.9, 34.2, 23.3, 18.8, 11.6; MS m/z 411 ($M^{\bullet+}$), 383, 346, 345, 317, 302, 271, 270 (100), 236, 160, 119, 95; $[\alpha]_D$ = +27° (c = 0.82).

More polar product **27a**: IR 1670; ^1H NMR 7.97–7.63 (m, 5 H), 6.32 (m, 1 H), 6.20 (m, 1 H), 4.05 (d, 1 H, J = 8), 3.53 (d, 1 H, J = 8), 0.94 (s, 3 H, CH_3), 0.79 (s, 3 H, CH_3), 0.70 (s, 3 H, CH_3); MS m/z 411 ($M^{\bullet+}$), 346, 302, 271, 270 (100), 236, 188, 174, 160, 95, 91; $[\alpha]_D$ = +24° (c = 0.59).

Diels–Alder Reaction between Cyclopentadiene (17) and Oxazoline 16. Preparation of Compound 28. This compound was prepared from oxazoline **16** (100 mg, 0.49 mmol), cyclopentadiene (**17**) (0.394 mL, 4.9 mmol, 10 equiv), and trifluoroacetic anhydride (90 μL, 0.63 mmol) in the presence of calcium carbonate (120 mg, 1.2 mmol) in dichloromethane at −78 °C for 45 min. Only one product [m/z 271 ($M^{\bullet+}$)] was detected by gas chromatography–mass spectrometry. Purification by flash chromatography (20 × 2 cm, hexane–ethyl acetate 85:15) afforded compound **28** (93 mg, 70%): IR 2950, 1665, 1050; ^1H NMR 6.20 and 5.97 (2 m, 2 H, C_5-H and C_6-H), 4.37 (d, 1 H, J = 8, C_{7a}-H), 3.77 (d, 1 H, J = 8, C_{3a}-H), 1.02 (s, 3 H, CH_3), 0.85 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3); MS m/z 271 ($M^{\bullet+}$), 256, 242, 230, 206, 134, 95 (100); $[\alpha]^{25}_D$ = +32° (c = 3.2). Anal. Calcd for $C_{18}H_{25}NO$: C, 79.66; H, 9.29; N, 5.16. Found: C, 79.61; H, 9.60; N, 5.07.

Diels–Alder Reaction between 1-(Phenylthio)-1,3-butadiene (18) and Oxazoline 16. Preparation of Compound 29. This compound was prepared from oxazoline **16** (20 mg, 0.097 mmol), diene **18** (162 mg, 1 mmol, 10 equiv), and trifluoroacetic anhydride (45 μL, 0.29 mmol, 3 equiv) in dichloromethane (2 mL) in the presence of calcium carbonate (60 mg, 0.6 mmol) at −20 °C for 20 min. Flash chromatography (hexane–ethyl acetate 80:20) afforded compound **29** (17 mg, 47%) which was not stable: IR 2950, 1665, 1190, 1010, ^1H NMR 7.23 (m, 5 H), 6 (m, 2 H, C_5-H and C_6-H), 4.47 (m, 1 H, $C_{1'}$-H), 4.05 (d, 1 H, J = 8, C_{7a}-H), 3.37 (d, 1 H, J = 8, C_{3a}-H), 3.23 (m, 1 H, $J_{H1'-H2'}$ = 4 (after double irradiation, $C_{2'}$-H)), 2.09 (d, 1 H, J = 5, C_7-H), 1.02 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3); MS m/z 367 ($M^{\bullet+}$), 334, 277, 258, 146 (100), 145, 95, 77; $[\alpha]_D$ = +22° (c = 3).

Diels–Alder Reaction between 2,3-Dimethyl-1,3-butadiene (19) and Oxazoline 16. Preparation of Compound 30. This compound was prepared from oxazoline **16** (118 mg, 0.575 mmol), diene **19** (1.29 mL, 11.5 mmol, 20 equiv), and trifluoroacetic anhydride (245 μL, 1.72 mmol, 3 equiv) in dichloromethane (4 mL) in the presence of calcium carbonate (300 mg, 3 mmol) at −40 °C during the introduction of the anhydride and then at −15 °C for 30 min. Gas chromatography–mass spectrometry showed two products corresponding to m/z 287 ($M^{\bullet+}$) in a ratio 84:16. The crude mixture was purified by flash chromatography and afforded compound **30** (93 mg, 56%): IR 2950, 1665, 1380, 1050; ^1H NMR 4.38 (d, 1 H, J = 8, C_{7a}-H), 3.83 (d, 1 H, J = 8, C_{3a}-H), 2.34 (m, 1 H, $C_{1'}$-H), 2.09 (d, 1 H, J = 5, C_7-H), 1.59 (s, 6 H, 2 CH_3), 1.07 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3); MS m/z (287 ($M^{\bullet+}$), 272, 258,

206, 152, 135, 108, 93; $[\alpha]_D = +21°$ ($c = 3.2$). Exact mass calcd for $C_{19}H_{27}NO$: 287.2241. Found: 287.2277.

Diels–Alder Reaction between 1,3-Cyclohexadiene (20) and Oxazoline 16. Preparation of Compound 31. This compound was prepared from oxazoline **16** (91 mg, 0.44 mmol), 1,3-cyclohexadiene (**20**) (0.837 mL, 8.8 mmol, 20 equiv), and trifluoroacetic anhydride (0.188 mL, 1.33 mmol, 3 equiv) in dichloromethane (3 mL) in the presence of calcium carbonate (200 mg, 2 mmol) at −40 °C during the introduction of the anhydride then at −15 °C for 30 min. One product m/z 285 ($M^{\bullet+}$) was detected by gas chromatography–mass spectrometry. Purification by flash chromatography (18 × 2 cm, hexane–ethyl acetate 80:20) afforded compound **31** (103 mg, 82%): IR 2950, 1665, 1050; ^{1}H NMR 6.30 and 6.15 (2 m, 2 H, C_5-H and C_6-H), 4.37 (d, 1 H, $J = 8$, C_{7a}-H), 3.77 (d, 1 H, $J = 8$, C_{3a}-H), 2.85 (m, 1 H, C_2-H), 2.07 (d, 1 H, $J = 5$, C_7-H), 1.02 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3); MS m/z 285 ($M^{\bullet+}$), 270, 256, 230, 229, 206, 175, 161, 134, 95 (100). $[\alpha]^{25}_D = +21°$ ($c = 3.14$). Exact mass calcd for $C_{19}H_{27}NO$: 285.2085. Found: 285.2104.

Diels–Alder Reaction between Phosphate Diene 21 and Oxazoline 16. Preparation of Compound 32. This compound was prepared from oxazoline **16** (18 mg, 0.087 mmol), diene **21** (162 mg, 0.435 mmol, 5 equiv), trifluoroacetic anhydride (0.037 mL, 0.261 mmol, 3 equiv), in dichloromethane (3 mL) in the presence of calcium carbonate (52 mg, 0.52 mmol) at −40 °C for 20 min. The crude mixture was analyzed by HPLC (column Resolve Si-5M, heptane–ethyl acetate 70:30, 1 mL/mn, 254 nm) and showed two products in a ratio 99:1 (retention time (major) 8.65 min, (minor) 8.10 min) and diene **21**. Purification of the crude mixture by flash chromatography (18 × 1 cm, hexane–ethyl acetate 60:40) afforded compound **32** as an oil (32 mg, 63%): IR 2950, 1665, 1620, 1600, 1030; ^{1}H NMR 7.23 (10 H, m), 5.68 (dd, 1 H, $J_{H6'-H1'} = 6$, C_6-H), 4.41 (d, 1 H, $J = 8$, C_{7a}-H), 4.33 (m, 1 H, $J_{H2'-H1'} = 4$, C_1-H), 3.73 (d, 1 H, $J = 8$, C_{3a}-H), 2.64 (m, 1 H, $J_{H2'-H1'} = 4$, C_2-H), 2.12 (d, 1 H, $J = 5$, C_7-H), 1.11 (s, 9 H, *tert*-butyl), 1.06 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3); MS m/z 579 ($M^{\bullet+}$), 523, 522 (100), 504, 503, 344, 327, 272, 251, 206, 95, 77. $[\alpha]^{25}_D = +16°$ ($c = 3.2$).

Diels–Alder Reaction between Diphenyl 1,3-Cyclopentadien-2-yl Phosphate (22a) and Oxazoline 16. Preparation of Compound 33. This compound was prepared from oxazoline **16** (102 mg, 0.5 mmol), diene **22** (628 mg, 2 mmol, 4 equiv), and trifluoroacetic anhydride (213 μL, 1.5 mmol, 3 equiv) in dichloromethane (5 mL) in the presence of calcium carbonate (200 mg, 2 mmol) at −78 °C for 2 h. HPLC analysis of the crude mixture (column Resolve Si-5M, heptane–ethyl acetate 70:30, 1 mL/mn, 254 nm) showed the presence of two products in a ratio 96:4 (retention time (major) 15.4 min, (minor) 14.1 min) and diene **22a**. The crude mixture, after purification by flash chromatography (20 × 2 cm, hexane–ethyl acetate 60:40) afforded **33** (171 mg, 66%) as a colorless oil: IR 2950, 1665, 1625, 1600, 1480, 1300, 1150, 1050; ^{1}H NMR 7.23 (m, 10 H), 5.48 (s, 1 H, C_6-H), 4.18 (d, 1 H, $J = 8$, C_{7a}-H), 3.69 (d, 1 H, $J = 8$, C_{3a}-H), 1.92 (d, 1 H, $J = 5$, C_7-H), 0.98 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3), 0.75 (s, 3 H, CH_3); MS m/z 519 ($M^{\bullet+}$) 501, 419 (100), 308, 262, 159, 95, 77. $[\alpha]^{20}_D = +17°$ ($c = 2$).

Diels–Alder Reaction between 1-Carbomethoxy-1,2-dihydropyridine (23) and Oxazoline 16. Preparation of Compound 34. This compound was prepared from oxazoline **16** (102 mg, 0.5 mmol), diene **23** (347 mg, 2.5 mmol, 5 equiv), and trifluoroacetic anhydride (213 μL, 1.5 mmol, 3 equiv) in dichloromethane (5 mL) in the presence of calcium carbonate (200 mg, 2 mmol) at −78 °C for 1 h. Two products m/z 344 ($M^{\bullet+}$) (ratio 94:6) were detected by gas chromatography–mass spectrometry. Purification by flash chromatography (20 × 2 cm, hexane–ethyl acetate 60:40) afforded compound **34** as a colorless oil (103 mg, 60%): IR 2950, 1690, 1665, 1430, 1400, 1100; ^{1}H NMR 6.37 (m, 2 H, C_7-H and C_8-H), 5.08 and 4.89 (2 m, 1 H, C_1-H), 4.36 (d, 1 H, $J = 8$, C_{7a}-H), 3.73 (d, 1 H, $J = 8$, C_{3a}-H), 3.67 (2 s, 3 H, CO_2CH_3), 3.23 (d, 1 H, $J = 10$, C_3-H_A), 2.98 (d, 1 H, $J = 10$, C_3-H_B), 2.85 (m, 1 H, C_6-H), 2.05 (d, 1 H, $J = 5$, C_7-H), 1.01 (s, 3 H, CH_3), 0.87 (s, 3 H, CH_3), 0.81 (s, 3 H, CH_3) (The NMR of this compound is complicated by the presence of carbamate rotamers); MS m/z 344 ($M^{\bullet+}$), 329, 285, 230, 206, 139, 138, 125; $[\alpha]^{20}_D = -99°$ ($c = 1.24$).

Preparation of Oxazoline 39. Amino alcohol **38** (700 mg, 4.2 mmol) afforded quantitatively oxazoline **39** (1 g, 11) after treatment with imino ether hydrochloride **14** as in the preparation of oxazoline **15**: IR 2950, 1665, 1380, 1050; ^{1}H NMR 4.2 (d, 1 H, $J = 8$, C_{7a}-H), 3.93 (d, 1 H, $J = 8$, C_{3a}-H), 3.67 (t, 2 H, $J = 7$, CH_2–CH_2–O), 2.02 (d, 1 H, $J = 5$, C_4-H), 1.13 (d, 6 H, $J = 7$, $(CH_3)_2CH$), 1 (s, 3 H, CH_3), 0.9 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3); MS m/z 265 ($M^{\bullet+}$), 250, 238, 222 (100), 207, 130, 95. $[\alpha]^{25}_D = +6.3°$ ($c = 3.42$ in $CHCl_3$). Anal. Calcd for $C_{16}H_{27}NO_2$: C, 72.41; H, 10.25; N, 5.28. Found: C, 72.34; H, 10.43; N, 5.28.

Preparation of Oxazoline 40. Oxazoline **40** (790 mg, 90%) was prepared by the same procedure as oxazoline **16**: IR 2950, 1665, 1600, 1380, 1050; ^{1}H NMR (200 MHz) 6.23 (dd, 1 H, $J_{HA-HB} = 11$, $J_{HA-HC} = 17$, $_{HA}>C=C<^{HC}_{HB}$), 6.02 (dd, 1 H, $J_{HC-HB} = 1$, $J_{HC-HA} = 17$, H_C), 5.67 (dd, 1 H, $J_{HB-HC} = 1$, $J_{HB-HA} = 11$, H_B), 4.28 (d, 1 H, $J = 8$, C_{7a}-H), 4.05 (d, 1 H, $J = 8$, C_{3a}-H), 2.06 (d, 1 H, $J = 5$, C_4-H), 1.07 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3); ^{13}C NMR (50 MHz) 164.7, 125.9, 125.8, 91.3, 76.1, 49.3, 49.0, 47.1, 32.4, 26.2, 23.6, 18.6, 15.1, 11.4; MS m/z 206 ($MH^{\bullet+}$), 152, 133, 95 (100); $[\alpha]^{25}_D = +92°$ ($c = 2.04$). Anal. Calcd for $C_{13}H_{19}NO$: C, 76.05; H, 9.33; N, 6.82. Found: C, 75.93; H, 9.23; N, 7.03.

Preparation of Amide 41. The amino alcohol **38** (338 mg, 2 mmol) was treated as in the preparation of amide **8** and afforded quantitatively the amide **41** (474 mg, 100%): mp 172–173 °C (ether); IR 3400, 2950, 1660, 1615; ^{1}H NMR 6.77 (1 H, qd, $J_{HA-CH_3} = 7.5$, $J_{HA-HB} = 15$, CH_A-CH_3), 6.22 (br s, 1 H, NH), 5.81 (dd, 1 H, $J_{HB-CH_3} = 1.5$, $J_{HB-HA} = 15$, –CH_B–CH_A–), 3.9 (s, 1 H, OH), 3.81 (d, 1 H, $J = 8$, C_2-H), 2.85 (d, 1 H, $J = 8$, C_3-H), 1.75 (dd, 3 H, $J_{CH_3-HA} = 7.5$, $J_{CH_3-HB} = 1.5$, CH_3—CH=), 1.72 (d, 1 H, $J = 5$, C_4-H), 1.05 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3); MS m/z 237 ($M^{\bullet+}$), 209, 134, 86, 69 (100); $[\alpha]^{25}_D = +81°$ ($c = 0.09$). Anal. Calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found: C, 70.58; H, 9.54; N, 5.70.

Preparation of Oxazoline 42. Amide **41** (474 mg, 2 mmol) was treated as above for the preparation of oxazoline **10**. Oxazoline **42** was obtained in 70% yield: IR 2950, 1665, 1620, 1050; ^{1}H NMR 6.49 (dq, 1 H, $J_{HA-CH_3} = 7.5$, $J_{HA-HB} = 15$, CH_A-CH_3), 5.84 (ddq, 1 H, $J_{HB-CH_3} = 1.5$, $J_{HB-HA} = 15$, CH_B=CH_A), 4.15 (d, 1 H, $J = 8$, C_{7a}-H), 3.94 (d, 1 H, $J = 8$, C_{3a}-H), 1.80 (dd, 3 H, $J_{CH_3-HA} = 7.5$, $J_{CH_3-HB} = 1.5$, CH_A-CH_3), 0.95 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3), 0.75 (s, 3 H, CH_3); ^{13}C NMR (50 MHz) 164.7, 139.2, 119.9, 91.1, 76.2, 49.0, 48.5, 46.9, 32.3, 26.2, 23.5, 18.7, 18.5, 18.3, 11.4; MS m/z 438, 423, 271, 256, 220, 219 ($M^{\bullet+}$), 191, 134, 95, 69; $[\alpha]^{25}_D = 64$ ($c = 1.16$).

Diels–Alder Reaction between Cyclopentadiene (17) and Oxazoline 40. Preparation of Compound 35. This compound was prepared from oxazoline **40** (52 mg, 0.25 mmol), cyclopentadiene (**17**) (200 μL, 2.5 mmol, 10 equiv), and trifluoroacetic acid (47 μL, 0.33 mmol, 1.3 equiv) in dichloromethane (2 mL) in the presence of calcium carbonate (66 mg, 0.66 mL) at −78 °C for 15 min. Two products m/z 271 ($M^{\bullet+}$) (ratio 78:22) were detected by gas chromatography–mass spectrometry. Purification by flash chromatography of the crude mixture afforded compound **35** (29 mg, 55%) as a colorless oil: IR 2950, 1665, 1050; ^{1}H NMR 6.16 and 6.02 (2 m, 2 H, C_5-H and C_6-H), 4.16 (d, 1 H, $J = 8$, C_{7a}-H), 3.92 (d, 1 H, $J = 8$, C_{3a}-H), 2.03 (d, 1 H, $J = 5$, C_4-H), 0.99 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3); MS m/z 271 ($M^{\bullet+}$), 256, 228, 206, 135, 108, 93, 55 (100); $[\alpha]^{20}_D = -33°$ ($c = 1.33$).

Diels–Alder Reaction between Diphenyl 1,3-Cyclopentadien-2-yl Phosphate (22a) and Oxazoline 40. Preparation of Compound 36. This compound was prepared from oxazoline **40** (20.5 mg, 0.1 mmol) and diene phosphate **22a** (94 mg, 0.3 mmol) in solution in dichloromethane (3 mL) in the presence of a suspension of calcium carbonate (60 mg, 0.6 mmol) and of trifluoroacetic anhydride (43 μL, 0.3 mmol) at −78 °C for 90 min. After usual treatment the residue was purified by column chromatography (eluant, heptane–ethyl acetate 63:35), the major adduct **36** was isolated (32 mg, 61%). IR 2950, 1665, 1620, 1600, 1480, 1050, 980; ^{1}H NMR 7.23 (m, 10 H), 5.51 (m, 1 H, C_6-H), 3.98 (d, 1 H, $J = 8$, C_{7a}-H), 3.77 (d, 1 H, $J = 8$, C_{3a}-H), 3.23 (m, 1 H, C_2-H), 1.96 (d, 1 H, $J = 5$, C_7-H), 0.91 (s, 3 H, CH_3), 0.88 (s, 3 H, CH_3), 0.79 (s, 3 H, CH_3); $[\alpha]_D = -12.6$ ($c = 2.2$). The ratio of the two diastereomer (64:36) was measured after alkaline hydrolysis of the enol phosphates (MeOH, CO_3K_2 (6 equiv), room temperature, 90 min) and separation of the corresponding ketones.

Diels–Alder Reaction between Cyclopentadiene (17) and Oxazoline 42. Preparation of Compound 37. This compound was prepared from oxazoline **42** (86 mg, 0.39 mmol), cyclopentadiene (**17**) (627 μL, 6.7 mmol, 20 equiv), and trifluoroacetic anhydride (72 mL, 0.51 mmol, 1.3 equiv) in dichloromethane (3 mL) in the presence of calcium carbonate (100 mg, 1 mmol) at −78 °C for 90 min. Two products m/z 285 ($M^{\bullet+}$) (ratio 86:14) were detected by gas chromatography–mass spectrometry. Purification by flash chromatography (18 × 1 cm, hexane–ethyl acetate 85:15) afforded compound **37** (70 mg, 62%) as a colorless oil: IR 2950, 1660, 1050; ^{1}H NMR 6.24 and 6.04 (2 m, 2 H, C_6-H and C_5-H), 4.16 (d, 1 H, $J = 8$, C_{7a}-H), 3.92 (d, 1 H, $J = 8$, C_{3a}-H), 1.17 (d, 3 H, $J = 7$, C_3-CH_3), 1.0 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3); MS m/z 285 ($M^{\bullet+}$), 270, 257, 242, 200, 152, 134, 108, 95; $[\alpha]^{25}_D = -103°$ ($c = 1.08$). Anal. Calcd for $C_{19}H_{27}NO$: C, 79.95; H, 9.54; N, 4.91. Found: C, 79.90; H, 9.59; N, 4.97.

Alkylation of Compound 24. Preparation of Oxazolinium Salt 43. A mixture of compound **24** (91 mg, 0.32 mmol) and benzyl bromide (0.04 mL, 0.32 mmol) was heated at 40 °C for 48 h. Excess of benzyl bromide was evaporated under vacuum. The crude salt **43** was used directly for the following hydrolysis.

Hydrolysis of Oxazolinium Salt 43. Preparation of Ester 44. To a solution of oxazolinium salt **43** (146 mg, 0.32 mmol) in THF (1 mL) was

added aqueous sodium hydroxide (4 mL, 1 N). The resulting mixture was heated for 5 h at 60 °C. After extraction with dichloromethane the ester **44** (116 mg, 92%) was isolated: IR 1740; ^{1}H NMR 7.38 (m, 5 H), 6.27 (m, 1 H), 6.07 (m, 1 H), 4.88 (d, J = 8, 1 H), 3.77 (m, 2 H), 3.10 (br s, 1 H), 2.77 (d, J = 8, 1 H), 1.17 (d, J = 7, 3 H, CH_3), 1.07 (s, 3 H, CH_3), 0.97 (s, 3 H, CH_3), 0.80 (s, 3 H, CH_3).

Hydrolysis of Ester 44. A solution of ester **44** (35 mg, 0.089 mmol) in methanol (1.5 mL) and aqueous sodium hydroxide (2.5 mL, 1.5 N) was stirred at 80 °C for 2 days. After dilution with water the resulting mixture was extracted with dichloromethane. After evaporation of the organic layer, the residue was purified by preparative TLC and afforded amino alcohol **6** (12.9 mg, 56%), $[\alpha]_D$ = −52° (c = 1.29).

The alkaline aqueous layer was acidified with hydrochloric acid (10%) and extracted with dichloromethane. The residue was purified by preparative TLC (ethyl acetate–heptane 70:30) and afforded the acid **45** (7 mg, 52%): $[\alpha]_D$ = +134° (c = 0.7 in $CHCl_3$); $[\alpha]_D$ = +119° (c = 0.56 in 95% EtOH) (lit.[27b] $[\alpha]_D$ = −151° (in 95% EtOH)).

Treatment of Oxazolines 24 and 28 with Benzyl Chloroformate. Preparation of Esters Carbamates 46 and 47. To a stirred solution (2 M) of oxazoline and sodium bicarbonate (2.2 equiv) in a mixture of dichloromethane–water (50:50) and benzyl chloroformate (1.1 equiv) was added dropwise at room temperature. The resulting mixture was stirred for 6 h and extracted with dichloromethane. After usual treatment the residue was purified by column chromatography. **46**: 93%; mp 84–85 °C (pentane); IR 3450, 2950, 1780, 1720, 1500, 1450, 1180; ^{1}H NMR (two conformers) 7.28 (m, 5 H), 6.23 (m, 1 H), 6.03 (m, 1 H), C_5-H and C_6-H, 5.12 (2 s, 2 H, CH_2-Ar), 4.95 (br s, 1 H, NH), 4.83 (d, J = 8, 1 H, C_3-H), 3.97 (2 d, J = 8, 1 H, C_2-H), 3.06 (m, 1 H), 2.45 (br s, 1 H), 2.33 (m, 1 H), 1.75 (d, J = 5, 1 H), 1.70 (m, 3 H), 1.60 and 1.30 (2 m, 4 H), 1.15 (d, J = 7, 3 H, C_3-CH_3), 1.02 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3); MS m/z 477 ($M^{\bullet+}$), 371, 328, 287, 286, 242, 196, 194, 135, 92, 91 (100); $[\alpha]_D$ = +25° (c = 1). Anal. Calcd for $C_{27}H_{35}NO_4$: C, 74.11; H, 8.06. Found: C, 74.38; H, 8.06. **47**: 82%; IR 3450, 2950, 1740, 1720, 1500, 1450, 1150; ^{1}H NMR (two conformers) 7.38 (m, 5 H), 6.13 and 5.92 (2 m, 1 H), C_5-H and C_6-H, 5.10 (2 H, 2 s, CH_2Ar), 4.95 (s, 1 H, NH), 4.83 (d, J = 8, 1 H, C_3-H), 3.93 (2 d, J = 8, 1 H, C_2-H), 312 (br s, 1 H), 2.87 (m, 3 H), 1.71 (d, J = 5, 1 H), 1.97–1.62 (m, 3 H), 1.40 and 1.23 (2 m, 4 H), 0.99 (s, 3 H, CH_3), 0.87 (s, 3 H, CH_3), 0.78 (s, 3 H, CH_3); MS m/z 423 ($M^{\bullet+}$) 196, 194, 135, 92, 91 (100); $[\alpha]_D$ = +28° (c = 4.77). Anal. Calcd for $C_{26}H_{33}NO_4$: C, 73.73; H, 7.85. Found: C, 73.62; H, 7.88.

Hydrolysis of Ester Carbamates 46 and 47. To a solution of esters carbamates **46** or **47** (0.3 mmol) in methanol (3.5 mL) was added an aqueous solution of sodium hydroxide (1.5 mL, 2.5 N). The reaction mixture was heated at 80 °C for 14 h and diluted with water. After extraction with dichloromethane the organic layer was washed with water, dried with magnesium sulfate, and evaporated under vacuum. The residue, dissolved in xylene and evaporated under vacuum in order to distill benzylic alcohol, afforded amino alcohol **7** (90%), $[\alpha]_D$ = −44° (c = 1.5). The aqueous layer after acidification with hydrochloric acid was extracted with ether. After usual treatment pure acids **45** and **48** were isolated, respectively. **45**: 96%; IR 3300, 2950, 1710, 1110; ^{1}H NMR 6.27 and 6.03 (2 m, 2 H, C_5-H and C_6-H), 3.12 (br s, 1 H, C_2-H), 2.48 (br s, 1 H, C_1-H), 2.40 (m, 1 H, C_3-H), 1.80 (m, 1 H, C_4-H), 1.55 and 1.48 (2 m, 2 H, C_7-H_2), 1.18 (d, J = 7, 3 H, C_3-CH_3); $[\alpha]_D$ = +131° (c = 3.14 in 95% EtOH) (Lit.[27b] $[\alpha]_D$ = −151° (in 95% EtOH)) (enantiomer of **45**). **48**: 89%; IR 3300, 2950, 1710, 1110; ^{1}H NMR 6.22 and 5.98 (2 m, 2 H, C_5-H and C_6-H), 3.32 (br s, 1 H, C_2-H), 2.95 (m, 2 H, C_3-H_2), 1.90 (m, 2 H, C_1-H and C_4-H), 1.33 (m, 2 H, C_7-H_2); $[\alpha]_D$ = +144° (c = 0.85, 95% EtOH) (Lit.[27a] $[\alpha]_D$ = +144° (95% EtOH)).

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Chemistry of Oxaziridines. 14.[1] Asymmetric Oxidation of Ketone Enolates Using Enantiomerically Pure (Camphorylsulfonyl)oxaziridine

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Abstract: The reagent-controlled asymmetric oxidation of tri- and tetrasubstituted ketone enolate anions **4** and **8** by enantiomerically pure (camphorylsulfonyl)oxaziridine **2** has been investigated. The stereoselectivities for oxidation of trisubstituted enolates **4a–d** are good to excellent, 60–95% ee, while those for tetrasubstituted enolates **4e** and **8** are lower; i.e., 21–30% ee. Isolated chemical yields for both types of enolate anions are good to excellent. The sodium enolate anions of **4a–d**, which could be oxidized at −78 °C, gave both higher yields and stereoselectivities than the corresponding lithium or zinc enolates, which required warming to higher temperatures for complete oxidation. The presence of HMPA generally had a deleterious effect on the stereoinduction. However, for oxidation of (*E*)- and (*Z*)-**4d** the highest ee's were observed in the presence of this additive. Investigation of the stereoselective trends reveals that the enolate substitution pattern and the enolate solution structure are the most important stereocontrol elements. The role that the enolate geometry has in the stereoinduction is less clear although *Z* enolates seem to exhibit higher stereoselectivities than the *E* enolates. The results obtained in this study have been formulated into a mechanistic rational involving an S_N2-type substitution of the enolate anion on oxaziridine **2** via an "open" transition state.

The α-hydroxy carbonyl structural unit is commonly found in many biologically active natural products such as sugars, pheromones, antibiotics, terpenes, and alkaloids. Enantiomerically pure α-hydroxy carbonyl compounds are also important synthons for the asymmetric synthesis of natural products[2] and are useful stereodirecting groups.[3] Consequently, numerous studies have

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