Pergamon

Tetrahedron: Asymmetry, Vol. 7, No. 2, pp. 375-378, 1996

0957-4166/96 $15.00 + 0.00

S0957-4166(96)00010-9

ASYMMETRIC DIELS-ALDER REACTION : CIS-1-ARYLSULFONAMIDO-2-INDANOLS AS HIGHLY EFFECTIVE CHIRAL AUXILIARIES

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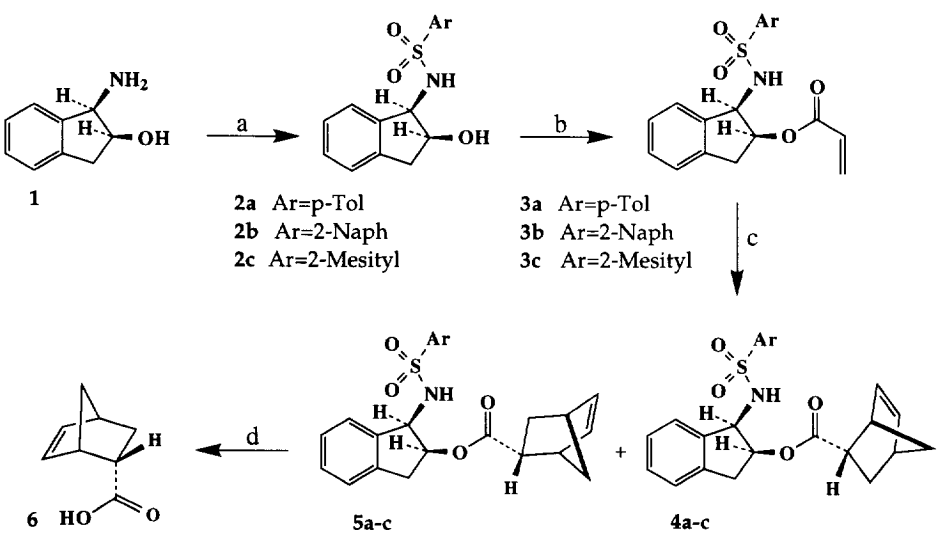
Summary. Lewis acid promoted Diels-Alder reaction of acrylate esters of *cis*-1-arylsulfonamido-2-indanols and cyclopentadiene provided exclusively *endo*-adducts with high *endo*-diastereoselectivities.

The Diels-Alder cycloaddition is one of the most powerful reactions in organic synthesis.[1] Because of its versatility in forming up to four new chiral centers in a single operation, there have been innumerable applications of this reaction in the construction of complex organic molecules.[1,2] Enantioselective synthesis of such cycloadducts is of tremendous synthetic importance. Consequently, over the years, a number of effective chiral auxiliaries[3] and chiral catalysts[4] have been developed for the asymmetric Diels-Alder reactions. Of key importance, the lack of ready availability of either enantiomer of the chiral auxiliaries as well as their removal after asymmetric induction often limits the chiral auxiliary mediated synthesis. Thus, readily accessible and versatile chiral auxiliaries would greatly enhance the utility of such asymmetric syntheses. Recently, we demonstrated that commercially available *cis*-1-amino-2-indanol derived oxazolidinone and arylsulfonamide derivatives are highly effective chiral auxiliaries for asymmetric aldol and asymmetric reductions of α-keto esters respectively. As part of our continuing interest in various asymmetric synthesis,[5] we have investigated Lewis acid promoted asymmetric Diels-Alder reactions of acrylate esters derived from *cis*-1-arylsulfonamido-2-indanols. Herein we report that the Diels-Alder reaction proceeded with complete *endo*-selectivites and high *endo*-diastereoselectivities. The chiral auxiliaries were removed under mild hydrolysis conditions and recovered fully.

Treatment of commercially available[6] (1R, 2S)-1-amino-2-indanol **1** with arylsulfonyl chlorides (1.2 equiv,) in CH_2Cl_2 in the presence of triethylamine (3 equiv.) at 23°C afforded the corresponding sulfonamide derivatives **2a-c** in high yields (90-93%) after silica gel chromatography.[7] Reaction of the resulting sulfonamido alcohols **2a-c** with acryloyl chloride (1.2 equiv.) in the presence of triethylamine in CH_2Cl_2 provided the corresponding acrylate esters **3a-c** (55-77% yield). Diels-Alder reaction of chiral dienophile **3a** and cyclopentadiene was carried out in CH_2Cl_2 at 0°C for 36 h. Analysis of the cycloadducts revealed that a mixture of *endo* and *exo*-adducts (80:20) were formed and virtually no *endo*-diastereoselectivity was observed (1:1

mixture of diastereomers by ^{1}H-NMR). On the other hand, various Lewis acid promoted cycloadditions of acrylate esters **3a-c** resulted in exclusively *endo*-adducts with very high diastereoselectivities. The reaction conditions and the results are summarized in Table-I. The diastereomeric mixture ratio was determined by ^{1}H-NMR (400 MHz) as well as by ^{13}C-NMR analysis of the cycloadducts after silica gel chromatography. As shown, the cycloaddition of acrylate ester **3a** and cyclopentadiene with 1-equivalent of $TiCl_4$ in CH_2Cl_2 at -78°C (entry 4) afforded the *endo*-adducts **4a** and **5a** with a diastereomeric ratio of 88:12 and 83% isolated yield.[8] When the reaction was carried out in the presence of 2-equiv. of $TiCl_4$, there was slight improvement in diastereoselectivity (mixture ratio 92:8). Similarly, $BF_3.OEt_2$ promoted (2 equiv.) cycloaddition afforded high diastereoselectivity (90:10) however, the reaction was rather slow and some starting dienophile was recovered (20-30%) after 11 h. The use of other Lewis acids such as Et_2AlCl and $SnCl_4$ also furnished the adducts with comparable selectivities. Interestingly, when the cycloaddition of the bulky acrylate ester **3b** and cyclopentadiene was carried out in the presence of 2-equivalents of $TiCl_4$ a very high diasteroselectivity was observed (diastereomer ratio 96:4; isolated yield 70%). The high degree of diastereoselection associated with the present asymmetric Diels-Alder process is probably due to effective metal chelation. We speculate that the corresponding metal of the Lewis acid is involved in chelation of the ester carbonyl as well as the oxygen of the sulfonamido group while the bulky aromatic unit on the sulfonamide group effectively shields one side of the prochiral olefinic moiety of the acrylate ester.

Scheme I



(a) $ArSO_2Cl$, Et_3N, DMAP, CH_2Cl_2, 23°C ; (b) CH_2=CHCOCl, Et_3N, CH_2Cl_2, 0°-23°C; (c) reaction conditions as shown in Table I ; (d) LiOH, THF-H_2O, 23°C.

Table 1. Lewis acid mediated Diels-Alder reactions of acrylate esters

Entry	Dienophile	Lewis acid (equiv.)	Temp (time)	Yields	Endo/Exo	Ratio(**4**/**5**)[a]
1.	**3a**	----	0°C (36 h)	85%	80 : 20	50 : 50
2.	**3a**	$BF_3.OEt_2$ (1.0)	-78°C (10 h)	85%	>99 : 1	88 : 12
3.	**3a**	$BF_3.OEt_2$ (2.0)	-78°C (11 h)	91%[b]	>99 : 1	90 : 10
4.	**3a**	$TiCl_4$ (1.0)	-78°C (10 h)	83%	>99 : 1	88 : 12
5.	**3a**	$TiCl_4$ (2.0)	-78°C (11 h)	87%	>99 : 1	92 : 8
6.	**3a**	Et_2AlCl (2.0)	-78°C (10 h)	80%[b]	>99 : 1	77 : 23
7.	**3a**	$SnCl_4$ (2.0)	-78°C (10 h)	85%	>99 : 1	86 : 14
8.	**3b**	$TiCl_4$ (2.0)	-78°C (10 h)	70%	> 99 : 1	96 : 4
9.	**3c**	$TiCl_4$ (2.0)	-78°C (10 h)	85%	> 99 : 1	86 : 14

[a] Diastereomeric ratios were determined by ^{1}H-NMR and ^{13}C-NMR spectroscopy

[b] based on recovered starting material

Esterification of racemic *endo* and *exo*-norbornene-2-carboxylic acids[9] with the sulfonamido alcohols **2a-c** by reaction with DCC and DMAP in CH_2Cl_2 at 23°C for 12 h provided the authentic *endo* - and *exo*-diastereomers (1:1 mixture) for comparison. The identities of *endo*- and *exo* -cycloadducts as well as *endo*-diastereomers were confirmed by comparison of ^{1}H-NMR and ^{13}C-NMR spectra of the authentic mixture (1:1) with the diastereomeric mixture obtained from various Lewis acid promoted cycloaddition reactions. The absolute configurations of all the new asymmetric centers of **4** and **5** were assigned after removal of the chiral sulfonamides and comparison of the optical rotations of the resulting norbornene-2-carboxylic acids with literature values.[10] For example, the cycloadducts resulting from the reaction in entry 8 were treated with aqueous lithium hydroxide in THF at 23°C for 24 h to provide the optically active norbornene-2(S)-carboxylic acid **6** (α_D^{23} -133, c, 1.1, $CHCl_3$; lit.[10] value; α_D^{23} -144.2, in $CHCl_3$). The enantiomeric excess of this asymmetric Diels-Alder reaction was calculated to be 91.5 % which is in agreement with the observed diastereomeric excess of **4b**/**5b** (92% de).[11] Similarly, ester hydrolysis of cycloadducts resulting from entry 5 provided norbornene-2(S)-carboxylic acid with 83% ee (α_D^{23} -120, c, 2.1, $CHCl_3$). The chiral auxiliaries were recovered (85-95%) after hydrolysis without loss of optical purity .

In summary, we have demonstrated that the acrylate esters of cis-1-arylsulfonamido-2-indanols derived from commercially available optically active *cis*-1-amino-2-indanols are efficient chiral auxiliaries for the Lewis acid promoted asymmetric Diels-Alder reaction. Further applications of aminoindanol derived chiral catalysts in asymmetric synthesis are in progress.

Acknowledgment: Financial support for this work was provided by the University of Illinois at Chicago. The authors thank Professor George Gould for helpful discussions.

References and Notes

1 (a) Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*, **1990**, Pergamon press; (b) Giuliano, R. M. *Cycloaddition Reactions in Carbohydrate Chemistry*, **1992**, American Chemical Society, washington, DC.

2. (a) Corey, E. J.; Letavic, M. A. *J. Am. Chem. Soc.* **1995**, *117*, 9616; (b) Furuta, K.; Iwanaga, K.; Yamamoto, H. *Tetrahedron Letters* **1986**, *27*, 4507; (c) Furuta, K.; Shimizu, S.; Miwa, Y.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 1481; (d) Kozikowski, A. P.; Ognyanov, V. I.; Chen, C,; Kurian, P.; Crews, F. T. *Tetrahedron Letters* **1993**, *34*, 219; (e) Waldmann, H. *Synthesis* **1994**, 535 and references cited therein.

3. (a) Oppolzer, W. *Comprehensive organic syntheses :Selectivity, Strategy and Efficiency in Modern Organic Chemistry;* Trost, B. M., Ed.; Pergamon Press: Oxford, **1991**; vol. 5, p 315; (b) Paquette, L. A. *Asymmetric Synthesis* , vol. 3 ; Morrison, J. D., Ed.; Academic Press, New York, **1984**, p 455; (c) Oppolzer, W. *Tetrahedron* **1987**, 1969; (d) Waldmann, H.; Braun, M. *Gazz. Chim. Ital.* **1991**, *121*, 277; (e) Helmchen, G.; Karge, R.; Weetman, J. *Modern Synthetic Methods*, vol. 4; Scheffold, R., Ed.; Springer; Heidelberg, **1986**; p 261; (f) Corey, E. J. *Pure Appl. Chem.* **1990**, *62*, 1209; (g) Corey, E. J.; Cheng, X-M.; Cimprich, K. A. *Tetrahedron Letters* **1991**, *32*, 6837; (h) Evans, D. A.; Chapman, K. T.; Bisaha, J. *Tetrahedron Letters* **1984**, *25*, 4071; (i) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1988**, *110*, 1238; (k) Kunz, H.; Ruck, K. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 336; (l) Waldman, H. *Kontakte (Darmstadt)* **1993**, *1*, 58; (m) Mathivanan, P.; Maitra, U. *J. Org. Chem.* **1995**, *60*, 364; (n) Gras, J-L.; Poncet, A.; Nouguier, R. *Tetrehedron Letters* **1992**, *33*, 3323.

4. (a) Corey, E. J.; Sarshar, S.; Lee, D.-H. *J. Am. Chem. Soc.* **1994**, *116*, 12089; (b) Corey, E. J.; Lee, D.-H. *Tetrahedron Asymmetry* **1995**, *6*, 3; (c) Corey, E. J.; Sarshar, S.; Bordner, J. *J. Am. Chem. Soc.* **1992**, *114*, 7938; (d) Corey, E. J.; Imwinkelreid, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493; (e) Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007; (f) Pindur, U.; Lutz, G.; Otto, C. *Chem. Rev.* **1993**, *93*, 741; (g) Deloux, L.; Srebnik, M. *Chem. Rev.* **1993**, *93*, 763; (h) Togni, A.; Venanzi, L. M. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 497; (i) Oh, T.; Reilly, M. *Org. Prep. Proceed. Int.* **1994**, *26*, 129.

5. (a) Ghosh, A. K.; Duong, T. T.; McKee, S. P. *J. Chem. Soc., Chem. Commun.* **1992**, 1673; (b) Ghosh, A. K.; Chen, Y. *Tetrahedron Letters* **1995**, *36*, 6811.

6. Available from Aldrich Chemical Co., Milwaukee, WI 53201 and Sepracor Inc., Marlborough, MA 01752.

7. **2a**: m.p. 136-138°C; α_D^{23} -33.5 (c, 2.6, $CHCl_3$) ; **2b**: m.p. 177-179°C; α_D^{23} -38.7 (c, 1.5, $CHCl_3$) ; **2c**: m.p. 144-146°C; α_D^{23} - 19.6 (c, 2.8, $CHCl_3$).

8. **4a** (from entry 5) : m.p. 169°C; $[\alpha]_D^{23}$ +7.96 (c , 1.85, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ ; 7.84 (d, 2 H, J = 8.3 Hz), 7.34 (d, 2 H, J = 8.1 Hz), 7.26 (m, 4 H), 6.15 (dd, 1 H, J = 5.6 , 3.0 Hz), 5.89 (dd, 1 H, J = 5.6 , 2.8 Hz), 5.18 (t, 1 H, J = 4.5 Hz), 5.09 (d, 1 H, J = 10.1 Hz), 4.93 (dd, 1 H, J = 10.2, 5.3 Hz), 3.10 (d, 1 H, J = 5.4 Hz), 3.05 (d, 1 H, J = 4.9 Hz), 2.90 - 2.77 (m, 3 H), 2.45 (s, 3 H), 1.83 (m, 1 H), 1.41 (m, 1 H), 1.29 - 1.2 (m, 2 H); MS (70 eV): m/z: 423 (M^+).

9. Berson, J. A.; Ben Efraim, D. A. *J. Am. Chem. Soc.* **1959**, *81*, 4083.

10. Berson, J.A.; Walia, J.S.; Remanick, A; Suzuki, S.; Reynolds-Warnhoff, P.; Willner, D. *J. Amer. Chem. Soc.* **1961**, *83*, 3986.

11. All new compounds gave satisfactory spectroscopic and analytical results.

(*Received in USA* 21 *November* 1995)