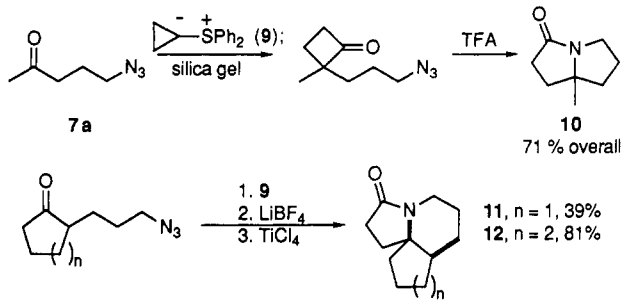
Scheme II



After the solution was allowed to stand for ca. 20 min at room temperature, the solvent was removed in vacuo, the residue subjected to a standard basic workup, and the product purified by column chromatography.[10,11] We have also determined that titanium tetrachloride (3.6–4.5 equiv) in CH_2Cl_2 is an excellent reagent for this transformation (cf. entries 2 vs 3, 6 vs 7, and 12 vs 13 in Table I).

A span of four atoms between the carbonyl group and the azide proved optimal (cf. entries 4 vs 6 and 11 vs 12). Thus, whereas **3a** reacted smoothly in TFA, similar treatment of **3c** resulted only in slow decomposition of the azide. Although a low yield of lactam **4c** could be obtained by prolonged dissolution in neat $BF_3{\cdot}OEt_2$, excellent results were realized when $TiCl_4$ was used. In addition, the insertion of a secondary azide proceeded uneventfully, demonstrating that the reaction was not overly sensitive to steric bulk as this site (entry 8).

Although we have not yet carried out detailed mechanistic studies, we favor the sequence of events drawn for the conversion **3a** → **4a** (Scheme I). The nucleophilic attack of the azide upon the protonated ketone is precedented in Boyer's work.[4] A comparison of entries 1 and 2 suggests that the reaction does not involve initial decomposition of the azide moiety: whereas the reaction **1a** → **2a** is complete within 1 h, treatment of **1b** in TFA for 1 h leads to the recovery of >90% starting material. We note that this mechanism is also consistent with higher reactivity of the four-carbon tether, because the antiperiplanar arrangement of the migrating bond and N_2^+ in intermediate **a** is ideally disposed for a stereoelectronically favored migration step.

We also demonstrate that this methodology should prove particularly useful for the rapid construction of complex ring systems when used in conjunction with modern methods of carbocycle synthesis (Scheme II). The addition of diphenylsulfonium cyclopropylide[12] to ketone **7a**, silica gel triggered rearrangement, followed by treatment with TFA gave the bicyclic lactam **10** in 71% overall yield. Two other tandem spiroannulation/ring adjustment reactions are also shown; lactams **11** and **12** were obtained as single diastereomers in the overall yields noted.

These examples demonstrate that the intramolecular Schmidt reaction is likely to have wide utility in the construction of polycyclic, nitrogen-containing materials. We are currently involved in the delineation of the scope of this process and its application to problems in alkaloid synthesis.

Acknowledgment. This work was supported by the National Institutes of Health. J.A. acknowledges an Eli Lilly granteeship (1989–1991).

Supplementary Material Available: Representative experimental procedures (3 pages). Ordering information is given on any current masthead page.

(10) The structure of **6b** was verified by X-ray crystallography to prove the regiochemistry of the reaction; details will be provided in the full paper. We thank Dr. Fusao Takusagawa of the University of Kansas Department of Chemistry for carrying out this determination.

(11) The conversion **5b** → **6b** could also be realized in 90% yield using 1.6 equiv of $BF_3{\cdot}OEt_2$ in CH_2Cl_2.

(12) See: Trost, B. M.; Scudder, P. H. *J. Am. Chem. Soc.* **1977**, *99*, 7601–7610 and references contained therein.

First Application of Attractive Intramolecular Interactions to the Design of Chiral Catalysts for Highly Enantioselective Diels–Alder Reactions

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The utility of chiral 1,3,2-oxazaborolidines[1] and 1,3,2-diazaborolidines[2] as catalysts in enantioselective synthesis has encouraged us to seek new members of this class which achieve selectivity through *attractive* interaction as well as the usual steric repulsion. This note describes a successful and practical methodology based on this approach, which we believe has wide implications in catalyst design and which deals specifically with catalysis of the Diels–Alder reaction.[3] Conceptually, we envisaged the possibility that the (*S*)-tryptophan-derived oxazaborolidine **1** would facilitate the Diels–Alder pathway represented by the transition-state assembly **2**, in which an attractive donor–acceptor interaction favors coordination of the dienophile at the face of boron which is cis to the 3-indolylmethyl substituent. In complex **2**, the π-basic indole and the π-acidic dienophile can assume a parallel orientation at the ideal separation (3 Å) for donor–acceptor interaction.[4] The product from such a catalytic reaction of cyclopentadiene, 2-bromoacrolein, and **1** is expected to be (2*R*)-2-bromobicyclo[2.2.1]hept-5-ene-2-carboxaldehyde (**3**). As described below, this surmise has been confirmed by experiment.

Reaction of *N*-(*p*-toluenesulfonyl)-(*S*)-tryptophan[5] with *n*-$BuB(OH)_2$ in 2:1 toluene–THF at reflux[6] with removal of water (CaH_2 in a Soxhlet thimble) gave after 6 h a solution of catalyst **1**, R = *n*-Bu, which showed a single ^{11}B NMR peak at 34 ppm (downfield from external $BF_3{\cdot}Et_2O$).[7] A solution of catalyst **1**, R = H,[7] was prepared in CH_2Cl_2 or $CDCl_3$ by the reaction of *N*-(*p*-toluenesulfonyl)-(*S*)-tryptophan with 1 equiv of $BH_3{\cdot}THF$ at 23 °C for 10 min (H_2 evolved immediately upon mixing). In the presence of 5 mol % of **1**, R = *n*-Bu, 2-bromoacrolein[8] and cyclopentadiene (ca. 5 equiv) underwent smooth Diels–Alder addition (−78 °C, 1 h) to give the (*R*)-bromo aldehyde **3** in 95% yield, 200:1 (R/S) enantioselectivity, and 96:4 (exo/endo CHO) diastereoselectivity; *N*-tosyltryptophan was efficiently recovered.[9]

(1) (a) Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551–5553. (b) Corey, E. J.; Bakshi, R. K.; Shibata, S.; Chen, C. P.; Singh, V. K. *J. Am. Chem. Soc.* **1987**, *109*, 7925–7926. (c) Corey, E. J.; Shibata, S.; Bakshi, R. K. *J. Org. Chem.* **1988**, *53*, 2861–2863. (d) Corey, E. J.; Bakshi, R. K. *Tetrahedron Lett.* **1990**, *31*, 611–614.

(2) Corey, E. J. *Pure Appl. Chem.* **1990**, *62*, 1209–1216.

(3) For previous studies of catalytic enantioselective Diels–Alder reactions, see: (a) Iwasawa, N.; Sugimori, J.; Kawase, Y.; Narasaka, K. *Chem. Lett.* **1989**, 1947–1950, and references cited. (b) Corey, E. J.; Imwinkelried, R.; Pikul, S.; Xiang, Y. B. *J. Am. Chem. Soc.* **1989**, *111*, 5493–5495. (c) Furuta, K.; Shimizu, S.; Miwa, Y.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 1481–1483. (d) Takemura, H.; Komeshima, N.; Takahashi, I.; Hashimoto, S.-I.; Ikota, N.; Tomioka, K.; Koga, K. *Tetrahedron Lett.* **1987**, *28*, 5687–5690. (e) Hashimoto, S.-I.; Komeshima, N.; Koga, K. *J. Chem. Soc., Chem. Commun.* **1979**, 437–438. (f) Takasu, M.; Yamamoto, H. *Synlett* **1990**, 194–196. (g) Sartor, D.; Saffrich, J.; Helmchen, G. *Synlett* **1990**, 197–198. (h) Corey, E. J.; Imai, N.; Zhang, H.-Y. *J. Am. Chem. Soc.* **1991**, *113*, 728–729.

(4) The expectation that **1** should be an effective accelerant for Diels–Alder reaction was strengthened by previous observations in our laboratory[2,3b] and that of Yamamoto.[3c]

(5) Prepared from (*S*)-tryptophan and 2.5 equiv of triethylamine in 10:1 H_2O–THF solution (0 °C) by addition of *p*-toluenesulfonyl chloride in THF and reaction at 23 °C for 3 h; mp 138–139 °C; $[\alpha]^{23}_D$ −42° (*c* 1, EtOH); 88%. The enantiomer was synthesized from (*R*)-tryptophan similarly.

(6) All reactions were performed under an inert atmosphere (Ar or N_2) and with rigorously dried solvents and glassware.

(7) The ^{11}B NMR data are consistent with structure **1**, R = *n*-Bu, as the major species.[1a] In the case of the BH_3-derived catalyst the ^{11}B NMR peak appears at 32.1 ppm.

(8) (a) Corey, E. J.; Snider, B. B. *J. Am. Chem. Soc.* **1972**, *94*, 2549–2550. (b) Prepared from acrolein by addition of Br_2 in CH_2Cl_2 at −78 °C and subsequent reaction with Et_3N; bp 50 °C (30 Torr).

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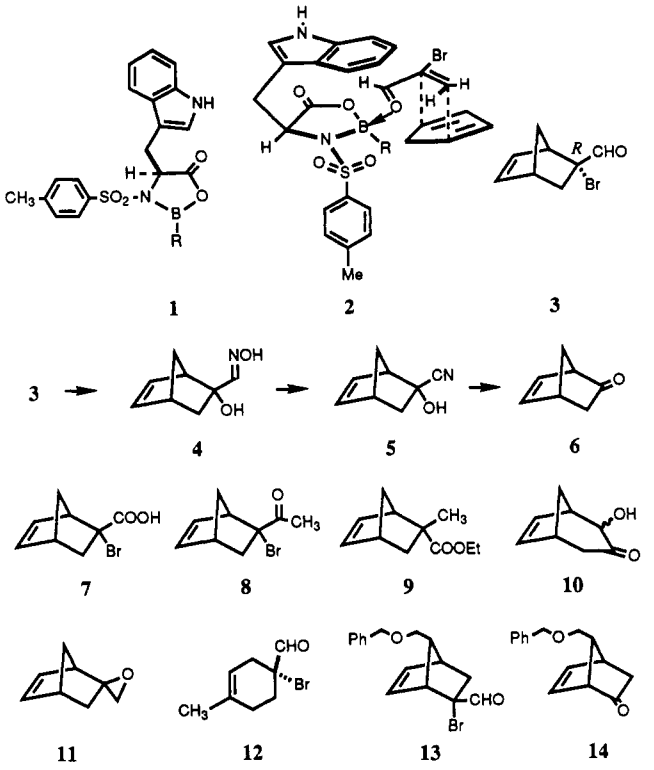
Chart I



Similar results were obtained for the catalyst **1**, R = H, under the same conditions: 98% yield, 98:2 (R/S) enantioselectivity and 97:3 (exo/endo CHO) diastereoselectivity. The minor, endo CHO, diastereomer could be removed to give pure exo adduct **3** by stirring the 94:6 exo–endo mixture with 4 mol % of aqueous $AgNO_3$ at 23 °C for 2 h and subsequent silica chromatography. The absolute configuration of the adduct from catalyst **1** was shown by conversion to the known dextrorotatory ketone **6**, $[\alpha]^{23}_D$ + 980° (*c* 0.3, $CHCl_3$),[10] via the sequence **3** → **4** (aqueous NH_2OH, 23 °C, 8 h, 61%); **4** → **5** → **6** (one flask) (TsCl–pyridine, 23 °C, 2 h; 1 M aqueous NaOH, 23 °C, 1 h, 86%).

2-Bromoacrolein is an outstanding dienophile in this catalytic Diels–Alder process not only because of the observed stereoselectivity (probably a consequence of a high s-cis preference) but also because of the exceptional synthetic versatility of the resulting adducts. To illustrate, **3** can be smoothly converted into **7** (aqueous $NaClO_2$),[11] **8** (CH_3Li; PCC), **9** (**8** with NaOEt–EtOH); **10** (aqueous K_2CO_3, 23 °C) (via the α-hydroxy aldehyde), and **11** ($NaBH_4$–EtOH; NaOH).[8a]

Isoprene and 2-bromoacrolein underwent Diels–Alder addition under catalysis by 5 mol % of **1**, R = H, at −40 °C for 48 h to form **12** (76%) with 96:4 enantioselectivity and complete position selectivity.[12]

The important intermediate for prostaglandin synthesis, **14**, was synthesized with remarkable ease. Reaction of the enantiomer of **1**, R = *n*-Bu or H, (5 mol %), 2-bromoacrolein and 5-(benzyloxymethyl)cyclopentadiene[13] (2.5 equiv) at −78 °C for 8 h in CH_2Cl_2 afforded the adduct **13** with 95:5 (exo/endo CHO) diastereoselectivity and greater than 96:4 enantioselectivity in 81–83% yield.[9,15] After removal of the minor endo aldehyde (stirring with 5 mol % aqueous $AgNO_3$) the product was transformed, by the two-flask sequence described above for **3** → **6**, into **14**, $[\alpha]^{23}_D$ −336° (*c* 0.9, $CHCl_3$) (92% ee; 54% overall yield), chromatographically and spectroscopically identical with an authentic sample of (±)-**14**.[14]

Of great mechanistic significance is the fact that the Diels–Alder reaction of cyclopentadiene and 2-bromoacrolein under catalysis of the oxazaborolidines corresponding to **1** from *N*-tosyl derivatives of (*S*)-valine or (*S*)-hexahydrophenylalanine gave the 2-(*S*)-enantiomer of **3** as major product with ca. 70% enantioexcess.[16] The *dramatically opposite* results for these amino acid derivatives and the (*S*)-tryptophan derivative **1** provide strong evidence for transition-state assembly **2**.

In conclusion, a new concept for the design of enantioselective catalysts has been supported by experiments which demonstrate a very practical and promising methodology for enantioselective synthesis.[17]

Supplementary Material Available: Procedures for the synthesis of **1**, **13**, and **14** together with spectroscopic and physical data (4 pages). Ordering information is given on any current masthead page.

(9) Diastereoselectivity was determined by 500-MHz ^1H NMR analysis. Enantioselectivity was determined *both* by 500-MHz ^1H NMR with the chiral shift reagent $Eu(tfc)_3$ (for **3**) or $Eu(hfc)_3$ (for **13**) (Aldrich) in $CDCl_3$ and by reduction with $NaBH_4$, conversion to the Mosher MTPA ester and ^1H NMR measurement. The figure given for enantioselectivity refers to the major (exo CHO) diastereomer.

(10) Paquette, L. A.; Doecke, C. W.; Kearney, F. R.; Drake, A. F.; Mason, S. F. *J. Am. Chem. Soc.* **1980**, *102*, 7228–7233.

(11) Corey, E. J.; Myers, A. G. *J. Am. Chem. Soc.* **1985**, *107*, 5574–5576.

(12) Absolute stereochemistry assigned by analogy with cyclopentadiene.

(13) Corey, E. J.; Koelliker, U.; Neuffer, J. *J. Am. Chem. Soc.* **1971**, *93*, 1489–1490.

(14) Corey, E. J.; Ravindranathan, T.; Terashima, S. *J. Am. Chem. Soc.* **1971**, *93*, 4326–4327.

(15) In this and the other Diels–Alder reactions described herein *N*-tosyltryptophan can be recovered efficiently for reuse.

(16) While the studies described herein were underway, results using various valine- and ethylglycine-derived oxazaborolidines as Diels–Alder catalysts appeared.[3f,8] In the reported cases the absolute stereocourse of the Diels–Alder addition was *opposite* to that observed for **1**, and the ee's averaged about 60%.

(17) This research was assisted financially by grants from the National Institutes of Health and the National Science Foundation.

Surface Reactions and Surface-Induced Dissociation of Polyatomic Ions at Self-Assembled Organic Monolayer Surfaces

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Chemical reactions involving molecules confined to specific environments are of growing interest in host–guest chemistry[1] and in surface science.[2] Reactions between gas-phase ionic reagents and molecules constrained to surfaces are potentially interesting and accessible examples of this general phenomenon. They have additional interest given the obvious analogy with conventional ion/molecule chemistry.[3] A few poorly characterized examples of chemical reactions between projectile ions and adsorbates present on surfaces have been reported,[4,5] and this study seeks to unambiguously confirm such reactions by employing self-assem-

(1) (a) *Crown ethers and analogs*; Patai, S., Rappoport, Z., Eds; Updates from the Chemistry of Functional Groups; John Wiley and Sons: New York, 1989. (b) Stoddart, J. F. Host Guest Chemistry. In *Annual Reports on the Progress of Chemistry, B*; Royal Society of Chemistry: London, 1988; Vol. 85, Chapter 12. (c) Smalley, R. E. *Sciences* **1991**, *March/April*, 22.

(2) Ceyer, S. T. *Science* **1990**, *249*, 133.

(3) (a) Bowers, M. T., Ed. *Gas Phase Ion Chemistry*; Academic Press: New York, 1979. (b) Graul, S. T.; Squires, R. R. *Mass Spectrom. Rev.* **1988**, *7*, 263. (c) Nibbering, N. M. M. *Adv. Phys. Org. Chem.* **1988**, *24*, 1.

(4) (a) Cooks, R. G.; Ast, T.; Mabud, Md. A. *Int. J. Mass Spectrom. Ion Processes* **1990**, *100*, 209. (b) Ast, T.; Mabud, Md. A.; Cooks, R. G. *Int. J. Mass Spectom. Ion Processes* **1988**, *82*, 131. (c) Bier, M. E.; Vincenti, M.; Cooks, R. G. *Rapid Commun. Mass Spectrom.* **1987**, *1*, 92.

(5) For a similar but independent idea and results, see the accompanying paper: Wysocki, V. H.; Jones, J. L.; Ding, J.-M. *J. Am. Chem. Soc.*, following paper in this issue.

0002-7863/91/1513-8967$02.50/0