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LANTHANIDE INDUCED INTRAMOLECULAR COUPLING OF ALDEHYDES AND KETONES WITH ELECTRON-DEFICIENT OLEFINS

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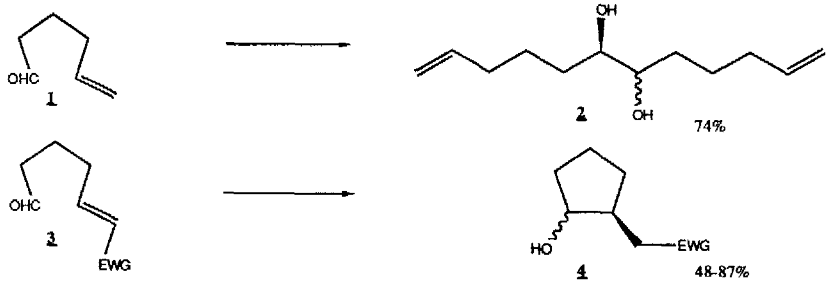
SUMMARY: Aldehydes or ketones with a δ,ε-olefin bearing a conjugating electron-withdrawing group undergo reductive cyclization with samarium iodide to afford five-membered rings. Diastereoselectivities of >250:1 have been obtained.

The application of lanthanide reagents to organic synthesis has become increasingly popular over the last five years.[1] Both samarium (II)- and ytterbium (II) halides have been effective in carbon-carbon bond forming reactions[2] and considerable attention has also been focussed on various intramolecular processes.[3] In this Letter we report our observations on the samarium iodide reductive cyclization of simple aldehydes and ketones with electron-deficient olefins to prepare substituted five-membered rings.[4]

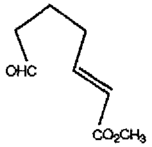
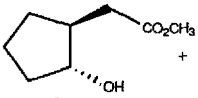
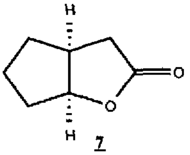
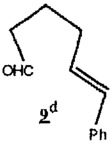
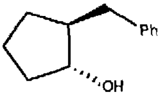
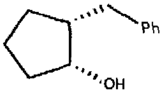
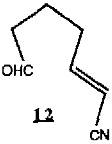
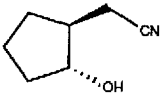
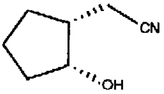
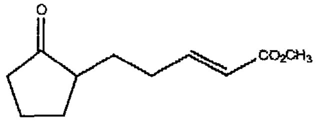
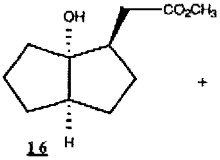
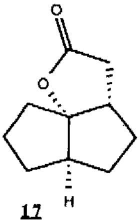
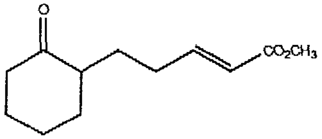
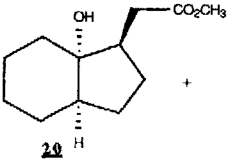
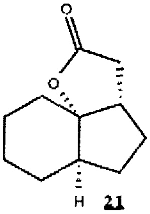
When 5-hexenal was reacted with SmI_2 (0.1M, 3 equiv) in THF at 0° C under dilute conditions (0.029M solution in aldehyde) with methanol as a proton donor, only the pinacol coupled product **2**[3(f)] could be isolated in 74% yield rather than the reductively cyclized product. However, when the same reaction conditions were applied to **3**, which possessed an electron-deficient olefin (EWG= CN, CO_2CH_3, Ph), the desired 2-substituted cyclopentyl alcohol **4** was obtained along with only minor amounts (ca. 5-15%) of the pinacol coupled byproduct. A number of substrates were examined which have been tabulated in Table I.



The yields for this reaction ranged from good to excellent for nearly all of the transformations depicted. The major diastereomeric product which was formed possesses a trans relationship between the hydroxyl and the substituted methylene appendage about the newly formed σ-bond.[5] Confirmation of the stereochemistry of the products was achieved by spectral comparison with known[6] compounds. In substrates involving an unsaturated methyl carboxylate moiety (entries 1, 2, 5, 6, and 7), the cis product was isolated as an annulated γ-lactone.[4,6(a),(b)] The trans:cis ratios generally ranged from ca. 2:1 to 3:1 for nearly every aldehyde tested. Moreover, the pinacol adduct was always observed as a minor byproduct in the reaction where aldehydes were used as starting compounds (entries 1-4), however, with the cyclic ketones (entries 5-7) no pinacol product was obtained. The cyclic ketones which posessed a trans disposed olefin (entries 5 and 7) produced the highest trans:cis ratios.

When we examined the relationship of the olefin geometry in the starting substrate vs. the

Table I

ENTRY	SUBSTRATE	CYCLIZED PRODUCTS	TRANS:CIS	YIELD[a]
		 6 +  7		
1.	5 E		3.1:1[b]	69%
2.	8 Z		1.8:1[b]	58%
3.	 9[d]	 10 +  11	2.5:1[b]	73%
4.	 12	 13 +  14	2.7:1[b]	72%
		 16 +  17		
5.	15 E		>250:1[c]	87%
6.	18 Z		1:1[c]	64%
7.	 19[e]	 20 +  21	11.5:1[c]	73%

[a] Yields refer to chromatographically homogeneous material with spectral data[6] (IR, ^{1}HNMR, ^{13}CNMR, MS) consistant with the structure shown. [b] Ratio determined by 300 MHz NMR. [c] Ratio determined by capillary GC on a 30m J&W DB1701 column. [d] The starting substrate in this example was a 5:1 E:Z mixture. [e] The starting substrate in this example was a 19:1 E:Z mixture.

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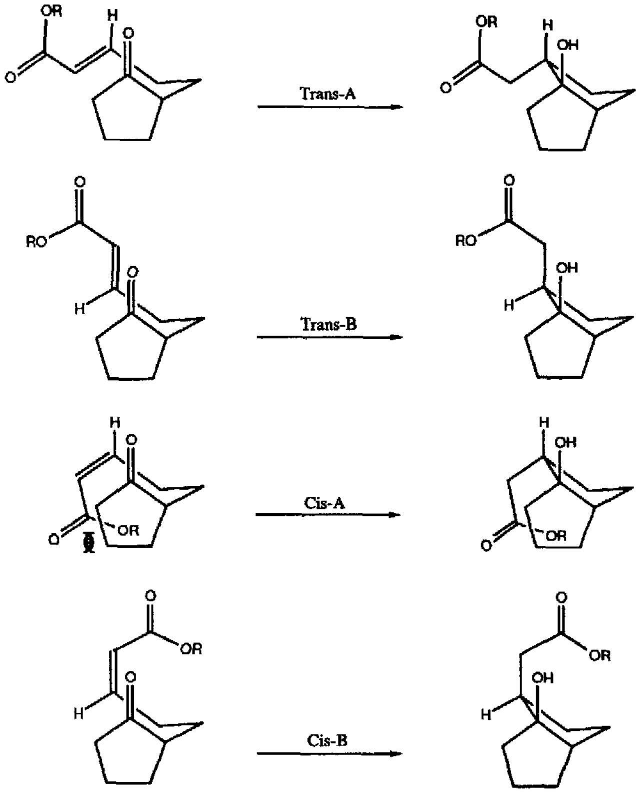
diastereoselectivity of the reductively cyclized products, we first compared aldehyde entries 1 and 2. Unfortunately, the E geometric isomer gave only a slightly better ratio favoring the trans disposed product in these two entries. *In marked contrast, when the two cyclopentanone cases in entries 5 and 6 were compared, a strong dependance of the product diastereoselectivity on the olefin geometry was observed.* The E geometric isomer **15** produced the trans product (>250:1) nearly exclusively, while the Z geometric isomer **18** led to an equal trans:cis mixture.

The preferred trans relationship of the major products in Table I is probably both steric and electronic in nature.[3d,g,h] Electrostatic repusions play a role in the transition state in addition to the expected nonbonding interactions between the oxygen anion and the developing methylene radical substituents. In the case of entry 5, where the product is almost solely trans, the steric constraints of the cyclopentanone ring only serve to amplify the electronically preferred trans arrangement of the appendages and favor[7] Trans-A over Trans-B, as shown in Scheme 1. The cis geometric isomer in entry 6 also has two similar conformations available, Cis-A and Cis-B. Conformation Cis-A, the electronically favored molecular geometry, has destabilizing steric interactions between the pendant α,β-unsaturated carboxylate moiety which nearly eclipses the cyclopentanone ring. Conformation Cis-B, the sterically favored molecular geometry, possesses unfavorable electrostatic interactions. The 1:1 trans:cis mixture probably results from both of these molecular geometries.

Scheme 1



Thus, the methodology described above provides an efficient reductive cyclization to produce 2-substituted cyclopentanols from simple aldehyde and ketone olefins mediated by the one electron transfer reagent SmI_2. With cyclic ketones, good to excellent stereocontrol over the two newly formed centers in the product can be achieved and the olefin geometry can play a crucial role in these cyclizations. This diastereoselectivity is the result of steric and electronic factors working in opposition or in concert.

REFERENCES AND NOTES

(1) For recent reviews on lanthanides in organic synthesis see: (a) Natale, N. R. Org.Prep.Proced. Int. **1983**, *15*, 387; (b) Kagan, H. B. "4f Elements in Organic Synthesis" in "Fundamental and Technological Aspects of Organo-f-Element Chemistry," Marks, T. J.; Fragala, I. L. Eds. R. Reidel, Boston, **1984**, p.49.

(2) (a) Girard, P. Namy, J. L.; Kagan, H. B. J. Am. Chem. Soc. **1980**, *102*, 2693; (b) Kagan, H. B.; Namy, J. L.; Girard, P. Tetrahedron **1981**, Suppl. 1, *37*, 175; (c) Souppe, J.; Namy, J. L.; Kagan, H.B. Tetrahedron Lett. **1982**, 3497; (d) Hou, Z.; Fujiwara, Y.; Jintoku, T.; Mine, N.; Yokoo, K.;

(3) (a) Molander, G. A.; Etter, J. B. Tetrahedron Lett. **1984**, *25*, 3281; (b) Okuda, Y.; Nakasukatsa, S.; Oshima, K.; Nozaki, H. Chem. Lett. **1985**, 481; (c) Molander, G. A.; Etter, J. B. J. Org. Chem. **1986**, *51*, 1778; (d) Molander, G. A.; Kenny, C. Tetrahedron Lett. **1987**, 4367; (e) Molander, G. A.; Etter, J. B.; Zinke, P. W. J. Am. Chem. Soc. **1987**, *109*, 453; (f) Molander, G. A.; Kenny, C. J. Org. Chem. **1988**, *53*, 2132; (g) Fukuzawa, S.; Nakanishi, A.; Fujinami, T.; Sakai, S. J. Chem. Soc. Chem. Comm. **1986**, 624; (h) Otsubo, K.; Inanaga, J.; Yamaguchi, M. Tetrahedron Lett. **1986**, 5763; (i) Fevig, T. L.; Elliott, R. L.; Curran, D. P. J. Am. Chem. Soc. **1988**, *110*, 5064.

(4) A similar reaction has been utilized in a synthesis of γ-lactones,[3(g)] see: (a) Fukuzawa, S.; Iida, M.; Nakanishi, A. Fujinami, T.; Sakai, S. J. Chem. Soc. Chem. Comm. **1987**, 920; (b) Fukuzawa, S.; Nakanishi, A., Fujinami, T.; Sakai, S. J. Chem. Soc. Perkin I **1988**, 1669.

(5) (a) Shono, T.; Nishiguchi, I.; Ohmizu, H.; Mitani, M. J. Am. Chem. Soc. **1978**, *100*, 545; b) Kariv-Miller, E.; Mahachi, T. J. J. Org. Chem. **1986**, *51*, 1041; (c) Pradhan, S. K.; Kadam, S. R.; Kolhe, J. N.; Radhakrishnan, S. V.; Sohani, V. B.; Thaker, J. J. Org. Chem. **1981**,*46*, 2622; (d) Corey, E. J.; Pyne, S. G. Tetrahedron Lett. **1983**, 2821; (e) Ikeda, T.; Nishiguchi, I.; Omizu, H.; Chem.Lett. **1976**, 1233

(6) For compounds 5-7, 15-21, 23, and 24 see: (a) Fox, D. P.; Little, R. D.; Baizer, M. M. J. Org. Chem. **1985**, *50*, 2202; (b) Little, R. D.; Fox, D. P.; Hijfte, L. V. Dannecker, R. Sowell, G. Wolin R. L.; Moens, L.; Baizer, M. M. J. Org. Chem. **1988**, *53*, 2287; for compounds 10 and 11 see: (c) Sehgal, R. K.; Koenigsberger, R. U.; Renate, U.; Howard, T. J. J. Chem. Soc. Perkin Trans. I **1976**, *2*, 191.

(7) (a) Belloti, D.; Cossy, J.; Pete, J. P.; Portella, C. Tetrahedron Lett. **1985**, 4591; (b) Beckwith, A. L. J. Tetrahedron **1981**, *37*, 3073.

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