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Communications

Silicon-Directed Nazarov Cyclizations. 8. Stereoelectronic Control of Torquoselectivity

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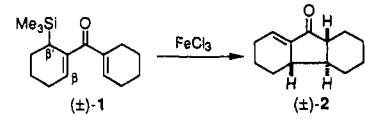
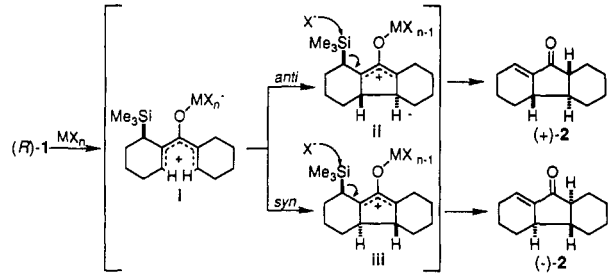
Summary: The silicon-directed Nazarov cyclization of the optically active β′-silyldivinyl ketones (+)-1 and (−)-1 proceeded with near perfect stereoselectivity. The direction of conrotatory electrocyclic ring closure was controlled by the remote silyl group such that carbon–carbon bond formation occurred in an anti S_E' sense to the silicon electrofuge.

A recent disclosure from these laboratories[1] reported a new variant of the silicon-directed Nazarov cyclization (SDNC),[2a,b] which was capable of constructing linear tricyclic compounds with various ring sizes (Scheme I). This reaction is notable for its facility and stereoselectivity. A unique feature of this cyclization which distinguishes it from the original variant with a β-silyl group is the presence of a silicon-bearing β′-stereogenic center. Thus, the educts are *intrinsically* chiral. In the original version, materials that were chiral by virtue of ring substitution (alkyl, aryl, and heteroatomic groups) were extensively investigated[2c,d] with regard to diastereoselection. In those cases the two, allowed conrotatory pathways led to diastereomeric products. The case at hand represents an interesting subset of this phenomenon since the original, silyl-bearing stereogenic center in **1** is destroyed. The two, opposite conrotatory pathways remain diastereomeric and result in two different orientations of the silyl moiety with respect to the π system (ii and iii, Scheme II). Now, however, the two complementary pathways lead to *enantiomers* of **2** (Scheme II). Therefore, to elucidate the influence of the silyl group on the sense of controtation, a nonracemic sample of **1** with known absolute configuration is required. *We report herein that the silyl moiety exerts near perfect control over the electrocyclization to* **2** *in an anti-*S_E' *sense.*

Scheme I



Scheme II



Initial attempts to prepare **1** in nonracemic form by silylcupration[3] proved fruitless. Thus, we resorted to classical resolution of a racemic intermediate as outlined in Scheme III. Allylsilane (±)-**3**[4] was prepared from 2,3-dibromocyclohexene as previously described.[1] Carboxylation of the vinyllithium[5] species derived from (±)-**3** afforded acid (±)-**4**,[4] which was reduced via a mixed anhydride[6] to alcohol (±)-**5**.[4] Resolution of (±)-**5** was accom-

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(3) (a) Fleming, I.; Thomas, A. P. *J. Chem. Soc. Commun.* **1986**, 1456. (b) Laycock, R.; Maynard, I.; Wickham, D.; Kitching, W. *Aust. J. Chem.* **1988**, *41*, 693.
(4) All new compounds were fully characterized by ^1H (300 MHz), ^{13}C (75.5 MHz) NMR, IR, MS, combustion analysis (±0.3%), and $[\alpha]_D$ (where appropriate).
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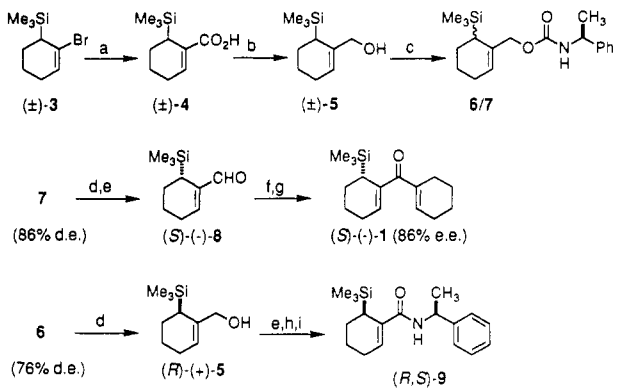
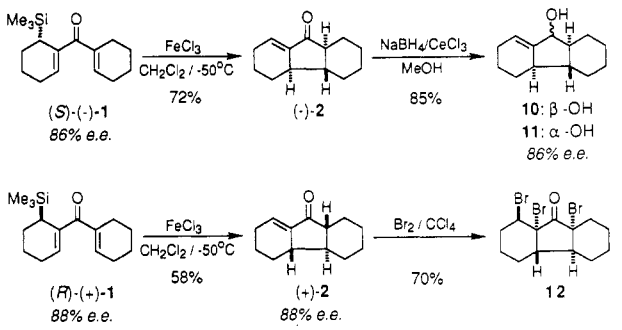
Scheme III[a]



[a] (a) *t*-BuLi, −78 °C, THF, then CO_2, Et_2O, −65 to 25 °C, 84%; (b) $ClCO_2Et$, THF, then $NaBH_4$, H_2O, 25 °C, 73%; (c) (*S*)-(1-phenylethyl)isocynate, toluene, 110 °C, 20 h, 80%; (d) $HSiCl_3$/Et_3N, toluene, 110 °C, 2.0 h, 75%; (e) MnO_2, CH_2Cl_2, 25 °C, 48 h, 71%; (f) cyclohexyltrisylhydrazone/*s*-BuLi, TMEDA/hexane, −78 to 25 °C, 75%; (g) $BaMnO_4$, CH_2Cl_2, 25 °C, 48 h, 70%; (h) $NaClO_2/H_2O_2$, 10 °C, 1 h, 76%; (i) (*S*)-(1-phenylethyl)amine/DCC/HOBT, THF, 25 °C, 1 h, 70%.

Scheme IV



plished by MPLC separation of the diastereomeric carbamates **6**[4] (t_R 11 min) and **7**[4] (t_R 12 min) derived from (*S*)-(1-phenylethyl)isocyanate[7a,b] (99% ee). Cleavage[7c] of the more polar diastereomer **7** (86% de) produced (−)-**5**[4] without racemization as judged by HPLC analysis of the *N*-(1-phenylethyl)carbamate derivative (86% de). The synthesis of (−)-**1**[4] continued by oxidation of (−)-**5** to aldehyde (−)-**8**[4] followed by 1,2-addition of cyclohexenyllithium[9] and oxidation of the resulting divinyl carbinol[10] to afford the target ketone. A parallel synthesis from the less polar carbamate **6** produced (+)-**1** with 88% ee. While the enantiomeric excess of (−)-**1** and (+)-**1** were safely assumed, the absolute configurations had to be independently established. This was accomplished by cleavage of the less polar carbamate **6** followed by oxidation[11] of the alcohol (+)-**5** to the acid (+)-**4**, which was coupled with (*S*)-(1-phenylethyl)amine to form **9**.[4] X-ray crystallographic analysis of **9**[12] established the configuration at the silyl-bearing center as *R* as shown in Scheme III.

The SDNC of (−)-**1** and (+)-**1** proceeded cleanly and rapidly to (−)-**2** and (+)-**2**,[1,4] respectively (Scheme IV). The enantiomeric purities of (−)-**2** and (+)-**2** were established by reduction[13] of each to a 4:1 mixture of alcohols **10** and **11**. *Pirkle analysis of both* ***10*** *and* ***11*** *showed their enantiomeric purities to be 86% ee for* (−)-***2*** *and 88% ee for* (+)-***2****, indicating completely stereoselective electrocyclizations.* After many unsuccessful attempts to prepare suitable, crystalline derivatives of **2** or **10**, we finally succeeded in establishing the absolute configuration of (+)-**2** by anomalous dispersion X-ray crystallographic analysis[14] of the derived tribromide **12**.[4] The correct configuration is depicted in Scheme IV. Thus, the tricyclic ketone (+)-**2** arises from a counterclockwise, conrotatory cyclization of (+)-**1** and corresponds to an anti-S_E' pathway[15,16] in the electrocyclization (Scheme I).

The factors governing the sense of conrotatory electrocyclic reactions (torquoselectivity)[17] have been reexamined recently. The electrocyclic interconversion of substituted 1,3-butadienes and cyclobutenes was once thought to be dominated by steric effects.[18] Dolbier[19] and Houk[20a] have now provided experimental support for the existence of a contrasteric component. Theoretical[20b] analysis identifies a strong stereoelectronic contribution that is substituent dependent. Neither of these steric or stereoelectronic considerations is applicable here. The cationic nature of this electrocyclization is surely responsible for the significant role played by the remote silicon substituent.[21] Examination of models clearly shows that only in the anti-conrotatory pathway does the silyl moiety experience continuous overlap with the cation system in the stereoelectronically correct alignment.[22] This feature was identified as the reason for the dramatic rate acceleration

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(11) Dalcanale, E.; Montanari, F. *J. Org. Chem.* **1986**, *51*, 567.

(12) Material for the X-ray analysis of **9** was obtained from racemic **4** and (*S*)-(1-phenylethyl)amine. The less polar diastereomer of **9** belongs to the same configurational family as **6**.

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(14) Least-squares refinement of the enantiomer converged at R = 0.045 and R_w = 0.053; of the 50 most enantiomer sensitive reflections measured, only 1 predicted the alternate enantiomer.

(15) An anti-S_E' pathway has been established for allylsilanes with a variety of electrophiles; however, cyclohexenysilanes show variable selectivity.[16] (a) Hayashi, T.; Konishi, M.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962. (b) Hayashi, T.; Konishi, M. Kumada, M. *Ibid.* **1982**, *104*, 4963. (c) Hayashi, T.; Okamoto, Y. Kabeta, K.; Hayihara, T. Kumada, M. *J. Org. Chem.* **1984**, *49*, 4224. (d) Hayashi, T.; Matsumoto, Y.; Ito, Y. *Organometallics* **1987**, *6*, 884. (e) Fleming, I.; Terrett, N. K. *J. Organomet. Chem.* **1984**, 264, 99. (e) Fleming, I. *Pure Appl. Chem.* **1988**, *60*, 71. (f) Wickham, G.; Kitching, W. *J. Org. Chem.* **1983**, *48*, 612. (g) Matassa, V. G.; Jenkins, P. R.; Kumin, A.; Damm, L.; Schreiber, J.; Felix, D.; Eschenmoser, A. *Isr. J. Chem.* **1989**, *29*, 321. For a syn-S_E' see: (h) Wetter, H.; Scherer, P.; Schweizer, W. B. *Helv. Chim. Acta* **1979**, *62*, 1985. (i) Wetter, H.; Scherer, P. *Helv. Chim. Acta* **1983**, *66*, 118.

(16) For example, we have found that epoxidation of 1-[(benzyloxy)methyl]-6-(trimethylsilyl)-1-cyclohexene is ca. 30% anti selective. However, we have recently established that *intramolecular* allylsilane–aldehyde condensations in 1-[(trialkylsilyl)methyl]cyclohexenes occur with >95% anti selectivity. Denmark, S. E.; Almstead, N. G., manuscript in preparation.

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(19) (a) Dolbier, W. R., Jr.; Koroniak, H.; Burton, D. J.; Heinze, P. L.; Bailey, A. P.; Shaw, G. S.; Hansen, S. W. *J. Am. Chem. Soc.* **1987**, *109*, 219. (b) Dolbier, W. R., Jr.; Koroniak, H.; Burton, D. J.; Bailey, A. P.; Shaw, G. S.; Hansen, S. W. *Ibid.* **1984**, *106*, 1871. (c) Dolbier, W. R., Jr.; Phansteil, O. *Tetrahedron Lett.* **1988**, *29*, 53.

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(21) For stereoelectronic effects in ring opening solvolysis of cyclopropyl halides, see ref 17c.

(22) (a) Lambert, J. B.; Wang, G.; Finzel, R. B.; Teramura, D. H. *J. Am. Chem. Soc.* **1987**, *109*, 7838. (b) Ibrahim, M. R.; Jorgensen, W. L. *Ibid.* **1989**, *111*, 819. (c) Lambert, J. B.; Wang, G. *J. Phys. Org. Chem.* **1989**, *1*, 169.

in the β′- silyl variant.[2] We have now demonstrated the stereochemical significance of this effect.

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Supplementary Material Available: A listing of crystal and positional parameters, bond lengths and angles, and torsional angles for **9** and **12** (23 pages). Ordering information is given on any current masthead page.

A Novel Oxidation of Internal Alkynes with Hydrogen Peroxide Catalyzed by Peroxotungsten Compounds

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Summary: Internal alkynes underwent a novel oxidation with aqueous hydrogen peroxide catalyzed by peroxotungsten compounds under two-phase conditions using chloroform as the solvent, giving α,β-epoxy ketones and α,β-unsaturated ketones as principal products. The epoxidation of α,β-unsaturated ketones by this catalyst–oxidant system appeared to involve the electrophilic attack of the peroxo species to the double bond.

In general, alkynes are converted into either 1,2-dicarbonyl compounds or carboxylic acids by permanganate,[1] ruthenium tetraoxide,[2] osmium tetraoxide,[3] thallium nitrate,[4] and metal peroxide like $(HMPA)MoO(O_2)_2$ in the presence of $Hg(OAc)_2$,[5] as well as peroxy acids.[6] Although hydrogen peroxide oxidation of acetylenes has been applied in fewer examples than peroxy acids,[7] it has recently been reported that alkynes are oxidized to keto aldehydes or 1,2-dicarbonyl compounds with hydrogen peroxide catalyzed by $NaMO_4$[8] or $(cetylpyridinium)_3PMO_{12}O_{40}$ (M: Mo or W)[9] in combination with $Hg(OAc)_2$, which is an essential component to complete the oxidation.

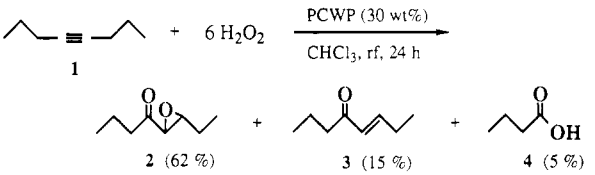
In a previous paper, we showed that treatment of 12-tungstophospholic acid or 12-molybdophosphoric acid in 35% H_2O_2 with cetylpyridinium chloride (CPC) in water easily produced peroxotungstophosphate (PCWP) or peroxomolybdophosphate (PCMP), respectively, containing the cetylpyridinium moiety as the counter cation.[10,11] The PCWP and PCMP thus prepared stoichiometrically oxidized not only a variety of substrates (i.e., olefins to epoxides, *sec*-alcohols to ketones, α,ω-diols to lactones, and 1,2-diols to carboxylic acids), but also catalyzed the oxidation of the same substrates with 35% H_2O_2.[10,11]

Table I. Oxidation of 4-Octyne (1) with 35% H_2O_2 Catalyzed by Several Peroxoheropoly Compounds[a]

				yield,[b] %		
run	catalyst	H_2O_2	conv, %	**2**	**3**	**4**
1	PCWP	6	98	54	12	12
2[c]	PCWP	6	98	32	–	73 (26)[d]
3	PCWP	3	92	47	13	7
4	PCWP	3 + 3[e]	98	62	15	5
5	PHWP	6	80	25	30	5
6	**5**	6	76	26	27	4

[a] 1 (3 mmol) was allowed to react with 35% H_2O_2 in the presence of catalyst (30 wt %) in $CHCl_3$ (7.5 mL) under refluxing for 24 h. [b] Determined by VPC analysis. Based on 1 used. Remainders were unidentified products. [c] *t*-BuOH was used as solvent. [d] Yield of propionic acid. [e] After 8 h, another portion of H_2O_2 was added.

We now find that the PCWP catalyzed a novel oxidation of internal alkynes with aqueous hydrogen peroxide to form α,β-epoxy ketones as the principal product (eq 1). This is the first catalytic transformation of internal alkynes into α,β-epoxy ketones.[12]



4-Octyne (1) was chosen as a model substrate and allowed to react with 35% H_2O_2 under the influence of several heteropoly compounds as catalysts (Table I).

The oxidation of 1 with 35% H_2O_2 (6 equiv) in the presence of a catalytic amount (30 wt %, 1.6 mol %) of PCWP under two-phase conditions using chloroform as the solvent produced 3,4-epoxy-5-octanone (**2**), 5-octen-4-one (**3**), and a small amount of cleaved product, butyric acid (**4**). The stereochemistry of **2** and **3** was determined by comparing their spectral data to those of authentic samples. Under homogeneous conditions using *tert*-butyl alcohol as the solvent, the yield of **2** decreased and a

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(12) It is reported that di-*tert*-butylacetylene is oxidized with MCPBA to form α,β-epoxy ketone through the 1,2-migration of methyl group.[6b]

0022-3263/90/1955-5545$02.50/0