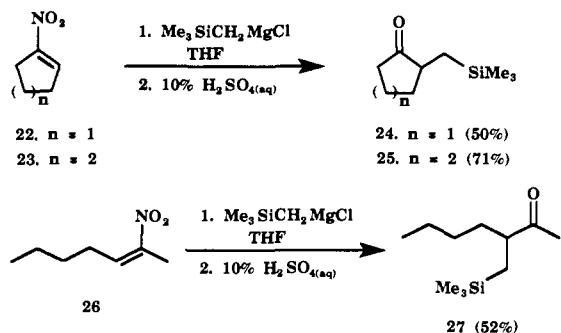


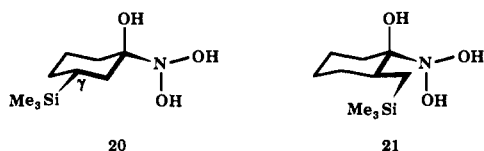
Scheme III



By the same procedure, we were able to convert the saturated silicon-containing nitro compound **8** to ketone **10** in excellent yield (91%, Scheme II). In contrast, the corresponding nitro compound **9**, without a γ -silyl group, gave ketone **11** in 16% yield under these mild conditions.

To prove the generality of the silicon-promoted Nef reaction, we reacted γ -silyl nitro compound **12** with KH and then with 3.5% aqueous HCl (Scheme II). The corresponding ketone **16** was obtained in 87% yield. Nonsilylated nitro compound **13**, however, gave ketone **17** in only 8% yield. Also, conversion of γ -silyl nitro compound **14** to ketone **18** (85% yield) was much more efficient than conversion of nonsilylated nitro compound **15** to ketone **19** (18% yield).

In the reaction **12** \rightarrow **16**, the possible intermediate **20** can hold a "W" conformation for the Si–C–C–N backbone. The carbocation resulting from the C–N bond cleavage¹⁶ in **20** can be stabilized by the γ -silicon. In the reaction **14** \rightarrow **18**, however,



the Si–C–C–N backbone in the intermediate may possess an "endo-Sickle" conformation¹⁷ (see **21**) or have a "W" conformation through a ring flip. Shiner et al. reported that a γ -silyl substituent enhances the solvolytic reactivity of secondary alkyl sulfonate esters by a factors of 10–100,^{4–6} the carbocation involved is stabilized by interaction with the back lobe of the Si–C bond in either a "W" or an "endo-Sickle" conformation.

To intensify the applicability of the silicon γ -effect to synthesis, we developed a "one-flask" method for the preparation of β -trimethylsilyl ketones from nitro olefins (Scheme III). We added 1-nitrocyclohexene (**23**) to a THF solution of $\text{Me}_3\text{SiCH}_2\text{MgCl}$ (1.1 equiv) at -20°C . After 30 min at 0°C , the solution was acidified to pH 3.0 by addition of 10% aqueous H_2SO_4 . The desired β -silyl ketone **25** was obtained in 71% yield. By the same procedure, we produced β -silyl ketone **24** in 50% yield from 1-nitrocyclopentene (**22**) and obtained β -silyl ketone **27** in 52% yield from 2-nitrohept-2-ene (**26**).

In conclusion, the γ -effect of silicon was found to facilitate the Nef reaction. The use of KH and aqueous HCl enabled conversion of nitro compounds with a γ -trimethylsilyl group to ketones much more efficiently than conversion of the corresponding nitro compounds without a silyl group. This unprecedented silicon-promoted Nef reaction was applied to a "one-flask" synthesis of β -silyl ketones from nitro olefins. β -Silyl ketones are valuable substrates for silicon-directed Norrish type I cleavage^{18,19} and can be used in the development of silicon-containing photodegradable polymers.

Acknowledgment. For financial support, we thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Council of the Re-

public of China (NSC 80-0208-M007-85). B.A.G. thanks Dr. Henry Sonneborn III for a fellowship.

Supplementary Material Available: General experimental and preparation details and analysis (including ^1H NMR and IR) of **6**, **8**, **10–12**, **14**, **16–19**, **22**, and **24–27** (9 pages). Ordering information is given on any current masthead page.

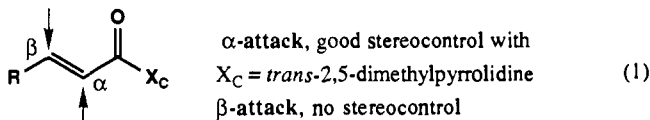
New Chiral Auxiliary for Asymmetric Thermal Reactions: High Regio- and β -Stereoselectivity in Asymmetric Radical Addition Reactions to Mixed Fumarimides

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Porter and Giese have recently reported the first examples of high α -stereoselection in the additions of achiral radicals to amide-substituted alkenes containing the 2,5-dimethylpyrrolidine auxiliary; however, there is no stereocontrol if the radicals attack the β -position (see eq 1).³ Because ester- or amide-based chiral auxiliaries normally direct attack of nucleophilic radicals to the β -position, a more natural approach is to develop auxiliaries that control β -stereochemistry. We now report high regio- and β -stereoselection in the addition of achiral radicals to a mixed fumarimide substituted with a new chiral auxiliary derived from Kemp's triacid.⁴



The chiral auxiliary used in this study is prepared from Kemp's triacid in six steps and 62% overall yield, as outlined in eq 2.⁵ Imide formation is accomplished in 91% yield by heating Kemp's triacid and urea in triglyme at 200°C . Treatment of the imide acid with SOCl_2 followed by 2-aminophenol gives the imide amide **2** in 92% yield. Two-step reduction of the imide with NaBH_4 and triethylsilane affords a lactam amide (84%), which upon heating with SOCl_2 affords the racemic auxiliary **3** in 89% yield. Resolution of the auxiliary is effected by acylation of the lactam with (–)-menthyl chloroformate, separation of the diastereomers by flash chromatography, and regeneration of the optically active auxiliaries with trifluoroacetic acid (40% and 36% yields). The absolute configuration of the enantiomers was determined by a single-crystal X-ray structure of one of the menthyl carbamate diastereomers.⁶ Standard lactam acylation procedures gave poor yields (<40%) of the desired fumarimide substrate **4**, so we developed a high-yielding hybrid of existing lactam acylation technology. The key to the success of this procedure is the in situ

(1) Dreyfus Teacher-Scholar, 1986–1991. NIH Research Career Development Awardee, 1987–1992. ICI Pharmaceuticals Awardee, 1990.

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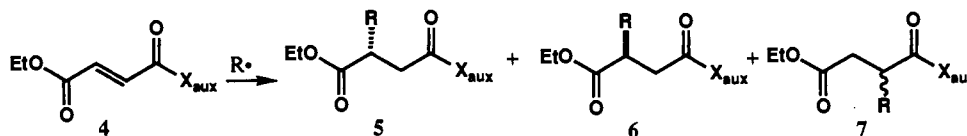
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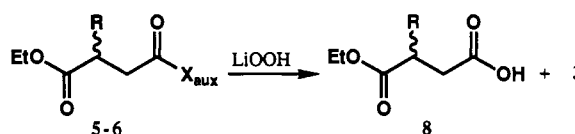
Table I. Asymmetric Radical Additions to Fumarimide 4



entry	substrate	R [*]	method ^a	temp, °C	ratio, 5:6:7 ^b	% yield
1	<i>rac</i> -4	<i>tert</i> -butyl	tin	80	78:19:3	64
2	<i>rac</i> -4	<i>tert</i> -butyl	mercury	25	88:9:3	— ^c
3	(<i>R</i>)-4	<i>tert</i> -butyl	mercury	0	88:9:3	69
4	<i>rac</i> -4	<i>tert</i> -butyl	mercury	-20	96:4:— ^d	— ^c
5	<i>rac</i> -4	<i>tert</i> -butyl	mercury	-40	97:3:— ^d	70
6	(<i>S</i>)-4	cyclohexyl	mercury	-20	94:6:— ^{d,e}	68
7	(<i>S</i>)-4	hexyl	mercury	0	82:18:— ^{d,e}	42

^a Tin: syringe pump addition of Bu₃SnH (0.66 M; 4.1 equiv) and AIBN (0.08 M; 0.5 equiv) in C₆H₆ added to 4 (0.16 M) and *tert*-butyl iodide (0.32 M; 4.0 equiv) in C₆H₆ at 80 °C for 6 h. Mercury: fumarimide 4 (0.08 M) and alkylmercuric halide (1.5 equiv) in CH₂Cl₂ stirred with excess solid NaBH₄ and H₂O for 2 h. ^b Ratios determined by capillary GC. ^c Not isolated. ^d Less than 3% detected. ^e Products are enantiomers of 5 and 6.

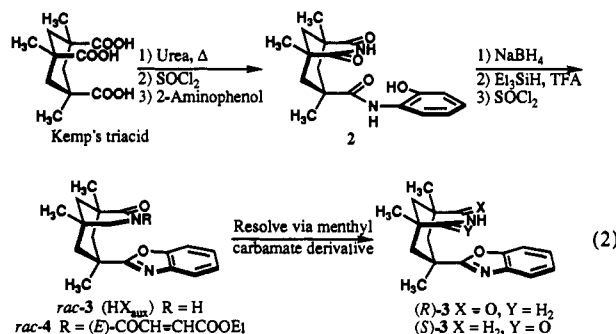
Table II. Cleavage of Radical Addition Products 5–6 to Succinates 8 and Auxiliary 3



entry	auxiliary	R	% yield of 8	[α] _D	confign	% recovery of 3 ^b
1	(<i>R</i>)-4	<i>tert</i> -butyl	95	+14.1°	<i>S</i>	82
2	(<i>S</i>)-4	cyclohexyl	87	-10.6° ^a	<i>R</i>	83
3	(<i>S</i>)-4	hexyl	79	-7.6° ^a	<i>S</i>	89

^a Rotation of diethyl ester. ^b Isolated yield after flash chromatography.

formation of an *N*-trimethylsilyl lactam⁷ (*n*-BuLi/Me₃SiCl, -78 °C); acylation of the *N*-silyl derivative of 3 with ethyl fumaryl chloride gives 4 in 83% yield.



Giese reactions with 4 were performed either by the "tin method"⁸ at 80 °C or by the "mercury method"⁹ at ambient temperature or below, and the results of these reactions are summarized in Table I. Syringe pump addition of a solution of Bu₃SnH (0.66 M; 4.1 equiv) and AIBN (0.08 M; 0.5 equiv) in C₆H₆ to a solution of *rac*-4 (0.16 M) and *tert*-butyl iodide (0.32 M; 4.0 equiv) in C₆H₆ at 80 °C over 6 h affords a mixture of the *tert*-butyl addition products 5, 6, and 7 in a ratio of 78:19:3, and the combined isolated yield after flash chromatography is 64% (Table I, entry 1). The product distribution was determined by VPC analysis of the crude reaction mixture, and the retention times of the products were correlated with authentic mixtures of each of the regioisomeric diastereomers.¹⁰ The extent of asym-

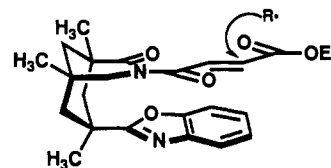


Figure 1. Transition-state model.

metric induction of the minor product 7 was not determined, but is assumed to be high.¹¹

Significantly higher selectivities were obtained at lower temperatures. Treatment of a CH₂Cl₂ solution of (*R*)-4 (0.08 M) and 1.5 equiv of *tert*-butylmercuric chloride with several equivalents each of solid NaBH₄ and H₂O at 0 °C gives a 69% isolated yield of 5, 6, and 7 in a 88:9:3 ratio (entries 2 and 3). Below 0 °C, the minor regioisomer is not detected and the diastereoselectivity increases to ≥96:4 (entries 4 and 5). The high regioselectivity (≥97:3) and β-stereoselectivity (≥91% de) are unprecedented in radical additions to chiral, unsymmetrical alkenes. Decreasing the steric bulk of the incoming radical has a measurable effect on the stereoselectivity of the addition: cyclohexyl (entry 6, 88% de) and hexyl (entry 7, 64% de) radicals afford the β-addition products in 68% and 42% isolated yields.¹²

The absolute configurations of the addition products were determined by removal of the chiral auxiliary and correlation of the succinic acid derivatives to compounds of known absolute configuration (see Table II). Unlike amide linkages to auxiliaries that are often difficult to hydrolyze or reduce,^{3a} these imide linkages are readily hydrolyzed with lithium hydroperoxide¹³ to

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(10) The authentic mixtures were prepared by acylation of the auxiliary with the racemic regioisomers of ethyl 3-(chlorocarbonyl)-*tert*-butylpropanoate.

(11) Experiments in progress indicate that the α-stereoselectivities in reactions of radicals bearing this chiral auxiliary range from 95:5 to as high as 99:1. J. Stack, unpublished results.

(12) Although we did not prepare authentic samples of the minor regioisomers and diastereomers, we detect no more than ~2% of the minor regioisomer by ¹H NMR spectroscopy.

give the carboxylic acid and the recovered auxiliary. These conditions allow isolation of the succinic half-ester **8** and the recovery of the chiral auxiliary in high yield. Comparing the sign of the rotation of the half-ester (entry 1) or the diethyl esters¹⁴ (entries 2 and 3) with compounds¹⁵ derived from enantiomerically pure alkylsuccinic acids¹⁶ allows assignment of the absolute configurations.

An explanation for the observed diastereoselectivity is provided by the model presented in Figure 1. This model has three key

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(15) (a) (*R*)-(-)-1-Ethyl 2-*tert*-butylsuccinate: $[\alpha]_{D}^{20} = -17.2^{\circ}$ ($c = 1.85$, CHCl_3). (b) (*S*)-(+)-Diethyl cyclohexylsuccinate: $[\alpha]_{D}^{20} = +14.9^{\circ}$ ($c = 2.3$, CHCl_3). (c) (*S*)-(-)-Diethyl hexylsuccinate: $[\alpha]_{D}^{20} = -13.5^{\circ}$.

(16) (a) (*R*)-(-)-*tert*-Butylsuccinic acid, $[\alpha]_{D}^{20} = -26.5^{\circ}$ ($c = 5$, acetone): Polański, T. *J. Chem. Soc., Perkin Trans. 1* **1988**, 629–37. (b) (*S*)-(+)-Cyclohexylsuccinic acid, $[\alpha]_{D}^{30} = +26.3^{\circ}$ ($c = 1.937$, EtOH): Naps, M.; Johns, I. B. *J. Am. Chem. Soc.* **1940**, *62*, 2450–7. (c) (*S*)-(-)-Hexylsuccinic acid, $[\alpha]_{D}^{15} = -26.6^{\circ}$ ($c = 4.00$, EtOH): Wren, H.; Burns, H. *J. Chem. Soc.* **1920**, *117*, 266–8.

features: (1) the imide carbonyls are opposed, (2) the fumarimide exists as an *s-cis* rotamer, and (3) the benzoxazole ring extends far enough to provide the necessary face-shielding required at the β -position for the asymmetric induction. The origin of the regioselectivity in the addition is not immediately apparent. Preliminary competition experiments between various fumarimide derivatives and diethyl fumarate indicate that the effect is *not* due to increased activation of the β -position of the alkene by the carboximide with respect to the carbethoxy substituent. We are now conducting additional experiments designed to help us understand this regioselectivity effect.

Acknowledgment. We gratefully acknowledge the support of this work by the National Institutes of Health. We also thank Professor N. A. Porter at Duke University for providing samples of two of the alkylsuccinic acids and for communicating to us his unpublished results on several occasions.

Supplementary Material Available: Experimental procedures for the preparation of fumarimide **4**, radical addition to **4** by the mercury method, and cleavage of addition products **5–7** to succinic acid derivative **8** and auxiliary **3** (2 pages). Ordering information is given on any current masthead page.

Book Reviews*

From CA to CAS Online. By Hedda Schulz. VCH: New York. 1988. xii + 227 pp. \$39.00. ISBN 0-89573-815-5. English translation of *Von CA bis CAS ONLINE*.

To search CAS ONLINE effectively, a scientist must develop a search strategy based on knowledge of the database. An important part of gaining this familiarity is learning to search the printed indexes in a systematic way. This book succeeds in providing a lucid explanation of the contents, organization, indexing policies, and chemical nomenclature principles of Chemical Abstracts. The first half of the book is devoted to searching Chemical Abstracts manually. For each type of index (Chemical Substance, Patent, General Subject, etc.) sample search questions are provided and the reader is guided through an appropriate search strategy. The author is particularly adept at pointing out changes in Chemical Abstracts over time and implications for the searcher. Various types of abstracts and CASSI entries are illustrated and deciphered. Other parts explained in detail include CASSI and the Registry Index.

The second half of the book, largely a contribution of H. R. Picher, provides an overview of searching CAS ONLINE and thoughtful comparisons of online and manual searching. Descriptions of the CA, CAOLD, and Registry Files are followed by illustrations of important steps and commands used in searching. The section devoted to the Registry File includes a basic introduction to structural searching. Although other hosts are listed with addresses and telephone numbers, emphasis is on STN, and examples are in STN command language. I was unable to find any reference to the Academic Program.

Although not as detailed as the CAS workbooks, this book brings together a wealth of practical information on manual and computerized searching in a clear and readable style. This book is recommended for novices and experienced searchers.

Margaret Manion, *University of Lowell*

Insect Neuropeptides. Chemistry, Biology, and Action. ACS Symposium Series No. 453. Edited by Julius J. Menn, Thomas J. Kelly, and Edward P. Masler (U.S. Department of Agriculture). American Chemical Society: Washington, DC. 1991. xii + 260 pp. \$59.95. ISBN 0-8412-1919-2.

This book was developed from a symposium sponsored by the 1989 International Chemical Congress of the Pacific Basin Societies, Honolulu, HA, December 17–22, 1989. It consists of a preface, a table of abbreviations and nomenclature, and 22 chapters in typescript form grouped under the following headings: Perspective; Developmental Neuropeptides; Homeostatic and Behavioral Neuropeptides; Reproductive Neu-

ropeptides; and Biochemistry and Molecular Biology. There are indexes of authors, their affiliations, and subjects.

Perspectives in Biochemistry. Volume 2. Edited by Hans Neurath (University of Washington). American Chemical Society: Washington, DC. 1991. x + 318 pp. \$19.95. ISBN 0-8412-1887-0.

This paperback book consists of a collection of concise reviews published in the journal *Biochemistry* in 1989 and 1990 under the heading *Perspectives in Biochemistry*. It consists of a Preface (1 page) and 29 reviews grouped under the following headings: Structure and Function of Proteins; Enzyme Structure and Mechanism; Membrane Proteins and Transmembrane Phenomena; Nucleic Acids and Protein Biosynthesis; Proteolytic Processing and Protein Degradation; Cell Growth and Regulation; and Bioenergetics. There are indexes of authors, their affiliations, and subjects.

Calcium Magnesium Acetate: An Emerging Bulk Chemical for Environmental Applications. Industrial Chemistry Library. Volume 2. Edited by D. L. Wise, Y. A. Levendis, and M. Metghalchi (Northeastern University). Elsevier: Amsterdam, Oxford, New York, and Tokyo. 1991. x + 511 pp. \$214.25. ISBN 0-444-88511-0.

CMA, the title compound, is a new bulk chemical emerging on the world market, and it is being used in multimillion ton quantities for two main applications: (1) as a noncorrosive, biodegradable road salt to replace sodium chloride for deicing, and (2) as an additive to coal-fired combustion units to facilitate combustion and to reduce the emission of sulfur in the stack gasses, thereby substantially lowering the formation of "acid rain".

The book contains a preface, biographical sketches of the editors, 18 chapters by different authors, and a subject index.

Photocatalysis Fundamentals and Applications. Edited by N. Serpone (Concordia University) and E. Pelizzetti (Università di Parma). Wiley-Interscience: New York. 1989. x + 650 pp. \$75.00. ISBN 0471-62603-1.

In the foreword, the editors state that their objective was to compile a book that could serve as a text for a course in the area of photocatalysis. This objective is clearly fulfilled. The organization and content of this book are such that it could serve as a text for a one-semester seminar course for chemistry, physics, and materials science students. In addition, the editors have avoided a problem common to books that are compiled from chapters written by different authors—that of individual chapters being specialized review articles and redundancy of the material covered by different authors. The editors have taken advantage of the expertise of the contributing authors and have compiled a text which will serve both the student and the more advanced scientist as an excellent source

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