Cantrill, J. A. Preece, J. F. Stoddart, Z.-H, Wang, A. J. P. White, D. J. Williams, *Org. Lett*. **1999**, *1*, 1917–1920; e) S. J. Cantrill, J. A. Preece, J. F. Stoddart, Z.-H. Wang, A. J. P. White, D. J. Williams, *Tetrahedron* **2000**, *56*, 6675–6681. The present research provides yet another beautiful example of anion-orchestrated self-assembly in the solid state.

[26] The thought processes that led to the design and synthesis of this 2:2 host–guest complex had their origins in the seminal work done by Cram in the 1970s on the face-to-face complexation of crown ethers with primary alkylammonium ions, see a) D. J. Cram, J. M. Cram, *Science* **1974**, *183*, 803–809; b) D. J. Cram, J. M. Cram, *Acc. Chem. Res.* **1978**, *11*, 5–14; c) "Container Molecules and Their Guests": D. J. Cram, J. M. Cram in *Supramolecular Chemistry* (Ed.: J. F. Stoddart, Royal Society of Chemistry, Cambridge, **1994**.

Novel Calcium Half-Sandwich Complexes for the Living and Stereoselective Polymerization of Styrene**

Sjoerd Harder,* Florian Feil, and Konrad Knoll

The many advantages of the anionic living polymerization of styrene (chain-length control, narrow molecular-weight distribution, chain-end functionalization, and particularly block-copolymerization) makes this technique the method of choice in the rational design of new styrene-based polymers.[1] The only disadvantage of this method is the lack of control of the polymers tacticity; control of tacticity offers many advantages in plastic material design.[2] Although stereoregular isotactic polystyrene was made in 1955 by use of classical Ziegler–Natta catalysts,[3] it never found any commercial application because of its extremely slow crystallization rate (crystallization times can be several days!). The discovery of its fast crystallizing syndiotactic form, obtained by polymerization with a titanocene half-sandwich complex, was therefore a revolution in polystyrene chemistry.[4] Syndiotactic polystyrene shows a low glass-transition temperature (104 °C) but high melting point (273 °C) with a high modulus and combines good electrical properties with an excellent solvent resistance.[5] The only disadvantage of stereocontrolled styrene polymerization by titanocene half-sandwiche complexes, however, is the lack of living character.

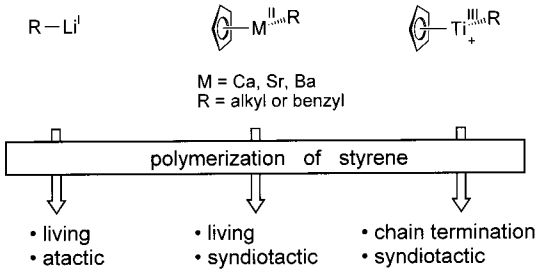
[*] Dr. S. Harder, Dipl-Chem. F. Feil
Fachbereich Chemie
Universität Konstanz
Postfach 5560, M738, 78457 Konstanz (Germany)
Fax: (+49) 7531-883137
E-mail: harder@chemie.uni-konstanz.de
Dr. K. Knoll
Kunststofflaboratorium, BASF AG
67056 Ludwigshafen (Germany)

[**] This work was generously supported by the BASF AG (Ludwigshafen (Germany)) and the university of Konstanz. We would like to acknowledge the following people for numerous discussions: Prof. Dr. H.-H. Brintzinger (Konstanz), Dr. H. Gausepohl, Dr. V. Warzelhan, and Dr. H. Weiss (Ludwigshafen).

Research to combine the favorable properties of anionic living polymerization and stereocontrolled coordination polymerization has come from both sides. Anionic polymerization with *n*BuLi initiators under certain reaction conditions can produce isotactic polystyrene,[6] but traces of water seem to be essential.[7] This observation has led to the use of mixed *n*BuLi/Li-alkoxide initiators; polymerizations, however, have to be carried out in apolar solvents at −30 °C and polymerization times can take up to 5 days with only 50% conversion.[8] Only 15% of the chains are highly isotactic, which indicates the presence of more than one reactive site at the proposed alkoxide initiator cluster. Recently it was discovered that a mixture of living polyisoprenyllithium and LiOH polymerizes styrene with high isotacticity and without atactic parts.[9]

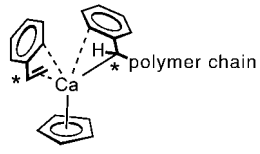
Attempts to make stereocontrolled coordination polymerization living are also under investigation. Under certain conditions, the polymerization of *para*-methylstyrene by titanium half-sandwich complexes shows living features, however, the system was not suitable for the living syndiotactic polymerization of styrene.[10]

Our approach to enable a living and a syndiospecific polymerization of styrene is based on "cross-breeding" the catalysts (RLi) used for classical anionic styrene polymerization and that for coordination polymerization (Scheme 1). A proposed catalytic species for coordination polymerization



Scheme 1.

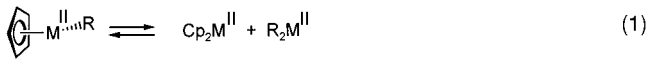
is a cationic Ti^{III} complex with a cyclopentadienyl spectator ligand and a growing chain. Syndiotactic stereocontrol proceeds through communication of the chiral chain-end and the stereogenic center on the coordinated monomer (**1**). A similar isolobal Group II metal compound could initiate the anionic (living) polymerization of styrene with syndiotactic insertions. We expect the polymerization to be living because of the considerable ionic (alkali metal like) character of the heavier alkaline-earth metals.[11] Syndiotactic insertion is anticipated on the basis of the very similar structure of [CpTiR$^+$] and the proposed Group II species. The use of non- or weak-coordinating solvents is a prerequisite for a coordination polymerization mechanism.



1

The apparent simplicity of the desired catalyst, $CpM^{II}R$ ($Cp = C_5H_5$), is in contrast to the inherent problems associated with this type of compound: a) the synthesis of reactive

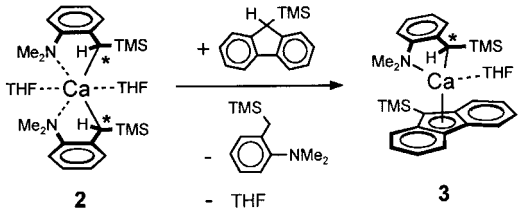
benzyls or alkyls of the heavier alkaline earth metals and b) the Schlenk equilibrium between heteroleptic and homoleptic species [Eq. (1)]: polymerization-active R_2M^{II} species



(1)

cannot be tolerated. We first developed simple synthetic methods for polymerization-active alkaline-earth benzyls.[12, 13] The Schlenk equilibrium can be directed to the heteroleptic side either by using large spectator ligands instead of Cp, this disfavors the homoleptic L_2M species by steric congestion, or by adding an excess of the polymerization-inactive L_2M species to the reaction mixture.

Attempts to polymerize styrene with heteroleptic benzylbarium mixtures were unsuccessful and only atactic polystyrene was obtained.[12] Here we describe our results with the first heteroleptic benzylcalcium compound (**3**), obtained by reaction of the polymerization-active homoleptic benzylcalcium compound (**2**)[13] with 9-Me_3Si-fluorene [Eq. (2); TMS = trimethylsilyl]. The crystal structure of **3** (Figure 1) shows a



(2)

distorted η^5 coordination for the fluorenyl ligand, a C,N bidentate coordination for the benzylic ligand, and coordination of one THF ligand. The NMR spectra of **3** (in benzene) show the exclusive presence of the heteroleptic species. Fast intermolecular ligand exchange processes were not observed on the NMR time scale. The chiral benzylic carbon causes two enantiotopic sides in the fluorenyl ligand: all the hydrogen atoms are unique at room temperature. Fast inversion of the chiral carbanion results in exchange of the two enantiotopic sides and is achieved by raising the temperature ($T_{coal} = 90\,^{\circ}C$; $\Delta G^{\neq} = 18.8$ kcal mol^{-1}). The energy barrier for inversion is concentration independent, which indicates a dissociative mechanism that involves Ca–C_α bond breaking (Scheme 2). Adding small amounts of THF[14] also results in fast inversion of the chiral center at room temperature by THF-assisted bond breaking (Scheme 2).

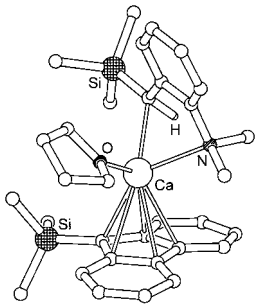
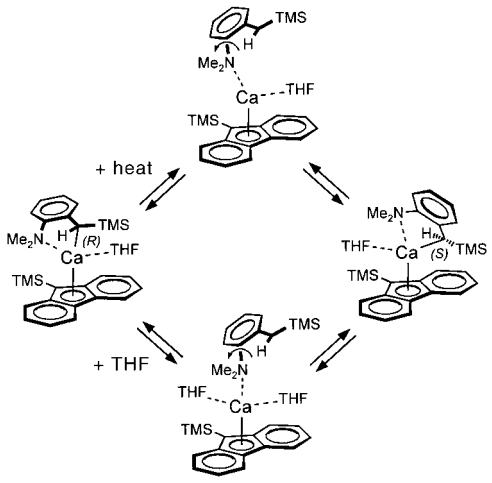


Figure 1. The crystal structure of **3** (only one of the two crystallographical independent but isostructural molecules is depicted). Hydrogen atoms (except for the benzylic hydrogen) have been omitted for clarity. Selected bond lengths [Å] for both independent molecules: Ca-C_α: 2.501(2) and 2.510(2); Ca-N: 2.462(2) and 2.470(2); Ca-O 2.305(2) and 2.310(2); Ca-fluorenyl contacts: 2.690(2), 2.733(2), 2.736(2), 2.785(2), 2.789(2) and 2.683(2), 2.732(3), 2.724(2), 2.771(2), 2.778(2).



Scheme 2.

The dibenzylcomplex (**2**) can be used as an initiator for the living polymerization of styrene.[13] The benzylic TMS substituent and the intramolecular coordinating Me_2N group stabilize the initiator thermodynamically as well as kinetically. The consequence is a sluggish initiation step compared to initiation with *sec*-butyllithium. This effect results in a tailing in the low molecular-weight range of the polymer obtained (Figure 2).[15] Polystyrene obtained with the heteroleptic

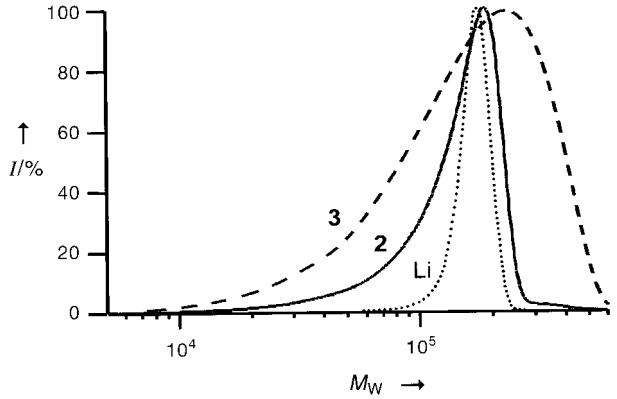


Figure 2. GPC traces of polystyrene obtained with a *sec*-butyllithium initiator (•••• $M_n = 1.091 \times 10^5$, P.D. = 1.039), the homoleptic dibenzylcalcium initiator (**2**) (—— $M_n = 1.093 \times 10^5$, P.D. = 1.369), and the heteroleptic fluorenyl-benzylcalcium initiator (**3**) (- - - -, $M_n = 0.996 \times 10^5$; P.D. = 2.262).

benzylcalcium complex (**3**) shows an even more extensive tailing in the low molecular weight part of the gel permeation chromatography (GPC) trace and consequently a relatively high polydispersion index. The observed tailing could also be explained by chain termination, however, several characteristics suggest living polymerization: a) good agreement between observed and calculated molecular weights (around 100000), b) linear pseudo first-order kinetic plots are obtained (Figure 3) c) the polymerization reactions were monitored by NMR spectroscopy: addition of new monomer after completed polymerization results in renewed styrene insertion, d) stepwise addition of styrene at certain time intervals shows no significant chain termination and polymers of the

  0044-8249/01/11322-4392 $ 17.50+.50/0

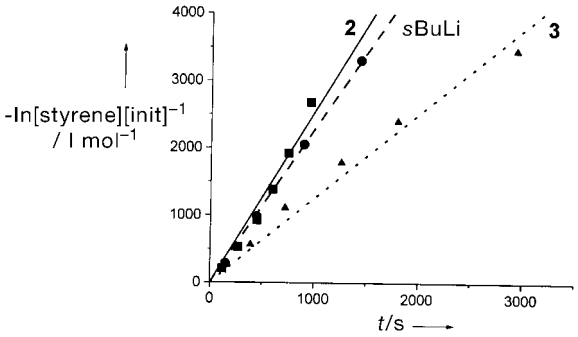


Figure 3. Graphical presentation of (ln[styrene])/[initiator] as a function of the polymerization time (estimated rate constants: (**2**) 2.55 L mol^{-1} s^{-1}, *sec*-BuLi 2.28 L mol^{-1} s^{-1}, and (**3**) 1.26 L mol^{-1} s^{-1}).

final calculated molecular weight are obtained, e) block copolymers with isoprene can be prepared.

The tacticity of the obtained polystyrene was checked by ^{13}C NMR spectroscopy (Figure 4). Polymer obtained with the heteroleptic benzylcalcium complex differs only slightly from the atactic material arising from alkyllithium initiation.

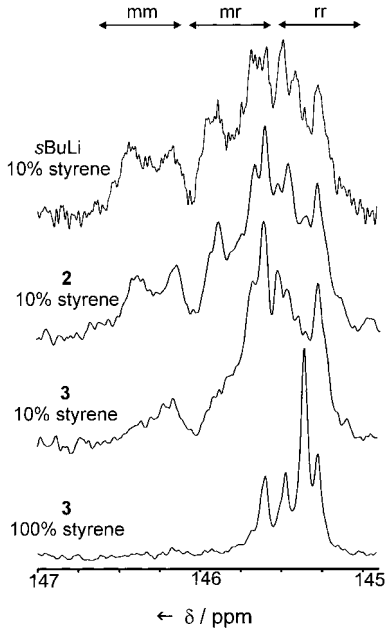
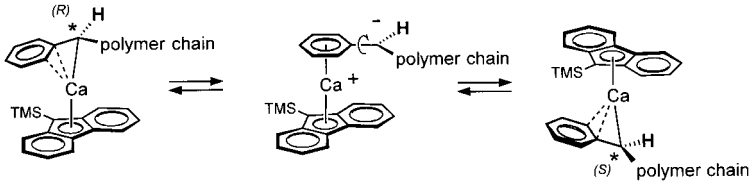


Figure 4. ^{13}C NMR signals of the phenyl C_{ipso} atom in the obtained polystyrene materials ([D$_2$]tetrachloroethane, $T = 100\,^{\circ}$C).

Although there is hardly preference for a syndiotactic insertion, a slight reduction of isotactic and atactic sequences is clearly evident (polymer obtained with heteroleptic benzylbarium complexes never showed any difference to material obtained by alkyllithium initiation). Polymerization at lower temperatures ($-20\,^{\circ}$C instead of the standard temperature of $+70\,^{\circ}$C) only shows a small increase of syndiotactic sequences.

Poor stereocontrol in the polymerization reactions might be a result of the configurationally instability of the chiral anionic chain-end. The barrier for inversion of the anionic chain end is probably lower than that of the chiral carbanion in **3**, which is stabilized by strong intramolecular N$\cdots$Ca coordination.[16] Inversion of the chiral chain end possibly proceeds without complete cleavage of the anion–cation bond: the Ca^{2+} ion binds to the phenyl ring followed by a rotation around the C_{ipso}–C_{α} bond (Scheme 3).

Inversion of the chain end results in racemization of the chiral centers and the formation of atactic polymer. To increase the polymerization rate in respect to the inversion rate, polymerizations in pure styrene were performed. Styrene as a solvent will hardly effect the inversion rates, but a 10-fold increase in insertion rates is expected with respect to the standard polymerization conditions (10% styrene in cyclohexane). NMR spectroscopic analyses of the polymer shows a drastic decrease of isotactic and atactic sequences. The largest



Scheme 3.

signal can be assigned to the pure syndiotactic pentad (rrrr; r = racemic dyad) and the three minor signals are related to polystyrene with high syndiotacticity (overall analysis: 76% rr, 84% r, 22% mr; m = meso dyad). Isotactic sequences are nearly non-existent (less than 2% mm). A slight improvement can be obtained by polymerization at $-20\,^{\circ}$C. All the polymers prepared show a homogenous syndiotacticity and can not be fractionated by extraction with methylethylketone (only minor amounts of low molecular weight chains were extracted). Polymerization experiments with variable intermittent styrene concentrations (in the range 10–100%) show a gradual improvement of stereocontrol with the styrene concentration. Polymerization experiments with 10% styrene in benzene as a solvent, show the same results as polymerization reactions in cyclohexane. Therefore, the increased syndiotacticity on increasing the styrene concentration is not a solvent effect. The results reported here confirm that the insertion step is syndiotactic to a high degree and inversion of the carbanionic chain end leads to stereo errors.

Currently we are also exploring the scope of using the heteroleptic benzylcalcium complex (**3**) in stereocontrolled polymerization of other monomers.

Experimental Section

All experiments were carried out under argon using predried solvents and Schlenk techniques. Styrene polymerizations were performed in a thermostated 100 mL stainless steel reactor at normal pressure (cyclohexane, 50 °C; unless stated otherwise) and quenched with oxygen-free methanol.

Synthesis of **3**: Crystalline bis(2-Me$_2$N-α-Me$_3$Si-benzyl)calcium · (THF)$_2$[13] (4.10 g, 6.86 mmol) and 9-Me$_3$Si-fluorene (1.63 g, 6.84 mmol) were dissolved in benzene (35 mL) and heated at 65 °C for 90 min. The solvent and volatiles of the orange-red solution were removed under oil-pump vacuum at 65 °C for 60 min. The remaining orange solid (after cooling) was obtained NMR pure in quantitative yield. Subsequent crystallization from benzene (15 mL) at 5 °C gave orange crystalline blocks in 73% yield (2.80 g, 5.03 mmol). The crystals contain benzene solvent which can be removed under vacuum. ^{1}H NMR (600 MHz, C_6D_6, 20 °C): $\delta = 0.34$ (s, 1H;

CH(TMS)), 0.42 (s, 9H; TMS-benzyl), 0.59 (s, 9H; TMS-fluorenyl), 0.95 (mb, 4H; THF), 1.93 and 1.96 (2 s, 6H; NMe_2), 2.59 (mb, 4H; THF), 6.12 (t, $^3J(H,H) = 7.5$ Hz, 1H; benzyl), 6.27 (d, $^3J(H,H) = 7.8$ Hz, 1H; benzyl), 6.31 (t, $^3J(H,H) = 7.5$ Hz, 1H; benzyl), 6.88 (d, $^3J(H,H) = 8.4$ Hz, 1H; benzyl), 7.04 (t, $^3J(H,H) = 7.5$ Hz, 1H; fluorenyl), 7.09 (t, $^3J(H,H) = 7.5$ Hz, 1H; fluorenyl), 7.24 (t, $^3J(H,H) = 7.2$ Hz, 1H; fluorenyl), 7.31 (t, $^3J(H,H) = 7.5$ Hz, 1H; fluorenyl), 7.93 (d, $^3J(H,H) = 7.8$ Hz, 1H; fluorenyl), 8.03 (d, $^3J(H,H) = 8.4$ Hz, 1H; fluorenyl), 8.14 (d, $^3J(H,H) = 8.4$ Hz, 1H; fluorenyl), 8.17 (d, $^3J(H,H) = 7.8$ Hz, 1H; fluorenyl); ^{13}C NMR (600 MHz, C_6D_6, 20 °C): $\delta = 2.43$ (TMS), 2.44 (TMS), 24.9 (THF), 41.8 (NMe), 44.5 (NMe), 44.9 (CH(TMS)), 68.5 (THF), aromatics: 87.0, 112.8, 116.5, 116.8, 119.4, 121.2, 121.4, 121.7, 121.9, 123.3, 124.2, 124.3, 124.4, 126.4, 128.3, 135.0, 140.7, 140.9, 147.0.

Crystal structure determination of **3**: Crystals grown from benzene solution contain up to three equivalents of benzene per Ca atom and crack upon cooling resulting in broad peak profiles and poor diffraction. Crystals grown from warm hexane also show solvent incorporation but remain stable upon cooling. Measurement on an Enraf Nonius CAD4 diffractometer at −90 °C, $Mo_{K\alpha}$, $2\theta_{max} = 50°$, 13501 independent reflections ($R_{int} = 0.011$), 10658 reflections observed with $I > 2\sigma(I)$. Crystal data: $C_{32}H_{45}CaNOSi_2$ triclinic, space group $P\bar{1}$, $a = 13.5981(13)$, $b = 16.8236(12)$, $c = 18.2031(15)$ Å, $\alpha = 70.779(6)$, $\beta = 77.084(7)$, $\gamma = 82.671(7)°$, $V = 3826.1(6)$ Å^3, $Z = 4$, $R = 0.0456$, $wR2 = 0.1466$, GOF = 1.08, $\rho_{max} = 0.57$ e Å^{-3}, $\rho_{min} = -0.44$ e Å^{-3}. The unit cell contains a hole with two severely disordered hexane molecules (confirmed by NMR analysis). Disorder was treated with the bypass method using the program SQUEEZE[17] incorporated in PLATON.[18] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-165023. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Received: July 4, 2001 [Z17423]

[1] K. Knoll in *Kunststoff Handbuch 4: Polystyrol* (Eds.: H. Gausepohl, R. Gellert), Hanser, München, **1996**, pp. 67–82; J. R. Wünsch in *Kunststoff Handbuch 4: Polystyrol* (Eds.: H. Gausepohl, R. Gellert), Hanser, München, **1996**, pp. 82–104.

[2] H. H. Brintzinger, D. Fischer, R. Mülhaupt, B. Rieger, R. M. Waymouth, *Angew. Chem.* **1995**, *107*, 1255; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1134; G. W. Coates, *Chem. Rev.* **2000**, *100*, 1223; L. Resconi, L. Cavallo, A. Fait, F. Piemontesi, *Chem. Rev.* **2000**, *100*, 1253.

[3] G. Natta, P. Pino, P. Corradini, F. Danusso, E. Mantica, G. Mazzanti, G. Moraglio, *J. Am. Chem. Soc.* **1955**, *77*, 1708.

[4] N. Ishihara, M. Kuramoto, M. Uoi, *Macromolecules* **1986**, *21*, 2464.

[5] M. Malanga, *Adv. Mater.* **2000**, *12*, 1869.

[6] R. J. Kern, *Nature* **1960**, *187*, 410.

[7] D. J. Worsfold, S. Bywater, *Makromol. Chem.* **1963**, *65*, 245.

[8] L. Cazzaniga, R. E. Cohen, *Macromolecules* **1989**, *22*, 4125.

[9] T. Makino, T. E. Hogen-Esch, *Macromolecules* **1999**, *32*, 5712.

[10] M. Kawabe, M. Murata, K. Soga, *Macromol. Rapid Commun.* **1999**, *20*, 569.

[11] C. Lambert, P. v. R. Schleyer, *Angew. Chem.* **1994**, *106*, 1187; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1129.

[12] A. Weeber, S. Harder, H. H. Brintzinger, K. Knoll, *Organometallics* **2000**, *19*, 1325.

[13] S. Harder, F. Feil, A. Weeber, *Organometallics* **2001**, *20*, 1044.

[14] Circa 4–5 equivalents result in fast inversion at room temperature. Addition of larger amounts of THF result in the crystallization of the solvent-separated ion pair: $[Me_3Si\text{-fluorenyl}^-]_2[Ca^{2+}(THF)_6]$.

[15] Polymerizations with the analogue but more reactive strontium complex show faster initiation and consequently less tailing (polydispersity (P.D.) = 1.218): F. Feil, S. Harder, *Organometallics* **2001**, accepted.

[16] Intramolecular chelation enhances the stability of carbanionic stereogenic centers: C. Strohmann, B. C. Abele, D. Schildbach, K. Strohfeldt, *Chem. Commun.* **2000**, 865.

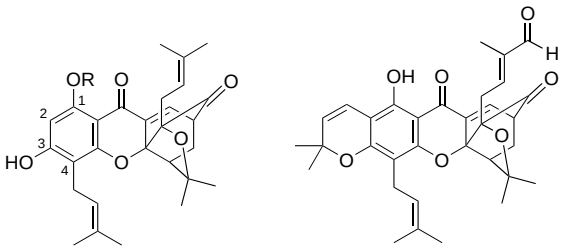
[17] P. A. van der Sluis, A. L. Spek, *Acta Crystallogr. Sect. A* **1990**, *46*, 194.

[18] A. L. Spek, *PLATON, A Multipurpose Crystallographic Tool*, Utrecht University, Utrecht, The Netherlands, **2000**.

"Biomimetic" Cascade Reactions in Organic Synthesis: Construction of 4-Oxatricyclo-[4.3.1.0]decan-2-one Systems and Total Synthesis of 1-*O*-Methylforbesione via Tandem Claisen Rearrangement/Diels–Alder Reactions**

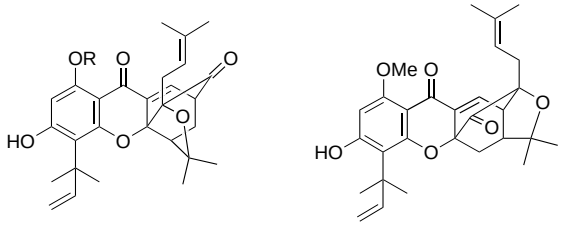
K. C. Nicolaou* and Jim Li

The intriguing 4-oxatricyclo[4.3.1.0]decan-2-one ring system is found in a growing class of biologically active natural products isolated from the genus *Garcinia* of the Guttiferae family of plants. Among the members of this class of compounds are forbesione (**2**, isolated from *Garcinia forbesii*),[1] morellin (**3**, from *G. morella*),[2] and the cytotoxic agents



1: R = Me: 1-*O*-methylforbesione
2: R = H: forbesione

3: morellin



4: R = H: bractatin
5: R = Me: 1-*O*-methylbractatin

6: 1-*O*-methylneobractatin

bractatin (**4**), 1-*O*-methylisobractatin (**5**), and 1-*O*-methylneobractatin (**6**), all of which were found in the species *G. bracteata*,[3] as well as lateriflorone (from *G. lateriflora*),[4]

[*] Prof. Dr. K. C. Nicolaou, J. Li
Department of Chemistry and The Skaggs Institute for Chemical Biology
The Scripps Research Institute
10550 North Torrey Pines Road, La Jolla, CA 92037 (USA)
Fax: (+1) 858-784-2469
and
Department of Chemistry and Biochemistry
University of California, San Diego
9500 Gilman Drive, La Jolla, CA 92093 (USA)
E-mail: kcn@scripps.edu

[**] We thank Drs. D. H. Huang, G. Siuzdak, and R. Chadha for NMR spectroscopic, mass spectrometric, and X-ray crystallographic assistance, respectively. This work was financially supported by the National Institutes of Health (USA), The Skaggs Institute for Chemical Biology, a graduate fellowship from The Skaggs Institute for Research (to J.L.), and grants from Abbott Laboratories, ArrayBiopharma, Boehringer Ingelheim, DuPont, Hoffmann-La-Roche, Merck, Pfizer, and Schering Plough.

Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.

  0044-8249/01/11322-4394 $ 17.50+.50/0