An Unexpected Tandem Reaction between N-Butadienyl-N-alkylketene \(N,O\)-Trimethylsilylacetics of Propionamide and Activated Dienophiles like \(N\)-Phenylmaleimide or Acryloyl Chloride

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Abstract. Starting from the \(N\)-butadienyl-\(N\)-alkylpropionamides 1a–1c the corresponding \(N,O\)-trimethylsilylacetics could be obtained using the mixture of LDA and trimethylsilyl chloride in THF. The unexpected reaction sequence Diels-Alder reaction/acylation between the \(N\)-butadienyl-\(N\)-alkylketene \(N,O\)-trimethylsilylacetal of propionamide (2a–2b) and \(N\)-phenylmaleimide produced tricyclic products rac-5a–rac-5b and bicyclic products rac-6a–rac-6b with high diastereoselectivity. The reaction of the \(N,O\)-trimethylsilylacetics 2a and 2c with acryloyl chloride in a similar sequence gave the bicyclic products rac-8a and rac-8c. The stepwise synthesis of bicyclic systems of this general structure could only be successfully executed in 26% yield treating the Diels-Alder product rac-10 with LDA.

Introduction

Nature has used sequential transformations in the biosynthetic processes leading to alkaloids, terpenoids, and steroids [1]. The beauty and the efficiency of these multistep reactions has motivated chemists to imitate these processes [2–5] since the time the biomimetic synthesis of tropinone has been reported by Robinson [6–8]. Tandem reactions always belonged to the most important processes in organic synthesis. Many of the so-called name reactions are more or less complex sequences of tandem reactions [9]. Especially in the synthesis of heterocycles tandem reactions are widely used [10–12]. For a long time, most tandem reactions were found by serendipity.

In recent years, more and more planned tandem reactions have been reported [13–15]. There are obvious advantages carrying out two or more steps in one pot: losses due to the workup can be reduced, the synthesis becomes more convergent, and finally it is possible to use sensitive intermediates, without isolating them.

Results and Discussion

Combining two synthetically important reactions should lead to processes with considerably enhanced synthetic potential. These arguments lead us to study the combination of the Diels-Alder reaction with the \([3,3]\)-sigmatropic rearrangement [16] (Scheme 1). The use of dienes substituted at C(1) with groups which can rearrange after the cycloaddition leads to 1,4-disubstituted cyclohex-2-enes. The tandem reaction allows the synthesis of the product by an alternative synthetic plan, than the one which is the result of a straightforward retrosynthetic analysis. The relative configuration at C(1) and C(4) of the cyclohexene ring system can be predicted by the rules governing the two reactions which are combined in the tandem process and the double bond situated between the two functional groups can be modified in a regio- and stereoselective way. In the case of the (E)-buta-1,3-dienyl-thiocyanate it has been shown, that a tandem reaction made up of a Diels-Alder reaction and of a \([3,3]\)-sigmatropic shift can be successfully accomplished. Using moderately acivated dienophiles it was possible to selectively trap the product of the tandem reaction by the addition of \(\text{EtOH}\) to the formed isothiocyanate. Only the selective trapping allowed to obtain good yields of the desired products. Using the (E)-buta-1,3-dienyl-thiocyanate as diene a tandem reaction made up of three separate steps, Diels-Alder reaction, a \([3,3]\)-sigmatropic shift, and finally the trapping of the isocyanate with \(\text{EtOH}\) has been developed.

\[\text{SCN} + \text{COOH}_3 \xrightarrow{110^\circ C} \text{COOCH}_3 \]

Scheme 1

\(~60\%~\)
als to rearrange the O-silyl derivative of an N,O-ketene acetal has been reported. Despite these facts we decided to study the behavior of the N-butadienyl-N-isopropylketene N,O-trimethylsilylacetal of propionamide 2a. The obvious starting material was the corresponding propionamide 1a, a moderately activated diene, which undergoes [4+2]-cycloaddition with a series of activated dienophiles [19][20]. The ketene N,O-acetal 2a was hoped to undergo the Diels-Alder reaction followed by a [3,3]-sigmatropic rearrangement. This process should lead to cyclohexene derivatives substituted at C(1) and C(4) with control of the relative configuration.

The synthesis of the ketene N,O-acetal 2a starting from the propionamide 1a was straightforward. Deprotonation of the amide in the presence of trimethylsilylimidazole [21] gave a 95% yield of isolated 2a as a liquid, which was extremely sensitive against hydrolysis (Scheme 2). Only the (Z)-diastereoisomer was obtained. This was independently proven by NOE experiments (Scheme 3): enhancements of the olefinic proton of 2a was observed, when the \( \alpha \) - and \( \beta \) -protons of the butadienyl portion were irradiated. At the same time, these results reveal the presence of two rotamers around the C–N bond. The A\( ^{1} \), B\( ^{1} \) system [22] between the substituent A on the nitrogen of the amide and the substituent on the \( \alpha \)-methylene group, in our case the Me group, has been cited to explain the (Z)-stereoselectivity during the deprotonation of N,N-dialkylamides [23]. If this argument is valid, the s-cis-conformation should be preferred for the starting material. NOE experiments using the dienamide 1a clearly indicate that already the starting material shows a conformational preference for the s-cis-conformation (Scheme 4). Also the dienamide 1a is present in two conformations around the C–N bond. The N-benzyl derivative 1b and the N-isopropyl derivative of the phenylacetic acid dienamide 1c could be transformed under the same reaction conditions into the corresponding ketene N,O-trimethylsilylacetals 2b and 2c.

The reaction of the ketene N,O-acetals 2a and 2b, respectively, with N-phenylmaleimide in THF at ambient temperature leads to product formation already at -78° (Scheme 5). Addition of MeOH to the reaction mixture and evaporation of the solvent yielded a raw material which was composed of two products 3a and 4a, respectively, and 3b and 4b, respectively, according to the TLC analysis. The two products 3a and 4a could be separated by fractional crystallisation from CHCl/\text{EtOH} ca. 1:1 in 66% overall yield. From the \( ^1 \)H-NMR spectra of both products, it was immediately clear that a cycloadDITION between the two substances had taken place.

Careful analysis of the 360-MHz \( ^1 \)H-NMR spectrum and decoupling experiments proved that it was not the expected tandem reaction Diels-Alder reaction/ [3,3]-sigmatropic shift which had taken place but an unexpected combination of a Diels-Alder reaction with an acylation step. The tricyclic product rac-3a as well as the bicyclic rac-4a were present each as one single diastereoisomer. The relative configuration at the ring junction for both products was all cis as one would expect from an endo-selective Diels-Alder reaction. A series of NOE experiments allowed to establish the relative positions of the H-atoms at the ring junction. More astonishing was the fact that the configuration at C(3) was also unique. The H-atoms at this position could be exchanged against deuterium without epimerization. Therefore, the observed relative configurations must be the thermodynamically more stable ones. The relative configuration was established by the following NOE experiments (Scheme 6). In the case of the tricyclic compound rac-3a a NOE enhancement of 7.3% could be observed.
irradiating H–C(3) and observing H–C(8). This assignment is also in good agreement with shift arguments. The Me group at C(3) resonates at extraordinary high field (0.59 ppm) which can be explained by the influence of the ring current of the nearby Ph group. The relative configuration of the bicyclic product rac-4a was assigned in an analogous way (Scheme 6). Using the N-benzyl derivative 2b as starting material similar results were obtained. A 10% yield of the tricyclic product rac-3b and a 40% yield the bicyclic product rac-4b were obtained (Scheme 5).

The tricyclic product rac-3a could be dehydrated treating it with CF₃COOH in CH₂OH. The vinylogous urea rac-5 was obtained in 78% yield. The spectral data are in good accordance with the proposed structure. The only surprising fact is the occurrence of a 5-J-coupling between CH₃–C(3) and H–C(9) of 1.8 Hz.

The ketene N,O-trimethylsilylacetals 2a and 2c could be brought to react with 2 equiv. of acryloyl chloride as dienophile. The bicyclic products rac-6a and rac-6c, respectively, could be isolated diastereomerically pure in 60 and 64% yield, respectively. The relative configuration at the ring junction as well as the relative configuration of CH₃–C(3) was unequivocally determined with the help of NOE experiments. Deuterium-exchange experiments showed that H–C(3) could be replaced by deuterium without changing the
ideal overlap between the C-H bond and the π-bonds of the two adjacent carbonyl groups.

Using crotonyl chloride and methacryl chloride as dienophile only minute amounts of cycloadducts could be detected in the 1H-NMR spectrum of the raw material. Disopropylamine is present in the reaction mixture, which stems from the synthesis of the ketene N,O-trimethylsilylacetal. Reaction of the disopropylamine with the acid chloride produces HCl, which immediately destroys the ketene acetal. In order to avoid the formation of HCl two sort of experiments were carried out. To remove the proton of the disopropylamine after the formation of the ketene N,O-trimethylsilylacetal 2a, a second equiv. of BuLi was added. This solution was treated with crotonyl chloride, methacryl chloride, and acryloyl chloride, respectively. In the first two cases almost no cycloadduct could be detected and even in the third case the product formation was highly reduced. Adding to the mixture containing 2a, LDA and acryloyl chloride 2 equiv. of LiCl allowed the reaction to proceed at a normal rate and a 56% yield of rac-6a could be isolated, comparable to the 60% yield obtained without the BuLi treatment. In the second sort of experiment 2a was isolated and the LiCl was precipitated by the addition of hexane. The soln. of 2a free of LiCl in CHCl₃ did not react with added N-phenylmaleimide as dienophile. The acylation of imides by ketene N,O-trimethylsilylacetal without the addition of Lewis acids is without precedent. The ease of this new tandem reaction composed of a Diels-Alder reaction and an acylation could be the consequence of the steric compression of the two reacting functional groups in the cycloadduct and of the action of LiCl as Lewis acid as the experiments reported above seem to indicate.

Finally, we decided to investigate if the product of the tandem reaction could not be obtained with similar ease using a stepwise procedure. The Diels-Alder reaction of the dienamides 1a and 7 with acryloyl chloride in CH₂Cl₂ at 0° overnight and treating the reaction mixture with CH₃OH allowed to isolate the mixture of the trans- and the cis-disubstituted cyclohexene rings rac-10 and rac-11 in 16 and 56% yield, respectively, and the acetamide derivatives of the cycloadduct rac-8 and rac-9 in 16 and 46% yield, respectively (Scheme 8). Attribution of the relative configuration by NMR methods proved to be difficult. The preference for one diastereoisomer under these relatively mild reaction conditions prompted us to assume that the major product of the cycloaddition is the cis-substituted product.
which is formed via an endo-transition state. To substantiate the tentative assignment the two diastereoisomeric cycloducts, rac-8 and rac-9 were reduced with Pd/C as catalyst to obtain the disubstituted cyclohexane derivatives rac-12 and rac-13 (Scheme 9). The \( ^1\)H-NMR data were much easier to interpret and allowed an unequivocal identification of the two diastereoisomers.

To check if the tandem reaction could be accomplished in a stepwise manner, rac-9 was transformed into the ketene N,O-trimethylsilylacetal rac-14 treating the amide with trimethylsilyl iodide and hexamethyldisilazane in CHCl\(_3\) (Scheme 10). The ketene N,O-acetal rac-14 was formed, but did not react any further. Treating the cyclohexene rac-9 with LDA at \(-85^\circ\)C in THF to form the lithium enolate instead allowed to isolate the bicyclic compound rac-15 in a moderate 26% yield (Scheme 11). The major side reaction was the base-catalyzed elimination of the deprotonated \(N\)-isopropyl acetamide to form methyl cyclohexa-1,3-dienyl-1-carboxylate in 14% yield. The structure of rac-15 could be secured by an X-ray analysis (Fig.). The structure clearly shows that the cyclohexene ring of rac-15 is in a half chair conformation, whereas the annulated lactam ring is in a boat conformation. This corresponds to the conformation which was predicted from the analysis of the NOE experiments in solution. This conformation of the bicyclic systems allows to remove the bulky \(N\)-isopropyl substituent as far from the ring system as possible. The (pro-S)-H\(\cdot\)C(3) is fixed in an axial position projecting towards the inside of the roof like molecule. The almost perfect alignment of this hydrogen with the \(\pi\)-orbitals of the two adjacent C=O bonds (dihedral angles: between \(\gamma\) and the (pro-S)-H\(\cdot\)C(3): 102.2\(^\circ\); between \(\beta\) and the (pro-S)-H\(\cdot\)C(3): 87.2\(^\circ\)) explains why the (pro-S)-H, which is sterically more hindered, undergoes the base catalysed deuterium exchange faster than the (pro-R)-H. At the same time the relatively short distance between the (pro-S)-H and H-C(8) (distance: 3.00 Å) and H-C(7) (distance: 3.76 Å) is a necessary condition for the observation of a NOE effect. At the same time the difference of the two distances explains why only the NOE enhancement with H-C(8) is observed. The X-ray analysis nicely complements the structural information deduced from the studies in solution and shows, that the conformation of these bicyclic systems must be very similar in the crystal and in solution.

In summary the ketene N,O-acetals 2a-2c undergo a tandem reaction Diels-Alder reaction/acylation reaction with unprecedented ease. The sequence Diels-Alder reaction first and acylation second is at the moment the preferred mechanistic hypothesis for this tandem process. This sequence explains without difficulties the observed relative configurations at the chiral centres formed. The second argument in favor of this sequence stems from the fact, that acylation between a ketene N,O-acetal and an imide without addition of a Lewis acid seems to be without precedent. The only Lewis acid present during this reaction is LiCl. As could be shown the presence of LiCl is necessary to obtain the products of the tandem reaction in good yield. The exact function of the LiCl could not be pinned down. The LiCl could catalyse the Diels-Alder reaction as well as the acylation process. Finally, the tandem process can in one case also be executed in a stepwise manner. The overall yield of the stepwise procedure is not very satisfactory which demonstrates one of the principal advantages of a tandem process.

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**Experimental**

**General.** All reactions were carried out under N\(_2\). Solvents were dried by distillation from drying agents as follows: THF (Na), Et\(_2\)O (CaH\(_2\)), CH\(_2\)Cl\(_2\) (CaH\(_2\)), MeOH (Mg), EtOH (Mg). Silica gel 50 (Merck) was used for flash chromatography (FC). M.p. were determined in open capillary
tubes on a Kofler melting point apparatus (Thermovar, C. Reichert AG, Vienna) and are uncorrected. IR spectra were in CDC$_3$ and CHCl$_3$ at room temp. (5.0 cm$^{-1}$ shifts) in paraffin oil or at ambotemp. during 12 h and the then violet soln. was hydrolyzed with MeOH (5 mol). After evaporation of the solvent on the rotavap the darkviolet residue was dissolved in CHCl$_3$ (30 ml) and washed with H$_2$O (10 x ml). The org. phase was dried over MgSO$_4$ and filtered over Celite/active carbon. Fractional crystallization of the violet soln. with CHCl$_3$/EtOAc at 0$^\circ$ gave rac-3a (1.4 g, 50% as white crystals. M. p. 197$^\circ$ (IRK): [3a]) 3320, 3100, 2980, 2960, 2830, 1685, 1650, 1595, 1530, 1350, 1150, 1105, 1050, 1010, 885, 830, 760, 745, 695. 1H-NMR (360 MHz, CDCl$_3$): 7.43-7.16 (m, 5, arom. H); 6.08 (dd, (j = 9.5, 7.3, 3.1, H-C(2)); 7.58 (m, = 9.5, H-C(4)); 4.94 (sept., J = 6.8, H-C(1)); 4.13 (br. s, OH); 3.90 (m, H-C(3a)); 3.12 (m, H-C(3)); 2.89 (m, H-C(2)); 2.85 (m, H-C(2)); 2.62 (g, H-C(6), H-C(2)); 2.11 (m, H-C(6)); 1.16, 1.13 (d, J = 6.8, CH$_2$(2) and CH$_2$(3)); 0.59 (d, = 6.8, CH$_3$-C(3)); 13C-NMR (100 MHz, CDCl$_3$): 147.5 (s, C(1)); 137.3, 137.1 (2d, C(1’), C(3’)); 126.0 (m, C(1)); 125.0 (s, C(2)); 126.0 (s, C(2)); 124.9 (s, C(2)); 111.0 (s, C(2’)); 119.3 (m, C(3)); 119.0 (m, C(3)); 5.0 (q, (CH$_3$)$_3$Si). 13C-NMR (90 MHz, CDC$_3$): 147.5 (s, C(1)); 137.3, 137.1 (2d, C(1’), C(3’)); 126.0 (m, C(1)); 125.0 (s, C(2)); 126.0 (s, C(2)); 124.9 (s, C(2)); 111.0 (s, C(2’)); 119.3 (m, C(3)); 119.0 (m, C(3)); 5.0 (q, (CH$_3$)$_3$Si). GC-MS: 239 (19, M$^+$), 224 (20, CH$_3$-C(5)), 116 (17), 106 (11), 73 (100), (CH$_3$)$_3$Si, 53 (11).

(Z)-N-[(E)-(E)-Buta-1,3-dienyl]-N-[(trimethylsilyl)oxy]prop-1-eneamine (2b). In a flame-dried three-necked flask fitted with magnetic stirrer, septum, and thermometer a soln. of Bzl (hexane, 8.8 ml, 14 mmol) was added dropwise to a soln. of anh. (i-Pr$_2$)NH (2.4 ml, 17.2 mmol) in THF (32 ml) at 0$^\circ$ and the mixture was stirred for 30 min at 0$^\circ$. The mixture was cooled to 78$^\circ$ and freshly distilled TMSCl (1.8 ml, 14 mmol) and a soln. of 1a (2.2 g, 13.2 mmol) in THF (10 ml) were added slowly at the same temp. After addition was complete, stirring was continued for 1 h at 78$^\circ$ and the mixture was warmed slowly to room temp. To get a NMR spectrum of 2a, 1 ml of the yellow soln. was taken, the volatile components were evaporated and the residue dissolved in CDC$_3$, which was filtered twice over basic Al$_2$O$_3$. The soln. was filtered directly in a dried NMR tube. Yield: 95% by GC. 1H-NMR (360 MHz, CDCl$_3$): 6.18 (dt, j = 16.7, 10.6, 10.3, H-C(3)); 6.15 (d, = 13.8, H-C($H_1$)); 5.26 (dd, J = 13.8, 10.6, H-C(4)); 4.71 (dd, J = 16.7, 10.3, H-C(4’)); 4.49 (dd, J = 10.3, 2.1, H-C(3)); 4.28 (g, J = 6.6, H-C(2)); 3.58 (sept., = 6.8, H-C(1’)); 1.51 (dd, J = 6.6, CH$_2$(3)); 1.13 (d, J = 6.8, 2xCH$_2$(2’)); 0.12 (s, (CH$_3$)$_3$Si). 13C-NMR (90 MHz, CDCl$_3$): 147.5 (s, C(1)); 137.3, 137.1 (2d, C(1’), C(3’)); 126.0 (m, C(1)); 125.0 (s, C(2)); 126.0 (s, C(2)); 124.9 (s, C(2)); 111.0 (s, C(2’)); 119.3 (m, C(3)); 119.0 (m, C(3)); 5.0 (q, (CH$_3$)$_3$Si). 13C-NMR (100 MHz, CDCl$_3$): 147.5 (s, C(1)); 137.3, 137.1 (2d, C(1’), C(3’)); 126.0 (m, C(1)); 125.0 (s, C(2)); 126.0 (s, C(2)); 124.9 (s, C(2)); 111.0 (s, C(2’)); 119.3 (m, C(3)); 119.0 (m, C(3)); 5.0 (q, (CH$_3$)$_3$Si). GC-MS: 239 (19, M$^+$), 224 (20, CH$_3$-C(5)), 116 (17), 106 (11), 73 (100), (CH$_3$)$_3$Si, 53 (11).

(Z)-N-Benzyl-N-[(E)-(E)-Buta-1,3-dienyl]-N-[(trimethylsilyl)oxy]prop-1-eneamine (2b). Analogously to the transformation of 1a to 2a, 2b (oil, 80%, by ‘H-NMR) was prepared from 1b (2.84 g, 13.93 mmol). 1H-NMR (360 MHz, CDCl$_3$): 7.36-7.10 (m, arom. H); 6.69 (d, J = 13.7, H-C(1’)); 6.24 (dt, J = 17.0, 10.3, H-C(3)); 5.18 (dd, J = 13.7, 10.3, H-C(2)); 4.72 (dd, J = 17.0, 10.3, H-C(4)); 4.57 (dd, J = 10.3, 1.6, H-C(4’)); 4.48 (s, (CH$_3$)$_3$Si); 4.12 (q, J = 6.7, H-C(2)); 1.54 (d, J = 6.7, H-C(3)); 0.21 (s, (CH$_3$)$_3$Si).
Methyl rac-trans-2-(N-Acetyl-N-isopropylamino)cyclohex-3-ene-1-carboxylate (rac-10) and Methyl rac-cis-2-(N-Acetyl-N-isopropylamino)cyclohex-3-ene-1-carboxylate (rac-11). Analogously to the transformation of 7 to rac-8 and rac-9, rac-10 and rac-11 were prepared from 1a (0.26 g, 1.65 mmol). In this manner rac-10 was obtained (oil, 93 mg, 16%). IR (CHCl₃): 3015, 3000, 2959, 2949, 1730, 1630, 1440, 1340, 1340, 1280, 1240, 1170, 1120, 1070, 1040, 960. 1H-NMR (400 MHz, CDCl₃): The signals of two rotamers were observed in a ratio of 67:33. Rotamer A: 5.92 (m, H-C(4)); 5.70 (d, J = 10.2, 1.7, H-C(3)); 4.69 (br, d, H-C(2)); 1.71 (t, CH₃-C(8)); 1.11 (s, CH₃(11)). Signals which were attributed to the Rotamer B were found at 5.80, 5.40, 3.95, 3.63, 1.22. 13C-NMR (100 MHz, CDCl₃): Rotamer A: 175.3 (C(7)); 171.4 (C(9)); 131.6 (C(12)); 127.9 (C(3)); 58.2 (C(6)); 50.8 (C(12)); 45.0 (C(1)); 26.7 (C(4)); 24.8 (C(6)); 24.2 (C(10)); 21.3 (C(2)), 21.1 (C(11)); Rotamer B: 175.1 (C(7)); 128.8, 115.9, 75.3, 43.0, 42.8, 24.3, 22.3, 21.9. MS: 240 (5 + M⁺); 239 (10, M⁺); 224 (1, M-C₅H₅⁺); 208 (5, M - 1 - OCH₃⁺); 197 (126, 197 (97), M-C₆H₄OH⁺); 180 (4, M - COOCH₃⁺); 164 (12, M-COOC₂H₅⁺); 154 (93, M - C₆H₅-COCH₃⁺); 139 (13), 122 (37), 111 (64), 103 (32), 95 (60), 79 (43), 40 (3). Further details see the supplementary information. The cis-product rac-9 was obtained (oil, 180 mg, 46%), which could be crystallized from CHCl₃/hexane to give white crystals.

Methyl rac-trans-2-(N-Acetyl-N-isopropylamino)cyclohex-3-ene-1-carboxylate (rac-12). A 10-mL autoclave was charged with rac-8 (100 mg, 0.42 mmol) and 10% Pd/C (60 mg, 0.06 mmol) and EtOH (5 mL). The autoclave was secured with H₂ (30) and shaken overnight under 5-6 bar H₂ pressure. The catalyst was then removed by filtration over Celite and washed with EtOH (50 mL). Evaporation of the filtrates and FC with
AcOEt/hexane 1:1 of the residue provided rac-12 (72 mg, 71 %) as a colorless oil. IR (CCl4): 2995, 2920, 2860, 2740, 1650, 1540, 1380, 1200, 1100, 1130, 1025, 940. 1H-NMR (400 MHz, CDCl3): 3.81 (dt, J = 11.8, 3.8, H-(C(8))); 3.06 (s, CH2O); 2.27 (sept, J = 6.8, H-(C(1))); 2.61 (dt, J = 11.5, 3.7, H-(C(3))); 1.21 (t, CH3(C(6))); 1.11 (t, CH3(C(4))); 1.08 (m, CH3(C(5))); 1.37 (t, CH(C(4))); 1.68 (dd, J = 8.6, CH2, CH3(C(3))). 13C-NMR (100 MHz, CDCl3): 175.3 (C(7)); 171.3 (C(9)); 30.1 (C(2)); 52.3 (CH2O); 47.7 (C(1)); 47.6 (C(11)); 31.0, 30.9, 26.1, 25.4 (C(5)), C(6), C(4), C(9); 24.3 (C(4a)); a yellow oil (1.6 mm, 1.0 ml) was obtained. A 1.6M soln. of BuLi (hexane, 15 ml) at -85°, stirring of the mixture at the same temp. for 3 h gave a light yellow oil. It was warmed up overnight to r.t. and poured onto sat. aq. NH4Cl soln. and extracted with Et2O (2 x 10 ml). The org. phase was washed with sat. aq. NaHCO3. Soln. (20 ml) then with sat. aq. NaCl soln. (2 x 30 ml). Drying over Na2SO4, evaporation of the solvent and FC with AcOEt/hexane 1:1 over 100 g of silica gel gave methyl cyclohexa-1,3-diene-1-carboxylate (16) [24] as a yellow oil (11 mg, 14 %).

Further elution furnished the more polar rac-11 as a yellow oil, which could be crystallized from CHCl3/hexane to give clear white crystals (30 mg, 26 %). M.p. 94–95° IR (CHCl3): 2995, 2920, 2860, 2740, 1640, 1530, 1250, 1080, 1050, 880, 750, 690. 1H-NMR (400 MHz, CDCl3): 5.82 (m, J = 10.2, H-(C(7))); 5.59 (br. d, J = 10.2, H-(C(8))); 4.98 (sept, J = 6.9, H-(C(1))); 4.26 (br. s, H-(C(8a))); 3.44 (d, J = 19.2, Hb-C(3)); 3.21 (d, J = 19.2, Hc-C(3)); 2.51 (m, H-(C(4a))); 2.45 (m, Hc-(C(5))); 1.97 (m, Hb-(C(6)), Hb-(C(5))); 1.81 (m, Hb-(C(5))); 1.23, 1.16 (2d, J = 6.9, CH2(C(2)), CH2(C(3))).

1H-NMR (100 MHz, CDCl3): 206.8 (C(2)); 166.4 (C(2)); 132.0 (C(7)); 128.8 (C(9)); 49.5 (C(8a)); 49.2 (C(9)); 47.2 (C(4a)); 45.2 (C(5)); 21.5 (C(4)); 20.9, 20.7 (C(C(2), C(C(3)))) MS: 208 (M+1), 207 (40, M*), 193 (22), 164 (17), 112 (16), 107 (22), 96 (18), 79 (75), 77 (59), 70 (100).

**X-Ray Crystal Structure Determination of rac-15**

H1, CH3NO2, Mw = 207.3, monoclinic, P21/c, a = 11.5(2), b = 8.95(2), c = 12.71(3) Å, V = 1129.3 Å3, Dcalc = 1.199 g·cm–3, ρcalc = 0.81, ρcalc = 1.45. Max shift/σ(a) = 0.001, residual density(e/Å3) max. 0.18. Neutral complex-atom scattering factors in StoeAED2 [25]. All further calculations were carried out using the SHELXS-86 [25].

**Table 1**

| No. | Ion Data | Remarks |
|-----|----------|---------|
| 1   | C        | Substance |
| 2   | H        | Substance |

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