A dirhodium(II)-catalyzed intramolecular C-H insertion reaction of 2-oxygen-substituted cyclohexyl diazoacetates 1a–f was investigated. In contrast to the trans-2-methoxy-1a and trans-2-(p-methoxybenzoxyl)cyclohexyl derivatives 1b, which, upon treatment with 1 mol% dirhodium(II) tetraacetate in boiling benzene, gave a complex mixture, the trans-2-(2-tert-butylidimethylsilyl)cyclohexyl derivative 1c gave, in addition to the β-lactone 3c (16%), cis- and trans-fused octahydrobenzo[9]furan-2-ones 2c in 22 and 18% yields, respectively. Similar treatment of the cis-isomer 1d gave the β-lactone 3d as the major product (34%) and cis- and trans-fused γ-lactones 2d (7 and 18% yields, respectively) as minor products. The (1R*,2R*,3R*)-3-benzoxyl-2-(2-tert-butylidimethylsilyl)cyclohexyl derivative 1e gave the γ-lactones 2e in 75% combined yield as a 5:2 mixture of cis- and trans-fused isomers, while the (1R*,2S*,3R*)-isomer 1f afforded the trans-fused γ-lactone 2f in 62% yield as a single product.

Key words dirhodium(II) tetraacetate; carbon--hydrogen insertion reaction; regioselectivity; octahydrobenzo[9]furan-2-one; β-lactone

A dirhodium(II)-catalyzed intramolecular C-H insertion reaction of α-diazoacarbonyl compounds has emerged as a valuable tool for the construction of carbo- and heterocyclic compounds. In connection with our synthetic studies on avermectin antibiotics, we have investigated the dirhodium(II)-catalyzed intramolecular C-H insertion reaction of 2-oxygen-substituted cyclohexyl diazoacetates 1 in the hope of obtaining 7-oxygen-substituted octahydrobenzofuran-2-ones 2. In the reaction of 1 there are theoretically four possible reaction pathways leading to isomeric γ-lactones 2 and 3, β-lactones 4, and oxonium ylides 5. To control the regiochemistry and, if possible, the stereochemistry of the reaction, we planned to examine the effect of oxygen-substituents in the cyclohexyl diazoacetates. In this paper, we describe results obtained with more readily accessible 2-oxygen-substituted cyclohexyl diazoacetates 1a–f, in which the diazoacetoxy group occupies an equatorial position.

Results

We began our investigations by examining the reaction of diazoacetates 1a–d. The trans-isomers 1a–c and the cis-isomer 1d were readily prepared starting from commercially available cyclohexene oxide and cis-1,2-cyclohexanediol, respectively (see Chart 1 and Experimental). The 1H-NMR spectra of 1a–c showed the 1,2-diaxial nature of the H-1 and H-2 protons (J1,2 = 8.0–9.0 Hz), confirming that both the oxygen-substituents adopt equatorial positions. On the other hand, the 1H-NMR spectrum of the cis-isomer 1d indicated the equatorial nature of H-2 (J1,2 = 2.7, J2,3 = 6.6, 2.7 Hz) and the axial disposition of H-1 (J1,2 = 2.7, J1,6 = 8.7, 2.7 Hz), suggesting that the 2-tert-butylidimethylsilyl)oxy (TBDMS) and diazoacetoxy groups occupy axial and equatorial positions, respectively.

In general, a solution of a diazoacetate 1 in benzene was added to a boiling benzene solution of 1 mol% of dirhodium(II) tetraacetate [Rh2(OAc)4] via a syringe pump over a period of 4–6 h. After removal of the solvent, the crude material was chromatographed on silica gel.

Treatment of the trans-2-methoxy-1a and 2-(p-methoxybenzoxyl)cyclohexyl derivatives 1b in this manner gave a complex mixture in each case; the γ-lactone 2b was isolated in only 4% yield as a mixture of two diastereoisomers from the reaction mixture of 1b. The structural assignment of 2b rests largely on the basis of spectral data (see Experimental).

In contrast, the reaction of the trans-2-(2-tert-butylidimethylsilyl)cyclohexyl derivative 1c under the same conditions gave the β-lactone 4c (16%), and the cis- and trans-fused γ-lactones 2c in 22 and 18% yields, respectively. The structure of the β-lactone 4c was assigned mainly on the basis of its IR spectrum (1825 cm−1). The stereochemistry of trans-2c was determined by comparison of the 1H-NMR coupling constants with those of the
related bicyclic trans-fused \(\gamma\)-lactone 10 derived from menthyl diazaoctoacetate\(^{10}\): the observed coupling constants between H-3 and H-3a (12.5 Hz) and between H-3a and H-7a (10.6 Hz) in trans-2c were in good agreement with the reported values for 10 \((J_{3,3a} = 12.4, J_{3a,7a} = 10.7\) Hz) (Table 2). The stereochemistry of cis-2c was deduced from differential nuclear Overhauser effect (NOE) experiments (Fig. 1); irradiation of the signal due to H-3 caused a 12% enhancement in the intensity of the signal due to H-7, and 5.5–7% enhancement was observed between
Table 1. Dirhodium(II)-Catalyzed Intramolecular C-H Insertion Reaction of α-Diazo ketones

<table>
<thead>
<tr>
<th>Entry</th>
<th>α-Diazo ketone</th>
<th>Conditions</th>
<th>Products (Yields)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1a</td>
<td>Benzene reflux, 5 h</td>
<td>A complex mixture</td>
</tr>
<tr>
<td>2</td>
<td>1b</td>
<td>Benzene reflux, 5 h</td>
<td>2b (4%)</td>
</tr>
<tr>
<td>3</td>
<td>1c</td>
<td>Benzene reflux, 6 h</td>
<td>cis-2c (22%), trans-2c (18%), 4c (16%)</td>
</tr>
<tr>
<td>4</td>
<td>1d</td>
<td>Benzene reflux, 5 h</td>
<td>cis-2d (7%), trans-2d (18%), 4d (34%)</td>
</tr>
<tr>
<td>5</td>
<td>1e</td>
<td>Benzene reflux, 4 h</td>
<td>(75% as a 5:2 mixture of cis-2e and trans-2e)</td>
</tr>
<tr>
<td>6</td>
<td>1f</td>
<td>Benzene reflux, 4 h</td>
<td>trans-2f (62%)</td>
</tr>
<tr>
<td>7</td>
<td>1f</td>
<td>Toluene reflux, 2 h</td>
<td>trans-2f (48%)</td>
</tr>
<tr>
<td>8</td>
<td>17</td>
<td>Benzene reflux, 5 h</td>
<td>cis-18 (31% as a 1:7 mixture of cis-18 and trans-18)</td>
</tr>
</tbody>
</table>

a) Reactions were carried out with 1 mol% of Rh₂(OAc)₄. b) A 4:1 mixture of two diastereoisomers. c) A 2:1 mixture of two diastereoisomers.

H-3a and H-7a. A similar treatment of the 1,2-cis-isomer 1d with Rh₂(OAc)₄ gave the β-lactone 4d (34%), and the cis- and trans-fused γ-lactones 2d in 7 and 18% yields, respectively.

Since the 2-TBDMS-oxyl group alone could not prevent β-lactone formation, we next investigated the reaction of the diazoacetacetates 1e and 1f having an additional axial benzyloxy group at the 3-position. Two isomeric compounds 1e and 1f were synthesized as shown in Chart 2. Thus, 3-(p-methoxybenzoylo)cyclohexene (11) was stereoselectively oxidized by a catalytic amount of osmium tetroxide and N-methylmorpholine N-oxide (NMO) to give the syn-diol 12,7,8 which was allowed to react with benzaldehyde dimethylacetal in the presence of p-toluene-sulfonylic acid, followed by ring-opening of the cyclic acetal with diisobutylaluminum hydride (DIBAL-H)9 and silylation to give 13 in 57% yield. Deprotection of the p-methoxybenzyl (PMB) group of 13 with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ)10 gave the mono alcohol, which was esterified with diketene, followed by
Table 2. The Vicinal Coupling Constants \( J_{2,3a}, J_{3a,7a} \) of trans-Fused \( \gamma \)-Lactones

<table>
<thead>
<tr>
<th>( \gamma )-Lactone</th>
<th>( R^1 )</th>
<th>( R^2 )</th>
<th>( R^3 )</th>
<th>( R^4 )</th>
<th>( J_{2,3a} ) (Hz)</th>
<th>( J_{3a,7a} ) (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>trans-2e</td>
<td>H</td>
<td>H</td>
<td>OTBDS</td>
<td>H</td>
<td>12.5</td>
<td>10.6</td>
</tr>
<tr>
<td>trans-2d</td>
<td>H</td>
<td>OTRBDS</td>
<td>H</td>
<td>H</td>
<td>13.0</td>
<td>11.1</td>
</tr>
<tr>
<td>trans-2e</td>
<td>H</td>
<td>H</td>
<td>OTBDS</td>
<td>OBN</td>
<td>12.7</td>
<td>11.1</td>
</tr>
<tr>
<td>trans-2f</td>
<td>H</td>
<td>OTRBDS</td>
<td>H</td>
<td>OBN</td>
<td>12.9</td>
<td>11.2</td>
</tr>
<tr>
<td>10&lt;sup&gt;th&lt;/sup&gt;</td>
<td>Me</td>
<td>H</td>
<td>iso-Pr</td>
<td>H</td>
<td>12.4</td>
<td>10.7</td>
</tr>
</tbody>
</table>

* a) Ref. 4a.

Fig. 1. The Result of NOE Experiments on \( \text{cis-2c} \)

diazo transfer reaction with \( p \)-toluenesulfonyl azide to afford \( \text{1e} \). The stereochemistry was assigned on the basis of the \( ^1\text{H}-\text{NMR} \) spectrum, which indicated that the diazaacetoxoacylated silyloxy groups both occupy equatorial positions and the benzyl group takes an axial position (see Experimental). Repetition of the same sequence starting from 3-(benzyl)oxy-cyclohexene (14)<sup>10</sup> produced \( \text{1f} \), whose \( ^1\text{H}-\text{NMR} \) spectrum showed that the benzyl and silyloxy groups adopt axial positions and the diazaacetoxoacylated group takes an equatorial position (see Experimental). The diazomalonate \( \text{17} \) was also prepared from \( \text{16} \) in a similar manner.

The diazaacetoxoacylated \( \text{1e} \), upon treatment with \( \text{R}_{2}(\text{OAc})_{2} \), gave an inseparable 5:2 mixture of \( \text{cis-} \) and \( \text{trans-} \)-fused \( \gamma \)-lactones \( \text{2e} \) in 75% combined yield. On the other hand, a similar treatment of the diazaacetoxoacylated \( \text{1f} \) in boiling benzene proceeded smoothly to give the \( \text{trans-} \)-fused \( \gamma \)-lactone \( \text{2f} \) as a single isomer in 62% yield. When the same reaction was carried out in boiling toluene, the yield of \( \text{trans-2f} \) was reduced to 48%. The diazomalonate \( \text{17} \) gave the corresponding \( \text{cis-} \) and \( \text{trans-} \)-fused \( \gamma \)-lactones \( \text{18} \) in 31% combined yield and in a ratio of 1:7.

**Discussion**

Taking into account the results of earlier studies on the \( \text{C-H} \) insertion reactions catalyzed by dirhodium(II) catalysts, it would appear that the most likely mechanism for the reactions of diazaacetates would involve initial overlap of the metal carbene’s \( p \)-orbital with the \( e \)-orbital of the reacting \( \text{C-H} \) bond, which leads to new \( \text{C-C} \) and \( \text{C-H} \) bond formation with the carbene carbon as the metal dissociates.<sup>4a,11</sup> In the \( \text{C-H} \) insertion reaction of the cyclohexyl diazooacetates, \( \gamma \)-lactone formation appears to be favored, although there are some exceptions, involving \( \beta \)-lactone formation.<sup>5</sup> However, the regioselectivity becomes complicated if an alkoxy group is introduced near the site of insertion, because the oxygen atom itself<sup>6f</sup> and the \( \text{C-H} \) bond adjacent to the oxygen atom<sup>12</sup> become the preferred sites of reaction. Indeed, the 2-methoxy and 2-(p-methoxybenzyl)oxy derivatives \( \text{1a, b} \) each gave a complex mixture, possibly as a result of the reaction of the carbonyl with the ether oxygen atom. To overcome such complications, we introduced a bulky TBDBMS-oxo group at the C-2 position; this was expected to cause a reduction of the reactivity at the ether oxygen atom as well as the \( \text{C-H} \) bond at the C-2 position. As expected, the 2-TBDBMS-oxo derivatives \( \text{1c, d} \) gave the \( \gamma \)-lactones in moderate yields, but the \( \beta \)-lactone formation could not be prevented. The regioselective formation of the \( \gamma \)-lactones was achieved by introduction of an additional axial benzyl group at the C-3 position, as seen in the cases of \( \text{1e, f and 17} \). The axial 3-benzyl group may destabilize the transition state \( \text{A} \) leading to the \( \beta \)-lactone by steric interference with the dirhodium complex.

The diastereoselectivity of the \( \text{C-H} \) insertion reaction of cyclohexyl diazooacetates is known to be influenced by the conformation of the diazooacetoxoacylated group.<sup>5</sup> When this group occupies an axial position, the insertion reaction occurs with the equatorial \( \text{C-H} \) bond to give the \( \text{cis-} \)-fused \( \gamma \)-lactones. However, in the case of the equatorial diazooacetoxoacylated group, the stereochemical outcome is less predictable. For example, \( \text{trans-4-tert-butylcyclohexyl diazooacetate}^{10} \) and methyl diazooacetoxoacylated<sup>4a</sup> having an equatorial diazooacetoxoacylated group give only the \( \text{trans-} \)-fused \( \gamma \)-lactones, while \( \text{trans-4-methylcyclohexyl diazooacetate}^{4a} \) affords a mixture of the \( \text{cis-} \) and \( \text{trans-} \)-fused \( \gamma \)-lactones.<sup>13</sup>

The reaction of \( \text{1c-e} \) in which the diazaacetoxoacylated group occupies an equatorial position, gave a mixture of the \( \text{cis-} \) and \( \text{trans-} \)-fused \( \gamma \)-lactones. On the other hand, \( \text{1f} \) and \( \text{17} \) possessing an equatorial diazaacetoxoacylated or diazomalonoxo group, an axial 2-TBDBMS-oxo and axial 3-benzyl groups, afforded exclusively or predominantly the \( \text{trans-} \)-fused \( \gamma \)-lactones as a result of the preferential equatorial \( \text{C-H} \) insertion reaction at the C-6 position. The decrease of the formation of the \( \text{cis-} \)-fused \( \gamma \)-lactones in the reaction of \( \text{1f} \) as well as \( \text{17} \) can be rationalized in terms of the steric factor: the transition state \( \text{B} \) leading to the \( \text{cis-} \)-fused \( \gamma \)-lactone seems to be disfavored by steric interference between the axial 2-TBDBMS-oxo group and dirhodium complex, which is absent in the transition state \( \text{C} \) leading to the \( \text{trans-} \)-fused \( \gamma \)-lactone.

In summary, the present work has revealed that steric effects of neighboring substituents play an important role in determining the regio- and stereoselectivity in the dirhodium(II)-catalyzed intramolecular \( \text{C-H} \) insertion reactions of the 2-oxygen-substituted cyclohexyl diazooacetates. It may be anticipated on this basis that the axial-diazaacetoxoacylated will show different behavior. Related work aimed at exploring this general area is in progress.

**Experimental**

All melting points were uncorrected. IR spectra were recorded using a
trans-2-Methoxyxycyclohexyl-1-yl Diazoacetoacetate (1a) This compound was prepared according to the reported procedure.14) Diketene (237 mg, 2.82 mmol) and triethylamine (517 mg, 5.12 mmol) were added to a solution of trans-2-methoxy-1-cyclohexanol15) (330 mg, 2.56 mmol) in tetrahydrofuran (THF) (10 ml) at 0°C. The mixture was stirred at room temperature for 9 h, then poured into H₂O (10 ml) and extracted with Et₂O (3 x 10 ml). The extract was washed with brine, dried (MgSO₄), and concentrated. The residue was chromatographed on silica gel (hexane-EtOAc, 7:1) to give the corresponding acetooacetoate (385 mg, 71%) as a colorless oil. The resulting acetooacetoate (312 mg, 1.46 mmol) was dissolved in CH₂CN (10 ml), then triethylamine (295 mg, 2.92 mmol) and p-toluene-sulfonyl azide (318 mg, 1.46 mmol) were added at room temperature. The mixture was stirred for 11 h, then poured into H₂O (30 ml), and extracted with Et₂O (3 x 20 ml). The extract was washed with brine, dried (MgSO₄), and concentrated. The residue was chromatographed on silica gel (hexane-EtOAc, 5:1) to give 1b (329 mg, 94%) as a colorless oil. IR (CCl₄, cm⁻¹): 1710, 1655. H-NMR (300 MHz, CDCl₃, δ): 1.2-1.5 (4H, m, 2 CH₂), 1.6-1.8 (2H, m, CH₂), 2.0-2.2 (2H, m, CH₂), 2.49 (3H, s, CH₃CO), 3.18 (1H, ddd, J = 13.2, 9.2, 4.5 Hz, CH₃), 3.37 (3H, s, OCH₃), 4.87 (1H, d, J = 9.6, 8.4, 4.6 Hz, CH-C). Anal. Calcd for C₁₃H₁₅N₂O₄: C, 54.99; H, 6.71; N, 11.66. Found: C, 55.02; H, 6.90; N, 11.34.

trans-2-(p-Methoxybenzoyloxy)-1-cyclohexyl (6) PMB alcohol (1.80 g, 13 mmol) was added to a solution of cyclohexene oxide (982 mg, 10 mmol) in benzene (15 ml) at 0°C, then boron trifluoride diethyl ether complex (10 drops) was added to the resulting mixture. The whole was stirred at room temperature for 9 h, then poured into H₂O (30 ml), and extracted with EtOAc (3 x 20 ml). The extract was washed with brine, dried (MgSO₄), and concentrated. The residue was chromatographed on silica gel (hexane-EtOAc, 3:1) to give 6 (166.67 g, 70%) as a colorless oil. IR (CCl₄, cm⁻¹): 1710, 1655. H-NMR (300 MHz, CDCl₃, δ): 0.75-2.4 (8H, m, 4 CH₂), 2.68 (1H, brs, OH), 2.9-3.6 (2H, m, C₂-Ch₂), 3.58 (3H, s, OCH₃), 4.31, 4.62 (1H each, ABq, J = 11.0 Hz, CH₂Ar), 6.80 (2H, d, J = 9.0Hz, Ar-H), 7.20 (2H, d, J = 9.0 Hz, Ar-H). Anal. Calcd for C₁₇H₁₈O₃: C, 71.16; H, 8.53. Found: C, 71.42; H, 8.88. Exact MS m/z: 236.1402 (Calcd for C₁₇H₁₈O₃, 236.1403).

trans-2-(tert-Butyldimethylsilyloxy)-2-(p-methoxybenzoyloxy)cyclohexane (9) p-Methoxybenzaldehyde dimethylacetal (1.09 g, 6 mmol) and anhydrous p-toluene-sulfonyl acid (34 mg, 0.2 mmol) were added to a solution of cis-1-2-cyclohexanediol (232 mg, 1.5 mmol) in toluene (10 ml) at room temperature under a nitrogen atmosphere. The mixture was refluxed for 1 h, then recooled to 0°C. Dibal-H (0.955 ml in hexane, 10.5 ml, 10 mmol) was added to the cooled solution. The mixture was stirred at the same temperature for 1.5 h, then methanol (2 ml) and a saturated ammonium chloride solution (2 ml) were added to the mixture. The resulting mixture was stirred for 1 h, then diluted with EtOAc (30 ml), dried (MgSO₄), and concentrated. The residue was chromatographed on silica gel (hexane-EtOAc, 5:1) to give cis-2-(p-methoxybenzoyloxy)-1-cyclohexanol (405 mg, 86%) as a colorless oil. According to a procedure similar to that described for the preparation of 7, 9 (378 mg, 74%) was obtained.
obtained from the alcohol (346 mg, 1.46 mmol), tert-butylidimethyl-
chlorosilane (332 mg, 2.20 mmol) and imidazole (199 mg, 2.96 mmol) as a
colorless oil. IR (CCl₄) cm⁻¹: 1610, 1510. 1H-NMR (300 MHz, CDCl₃)
δ: 0.04 (3H, s, SiCH₃), 0.05 (3H, s, SiCH₃), 0.89 (9H, s, tert-But), 1.15–1.19
(8H, m, 4 × CH₂), 3.33 (1H, dt, J = 8.3, 2.8 Hz, C₂, CH₃), 3.78 (3H, s,
OCH₃), 3.85–3.95 (1H, m, C₂, CH₃), 4.47, 4.58 (1H each, Abq, J = 11.8 Hz,
CH₂Ar), 6.85 (2H, d, J = 8.7 Hz, Ar-H), 7.27 (2H, d, J = 8.7 Hz, Ar-H).
Anal. Caled for C₁₇H₂₃NO₂Si:C 68.52; H 8.7; Found: C 68.98; H 9.99.

cis-2-(Tert-Butyldimethylsiloxy)cyclohex-1-yl Diazoacetate (1d)
According to a procedure similar to that described for the preparation of
8, (1R,2S,3R,4S)-3-Benzoyl-2-(tert-butyldimethylsiloxy)cyclohex-1-
yl Diazoacetate (1e) According to a procedure similar to that described for
the preparation of 8, (1R,2S,3R,4S)-3-Benzoyl-2-(tert-butyldimethylsiloxy)
1-cyclohexanol (192 mg, 75%) was obtained from 13 (331 mg, 0.72 mmol) and DDQ (197 mg, 0.87 mmol). Following a procedure
similar to that described for the preparation of 1a, the resulting alcohol
(182 mg, 0.94 mmol) was allowed to react with dienone (65 mg, 0.65 mmol) and triethylamine (109 mg, 1.08 mmol) to give the corre-
sponding acetate (127 mg, 56%), which was then treated with p-
toluenesulfonyl azide (71 mg, 0.36 mmol) and triethylamine (61 mg, 0.6
mmol) to afford 1f (110 mg, 83%) as a colorless oil. IR (CCl₄) cm⁻¹:
2130 (C = N), 1720, 1660. 1H-NMR (300 MHz, CDCl₃) δ: 0.01 (3H, s,
SiCH₃), 0.08 (3H, s, SiCH₃), 0.90 (9H, s, tert-But), 1.4–2.0 (6H, m,
3 × CH₂), 2.46 (3H, s, CH₂O), 3.57 (1H, brd, J = 7.2 Hz, C₂, CH₃), 3.82 (1H
and triethylamine (109 mg, 1.08 mmol) to give the corre-

(1R,2S,3R,4S)-1-Benzoyl-2-(tert-butyldimethylsiloxy)-3-(p-
methoxybenzyl) cyclohexane (11)
2-Cyclohexen-1-ol (980 mg, 10 mmol) was added to a suspension of sodium hydride (60% dispersion in mineral oil, 1.45g, 36mol) in THF (18ml) and DMF
(6ml). The mixture was stirred under a nitrogen atmosphere. The mixture was vigorously
stirred for 30min, then PMB chloride (5.16g, 33mmol) and triet-
butylammonium iodide (369 mg, 1mmol) were added. The mixture was heated to 50°C. The solution was worked up, washed with
dried MgSO₄, and concentrated. The residue was chromatographed on silica gel (hexane-EtOAc, 50:1) to give 11 (1.05g, 84%) as a
white solid. IR (CCl₄) cm⁻¹: 3030–3050, 2960, 2870, 1605, 1505. 1H-
NMR (60 MHz, CDCl₃) δ: 1.3–1.4 (6H, m, 3 × CH₂), 1.75 (3H, s,
CH₃), 3.78 (1H, m, OCH₂), 3.86 (4H, m, CH₂O), 7.05 (2H, t, J = 8.2 Hz,
Ar-H), 7.34 (2H, d, J = 8.2 Hz, Ar-H). Anal. Caled for C₂₁H₂₃NO₂Si:C
56.44; H 8.29, N. 8.23. Found: C 56.52; H 8.41; N, 8.45.

(1R,2S,3R,4S)-3-(p-Methoxybenzyl)-1,2-cyclohexanediol (12)
Oxime tetracetate (a 4% aqueous solution, 0.7 ml, 1.66 mmol) was added to
the above solution (44 mg, 0.14 mmol). The mixture was allowed to stand at
room temperature for 2.2ml (7.97 mmol) in THF (25 ml) at room temperature. The mixture was stirred
for 5h, then diluted with water (30 ml), and extracted with EtOAc
(3 × 20 ml). The extract was washed with brine, dried (MgSO₄), and
concentrated. The residue was chromatographed on silica gel (hexane-EtOAc, 1:1) to give 12 (1.27g, 79%) as a colorless oil. IR (CCl₄) cm⁻¹:
3500–3700, 1610, 1510. 1H-NMR (500 MHz, CDCl₃) δ: 1.15–1.3 (3H, m,
CH₃), 1.49 (3H, s, brs, OH), 3.52 (3H, s, OCH₃), 4.91 (1H, d, J = 6.2 Hz,
Ar-H), 5.46 (1H, d, J = 6.2 Hz, Ar-H), 5.85 (2H, d, J = 8.5 Hz, Ar-H).
Anal. Caled for C₁₈H₂₃NO₂Si:C, H, O. Found: C 77.24; H, 8.34.

(1R,2S,3R,4S)-1-Benzoyl-2-(tert-butyldimethylsiloxy)-3-(p-
methoxybenzyl) cyclohexane (13)
The procedure was essentially the same as that used for the preparation of 9. Compound 12 (252 mg, 1mmol) was allowed to react with benzaldeyde dimethylacetal (0.3
mmol) and p-toluenesulfonic acid (2mg, 0.01 mmol) in toluene (5ml) at room temperature for 5h under a nitrogen atmosphere. The crude mixture was treated with DIBAL-H (1.5ml in toluene, 3.3ml, 55mol) at 0°C for 1h. Work-up gave (1R,2S,3R)-2-benzoyl-6-(p-
methoxybenzyl)1-cyclohexanol (257mg, 75%) as a colorless oil. The resulting alcohol (324 mg, 0.95 mmol) was then treated with tert-
butyldimethylchlorosilane (429 mg, 2.85 mmol) and imidazole (258 mg, 3.8 mmol) to give 13 (331 mg, 76%) as a colorless oil. IR (CCl₄) cm⁻¹:
1615, 1510. 1H-NMR (300 MHz, CDCl₃) δ: 0.01 (3H, s, SiCH₃), 0.04 (3H, s, SiCH₃), 0.88 (9H, s, tert-But), 1.4–1.55 (4H, m, 2 × CH₂), 1.7–1.8
(2H, m, CH₂), 2.5–3.65 (2H, m, C₂, CH₃), 3.79 (3H, s, OCH₃), 3.85–3.95 (1H, m, C₂, CH₃), 4.45, 4.50 (1H each, Abq, J = 11.5 Hz, CH₂Ar), 4.53, 4.59 (1H each, Abq, J = 12.2 Hz, CH₂Ar), 6.86 (2H, d, J = 8.4 Hz, Ar-H), 7.23 (2H, d, J = 8.4 Hz, Ar-H), 7.25–7.4 (5H, m, Ar-H). Anal. Caled for C₂₃H₂₇NO₂Si:C 71.01; H, 8.83. Found: C 70.78; H, 9.00.

(1R,2S,3R,4S)-1-Benzoyl-2-(tert-butyldimethylsiloxy)-3-(p-
methoxybenzyl) cyclohexane (14)
2-Cyclohexen-1-ol (980 mg, 10 mmol) was added to a suspension of sodium hydride (60% dispersion in mineral oil, 1.45g, 36mol) in THF (18ml) and DMF
(6ml). The mixture was stirred under a nitrogen atmosphere. The mixture was vigorously
stirred for 30min, then PMB chloride (5.16g, 33mmol) and triet-
butylammonium iodide (369 mg, 1mmol) were added. The mixture was heated to 50°C. The solution was worked up, washed with
dried MgSO₄, and concentrated. The residue was chromatographed on silica gel (hexane-EtOAc, 1:1) to give the corresponding acetate (232mg, 52%) as a colorless oil. The resulting malonate (100mg, 0.22 mmol) was dissolved in
CH₂CN (7ml), and then 1,8-diazabicyclo[3.4.0]undec-7-ene (DBU)
(0.05 ml, 0.33 mmol) and p-toluene sulfonil amide (51 mg, 0.26 mmol) were added to this solution at room temperature. The mixture was stirred for 17 h, then poured into H₂O (20 ml), and extracted with EtO₂ (3 x 10 ml). The extract was washed with brine, dried (MgSO₄), and concentrated. The residue was chromatographed on silica gel (benzene-acetone, 70:1) to give 17 (90 mg, 86%) as a colorless oil. IR (CCl₄) cm⁻¹: 1310 (C = N₂), 1760, 1760, 1690. ¹H-NMR (300 MHz, CDCl₃): δ = 0.01 (3H, s, CH₃), 0.02 (3H, s, CH₃), 0.37 (8H, s, tert-Bu), 1.45-1.59 (9H, m, 3x CH₃), 1.37 (3H, t, J = 7.1 Hz, CH₃), 2.94-3.55 (11H, m, C₂H₅, 3.93-4.01 (1H, m, C₂H₅), 4.31 (2H, qd, δ = 7.1, 1.3 Hz, OCH₂), 4.58 (2H, s, CH₂Ar), 5.26 (1H, dt, J = 9.0, 3.0 Hz, C₂H₅), 7.2-7.4 (5H, m, Ar-H). Exact FAB-MS m/z: 477.2407 (Calcd for C₂₆H₂₄N₂O₂ SiH⁺: 477.2436). ¹³C-NMR (75 MHz, CDCl₃) for the major isomer: δ = 2.0-1.2 (9H, s, CH₃), 1.45-1.59 (9H, m, 3x CH₃), 1.37 (3H, t, J = 7.1 Hz, CH₃), 2.94-3.55 (11H, m, C₂H₅, 3.93-4.01 (1H, m, C₂H₅), 4.31 (2H, qd, δ = 7.1, 1.3 Hz, OCH₂), 4.58 (2H, s, CH₂Ar), 5.26 (1H, dt, J = 9.0, 3.0 Hz, C₂H₅), 7.2-7.4 (5H, m, Ar-H). Exact FAB-MS m/z: 477.2407 (Calcd for C₂₆H₂₄N₂O₂ SiH⁺: 477.2436). ¹³C-NMR (75 MHz, CDCl₃) for the minor isomer: δ = 2.0-1.2 (9H, s, CH₃), 1.45-1.59 (9H, m, 3x CH₃), 1.37 (3H, t, J = 7.1 Hz, CH₃), 2.94-3.55 (11H, m, C₂H₅, 3.93-4.01 (1H, m, C₂H₅), 4.31 (2H, qd, δ = 7.1, 1.3 Hz, OCH₂), 4.58 (2H, s, CH₂Ar), 5.26 (1H, dt, J = 9.0, 3.0 Hz, C₂H₅), 7.2-7.4 (5H, m, Ar-H). Exact FAB-MS m/z: 477.2407 (Calcd for C₂₆H₂₄N₂O₂ SiH⁺: 477.2436).
reaction was carried out in refluxing toluene, trans-2f (44 mg, 48%) was obtained from If (100 mg, 0.22 mmol) and Rh₂(OAc)₄ (1 mg).

The Intramolecular C–H Insertion Reaction of 17 Following the general procedure, 17 (10 mg, 0.19 mmol) was treated with Rh₂(OAc)₄ (0.3 mg) and the crude material was chromatographed on silica gel (hexane-EtOAc, 20:1) to give an inseparable 1:7 mixture of ethyl (3R,3aS*,6R*),7S*),7aR*)- and (3S,3aR*,6R*,7S*,7aR*)-6-benzoyl-7-(tert-butylmethylsilyl)oxy-2-oxo-3,3a,4,5,6,7,7a-octahydrobenzofuran-3-carboxylates (cis-18 and trans-18) (26 mg, 31%) as a colorless oil. IR (CCl₄ cm⁻¹): 1790, 1735. ¹H-NMR (300 MHz, CDCl₃) for the major isomer δ: 0.02 (3H, s, SiCH₃), 0.06 (3H, s, SiCH₃), 0.87 (9H, s, tert-Bu), 1.60–1.90 (4H, m, 2 × CH₂), 1.31 (3H, t, J = 7.1 Hz, CH₃), 2.97 (1H, qd, J = 13.0, 6.0 Hz, C₃H₂), 3.25 (1H, d, J = 13.1 Hz, C₃H₂), 3.6–3.65 (1H, m, C₃H₂), 4.2–4.3 (2H, m, C₃H₂ and C₃H₂), 4.26 (2H, q, J = 7.1 Hz, CH₂O), 4.47, 4.60 (1H each, ABq, J = 11.8 Hz, CH₂Ar), 7.25–7.34 (5H, m, Ar-H). ¹³C-NMR (75 MHz, CDCl₃) for the major isomer δ: −5.2, −4.9, 14.1, 18.0, 22.9, 24.5, 25.6 (3), 39.2, 52.7, 61.8, 67.1, 78.2, 71.4, 81.9, 127.5 (2), 127.9, 128.5 (2), 133.7, 167.6, 171.4. Exact FAB-MS m/z: 449.2354 (Ca. for C₅₂H₄₃O₇Si·H⁺: 449.2360).

References and Notes


7) A similar stereoselectivity was reported in the osmium tetroxide oxidation of trans-1,2-dibenzoyl-3-cyclohexene.₄⁶


13) Doyle and co-workers have recently reported regio- and diastereosecontrol in the intramolecular C–H insertion reactions of chiral cis- and trans-2-methylcyclohexyl diazoacetates using chiral diiodomethane carboxamidates.₄⁶
