

The Novel Sequence Diels-Alder Reaction/Ireland-Claisen Rearrangement Applied to Acyclic Dienophiles: New Insights into the Selectivity of the Ireland-Claisen Rearrangement

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Dedicated with admiration and respect to Professor Albert Eschenmoser in honour of his scientific achievements and his enthusiasm as a teacher

Abstract: The new dienes **4a-d**, **7** and **11** reacted in good yields with acyclic dienophiles like methyl acrylate and diethyl fumarate in the tandem process Diels-Alder reaction/Ireland-Claisen rearrangement. Analysis of the relative configuration of products **5**, **6**, **8-10** and **12** indicated that preference for the chair or boat transition state of the Ireland-Claisen rearrangement is strongly influenced by the relative configuration of the substituents of the cyclohexene ring.

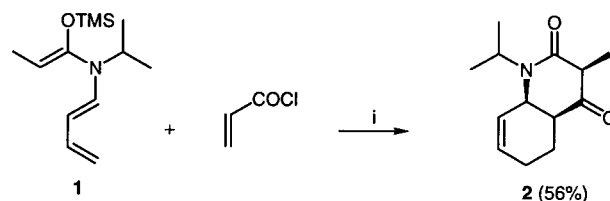
Key words: Diels-Alder reaction, Ireland-Claisen rearrangement, tandem reaction, diastereoselectivity, high pressure

Combining two or more reactions into one synthetic operation has become a popular higher order strategy with the goal to reduce the length of the synthesis of a specific target molecule.¹ Beautiful applications of this strategy to the synthesis of complex molecules have been reported.² Some of the reported syntheses were motivated simultaneously by the idea to decrease the number of steps as by the intention to imitate the biosynthesis by a biomimetic process.³ Impressive advances in our understanding of mechanism and in the number of reactions and reaction conditions available have in recent years allowed to develop numerous examples of these reaction sequences combining several mechanistically distinct steps into one synthetic operation. Such reaction sequences have been designated as "domino",^{1d} "tandem",^{1c,1f-h} "cascade",⁴ "serial" and "sequential"^{1a} processes, just to name a few.

Combining two well-known stereoselective reactions like the Diels-Alder reaction and sigmatropic rearrangements should create an attractive synthetic process.⁵ There are different reasons for the attractiveness of such processes. The sequence belongs to the class of heterogenerative coupled transformations,^{1a} as the first bond-forming reaction sets the stage for the next event generating new functionalities which were not present in the starting materials. Heterogenerative processes can be used with at least comparable if not greater advantage in synthesis than their homogenerative counterparts.^{1a} Unusual substitution pattern of six-membered rings can be obtained directly.^{5a,6} Choosing a sigmatropic rearrangement which will create

an additional C-C bond, a total of 3 C-C bonds will be formed in such a process. Not only the relative configuration in the six-membered ring but also at the exocyclic chiral centre will be controlled by the configuration at the double bond and by the geometry of the transition state for the sigmatropic rearrangement.

Our first trials to realise this synthetic strategy were based on the use of *N*-butadienyl-*N*-alkyl *N,O*-trimethylsilyl ketene acetals **1** (Scheme 1).⁷ The sequence leading to bicyclic product **2** was a Diels-Alder reaction/acylation process. It is well-known that the temperatures needed for the sigmatropic rearrangements of *O*-allyl *O,O*-trimethylsilyl ketene acetals is much lower than those for the corresponding *N,O*-silyl ketene acetals.⁸

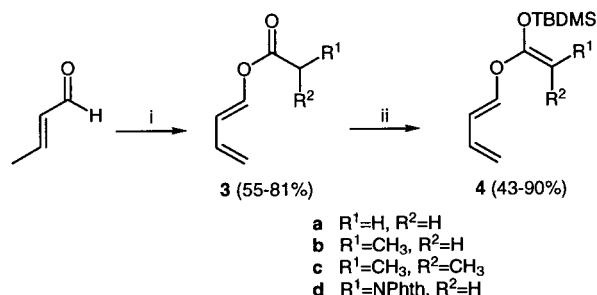


Scheme 1 Reaction conditions: i) THF, -78 °C → rt, MeOH

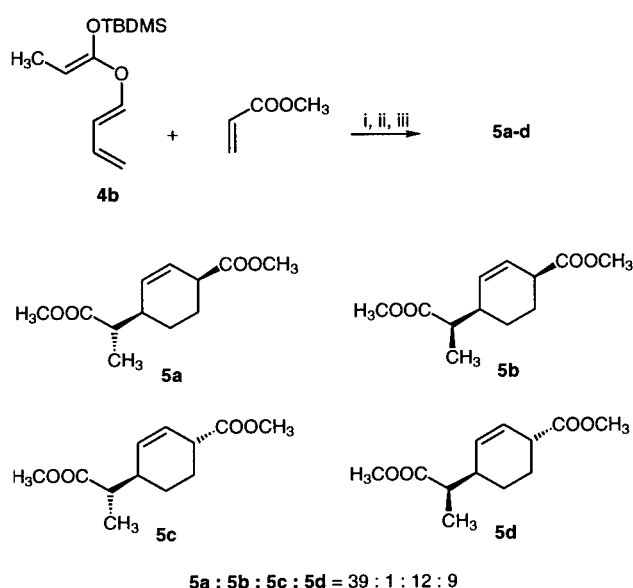
We have recently developed a method to obtain the *O*-butadienyl *O,O*-trialkylsilyl ketene acetals **4a-d** in good yields and with excellent diastereoselectivities in two steps (Scheme 2).⁹ The ketene acetals **4a-d** reacted readily with cyclic dienophiles like *N*-phenyl maleimide.⁹ In this letter we report an extension of this strategy to the reaction of our *O*-butadienyl *O,O*-*tert*-butyldimethylsilyl ketene acetals **4** with acyclic dienophiles.

As butadienes **4** are not very reactive in Diels-Alder reactions we tried to promote the reaction sequence using high pressure.¹⁰ Treating dienes **4b**, **4c** with *tert*-butyl acrylate in the presence or in the absence of radical inhibitors like 2,6-di-*tert*-butyl-*p*-cresol only lead to polymerisation. However, reaction of methyl acrylate with butadiene **4b** in dichloromethane at 40 °C under 12 kbar pressure allowed to isolate the products **5a-d** in good yield (Scheme 3). The

four diastereomeric products of this reaction were isolated in 61% overall yield as methyl esters **5a-d** after hydrolysis with fluorosilicic acid according to DeShong,¹¹ and esterification with trimethylsilyl diazomethane. The facial selectivity of the reaction was 1.9:1 (*endo* : *exo*) and the diastereoselectivity for the Ireland-Claisen reaction was 39:1 for the *endo*-product (**5a** : **5b**) and 1.3:1 for the *exo*-product (**5c** : **5d**).



Scheme 2 Reagents: i) KO^tBu, THF, -78 °C, then R¹R²CHCOCl, THF, -78 °C → -50 °C; ii) LiHMDS, TBDMSCl, THF, 2-MeTHF, HMPA, -115 °C, 1.5h



Scheme 3 Reagents: i) CH₂Cl₂, 40 °C, 12 kbar, 3h; ii) H₂SiF₆, DME, r.t.; iii) Me₃SiCHN₂, THF/MeOH (10:4), rt, 1h, 61%

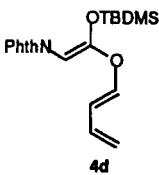
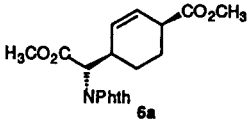
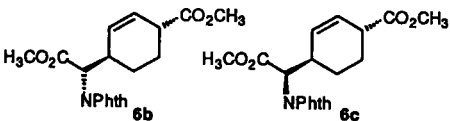
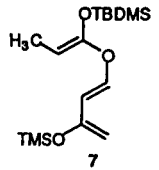
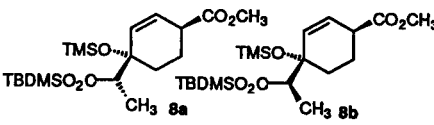
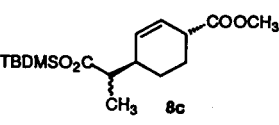
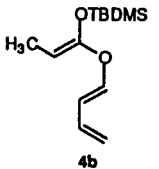
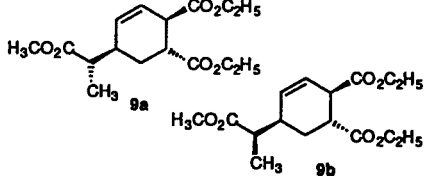
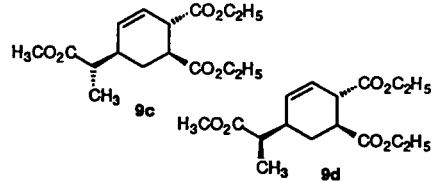
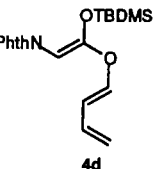
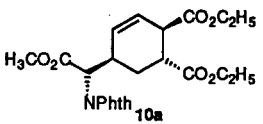
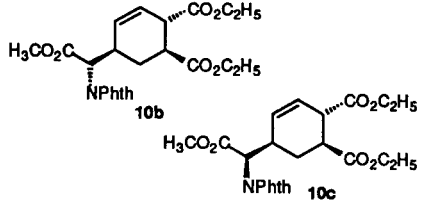
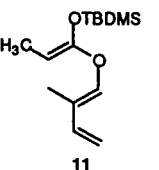
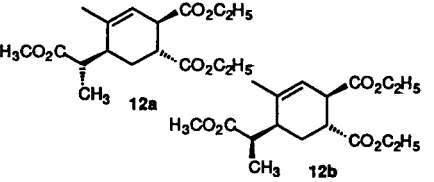
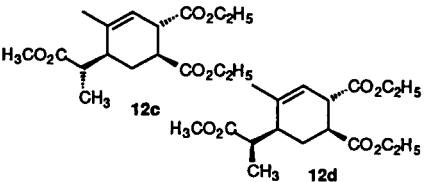
Thermal reaction of diene **4d** was achieved using a large excess of methyl acrylate and heating to 140 °C for 3h. Using the same procedure as for the high pressure reaction the products **6a-c** were isolated as their methyl ester in 60% yield (Table 1). The *endo-exo* selectivity was slightly lower than for the high pressure reaction namely 1.1:1 (*endo* : *exo*). For the *endo*-product only one single diastereoisomer **6a** could be identified, whereas the *exo*-product was a mixture of 8:1 (**6b** : **6c**) of the two diastereoisomers. Using the more reactive diene **7** the reaction temperature could be lowered to 120 °C. Unfortunately,

the product did not resist to the standard sequence of transformations to the methyl ester. Under these conditions the allylic trimethylsilyl ether was eliminated. Without any optimisation the products **8a-c** of the sequence Diels-Alder reaction/Claisen-Ireland rearrangement were purified as their *tert*-butyldimethylsilyl ester by flash-chromatography. The yield was low (17%), because of decomposition of the product on silica gel. The facial selectivity for the Diels-Alder reaction was considerably higher 5.2:1 (*endo* : *exo*). Surprisingly, the diastereoselectivity of the Ireland-Claisen rearrangement was low for the *endo*-product 1.9:1 (**8a** : **8b**). For the *exo*-product **8c** we were unable to determine the relative configuration and the diastereoisomeric ratio could only be guessed (≈ 2.5:1).

Using the more reactive dienophile diethyl fumarate the temperature for the sequence Diels-Alder reaction/Ireland-Claisen rearrangement could be lowered to 125 °C. The products were isolated as their methyl esters **9**, **10** and **12** in 40 to 64% yield (Table 1). The facial selectivity for the Diels-Alder reaction is in all cases about 1.5:1 (*endo* : *exo*). The diastereoselectivity of the Ireland-Claisen rearrangement is high for the *endo*-products and much lower for the *exo*-products.

The attribution of the relative configuration is based on extensive 1D- and 2D-¹H NMR measurements. The coupling constants of the protons on the cyclohexene ring are in good agreement with a half-chair conformation. In the case of the products obtained using methyl acrylate as dienophile the acetic acid side-chain prefers the *pseudo equatorial* position. In this conformation the proton at the ring carbon bearing the acetic acid side chain is preferentially in a *pseudo axial* position, which leads to characteristic coupling constants with its immediate neighbours. The conformation of the methyl ester is *pseudo axial* for the product of the *endo* Diels-Alder reaction and *pseudo equatorial* for the product of the *exo* Diels-Alder reaction. In the case of the products obtained from diethyl fumarate the results of the ¹H NMR measurements are in accordance with a half-chair conformation where the two ester functions are in a *pseudo equatorial* conformation. The acetic acid side-chain is therefore in a *pseudo axial* position for the products of the *endo*-selective Diels-Alder reaction and in a *pseudo equatorial* position for the products of the *exo*-selective Diels-Alder reaction. The attribution of the relative configuration of the exocyclic chiral centre was more difficult. Our attribution is based on the X-ray structure obtained for the product of the reaction of *N*-phenyl maleimide and diene **4d**.⁹ The coupling constant between the exocyclic chiral centre and the ring carbon bearing the acetic acid side-chain for this product was 8.9 Hz. For the *endo* Diels-Alder products **6a** and **10a** and for the *exo*-Diels-Alder products **6b** and **10b** large coupling constants between the proton at the exocyclic chiral centre and the adjacent ring proton (between 7.6 and 9.6 Hz) were observed, whereas the diastereoisomeric products **6c** and **10c** showed small coupling constants (between 3.7 and 5.4 Hz). Molecular mechanics calculations using the

Table 1: Tandem reactions using methyl acrylate and diethyl fumarate as dienophiles

Entry	Diene	Endo - Product(s)	Exo - Product(s)	Yield [%] (Diastereomeric Ratio)
1 ^a				60% 6a:6b:6c (10:8:1)
2 ^a				17% 8a:8b:8c ^{b,c} (17:9:5)
3 ^d				64% 9a:9b:9c:9d (21:1:9:5)
4 ^d				40% 10a:10b:10c (28:14:5)
5 ^d				63% 12a:12b:12c (15:1:6:4)

^a The cycloadditions of the examples 1 and 2 were performed heating an excess methyl acrylate together with the diene at 120-140°C (1h-3h). ^b The product of the reaction sequence was directly isolated without hydrolysis nor esterification. ^c The relative configuration was attributed in analogy to the cycloadducts 5 and 6. ^d The cycloadducts of the examples 3 to 5 were obtained reacting 2.3 eq. of diethyl fumarate with the corresponding diene at 125°C for 3h.

MM' programme indicated that the products of the tandem reaction should prefer one conformation. The substituents at the exocyclic centre try to avoid steric interactions with the vinylic proton in the cyclohexene ring. This conformational bias allows to tentatively assign the relative configuration at the exocyclic chiral centre. The dihedral angle between the proton at the exocyclic chiral carbon centre and the proton at the ring carbon bearing the acetic acid side chain is predicted to be near to 180° (*anti periplanar*) for the products obtained via a boat transition state. However for the products obtained via a chair transition state the dihedral angle should be near to 60° (*synclinal*). We used this argument for the attribution of the relative configuration.

As a consequence of this attribution, the Ireland-Claisen rearrangement is highly selective for a boat transition state of the cyclohexene rings obtained via *endo* Diels-Alder

reaction. In contrast, rearrangement of the cyclohexenes obtained via *exo* Diels-Alder reaction was considerably less, in most cases even almost unselective. The preference for the boat respectively chair transition state for the Ireland-Claisen rearrangement has been studied.^{8d,12} However, the fact that the relative configuration of the other substituents at the cyclohexene ring greatly influences the diastereoselectivity of the rearrangement has not been generally recognised so far. The diastereoselectivity of the Ireland-Claisen rearrangement in acyclic cases is mainly in favour of the chair transition state. We attribute the shift of the diastereoselectivity to the boat transition state in the case of the *endo* adducts to the steric hindrance of the OTBDMS group with the ring during the transition state (Figure 1). We assume that the cyclohexene ring is in a clear half-chair conformation. This half-chair conformation is in agreement with the result of an X-ray structure determination of a Diels-Alder adduct and with

our MM'-calculations. For the *exo* adducts the conformation of the cyclohexene ring has to be different during the transition state. The flattening of the cyclohexene ring should help to avoid the steric interactions which we invoked for the *endo* adducts and this should lead to a reduced selectivity.

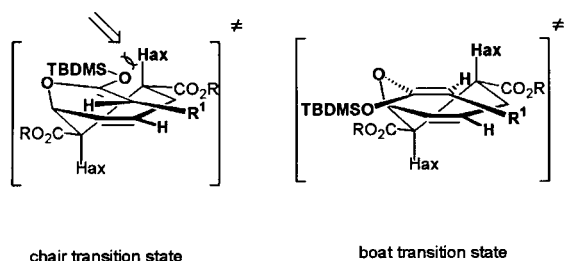


Figure 1 Chair and boat transition states for the Ireland-Claisen rearrangement.

In conclusion we have developed an efficient route for the conversion of the dienes **4a-d** into substituted cyclohexenes via the sequence Diels-Alder reaction/Claisen-Ireland rearrangement followed by a two-step procedure to obtain the methyl esters. The conversion occurs in good overall yields over the four synthetic steps and with good diastereoselectivities for the *endo* Diels-Alder product. This transformation allows to control not only the chiral centres in the cyclohexene ring but also the relative configuration at the exocyclic centre. This protocol should be applicable in natural product synthesis.

Preparation of compounds 5a-d: A solution of **4b** (933.3 mg, 3.88 mmol) and methyl acrylate (727.6 mg, 8.45 mmol) in CH_2Cl_2 (5 ml) was heated at 40 °C under 12 kbar in a sealed teflon tube. The solvent was removed in vacuo and to the crude material dissolved in DME (8 ml) H_2SiF_6 25% in H_2O (0.5 ml, 1 mmol) was added at r.t. After stirring for 0.5 h the solvent was removed in vacuo and DME (2 x 20 ml) was added and then removed in vacuo to dry the reaction mixture by azeotropic distillation. To the colourless oil dissolved in THF/MeOH (20 ml/4 ml) a 2M solution of trimethylsilyl diazomethane (2 ml, 4 mmol) was added. After stirring for 1 h the excess trimethylsilyl diazomethane was destroyed by dropwise addition of acetic acid. Removal of the solvent in vacuo and flash column chromatography (EtOAc / hexane = 1:4) afforded 538 mg (61%) of the mixture of diastereoisomers. Selected data for **5**: Mixture of diastereoisomers **5a-d**: IR: 3029, 2952, 2869, 1736, 1451, 1435, 1258, 1199, 1168; MS (DCI, NH_3) m/z 226 (4, M^+), 166 (53), 107 (41), 79 (100); Anal. calcd. for $\text{C}_{12}\text{H}_{18}\text{O}_4$: C 63.42, H 7.98; found: C 63.39, H 7.96. **5a**: ^1H NMR (400 MHz, CDCl_3): 5.76 (*dtd*, $^3J = 10.2$ Hz, $J = 2.2$ Hz, $J = 1.2$ Hz, 1H, H-2); 5.58 (*dtd*, $^3J = 10.0$ Hz, $J = 1.4$ Hz, $J = 0.8$ Hz, 1H, H-3); 3.62 (*2s*, 6H, $\text{H}_3\text{C}1.2$, $\text{H}_3\text{C}4.1''$); 3.05-2.97 (*m*, 1H, H-1); 2.45-2.30 (*m*, 2H, H-4, H-4.1); 2.00 (*ddt*, $^2J = 13.3$ Hz, $J = 6.2$ Hz, $J = 2.9$ Hz, 1H, H_a-6); 1.71-1.58 (*m*, 2H, H_a-6 , H_b-

C5); 1.47 (*dddd*, $^2J = 13.4$ Hz, $J = 11.6$ Hz, $J = 8.4$ Hz, $^3J = 3.1$ Hz, 1H, H_a-5); 1.06 (*t*, $^3J = 6.8$ Hz, 3H, $\text{H}_3\text{C}4.2$); ^{13}C NMR (100 MHz, CDCl_3): 176.0, 174.0, 131.9, 125.2, 51.6, 51.3, 43.7, 39.9, 37.5, 23.4, 22.3, 13.6. **5b**: ^{13}C NMR (100 MHz, CDCl_3): 130.6, 125.6, 43.3, 39.5, 37.4, 24.3, 23.2, 13.8. **5c**: ^1H NMR (400 MHz, CDCl_3): 5.76 (*m*, 1H, H-C(2)); 5.55 (*ddd*, $J = 2.5$ Hz, $J = 1.2$ Hz, 1H, H-3); 3.63, 3.61 (*2s*, 6H, $\text{H}_3\text{C}1.2$, $\text{H}_3\text{C}4.1''$); 3.05-2.97 (*m*, 1H, H-1); 2.45-2.30 (*m*, 2H, H-4, H-4.1); 1.95 (*m*, 1H, H-6); 1.79-1.72 (*m*, 1H, H-5); 1.71-1.58 (*m*, 1H, H-6); 1.30 (*qd*, $^2J \approx ^3J \approx ^3J = 12.8$ Hz, $^3J = 2.7$ Hz, 1H, H_a-5), 1.06 (*t*, $^3J = 7.0$ Hz, 3H, $\text{H}_3\text{C}4.2$); ^{13}C NMR (100 MHz, CDCl_3): 175.7, 174.5, 131.3, 125.7, 51.7, 51.4, 43.5, 41.5, 37.8, 24.9, 24.3, 13.2. **5d**: ^1H NMR (400 MHz, CDCl_3): 5.76 (*m*, 1H, H-2); 5.69 (*dm*, $^3J = 10.3$ Hz, 1H, H-3); 3.62 (*2s*, 6H, $\text{H}_3\text{C}1.2$, $\text{H}_3\text{C}4.1''$); 3.05-2.97 (*m*, 1H, H-1); 2.45-2.30 (*m*, 2H, H-4, H-4.1); 1.95 (*m*, 1H, H-6); 1.79-1.72 (*m*, 1H, H-5); 1.71-1.58 (*m*, 1H, H-6); 1.28 (*qd*, $^2J \approx ^3J \approx ^3J = 12.7$ Hz, $^3J = 3.1$ Hz, 1H, H_a-5); 1.09 (*t*, $^3J = 6.8$ Hz, 3H, $\text{H}_3\text{C}4.2$); ^{13}C NMR (100 MHz, CDCl_3): 175.8, 174.1, 130.2, 125.9, 51.7-51.4, 43.8, 40.2, 37.9, 25.8, 24.8, 13.5.

Typical procedure for the synthesis 9a-d: The mixture of diethyl fumarate (481.1mg, 2.80mmol) and diene **4b** (269.7 mg, 1.12 mmol) was stirred at 125 °C for 3h. DME (5 ml) and H_2SiF_6 25% in H_2O (0.2 ml, 0.4 mmol) was added and the solution stirred for 0.5 h. Two times 25 ml of DME were added and removed in vacuo. The oily residue was dissolved in THF/MeOH (10 ml/4 ml) and a 2M solution of trimethylsilyl diazomethane (1.0 ml, 2.0 mmol) was added and the solution stirred for 1 h. Removal of the solvent in vacuo and flash column chromatography (CH_2Cl_2 / Et_2O / hexane = 7:1:6) afforded 225.8 mg (64%) of the mixture of the diastereoisomers. Selected data for **9**: Mixture of diastereoisomers **9a-d**: IR : 2982, 2954, 2908, 1734, 1196, 1166; MS (DCI, NH_3): m/z 330 (12), 314 (15), 313 (100), 267 (54), HR-MS (DCI, isobutane): m/z calc. for $\text{C}_{16}\text{H}_{25}\text{O}_6$: 313.1646, found: 313.1652; Anal. calcd. for $\text{C}_{16}\text{H}_{24}\text{O}_6$: C 61.52, H 7.74; found: C 61.63, H 7.85. **9a**: ^1H NMR (400 MHz, CDCl_3): 5.80 (*ddd*, $^3J = 10.2$ Hz, $^3J = 3.8$ Hz, $^4J = 1.9$ Hz, 1H, H-3); 5.62 (*dt*, $^3J = 10.2$ Hz, $^3J \approx ^4J = 2.7$ Hz, 1H, H-4); 4.12 (*q*, $^3J = ^3J = 7.1$ Hz, 4H, $\text{H}_2\text{C}1.2$, $\text{H}_2\text{C}2.2$); 3.64 (*s*, 3H, $\text{H}_3\text{C}5.1''$); 3.49 (*ddt*, $^3J = 6.0$ Hz, $^3J = 3.7$ Hz, $^4J \approx ^5J = 2.3$ Hz, 1H, H-2); 3.00 (*ddd*, $^3J = 8.4$ Hz, $^3J = 6.1$ Hz, $^3J = 3.9$ Hz, 1H, H-1); 2.47-2.37 (*m*, 2H, H-5, H-5.1); 1.90 (*ddd*, $^3J = 13.7$ Hz, $^3J = 8.4$ Hz, $^3J = 5.3$ Hz, 1H, H-6_b); 1.82 (*ddd*, $^3J = 13.6$ Hz, $^3J = 5.9$ Hz, $^3J = 4.0$ Hz, 1H, H-6_a); 1.23 (*t*, $^3J = ^3J = 7.1$ Hz, 3H, $\text{H}_3\text{C}1.3$, $\text{H}_3\text{C}2.3$); 1.14 (*d*, $^3J = 6.7$ Hz, 3H, $\text{H}_3\text{C}5.2$). ^{13}C NMR (100 MHz, CDCl_3): 175.8, 174.0, 172.4, 130.6, 124.4, 60.9, 51.5, 43.4, 42.7, 38.5, 35.5, 25.4, 14.4, 14.1. **9c**: ^1H NMR (400 MHz, CDCl_3): 5.76 (*dt*, $^3J = 10.2$ Hz, $^3J \approx ^4J = 2.3$ Hz, 1H, H-3); 5.68 (*ddt*, $^3J = 10.2$ Hz, $^3J = 2.7$ Hz, $^4J \approx ^5J = 1.3$ Hz, 1H, H-4); 4.18-4.07 (*m*, $\text{H}_2\text{C}1.2$, $\text{H}_2\text{C}2.2$); 3.64 (*s*, 3H, $\text{H}_3\text{C}5.1''$); 3.44 (*dm*, $^3J = 10.7$ Hz, 1H, H-2); 2.88 (*ddd*, $^3J = 13.1$ Hz, $^3J = 10.7$ Hz, $^3J = 2.9$ Hz, 1H, H-1); 2.62-2.57 (*m*, 1H, H-5); 2.47-2.37 (*m*, 1H, H-5.1); 2.02 (*dm*, $^3J \approx 12.6$ Hz, 1H, H-6_b); 1.43 (*q*, $^3J \approx ^3J \approx ^3J = 12.8$ Hz, 1H,

H-6_a); 1.22 (*t*, $^3J = ^3J = 7.1$ Hz, 3H, H₃C1.3, H₃C2.3); 1.11 (*d*, $^3J = 7.1$ Hz, 3H, H₃C5.2). ¹³C NMR (100 MHz, CDCl₃): 175.5, 174.4, 172.7, 129.7, 125.0, 60.7, 51.6, 44.3, 43.1, 42.0, 38.3, 29.4, 14.1, 13.2. **9d**: ¹H NMR (400 MHz, CDCl₃): ≈5.76 (*dm*, $^3J = 10.1$ Hz, 1H, H-3); 5.55 (*dm*, $^3J = 10.3$ Hz, 1H, H-4); 4.18-4.07 (*m*, H₂C1.2, H₂C2.2); 3.66 (*s*, 3H, H₃C5.1"); 3.43 (*dm*, $^3J = 10.2$ Hz, 1H, H-2); 2.86 (*ddd*, $^3J = 13.1$ Hz, $^3J = 10.4$ Hz, $^3J = 2.9$ Hz 1H, H-1); 2.62-2.57 (*m*, 1H, H-5); 2.47-2.37 (*m*, 1H, H-5.1); ≈2.02 (*dm*, $^3J \approx 12.8$ Hz, 1H, H-6_b); 1.38 (*q*, $^3J \approx ^3J \approx 12.5$ Hz, 1H, H-6_a); 1.23 (*t*, $^3J = ^3J = 7.1$ Hz, 3H, H₃C1.3, H₃C2.3); 1.09 (*d*, $^3J \approx 7.7$ Hz, 3H, H₃C5.2). ¹³C NMR (100 MHz, CDCl₃): 175.4, 174.5, 172.6, 130.7, 124.8, 60.7, 51.6, 44.3, 43.5, 41.9, 38.2, 28.1, 14.0, 13.1.

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References and Notes

- (1) a) Wender P.A., Miller B.L. In *Organic Synthesis: Theory and Applications Vol. 2*; Hudlicky T., Ed.; JAI Press: Greenwich, 1993; p.27; b) Wender P.A. *Chem. Rev.* **1996**, *96*, 1; c) Tietze L.F., Beifuss U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 131; d) Tietze L.F. *Chem. Rev.* **1996**, *96*, 115; e) Ho T.-L. *Tandem Organic Reactions*; J. Wiley: New York, 1992; f) Hudlicky T. *Chem. Rev.* **1996**, *96*, 3; g) Bunce R.A. *Tetrahedron* **1995**, *51*, 13103; h) Denmark S.E., Thorarensen A. *Chem. Rev.* **1996**, *96*, 137.
- (2) Wender P.A., Howbert J.J. *J. Am. Chem. Soc.* **1981**, *103*, 688.
- (3) a) Johnson W.S. *Angew. Chem., Int. Ed. Engl.* **1976**, *88*, 33; b) Still W.C., Romero A.G. *J. Am. Chem. Soc.* **1986**, *108*, 2105; c) Schreiber S.L., Sammakia T., Hulin B., Schulte G. *J. Am. Chem. Soc.* **1986**, *108*, 2106; d) Heathcock C.H., Hansen M.M., Ruggeri R.B., Kath J.C. *J. Org. Chem.* **1992**, *57*, 2544.; e) Heathcock C.H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 665.
- (4) Padwa A., Weingarten M.D. *Chem. Rev.* **1996**, *96*, 223.
- (5) a) Neuschütz K., Velker J., Neier R. *Synthesis* **1998**, 227; b) Huber S., Stamouli P., Neier R. *J. Chem. Soc., Chem. Commun.* **1985**, 533; c) Huber S., Stamouli P., Jenny T., Neier R. *Helv. Chim. Acta* **1986**, *69*, 1898.
- (6) Schoepfer J., Marquis C., Pasquier C., Neier R. *J. Chem. Soc., Chem. Commun.* **1994**, 1001.
- (7) a) Baak M., Rubin Y., Franz A., Stoeckli-Evans H., Bigler L., Nachbauer J., Neier R. *Chimia* **1993**, *47*, 233; b) Franz A., Eschler P.-Y., Tharin M., Stoeckli H., Neier R. *Synthesis* **1996**, 1239; c) Franz A., Eschler P.-Y., Tharin M., Neier R. *Tetrahedron* **1996**, *52*, 11643.
- (8) a) Ireland R.E., Willard A.K. *J. Org. Chem.* **1974**, *39*, 421; b) Ireland R.E., Mueller R.H. *J. Am. Chem. Soc.* **1972**, *94*, 5897; c) Ireland R.E., Mueller R.H., Willard A.K. *J. Am. Chem. Soc.* **1976**, *98*, 2868; d) Wipf P. In *Comprehensive Organic Synthesis, Vol. 5*; Trost B.M., Fleming I., Eds.; Pergamon Press: New-York, 1991; p.827.
- (9) a) Velker J. Ph.D. thesis; Université de Neuchâtel: Neuchâtel, 1998.
- (10) Klaerner F.-G., Diedrich M.K. In *The Chemistry of Dienes and Polyenes, Vol 1*; Rappoport Z., Ed.; John Wiley and Sons Ltd.: Chichester, 1997.
- (11) Pilcher A.S., DeShong P. *J. Org. Chem.* **1993**, *58*, 5130.
- (12) Ireland R.E., Wipf P., Xiang J. *J. Org. Chem.* **1991**, *56*, 3572.