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Facial selectivity in addition reactions to the highly strained enone in tricyclo[5.2.1.0^{2,6}]deca-2(6),8-dienone and tricyclo[5.2.1.0^{2,6}]dec-2(6)-enone☆

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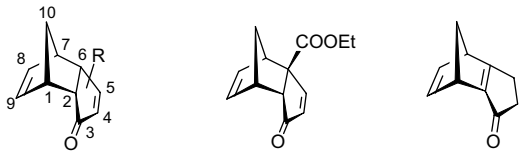
ABSTRACT

Tricyclo[5.2.1.0^{2,6}]deca-2(6),8-dien-3-one contains a highly strained central double bond due to geometrical constraints imposed by the tricyclic skeleton which does not allow optimal sp^2 hybridization at the C_2 and C_6 bridgehead positions. Michael addition of various nucleophiles (alkoxides, cyanide, and malonate) under protic conditions resulted in an exclusive *exo*-facial selectivity. This preference can be explained by steric and electronic factors. Michael additions using lithium dialkylcuprates resulted in predominant formation of *endo*-products, but also some *exo*-products were obtained. These *exo*-products arising from *endo*-approach may be the result of coordination of the cuprate with both the enone moiety and the olefinic C_8–C_9 bond. Michael additions to tricyclo[5.2.1.0^{2,6}]dec-2(6)-en-3-one, which lacks this C_8–C_9 double bond showed exclusive *exo*-facial selectivity to give *exo*-products. Besides these additions were all considerably slower than those to tricyclo[5.2.1.0^{2,6}]deca-2(6),8-dien-3-one proving significant electronic participation of the C_8–C_9 double bond in reactions with this substrate.

1. Introduction

The *endo*-tricyclo[5.2.1.0^{2,6}]decadienone system **1** is a versatile and useful synthon for the synthesis of a great variety of cyclopentenoids.[1,2] Its rigid structure, the presence of several easily accessible positions for functionalization, and the ability to undergo [4+2] cycloreversion[3] underly the importance of this polycyclic structure in synthetic organic chemistry. Moreover, the availability of both antipodes of **1** in enantiopure form makes it extremely useful for the enantioselective synthesis of a variety of cyclopentenoids and related natural products.[1]



1 **2** (Herz ester) **3**

Starting from the readily available Herz ester **2**,[4] chemical transformations involving 1,4-reduction of the enone system to **4**, followed by the Barton radical decarboxylation process[5] allow the introduction of a phenylselenyl group at the C_6 position in the tricyclodecadienone system[6] (Scheme 1). The synthesis of the reactive and strained tricyclodecadienone **3** was achieved by oxidative elimination of the 6-phenylselenyl group from phenylselenyl-*endo*-tricyclodecenone **6** (Scheme 1).[5]

Tricyclodecadienone **3** is a novel unsaturated tricyclic structure, which is characterized by a central enone system that forms a common structural element of both the rigid norbornene moiety and the annulated cyclopentenone ring. As a result of the geometrical constraints imposed by the tricyclic skeleton, which does not allow optimal sp^2 hybridization at the C_2 and C_6 bridgehead positions, the central C_2–C_6 enone double bond is highly strained and therefore highly reactive.

Steric energy calculation (MM2) for **3** gave a value of 40 kcal/mol of which a large contribution originates from the central C_2–C_6 double bond. Comparing **3** with **1** (R=H), which contains 31 kcal/mol steric energy, clearly reveals the effect of the central double bond and the outer enone double bond on the strain energy. Furthermore, the heat of formation of **1** (R=H) is 14 kcal/mol less than for **3**, indicating a more reactive enone system in tricyclodecadienone **3** than in **1** (R=H).

New functionalities may be introduced by nucleophilic addition to tricyclodecadienone **3** (Scheme 2). Whether *endo*-tricyclic compound **7** or *exo*-tricyclic **8** is formed depends on steric and electronic factors as well as on the stability of the intermediates and/or the final products. The main goal of this study was to establish the factors that determine the facial selectivity in nucleophilic additions to the tricyclo[5.2.1.0^{2,6}]deca-2(6),8-dienone system **3**.

☆ Preliminary account (without experimental part): Mao, X. S.; Volkers, A. A.; Klunder, A. J. H.; Zwanenburg, B. *Chin. Chem. Lett.*, **2001**, *12*, 581; published without permission of the senior author (B.Z.).

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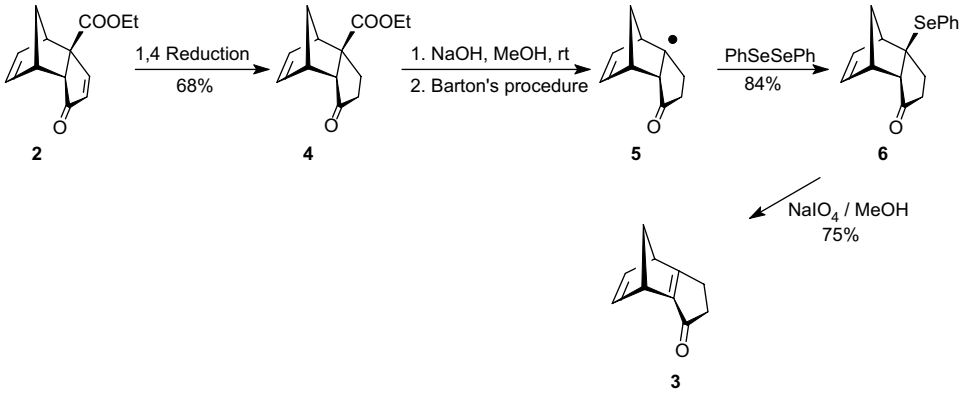


Scheme 1.

2. Results and discussion

2.1. Addition reactions under protic conditions

The Michael addition of a series of nucleophiles to **3** was investigated under protic conditions. The alkoxy nucleophiles were generated in an alcoholic solvent. As depicted in Scheme 2, the nucleophile can approach the enone either from the *exo*- or the *endo*-face. Although the addition of the nucleophiles is in principle an equilibrium, protonation of the initially formed product anions **9** and **10**, respectively, in a protic medium will be much faster than the reverse reaction to the starting material because of the low acidity of the conjugate acid of such ions. This implies that the outcome of these addition reactions to **3** is kinetically controlled. The cyanide and malonate ions were generated in acetonitrile, which is seemingly aprotic. Cyanide however, contains some water resulting in protic conditions. Also, in the malonate case, by intramolecular transfer of the malonate proton the product anion cannot revert to starting material and therefore the reaction is still kinetically controlled.

The experiments clearly show an exclusive *exo*-facial selectivity as only C_6 substituted *endo*-tricyclodecenones **7** were obtained (Table 1). The kinetically controlled product formation is governed by steric and/or electronic factors. Sterically, the methylene bridge is less demanding than the ethylene bridge[7] and therefore facial attack from the *exo*-face of the cyclopentenone moiety in **3** is kinetically favored over *endo*-facial addition. Electronically, addition from the *exo*-face may also be favored as considerable orbital interaction between the enone π-system and the olefinic C_8–C_9 bond may exist leading to an effective shielding of the *endo*-face of **3** for incoming nucleophiles. On the other hand *exo*-facial attack is promoted by stabilization of the emerging σ*-orbital by the norbornene π-system, which enhances incipient bond formation from the *exo*-face.[8]

The difference in product stability, i.e., **7** versus **8** is very minor as was apparent from AM1 calculations. The difference in heat of formation of these products amounts to 0.5–2.0 kcal/mol. Hence, the product ratio is not determined by a process involving product control.

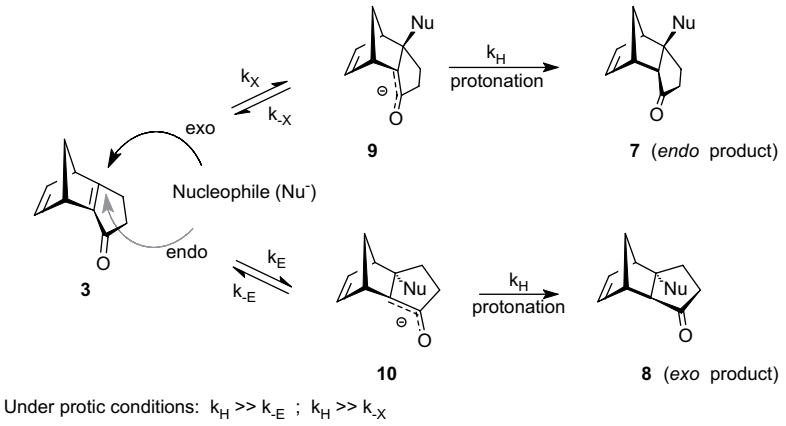
2.2. Addition reactions under aprotic conditions

Michael additions under aprotic conditions were also investigated using lithium dialkylcuprates as the nucleophilic reagents in diethyl ether. The results of these addition reactions are shown in Table 2. Interestingly, this mode of nucleophilic addition leads to the formation of minor amounts of *exo*-products **8h**,**i**. This observation implies that the addition of lithium dialkylcuprates preferentially takes place by an *exo*-facial attack giving *endo*-products **7h**,**i**, but some *endo* reaction occurs as well. These cuprate

Table 1
Addition reactions under protic conditions to **3**

Entry	Solvent	Base	Nucleophile	Time	Product	Yield (%)
a	*t*-BuOH	NaOH	*t*-BuO^-	3 days	**7a** (Nu=OH)	67
b	MeOH	NaOH	MeO^-	15 min	**7b** (Nu=OMe)	99
c	EtOH	NaOH	EtO^-	35 min	**7c** (Nu=OEt)	97
d	*n*-BuOH	NaOH	*n*-BuO^-	2 h	**7d** (Nu=OBu)	65
e	*i*-PrOH	NaOH	*i*-PrO^-	6 h	**7e** (Nu=O*i*-Pr) and **7a**	35 and 20
f	MeCN		CN^-	3 days	**7f** (Nu=CN)	95
g	MeCN	NaH	$CH(COOEt)_2^-$	5 days	**7g** (Nu=CH $(COOEt)_2$)	73

Reactions at room temperature.



Scheme 2.

Table 2
Addition reactions of lithium dialkylcuprates to **3** in Et_2O

Entry	Nucleophile	Temp (°C)	Time	Product	Yield (%)
h	$(CH_3)_2CuLi$	−78	15 min	**7h**+**8h** (10:1)	82
i	$(C_4H_9)_2CuLi$	−78	15 min	**7i**+**8i** (19:1)	92

Table 3
Michael addition to tricyclodecenone **14**

Entry	Nucleophile	Temp (°C)	Time	Product	Yield (%)
b	MeOH/NaOH	rt	20 h	**15b**	65 (+30% recovered **14**)
h	$(CH_3)_2CuLi/Et_2O$	−78	2 h	**15h**	82
i	$(C_4H_9)_2CuLi/Et_2O$	−78	2 h	**15i**	85

additions are therefore not completely stereoselective in contrast to the reactions with nucleophiles under protic conditions.

Cuprates are rather bulky reagents and accordingly a complete stereoselective reaction from the sterically less demanding *exo*-face would have been expected. Going from methyl to butyl cuprates a considerably enhanced selectivity for the *endo*-product is observed, but still some *exo*-product is produced with the most bulky nucleophile. Thus, steric approach control is the main controlling factor in this nucleophilic reaction. However, in comparison with the reaction under protic conditions, which is completely stereoselective, the cuprate reaction cannot be explained solely by steric governing factors. Some electronic effect must be involved as well to account for the formation of some *exo*-product.

It is suggested that the cuprates may coordinate with the enone moiety and the olefinic C_8–C_9 bond to give a d–π cuprate complex, whereby the nucleophilic species is favorably positioned at the *endo*-face of substrate **3** producing the *exo*-product. This special behavior of lithium dialkylcuprate in enone addition reactions to **3** is not unique as similar selectivities were observed in the addition of lithium dialkyl- and diarylcuprates to tricyclodecadienone **1** (R=H).[9] The special nature of the cuprate addition reaction involving complexation with the C_8–C_9 olefinic bond[10] can be verified by investigating the facial selectivity of lithium dialkylcuprate addition reactions to tricyclodecenone **14**, lacking the C_8–C_9 double bond.

2.3. Nucleophilic addition reactions to tricyclodecenone 14

In order to test the aforementioned hypothesis, tricyclodecenone **14** was subjected to nucleophilic addition reactions. The synthesis of **14** is depicted in Scheme 3. Starting with Herz ester **2**, palladium catalyzed hydrogenation gave the completely reduced tricyclodecanone ester **11**. After hydrolysis and decarboxylation under Barton conditions[5] with diphenyl diselenide as trapping agent, phenylselenyl-*endo*-tricyclodecanone **13** was obtained in good yield. Oxidative elimination of the phenylselenyl group afforded the desired tricyclodecenone **14** in high yield.

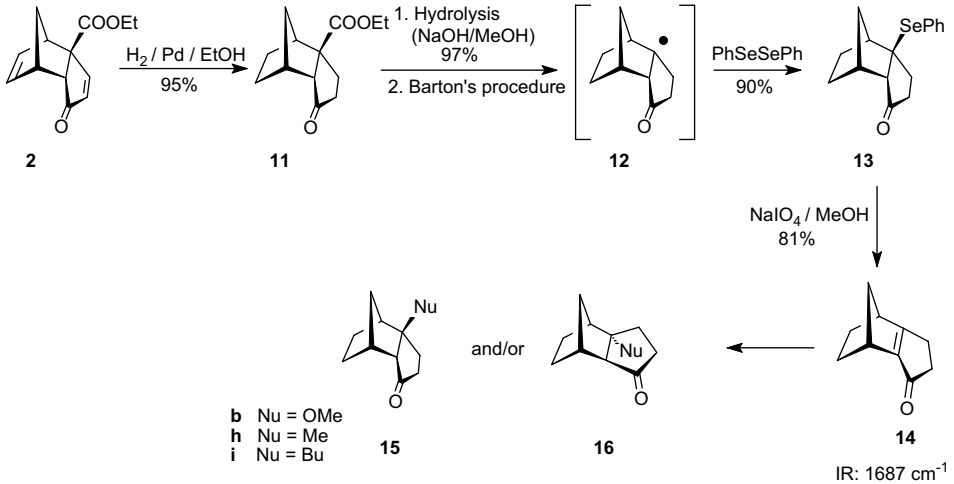
Michael additions to **14** were studied under aprotic and protic conditions using two lithium dialkylcuprates and sodium hydroxide in methanol, respectively (Scheme 3). The experimental results are collected in Table 3.

All of these addition reactions took place with complete *exo*-facial selectivity, as only *endo*-product was obtained. It should be noted however, that these additions were considerably slower than those to substrate **3**. The addition of methoxide to **3** was complete in 15 min affording the product **7b** in quantitative yield, whereas the same reagent reacted with **14** in 20 h providing product **15b** in 65% yield only, with a recovery of 35% of starting material **14**. Lithium dialkylcuprate addition reactions to **14** were at least eight times slower than the corresponding additions to **3**.

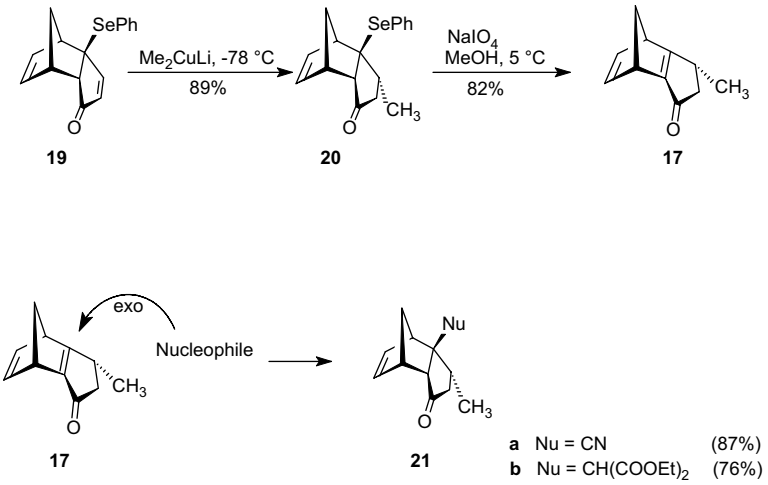
The complete *exo*-selectivity for the lithium dialkylcuprate addition reactions indicates that the stereoselectivity is fully governed by steric factors, i.e., by the difference in steric demand of the ethylene and methylene bridge. The absence of the C_8–C_9 double bond prevents complexation of the cuprate, thus the differentiation is purely steric. Apparently, this difference is large enough to cause complete *exo*-facial selectivity. An additional and even more convincing proof for significant electronic participation of the norbornene double bond in **3** is the considerable and consistent decrease in reaction rates when **14** is compared with **3** in the lithium dialkylcuprate reaction. The stabilizing interaction between the norbornene double bond and the emerging σ*-orbital during the reaction with **3** clearly speeds up the addition reaction.

2.4. Synthesis and chemical properties of 5-substituted tricyclodecadienones

Additions to the central double bond in tricyclic enone **3** generally take place with a remarkable high *exo*-facial selectivity as was described in the preceding sections. In order to study the influence of an additional substituent at the C_5 position, the facial

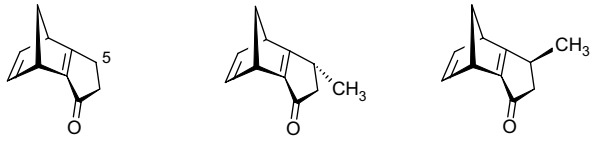


Scheme 3.



Scheme 4.

selectivity of the nucleophilic additions to 5-*endo*- and 5-*exo*-methyltricyclodecadienone **17** and **18** was investigated.



5-*endo*-Methyl substituted tricyclodecenedione **17** was prepared as described previously (Scheme 4). The Michael addition reaction to enone **17** was studied using cyanide and diethylmalonate as the nucleophile (Scheme 4). Applying these nucleophiles **17** proved to be much less reactive than tricyclic enone **3**.

Both nucleophilic additions occur in reasonable yields only in the presence of 15-crown-5-ether. Both reactions proceeded with complete *exo*-facial stereochemistry to give exclusively *endo*-tricyclodecadienones **21a** and **21b**, respectively, in good yield. The considerable lower reactivity of enone **17** toward nucleophilic addition as compared with parent compound **3** is not so easy to explain. Sterically, the methyl group at C_5 cannot interfere with the incoming nucleophile, as it is positioned *anti* to its approach trajectory and therefore no change in reactivity is expected. Electronically, according to the Cieplak theory, this C_5-methyl group is just expected to accelerate this addition as the slightly electron-donating C_5–CH_3 σ-bond stabilizes the σ*-bond, which is formed when the nucleophile approaches from the *exo*-face of the cyclopentenone moiety.[8] A possible reason for the decrease in rate could be the increasing steric interaction between the *endo*-C_5 methyl group and the norbornene C_8–C_9 double bond as the result of the changing hybridization at C_6 during the process of bond formation. Inspection of molecular models supports this view.

Unfortunately, the corresponding 5-*exo*-methyl tricyclodecadienone **18** could not be prepared, and therefore its behavior toward nucleophiles could not be investigated.

In conclusion, the results described in this paper demonstrate a higher preference for *exo*-facial attack of the central enone moiety of tricyclodecadienone **3**. This facial selectivity can be explained by invoking steric approach control in a kinetically controlled process. The steric differentiation by the methylene and ethylene group is caused by their difference in spatial demand and the electronic repulsion exerted by the olefinic group. In addition to the pure steric effects, an orbital interaction between the enone system and the olefinic C_8–C_9 bond may exist also favoring an *exo*-facial approach of the nucleophile. Moreover, *exo*-facial attack is promoted by stabilization of the emerging σ*-orbital by the norbornene π system, which assists the incipient bond formation. The participation of the norbornene double bond is also clearly demonstrated by the low reactivity of tricyclodecenone **14**, which lacks such an olefinic bond. During the addition of lithium dialkylcuprates under aprotic conditions coordination of the cuprate reagent with the norbornene double bond is probably responsible for the somewhat diminished *exo*-facial selectivity.

3. Experimental section

3.1. General remarks

The AM1 calculations were carried out using the MOPAC 98 package. FTIR spectra were recorded on a Biorad WIN-IR FTS-25 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained on a Bruker AM-400, a Bruker AC-300, and a Bruker AC-100 at T=298 K unless other stated. Chemical shifts were reported relative to TMS. Mass spectrometric (MS) analyses were measured on a double focussing VG Analytical 7070E mass spectrometer. GC–MS analyses were performed using a Varian Saturn II GC–MS ion trap system, equipped with a Varian 8100 autosampler. Separation was carried out on a fused silica HP-1 capillary column (DB-5, 30 m×0.25 mm). Helium was used as a carrier gas and electron impact (EI) was used as ionization mode. Elemental analyses were performed on a Carlo Erba Instruments CHNS-O 1108 Elemental Analyzer. Optical rotations were measured with a Perkin Elmer 241 Polarimeter. Melting points were determined with a Reichert Thermopan microscope and are uncorrected. Gas chromatographic (GC) analyses were performed on a Hewlett-Packard HP5890A or a Hewlett-Packard HP5890II gas chromatograph (flame ionization detector, FID) using a capillary column (HP-1, 25 m×0.32 mm×0.17 μm) and nitrogen at 2 mL/min (0.5 atm) as the carrier gas. The GC temperature programs employed were either from 50 °C (5 min isothermal) to 250 °C at 15 °C/min followed by 2 min at 250 °C (isothermal) or from 100 °C to 250 °C at 15 °C/min followed by 10 min at 250 °C (isothermal). Column chromatography was carried out at ambient pressure using Merck Kieselgel 60. Thin layer chromatography (TLC) was carried out on Merck precoated silicagel 60 F_{254} plates (0.25 mm) using the eluents indicated. Spots were visualized with UV, by reaction with I_2 or molybdate spray. Solvents were dried using the following methods: dichloromethane and hexane were

distilled from calcium hydride, diethyl ether was distilled from sodium hydride, ethyl acetate was distilled from potassium carbonate, and toluene was distilled from sodium. THF was distilled first from calcium hydride and then from sodium with benzophenone as indicator under argon, directly prior to use. All other solvents were of analytical grade.

3.2. General procedure A for the nucleophilic addition of alcohols to tricyclo[5.2.1.$0^{2,6}$]deca-2(6),8-dien-3-one 3

To a solution of tricyclo[5.2.1.$0^{2,6}$]deca-2(6),8-dien-3-one **3**[5] (0.5 mmol) in alcohol (2 mL) was added dropwise 2.5 N NaOH aq (0.2 mL) solution at 0–5 °C (ice-water) under a nitrogen atmosphere. The mixture was stirred until the reaction was complete according to GC and then quenched with aqueous ammonium chloride (100 mL), and the aqueous phase extracted with ether (3×100 mL). The combined organic phase was washed with water (3×), dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. Analytically pure samples were obtained by preparative TLC or crystallization.

3.3. General procedure B for the lithium dialkylcuprate addition reaction to tricyclo[5.2.1.$0^{2,6}$]deca-2(6),8-dien-3-one 3

A solution of RLi (ca. 4 equiv) in hexane was gradually added to a suspension of dry CuI (ca. 2 equiv) in dry ether (40 mL) at −30 °C under an argon atmosphere. After stirring the mixture for 15 min at −30 °C, the mixture was cooled to −78 °C, then a solution of tricyclodecadienone **3** (1 mmol) in ether (10 mL) was gradually added. The mixture was stirred at −78 °C until the reaction was complete according to GC and then quenched with aqueous ammonium chloride (100 mL), and the aqueous phase extracted with ether (3×100 mL). The combined organic phase was washed with water (3×), dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. Analytically pure samples were obtained by preparative TLC.

3.3.1. 6-Hydroxy-endo-tricyclo[5.2.1.$0^{2,6}$]dec-8-en-3-one *7a*

Following general procedure A using *tert*-butyl alcohol (2 mL), 2.5 N NaOH (0.2 mL), and tricyclodecenone **3** (0.059 g, 0.4 mmol) at room temperature for 72 h, alcohol **7a** (0.030 g) was obtained as a white solid in 46% yield after purification by preparative TLC on silica-gel (EtOAc/hexane=1:2).

3.3.2. An improved procedure for the preparation of *7a*

To a solution of tricyclodecadienone **3** (0.120 g, 0.8 mmol) in *tert*-butyl alcohol (5 mL) was added dropwise 1.25 N NaOH aq (5 mL) at 0–5 °C (ice-water) under a nitrogen atmosphere. The mixture was stirred at room temperature until the reaction was complete (GC: 7 h). After the general work-up and purification procedure according to procedure A, **7a** (0.086 g, 65%) was obtained as a white solid. A pure sample was obtained by recrystallization from diisopropyl ether, mp 73–75 °C (colorless crystals).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.21 (m, 2H, H_9, H_8), 3.21 (m, 1H, H_1), 2.85 (m, 1H, H_7), 2.64 (d, $^3J_{2,1}$=4.5 Hz, 1H, H_2), 2.52 (m, 1H, H_{4x}), 2.06 (m, 4H, H_{4n}, H_{5x}, H_{5n}, H_{10s}), 1.96 (br s, 1H, O*H*), 1.80 (d, $^2J_{10s,10a}$=8.0 Hz, 1H, H_{10a}). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 204.6 (quat.), 137.7, 134.8 (*tert*), 87.5 (quat.), 63.5, 54.9, 45.8 (*tert*), 50.9, 42.4, 33.7 (*sec*). IR ($CDCl_3$): ν 3580 (O–H), 2960 (C–H), 2938 (C–H), 1735 (C=O), 1248 (C–O) cm^{-1}. GC–MS (EI): *m*/*e* (%) 163 (<1, M^+-H), 99 (100, $M^+-C_5H_5$), 66 (38, $C_5H_6^+$). HRMS (EI): *m*/*e* 164.0835 [calcd for $C_{10}H_{12}O_2$ (M^+) 164.0837].

3.3.3. 6-Methoxy-endo-tricyclo[5.2.1.$0^{2,6}$]dec-8-en-3-one *7b*

Following general procedure A using methanol (2 mL), 2.5 N NaOH (0.2 mL), and tricyclodecadienone **3** (0.059 g, 0.4 mmol) at 0–5 °C for 15 min, methoxytricyclodecenone **7b** (0.070 g) was obtained as a colorless oil in 99% yield after purification by preparative TLC on silica-gel (EtOAc/hexane=1:2). The spectral data were in agreement with the literature.[6]

3.3.4. 6-Ethoxy-endo-tricyclo[5.2.1.$0^{2,6}$]dec-8-en-3-one *7c*

Following general procedure A using ethanol (2 mL), 2.5 N NaOH (0.2 mL), and tricyclodecadienone **3** (0.059 g, 0.4 mmol) at 0–5 °C for 1 h, ethoxytricyclodecenone **7c** (0.075 g) was obtained as a colorless oil in 97% yield after purification by preparative TLC on silica-gel (EtOAc/hexane=1:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.21 (dd, $^3J_{9,8}$=5.7 Hz, $^3J_{9,1}$=2.8 Hz, 1H, H_9), 6.14 (dd, $^3J_{8,9}$=5.7 Hz, $^3J_{8,7}$=2.8 Hz, 1H, H_8), 3.57 (m, ^3J=5.9 Hz, 1H, C*H*$_2$CH$_3$), 3.49 (m, ^3J=5.9 Hz, 1H, C*H*$_2$CH$_3$), 3.16 (m, $^3J_{1,9}$=2.8 Hz, $^3J_{1,2}$=4.5 Hz, 1H, H_1), 3.13 (d, $^3J_{7,8}$=2.8 Hz, 1H, H_7), 2.71 (d, $^3J_{2,1}$=4.5 Hz, 1H, H_2), 2.46 (m, 1H, H_{4x}), 2.19 (m, 1H, H_{5x}), 2.06 (m, 1H, H_{4n}), 2.02 (d, $^2J_{10s,10a}$=8.0 Hz, 1H, H_{10s}), 1.87 (m, 1H, H_{5x}), 1.71 (d, $^2J_{10s,10a}$=8.0 Hz, 1H, H_{10a}), 1.21 (t, ^3J=5.9 Hz, 3H, CH$_2$C*H*$_3$). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 219.3 (quat.), 138.5, 134.4 (*tert*), 92.5 (quat.), 62.1 (*tert*), 58.6, 50.4 (*sec*), 49.9, 45.5 (*tert*), 42.3, 28.4 (*sec*), 16.1 (prim.). IR ($CDCl_3$): ν 2979 (C–H), 2944 (C–H), 2874 (C–H), 1726 (C=O), 1075 (C–O) cm^{-1}. GC–MS (EI): *m*/*e* (%) 192 (<1, M^+), 127 (100, $M^+-C_5H_5$), 66 (<1, $C_5H_6^+$). HRMS (EI): *m*/*e* 192.1149 [calcd for $C_{12}H_{16}O_2$ (M^+) 192.1150].

3.3.5. 6-n-Butoxy-endo-tricyclo[5.2.1.$0^{2,6}$]dec-8-en-3-one *7d*

Following general procedure A using *n*-butanol (2 mL), 2.5 N NaOH (0.2 mL), and tricyclodecadienone **3** (0.059 g, 0.4 mmol) at room temperature for 2 h, *n*-butoxytricyclodecenone **7d** (0.058 g) was obtained as a colorless oil in 65% yield after purification by preparative TLC on silica-gel (EtOAc/hexane=1:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.21 (dd, $^3J_{9,8}$=5.6 Hz, $^3J_{9,1}$=2.8 Hz, 1H, H_9), 6.13 (dd, $^3J_{8,9}$=5.7 Hz, $^3J_{8,7}$=2.8 Hz, 1H, H_8), 3.52 (m, ^3J=5.9 Hz, 1H, OC*H*$_2$CH$_2$CH$_2$CH$_3$), 3.46 (m, ^3J=5.9 Hz, 1H, OC*H*$_2$CH$_2$CH$_2$CH$_3$), 3.16 (m, $^3J_{1,9}$=2.8 Hz, $^3J_{1,2}$=4.5 Hz, 1H, H_1), 3.13 (d, $^3J_{7,8}$=2.8 Hz, 1H, H_7), 2.70 (d, $^3J_{2,1}$=4.5 Hz, 1H, H_2), 2.47 (m, 1H, H_{4x}), 2.19 (m, 1H, H_{5x}), 2.07 (m, 1H, H_{4n}), 2.01 (d, $^2J_{10s,10a}$=8.3 Hz, 1H, H_{10s}), 1.82 (m, 1H, H_{5n}), 1.71 (d, $^2J_{10s,10a}$=8.3 Hz, 1H, H_{10a}), 1.55 (m, ^3J=7.4 Hz, 2H, CH$_2$C*H*$_2$CH$_2$CH$_3$), 1.37 (m, ^3J=7.4 Hz, 2H, CH$_2$CH$_2$C*H*$_2$CH$_3$), 0.93 (d, ^3J=7.4 Hz, 3H, CH$_2$CH$_2$CH$_2$C*H*$_3$). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 219.4 (quat.), 138.5, 134.5 (*tert*), 92.4 (quat.), 63.0 (*sec*), 62.1, 49.9, 45.5 (*tert*), 50.4, 42.3, 32.6, 28.3, 19.5 (*sec*), 13.9 (prim.). IR ($CDCl_3$): ν 2963 (C–H), 2938 (C–H), 2874 (C–H), 1726 (C=O), 1081 (C–O) cm^{-1}.

GC–MS (EI): *m*/*e* (%) 220 (<1, M^+), 155 (100, $M^+-C_5H_5$), 66 (22, $C_5H_6^+$). HRMS (EI): *m*/*e* 220.1463 [calcd for $C_{14}H_{20}O_2$ (M^+) 220.1463].

3.3.6. 6-Isopropoxy-endo-tricyclo[5.2.1.$0^{2,6}$]dec-8-en-3-one *7e*

Following general procedure A using *iso*-propyl alcohol (2 mL), 2.5 N NaOH (0.2 mL), and tricyclodecadienone **3** (0.059 g, 0.4 mmol) at room temperature for 6 h, isopropoxytricyclodecenone **7e** (0.029 g) was obtained as a colorless oil in 35% yield after purification by preparative TLC on silica-gel (EtOAc/hexane=1:3). Also byproduct hydroxytricyclodecenone **7a** (0.014 g) was obtained as white amorphous solid in 20% yield.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.20 (dd, $^3J_{9,8}$=5.6 Hz, $^3J_{9,1}$=2.8 Hz, 1H, H_9), 6.13 (dd, $^3J_{8,9}$=5.7 Hz, $^3J_{8,7}$=2.8 Hz, 1H, H_8), 3.87 (m, ^3J=5.9 Hz, 1H, C*H*(CH$_3$)$_2$), 3.16 (m, $^3J_{1,9}$=2.8 Hz, $^3J_{1,2}$=4.5 Hz, 1H, H_1), 3.10 (d, $^3J_{7,8}$=2.8 Hz, 1H, H_7), 2.69 (d, $^3J_{2,1}$=4.5 Hz, 1H, H_2), 2.50 (m, 1H, H_{4x}), 2.18 (m, 1H, H_{5x}), 2.07 (m, 1H, H_{4n}), 2.06 (d, $^2J_{10s,10a}$=8.0 Hz, 1H, H_{10s}), 1.87 (m, 1H, H_{5n}), 1.72 (d, $^2J_{10s,10a}$=8.0 Hz, 1H, H_{10a}), 1.21 (d, ^3J=5.9 Hz, 6H, CH(C*H*$_3$)$_2$). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 219.2 (quat.), 138.6, 134.5 (*tert*), 93.1 (quat.), 66.9, 62.7, 51.1 (*tert*), 50.4 (*sec*), 45.6 (*tert*), 42.3, 29.7 (*sec*), 25.0 (2X) (prim.). IR ($CDCl_3$): ν 2977 (C–H), 2945 (C–H), 2868 (C–H), 1727 (C=O), 1046 (C–O) cm^{-1}. GC–MS (EI): *m*/*e* (%) 206 (<1, M^+), 141

(100, $M^+-C_5H_5$), 66 (18, $C_5H_6^+$). HRMS (EI): *m/e* 206.1307 [calcd for $C_{13}H_{18}O_2$ (M^+) 206.1307].

3.3.7. 5-Oxo-endo-tricyclo[5.2.1.0^{2,6}]dec-8-ene-2-carbonitrile **7f**

To a solution of tricyclodecadienone **3** (0.170 g, 1.16 mmol) in acetonitrile (50 mL) was added KCN (0.300 g, 4.6 mmol) and the suspension was stirred for 3 days at room temperature to complete the reaction. After filtration over Celite and removal of the solvent under reduced pressure, product **7f** (0.190 g) was obtained as a colorless oil in 95% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.28 (dd, $^3J_{8,9}$=5.7 Hz, $^3J_{8,7}$=3.0 Hz, 1H, H_9), 6.23 (dd, $^3J_{9,8}$=5.7 Hz, $^3J_{9,1}$=3.2 Hz, 1H, H_8), 3.42 (br s, 1H, H_7), 3.38 (br s, 1H, H_1), 3.28 (d, $^3J_{2,1}$=4.6 Hz, 1H, H_2), 2.38 (m, 2H, H_5), 2.1–2.0 (m, 2H, H_4), 1.94 (d, $^2J_{10s,10a}$=8.6 Hz, 1H, H_{10s}), 1.64 (d, $^2J_{10a,10s}$=8.6 Hz, 1H, H_{10a}). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 215.4 (quat.), 138.6, 133.4 (*tert*), 125.6 (quat.), 61.3, 53.2 (*tert*), 52.0 (*sec*), 47.0 (*tert*), 49.9 (*sec*), 44.0 (quat.), 28.3 (*sec*). IR (CCl_4): ν 2978 (C–H), 2867 (C–H), 2230 (C≡N), 1744 (C=O) cm^{-1}. GC–MS (EI): *m/e* (%) 173 (<1, M^+), 107 (2, $M^+-C_5H_5$), 66 (100, $C_5H_6^+$). HRMS (EI): *m/e* 173.0841 [calcd for $C_{11}H_{11}NO$ (M^+) 173.0841].

3.3.8. Diethyl 2-(5-oxo-endo-tricyclo[5.2.1.0^{2,6}]dec-8-en-2-yl)malonate **7g**

To a solution of diethylmalonate (0.40 g, 2.5 mmol) in acetonitrile (60 mL) was added NaH (0.08 g, 2.0 mmol, 60% dispersion in mineral oil). After 30 min stirring at room temperature, tricyclodecadienone **3** (0.120 g, 0.75 mmol) was added. The reaction mixture was monitored (GC/TLC) and stirred for 5 days at room temperature and then aqueous work-up afforded the crude product. Product **7g** (0.168 g, 0.55 mmol) was obtained as a colorless oil in 73% yield after purification by column chromatography on silica-gel (EtOAc/hexane=1:12).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.32 (dd, $^3J_{8,9}$=5.6 Hz, $^3J_{8,7}$=3.4 Hz, 1H, H_9), 6.20 (dd, $^3J_{9,8}$=5.6 Hz, $^3J_{9,1}$=2.9 Hz, 1H, H_8), 4.21 (m, 4H, OCH_2CH_3), 3.62 (s, 1H, $CH(COOEt)_2$), 3.20 (br s, 1H, H_7), 3.10 (br s, 1H, H_1), 2.72 (d, $^3J_{2,1}$=4.5 Hz, 1H, H_2), 2.31 (m, 2H, H_5), 2.0–1.7 (m, 2H, H_4), 1.57 (s, 2H, H_{10}), 1.32 (t, ^3J=7.1 Hz, 3H, OCH_2CH_3), 1.25 (t, ^3J=7.1 Hz, 3H, OCH_2CH_3). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 220.5, 169.0, 168.6 (quat.), 136.5, 136.3, 61.8 (*tert*), 61.4 (2X) (*sec*), 60.9 (*tert*), 52.9 (quat.), 51.4 (*sec*), 49.9 (*tert*), 47.9, 41.0 (*sec*), 26.9 (*tert*), 14.1, 14.0 (prim.). IR (CCl_4): ν 2983 (C–H), 2865 (C–H), 1750 (C=O), 1732 (C=O, br s) cm^{-1}. MS (CI): *m/e* (%) 307 (1, M+H$^+$), 241 (100, M+H$^+-C_5H_6$), 66 (52, $C_5H_6^+$). HRMS (EI): *m/e* 306.1466 [calcd for $C_{17}H_{22}O_5$ (M^+) 306.1467].

3.3.9. 6-Methyl-endo-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one **7h** and 6-methyl-exo-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one **8h**

Following general procedure B using 1.6 M MeLi (2.5 mL, 4 mmol), CuI (0.380 g, 2 mmol), and tricyclodecadienone **3** (0.116 g, 0.8 mmol) the reaction was completed in 15 min. A mixture (0.106 g) of **7h** (91%) and **9h** (9%) was obtained as a colorless oil in 82% total yield after purification by preparative TLC on silica-gel (EtOAc/hexane=1:7).

*3.3.9.1. Compound **7h**.* ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.31 (dd, $^3J_{8,9}$=5.7 Hz, $^3J_{8,7}$=2.8 Hz, 1H, H_8), 6.12 (dd, $^3J_{9,8}$=5.7 Hz, $^3J_{9,1}$=2.8 Hz, 1H, H_9), 3.16 (m, $^3J_{1,9}$=2.8 Hz, $^3J_{1,2}$=4.5 Hz, 1H, H_1), 2.64 (d, $^3J_{7,8}$=2.8 Hz, 1H, H_7), 2.40 (d, $^3J_{2,1}$=4.5 Hz, 1H, H_2), 2.26 (m, 1H, H_{4x}), 2.05 (m, 1H, H_{4n}), 1.75 (m, 1H, H_{5n}), 1.72 (d, $^2J_{10s,10a}$=8.0 Hz, 1H, H_{10s}), 1.62 (m, 1H, H_{5x}),1.60 (d, $^2J_{10a,10s}$=8.0 Hz, 1H, H_{10a}), 1.39 (s, 3H, CH_3). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 222.0 (quat.), 137.4, 135.5 (*tert*), 62.5, 53.7, 47.4 (*tert*), 47.7 (quat.), 50.7, 41.5, 31.6 (*sec*), 29.7 (prim.). IR ($CDCl_3$): ν 2965 (C–H), 1720 (C=O) cm^{-1}. GC–MS (EI): *m/e* (%) 162 (<1, M^+), 97 (84, $M^+-C_5H_5$), 66 (100, $C_5H_6^+$). HRMS (EI): *m/e* 162.1044 [calcd for $C_{11}H_{14}O$ (M^+) 162.1044].

*3.3.9.2. Compound **8h**.* The spectrum below was recorded from a mixture of **7h** and **8h**.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.25 (dd, $^3J_{8,9}$=5.7 Hz, $^3J_{8,7}$=2.8 Hz, 1H, H_8), 6.18 (dd, $^3J_{9,8}$=5.7 Hz, $^3J_{9,1}$=2.8 Hz, 1H, H_9), 3.06 (m, $^3J_{1,9}$=2.8 Hz, $^3J_{1,2}$=4.5 Hz, 1H, H_1), 2.58 (d, $^3J_{7,8}$=2.8 Hz, 1H, H_7). The other signals overlap with ^{1}H NMR signals of **7h**.

3.3.10. 6-n-Butyl-endo-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one **7i** and 6-n-butyl-exo-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one **8i**

Following general procedure B using 1.6 M *n*-BuLi (2.4 mL, 3.8 mmol), CuI (0.380 g, 2 mmol), and tricyclodecadienone **3** (0.120 g, 0.82 mmol) the reaction was completed in 15 min. A mixture (0.154 g) of **7i** (95%) and **8i** (5%) was obtained as a colorless oil in 92% total yield after purification by preparative TLC on silica-gel (EtOAc/hexane=1:7).

*3.3.10.1. Compound **7i**.* ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.29 (dd, $^3J_{8,9}$=5.7 Hz, $^3J_{8,7}$=2.8 Hz, 1H, H_8), 6.13 (dd, $^3J_{9,8}$=5.7 Hz, $^3J_{9,1}$=2.8 Hz, 1H, H_9), 3.14 (m, $^3J_{1,9}$=2.8 Hz, $^3J_{1,2}$=4.5 Hz, 1H, H_1), 2.78 (d, $^3J_{7,8}$=2.8 Hz, 1H, H_7), 2.44 (d, $^3J_{2,1}$=4.5 Hz, 1H, H_2), 2.20 (m, 1H, H_{4x}), 2.06 (m, 1H, H_{4n}), 1.75 (m,1H, H_{5n}), 1.70 (d, $^2J_{10s,10a}$=8.0 Hz, 1H, H_{10s}), 1.61 (t, J=5.9 Hz, 2H, $CH_2CH_2CH_2CH_3$), 1.62 (m, 1H, H_{5x}), 1.55 (d, $^2J_{10a,10s}$=8.0 Hz, 1H, H_{10a}), 1.40 (m, 4H, $CH_2CH_2CH_2CH_3$), 0.93 (t, ^3J=5.9 Hz, 3H, $CH_2CH_2CH_2CH_3$). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 222.2 (quat.), 137.2, 135.8 (*tert*), 61.1 (*tert*), 51.8 (quat.), 51.2, 47.2 (*tert*), 50.3, 41.9, 41.5, 28.5, 27.5, 23.4 (*sec*), 14.0 (prim.). IR ($CDCl_3$): ν 2961 (C–H), 2933 (C–H), 2874 (C–H), 1722 (C=O) cm^{-1}. GC–MS (EI): *m/e* (%) 204 (<1, M^+), 139 (100, $M^+-C_5H_5$), 65 (6, $C_5H_5^+$). HRMS (EI): *m/e* 204.1473 [calcd for $C_{14}H_{20}O$ (M^+) 204.1514].

*3.3.10.2. Compound **8i**.* The spectrum below was recorded from a mixture of **7i** and **8i**.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.21 (dd, $^3J_{8,9}$=5.7 Hz, $^3J_{8,7}$=2.8 Hz, 1H, H_8 or H_9), 6.16 (dd, $^3J_{9,8}$=5.7 Hz, $^3J_{9,1}$=2.8 Hz, 1H, H_9 or H_8), 3.06 (br, 1H, H_1), 2.66 (br, 1H, H_7). The other signals overlap with ^{1}H NMR signals of **7h**. ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 222.0 (quat.), 137.6, 136.4 (*tert*), 60.4 (*tert*), 53.4 (quat.), 52.1, 47.3 (*tert*), 50.3, 46.1, 40.2, 30.6, 27.7, 23.3 (*sec*), 13.7 (prim.).

3.3.11. Ethyl 5-oxo-endo-tricyclo[5.2.1.0^{2,6}]decane-2-carboxylate **11**

A mixture of Herz ester **2** (4.36 g, 20 mmol) and palladium (0.436 g, 10%) on activated carbon in absolute ethanol (120 mL) was hydrogenated (1 atm) at room temperature. The reaction was completed after 7 h (GC). The mixture was filtered and concentrated in vacuo to give almost pure product **11** (4.2 g) as a colorless oil in 95% yield. An analytical pure sample was obtained by column chromatography on silica-gel (EtOAc/hexane=1:10).

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.17 (q, ^3J=7.1 Hz, 2H, CH_2CH_3), 3.10 (d, ^3J=5.7 Hz, 1H, H_6), 2.77 (d, $^3J_{2,1}$=3.9 Hz, 1H, H_7), 2.63 (dd, $^3J_{1,2}$=3.9 Hz, $^3J_{1,9}$=5.7 Hz, 1H, H_1), 2.48 (m, 1H, H_{4x}), 2.37–2.19 (m, 2H), 2.05–1.96 (m, 1H, H_{4n}), 1.64–1.53 (m, 3H), 1.48–1.42 (m, 2H), 1.30–1.25 (m, 1H), 1.27 (t, ^3J=7.1 Hz, 3H, CH_2CH_3). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 220.4, 177.0 (quat.), 61.0 (*tert*), 58.6 (quat.), 57.4, 45.6, 41.0 (*tert*), 40.9, 40.8, 25.7, 24.7, 23.1 (*sec*), 14.1 (prim.). IR ($CDCl_3$): ν 2979 (C–H), 2944 (C–H), 2874 (C–H), 1726 (C=O), 1075 (C–O) cm^{-1}. GC–MS (EI): *m/e* (%) 223 (6, M^++1), 222 (2, M^+), 155 (68, $M^+-C_5H_8$+1), 149 (100, $M^+-CO_2C_2H_5$). HRMS (EI): *m/e* 222.1256 [calcd for $C_{13}H_{18}O_3$ (M^+) 222.1256].

3.3.12. 6-Phenylselenyl-endo-tricyclo[5.2.1.0^{2,6}]decan-3-one **13**

Starting with acid **22** (2.91 g, 15 mmol), following the literature procedure[11] using *N*-hydroxypyridin-2-thione sodium salt (2.68 g, 18 mmol) and diphenyl diselenide (7.8 g, 25 mmol) product **13** (4.1 g, 13.4 mmol) was obtained in 90% yield after purification by column chromatography on silica-gel (EtOAc/heptane=1:20), mp 87–88 °C (colorless amorphous solid).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (m, 2H, C_6H_5), 7.30 (m, 3H, C_6H_5), 2.63 (dd, $^3J_{1,2}$=4.5 Hz, $^3J_{1,9}$=4.5 Hz, 1H, H_1), 2.58 (d, ^3J=4.5 Hz, 2H, H_7 and H_2), 2.49–2.40 (m, 2H), 2.32–2.22 (m, 3H), 1.61–1.55 (m, 3H), 1.52–1.42 (m, 1H), 1.23–1.18 (m, 1H). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 219.3, 129.0, 59.0 (quat.), 136.4, 128.9 (2X), 128.5 (2X), 62.1, 49.1, 41.6 (*tert*), 42.0, 41.5, 31.0, 24.7, 24.3 (*sec*). IR ($CDCl_3$): ν 2970, 2886 (C–H), 1728 (s, C=O) cm^{-1}. GC–MS (EI): *m/e* (%) 307 (3, M^++H), 305 (2, M^+−H), 149 (100, M^+−PhSe). HRMS (EI): *m/e* 306.0523 [calcd for $C_{16}H_{18}OSe$ (M^+) 306.0523].

3.3.13. *Tricyclo[5.2.1.0^{2,6}]dec-2(6)-en-3-one* **14**

Phenylselenyltricyclodecanone **13** (0.305 g, 1 mmol) in methanol (50 mL) was treated with a solution of sodium periodate (0.236 g) in water (1 mL) at 0–5 °C (ice-water) for 2 h. Methanol was evaporated and the crude product was purified by preparative TLC on silica-gel (EtOAc/hexane=1:2) to give tricyclodecenone **14** (0.120 g) as a colorless oil in 81% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.18 (br s, 1H, H_1), 3.10 (br s, 1H, H_7), 2.68 (d, J=17.1 Hz, 2H, H_4), 2.50 (d, J=17.1 Hz, 2H, H_5), 1.90 (m, 1H, H_{8x}), 1.79 (m, 2H, H_{9x} and H_{10s}), 1.48 (d, J=8.7 Hz, 1H, H_{10}), 1.10 (m, 2H, H_{8n} and H_{9n}). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 201.8, 190.5, 150.9 (quat.), 50.6, 39.9 (*sec*), 43.9, 37.6 (*tert*), 26.0, 24.9, 24.3 (*sec*). IR ($CDCl_3$): ν 2971, 2926, 2876 (C–H), 1687 (C=O) cm^{-1}.

GC–MS (EI): *m/e* (%) 149 (100, M^++H), 148 (5, M^+), 92 (25, $M^+-CH_2CH_2CO$). HRMS (EI): *m/e* 148.0887 [calcd for $C_{10}H_{12}O$ (M^+) 148.0888].

3.3.14. *6-Methoxy-endo-tricyclo[5.2.1.0^{2,6}]decan-3-one* **15b**

Following general procedure A using methanol (2 mL), 2.5 N NaOH (0.2 mL), and tricyclodecenone **14** (0.080 g, 0.54 mmol) at 0–5 °C for 15 min, then at room temperature for 20 h methoxytricyclodecanone **15b** (0.063 g) was obtained as a colorless oil in 65% yield after purification by preparative TLC on silica-gel (EtOAc/hexane=1:3). Starting material **14** (0.024 g) was recovered in 30% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 (s, 3H, OCH_3), 2.63 (s, 1H, H_1), 2.61 (s, 1H, H_7), 2.56 (m, 1H, H_{5n}), 2.39 (d, J=6.0 Hz, 1H, H_2), 2.25 (m, 1H, H_{4n}), 2.23 (m, 1H, H_{4x}), 2.06 (m, 1H, H_{5x}), 1.92 (dt, $^2J_{10a,10s}$=9.1 Hz, $^4J_{10a,8n,\ and\ 9n}$=1.7 Hz, 1H, H_{10a}), 1.64 (m, $^2J_{8x,8n}$=12.6 Hz, $^3J_{8x,9}$=3.5 Hz, 1H, H_{8x}), 1.43 (m, 1H, H_{9x}), 1.36 (d, $^2J_{10s,10a}$=9.1 Hz, 1H, H_{10s}), 1.28 (m, 1H, H_{8n}), 1.18 (m, 1H, H_{9n}). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 219.9, 91.7 (quat.), 61.7 (prim.), 49.8, 43.7 (*tert*), 41.8 (*sec*), 40.5 (*tert*), 39.2, 25.5, 24.5, 22.8 (*sec*). IR ($CDCl_3$): ν 2970 (C–H), 2890 (C–H), 1728 (C=O) cm^{-1}. GC–MS (EI): *m/e* (%) 180 (45, M^+), 165 (19, M^+-CH_3), 149 (100, M^+-OCH_3), 113 (46, $M^+-C_5H_7^+$). HRMS (EI): *m/e* 180.1145 [calcd for $C_{11}H_{16}O_2$ (M^+) 180.1150].

3.3.15. *6-Methyl-endo-tricyclo[5.2.1.0^{2,6}]decan-3-one* **15h**

Following general procedure B using 1.6 M MeLi (2.5 mL, 4 mmol), CuI (0.380 g, 2 mmol), and tricyclodecenone **14** (0.110 g, 0.75 mmol) the reaction was completed in 2 h. Methyltricyclodecanone **15h** (0.100 g) was obtained as a colorless oil in 82% yield after purification by preparative TLC on silica-gel (EtOAc/hexane=1:7).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.54 (dd, J=8.0, 4.0 Hz, 1H), 2.47–2.38 (m, 1H, H_{4x}), 2.31–2.21 (m, 1H), 2.12–2.03 (m, 3H), 1.77 (d, $^2J_{10s,10a}$=9.8 Hz, 1H, H_{10s}), 1.62–1.48 (m, 3H), 1.47–1.42 (m, 1H), 1.39 (d, $^2J_{10s,10a}$=9.8 Hz, 1H, H_{10s}), 1.22–1.15 (m, 1H), 1.17 (s, 3H, CH_3). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 223.0 (quat.), 61.7, 48.5 (*tert*), 47.5 (quat.), 41.7, 40.3 (*sec*), 41.6, 30.3 (*tert*), 29.8, 24.4, 24.1 (*sec*). IR ($CDCl_3$): ν 2964 (C–H), 2885 (C–H), 1717 (C=O) cm^{-1}. GC–MS (EI): *m/e* (%) 165 (20, M^++1), 164 (1, M^+), 97 (100, $M^+-C_5H_8$), 67 (8, $C_5H_8^+-1$). HRMS (EI): *m/e* 164.1197 [calcd for $C_{11}H_{16}O$ (M^+) 164.1201].

3.3.16. *6-n-Butyl-endo-tricyclo[5.2.1.0^{2,6}]decan-3-one* **15i**

Following general procedure B using 1.6 M *n*-BuLi (2.0 mL, 3.2 mmol), CuI (0.314 g, 1.65 mmol), and tricyclodecenone **14** (0.110 g, 0.75 mmol) the reaction was completed in 2 h. *n*-Butyltricyclodecanone **15i** (0.102 g) was obtained as a colorless oil in 85% yield after purification by preparative TLC on silica-gel (EtOAc/hexane=1:7).

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.53 (dd, $^3J_{1,2}$=4.5 Hz, $^3J_{1,9}$=4.5 Hz, 1H, H_1), 2.44–2.34 (m, 1H), 2.31–2.21 (m, 1H), 2.20 (br, 1H, H_7), 2.08 (d, $^3J_{2,1}$=4.5 Hz, 1H, H_2), 2.01–1.94 (m, 1H), 1.75 (d, $^2J_{10s,10a}$=9.8 Hz, 1H, H_{10s}), 1.70–1.64 (m, 1H), 1.56–1.39 (m, 4H), 1.34 (d, $^2J_{10a,10s}$=9.8 Hz, 1H, H_{10a}), 1.33–1.17 (m, 6H), 0.91 (t, ^3J=7.1 Hz, 3H, CH_2CH_3). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 223.3 (quat.), 60.6 (*tert*), 51.1, 50.4, 41.4 (*tert*), 42.3, 41.6, 40.0, 26.9, 26.5, 24.9, 24.1, 23.4 (*sec*), 14.0 (prim.). IR ($CDCl_3$): ν 2964 (C–H), 2938 (C–H), 2885 (C–H), 2864 (C–H), 1718 (C=O), 1183 (C–H) cm^{-1}. GC–MS (EI): *m/e* (%) 207 (53, M^++1), 139 (100, $M^+-C_5H_8$+1), 67 (7, $C_5H_8^+-1$). HRMS (EI): *m/e* 206.1669 [calcd for $C_{14}H_{22}O$ (M^+) 206.1670].

3.3.17. *endo-3-Methyl-5-oxo-endo-tricyclo[5.2.1.0^{2,6}]dec-8-ene-2-carbonitrile* **21a**

To a solution of methyltricyclodecadienone **17**[6] (0.150 g, 0.94 mmol) in ether (60 mL) were added KCN (0.200 g, 3.1 mmol) and 18-crown-6 ether (0.264 g, 1 mmol). The suspension was stirred overnight at room temperature to complete the reaction. After standard work-up procedure and purification by column chromatography on silica-gel (EtOAc/hexane=1:8), product **21a** (0.153 g, 0.82 mmol) was obtained as a colorless oil in 87% yield.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.26 (dd, $^3J_{8,9}$=5.7 Hz, $^3J_{8,7}$=3.0 Hz, 1H, H_9), 6.19 (dd, $^3J_{9,8}$=5.7 Hz, $^3J_{9,1}$=2.8 Hz, 1H, H_8), 3.40 (br s, 1H, H_7), 3.36 (br s, 1H, H_1), 3.34 (d, $^3J_{2,1}$=5.2 Hz, 1H, H_2), 2.75 (m, 1H, H_5), 2.32 (dd, ^2J=18.8 Hz, ^3J=9.5 Hz, 1H, H_{4x}), 1.95 (d, $^2J_{10s,10a}$=9.3 Hz, 1H, H_{10s}), 1.80 (dd, ^2J=18.8 Hz, ^3J=12.5 Hz, 1H, H_{4n}), 1.78 (d, $^2J_{10a,10s}$=9.3 Hz, 1H, H_{10a}), 1.26 (d, ^3J=7.0 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 215.1 (quat.), 138.6, 134.0 (*tert*), 125.4 (quat.), 62.0 (*tert*), 52.5 (*sec*), 51.0, 47.3 (*tert*), 48.0 (quat.), 47.0 (*sec*), 36.2 (*tert*), 15.1 (prim.). IR (CCl_4): ν 2976 (C–H), 2880 (C–H), 2231 (C≡N), 1743 (C=O) cm^{-1}. GC–MS (EI): *m/e* (%) 187 (<1, M^+), 66 (100, $C_5H_6^+$). HRMS (EI): *m/e* 187.0995 [calcd for $C_{12}H_{13}NO$ (M^+) 187.0997].

3.3.18. *Diethyl 2-(endo-3-methyl-5-oxo-endo-tricyclo[5.2.1.0^{2,6}]dec-8-en-2-yl)malonate* **21b**

To a solution of diethylmalonate (0.40 g, 2.5 mmol) in toluene (40 mL) was added NaH (0.08 g, 60%, 2.0 mmol). After 30 min stirring at room temperature, methyltricyclodecadienone **17**[6] (0.101 g, 0.63 mmol) in DMSO (2 mL) and 15-crown-5-ether (0.220 g, 1 mmol) were added. The reaction mixture was heated under reflux until completion (GC/TLC: 4 days) and then aqueous work-up afforded the crude product. Product **21b** (0.152 g, 0.48 mmol) was obtained as a colorless oil in 76% yield after purification by column chromatography on silica-gel (EtOAc/hexane=1:5).

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.37 (dd, $^3J_{8,9}$=5.6 Hz, $^3J_{8,7}$=3.2 Hz, 1H, H_9), 6.14 (dd, $^3J_{9,8}$=5.6 Hz, $^3J_{9,1}$=3.0 Hz, 1H, H_8), 4.20 (m, 4H, OCH_2CH_3), 3.60 (s, 1H, $CH(COOEt)_2$), 3.31 (br s, 1H, H_7), 3.14 (br s, 1H, H_1), 3.01 (m, 1H, H_5), 2.72 (d, $^3J_{2,1}$=4.8 Hz, 1H, H_2), 2.46 (dd, ^2J=18.7 Hz, ^3J=9.6 Hz, 1H, H_{4x}), 1.66 (dd, ^2J=18.7 Hz, ^3J=11.0 Hz, 1H, H_{4n}), 1.70 (d, $^2J_{10s,10a}$=9.1 Hz, 1H, H_{10s}), 1.66 (d, $^2J_{10a,10s}$=9.1 Hz, 1H, H_{10a}), 1.31 (t, ^3J=7.1 Hz, 3H, OCH_2CH_3), 1.26 (t, ^3J=7.1 Hz, 3H, OCH_2CH_3), 0.98 (d, ^3J=7.0 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, H-dec, $CDCl_3$): δ 218.7, 169.0, 168.5 (quat.), 136.9, 136.4, 62.7 (*tert*), 61.6, 61.4 (*sec*), 60.7 (*tert*), 56.4 (quat.), 50.9, 50.0 (*sec*), 49.2, 47.4, 32.3 (*tert*), 16.9, 14.1, 14.0 (prim.). IR (CCl_4): ν 2980 (C–H), 2860 (C–H), 1731 (C=O, br s) cm^{-1}. MS (CI): *m/e* (%) 321 (1, M+H$^+$), 255 (100,

$M+H^+-C_5H_6$), 66 (29, $C_5H_6^+$). HRMS (EI): *m*/*e* 320.1623 [calcd for $C_{18}H_{24}O_5$ (M^+) 320.1624].

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