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A Facile Approach to Norbornene-annulated Cyclopentenones, A Novel Class of Tricyclodecadienones

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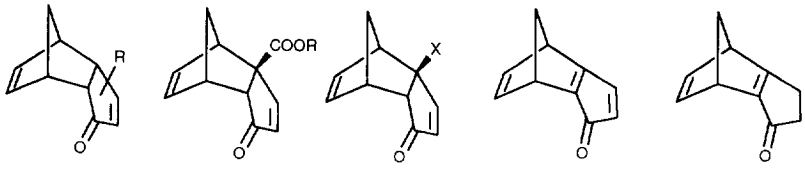
Abstract: *An efficient synthesis of norbornene annulated cyclopentenones* **5** *and* **18** *starting from readily available tricyclodecadienone carboxylic acid* **2a** *is described. Parent tricyclo[5.2.1.0^{2,6}]deca-di-2(6),8-ene* **5**, *an hitherto unknown compound, has been obtained in good yield by subjecting bromide* **7b** *to base induced elimination or by oxidative deselenylation of* **7c**. *5-Substituted analogues* **18** *are conveniently obtained from phenylselenide* **3c** *by stereoselective conjugate cuprate addition followed by oxidative elimination of the seleno group. Dehydrobromination of epoxy bromide* **21** *affords norbornene-annulated cyclopentadienone* **22** *which immediately undergoes stereoselective 1,4-addition at the strained C_2-C_6 enone moiety to give* **23**. *These novel norbornene annulated cyclopentenones can be considered as the synthetic equivalent of 2-cyclopentynones.*

Introduction

The tricyclo[5.2.1.0^{2,6}]decadienone system **1** constitutes a versatile synthetic equivalent of cyclopentadienone[1,2]. Its rigid structure, the presence of a reactive α,β-enone system and the ability of the tricyclic skeleton to undergo [4+2]-cycloreversion are instrumental in the synthesis of a variety of functionalized cyclopentenones with defined stereochemistry and chirality[1,2]. The *endo*-tricyclodecadienone system, racemic as well as enantiopure, is conveniently accessible via carboxylic acid **2a**, which in turn is readily available from the Diels-Alder adduct of benzoquinone and cyclopentadiene[3].



1 **2a** R=H **2b** R=C_2H_5 **3a** X= Br **3b** X= OCH_3 **4** **5**

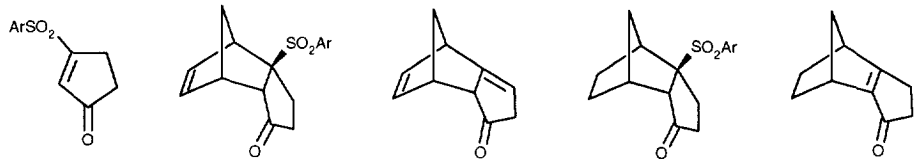
In the preceding paper, the synthesis of a series of 6-substituted tricyclodecadienones **3** starting from **2a** employing Barton's radical chain decarboxylation methodology is described[4]. Bromodecarboxylation of **2a** appeared to be particularly suitable for a high yield synthesis of bridgehead bromide **3a**. Dehydrobromination of **3a** using selected basic conditions is an efficient process to give elusive

norbornene-annulated cyclopentadienone **4** as a transient intermediate in nearly quantitative yield. Although this cyclopentadienone is still too reactive to be isolated its bicyclic structure retards its [4+2]-dimerization to such an extent that nucleophilic conjugate addition and crossed Diels-Alder reactions can compete efficiently. This is exemplified by the alkaline methanolysis of bromide **3a** which produces bridghead methyl ether **3b** in excellent yield (>80%). The exclusive formation of **3b** shows that **4** can be effectively intercepted by a nucleophile in a regio- and stereospecific conjugate addition involving the central C_2-C_6 enone moiety which is evidently more strained than the peripheral C_4-C_5 enone function. The efficient two step synthesis of **4** from acid **2a** suggests that this sequence of steps may also be applicable to the synthesis of the interesting hitherto unknown positional isomer of **1** *viz.* tricyclo[5.2.1.$0^{2,6}$]deca-2(6),8-dien-3-one **5**. The absence of the peripheral enone moiety as present in **4** will probably lead to considerable chemical stability and accordingly it may be expected that this tricyclodecadienone **5** is isolable despite its constrained C_2-C_6 enone system. In this paper the successful synthesis of **5** and some of its derivatives is described.

Results and discussion

Norbornene-annulated cyclopentenone **5** is essentially the Diels-Alder adduct of cyclopentadiene and 2-cyclopentynone. Although this direct route to **5** is obviously blocked by the non-availability of 2-cyclopentynone, even as a transient intermediate, the use of an appropriate synthetic equivalent may, however, circumvent this synthetic problem. Kienzle and Minder applied β-arylsulfonylcyclopentenones **6** for this purpose[5]. With cyclopentadiene the corresponding tricyclodecadienones **7a** were obtained as an *endo*/*exo*-mixture (2:1 ratio) in 60-80% yield (Scheme 1). Attempts to eliminate the arylsulfonyl group in **7a** by a variety of basic reagents did not produce the desired ketone **5** but only led to its isomer **1** (R=H). Although the authors suggest that **1** is the result of β,γ-, and not of α,β-elimination, involving the initial formation of **8**, this seems highly unlikely as the γ-hydrogen at C_5 is not activated at all. Most interestingly, reducing the C_8-C_9 double bond in **7a** and repeating the elimination procedure now smoothly converted **9** into the C_2-C_6 enone **10** in 60-80% yield. (Scheme 1). This result indicates that the C_8-C_9

Scheme 1



6 **7a** **8** **9** **10**

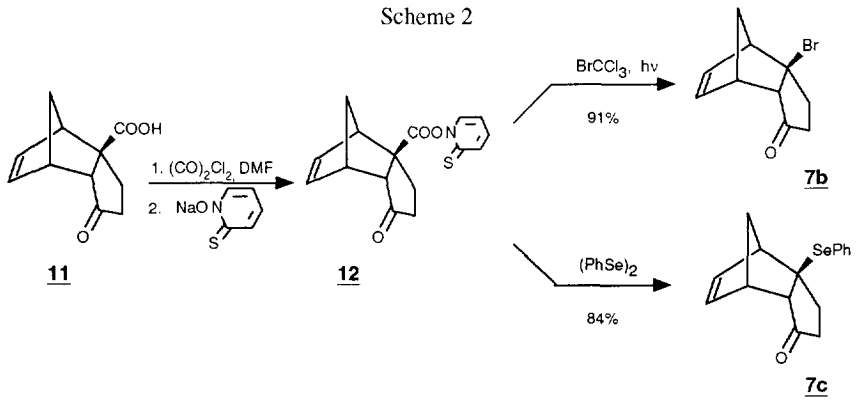
double bond in the β-elimination of sulfone **7a** plays a decisive role in the product formation.

An effective route to 6-substituted tricyclodecenones **7** is Barton's radical chain decarboxylation[6] of the corresponding carboxylic acid **11** (Scheme 2). As was demonstrated for **3** in the preceding paper[4], both the 6-bromo and 6-selenyl compounds **7b** and **7c** are available using this methodology. Both compounds may then undergo α,β-elimination to form **5** either by base induced dehydrobromination or oxidative *syn*-deselenylation. These conversions may be much more effective than the elimination of sulfinic acid

from sulfone **7a**.

The bromodecarboxylation of tricyclic acid **11** which is readily available by lithium aluminum hydride reduction of tricyclic ester **2b** ($R=C_2H_5$)[1i,7] and subsequent basic hydrolysis, was accomplished using essentially the same procedure as reported for the transformation of carboxylic acid **2a** into enone bromide **3a**. Conversion of **11** into the corresponding acid chloride with oxalyl chloride, followed by treatment with the sodium salt of N-hydroxypyridine-2-thione afforded the N-acyloxypyridine-2-thione ester **12** which was immediately exposed to bromotrichloromethane at reflux temperature to give 6-bromo compound **7b** in an excellent overall yield of 91% (Scheme 2).

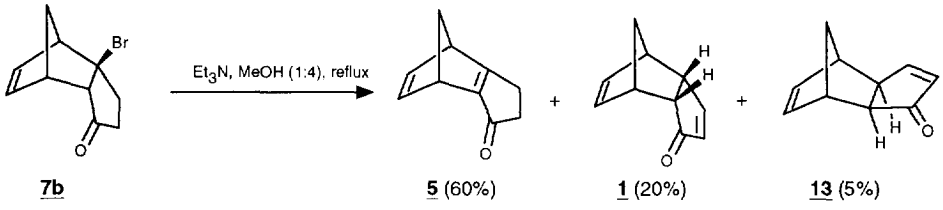
Scheme 2



Phenylselenyldecarboxylation of **11** also proceeded smoothly with diphenyl selenide in toluene as the radical trapping agent. 6-Phenylselenyltricyclodecadienone **7c** was obtained in 84% yield as a nice crystalline material.

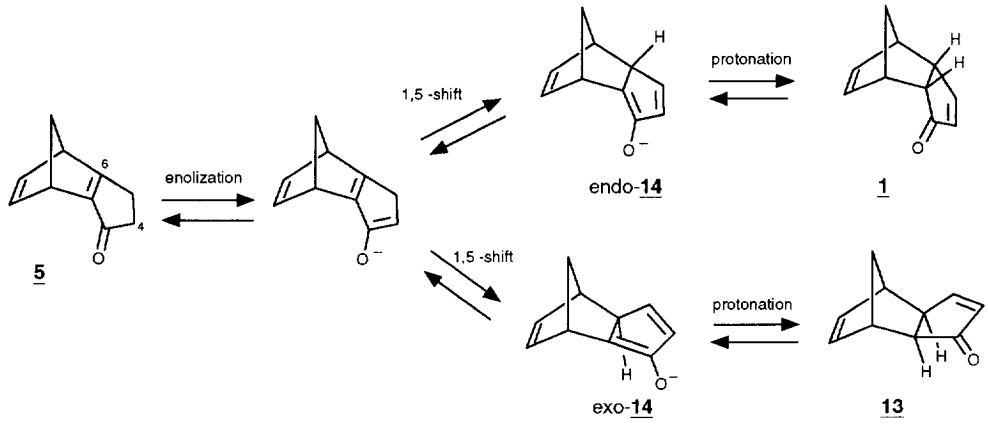
6-Bromotricyclodecenone **7b** showed similar reactivity towards triethylamine in methanol (1:4) as did as tricyclodecadienone bromide **3a**. At room temperature hardly any elimination of bromide was observed whereas at reflux temperature the reaction was complete within 30 minutes. Capillary gas chromatography revealed the formation of three products in a ratio 12:4:1, which, on basis of their ^{1}HNMR-spectra were identified as the desired enone **5**, and *endo*- and *exo*-tricyclodecadienone **1** (R=H) and **13**, respectively (Scheme 3). Pure **5** was readily obtained in 60% yield by flash chromatography over

Scheme 3



silica gel. The formation of *endo*- and *exo*-tricyclodecadienone (**1** and **13**) in this bromo-elimination of **7b** is readily explained by rearrangement of the initially formed **5** involving the base induced enolization process depicted in Scheme 4. Deprotonation at C_4 leads to the cyclopentadienolate intermediate which by

Scheme 4



a series of 1,5 proton shifts eventually forms either *endo*-**14** or *exo*-**14**. Subsequent stereospecific protonation of these enolates at C_2 then leads to observed mixture of *endo*- and *exo*-tricyclodecadienones (**1** and **13**). The occurrence of such a base catalyzed process was conveniently demonstrated by treating **5** under identical conditions as applied by Kienzle and Minder[5] using diazabicyclo[5.4.0]undecene (DBU) in tetrahydrofuran. After stirring for 3 days quantitative conversion of **5** into a mixture of *endo*-**1** and *exo*-**13** in a ratio of 8:3 was observed. This result not only explains the failure of the Swiss group to isolate **5** but also shows that the choice of the base used in the preparation of **5** is crucial. The thermodynamic bias which is the reason for the rapid base induced isomerization of **5** was substantiated by both force field (MM2) and semi-empirical (AM1) calculations[8] (Table 1).

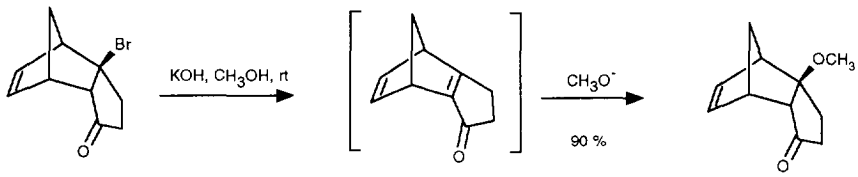
Table 1. Calculated heat of formation(AM1) and strain energy(MM2)

	1	**5**	**13**
Heat of formation (AM 1) Kcal/mol	27.62	41.13	25.85
Strain energy (MM2) Kcal/mol	30.49	39.76	28.92

After the successful synthesis of tricyclic enone **5** using the non-nucleophilic base triethylamine, the question arose whether a more nucleophilic base system, such as potassium hydroxide in methanol could be used for the preparation of 6-methoxy-*endo*-tricyclodecenone **7d**. At room temperature bromide **7b** rapidly reacted with this reagent to give **7d** in 90% yield (Scheme 5)[1i,7]. No enone **5** was detected in the product mixture. The formation of **7d** is clearly the result of rapid conjugate addition of methoxide to relatively strained C_2-C_6 enone moiety of initially formed **5**. This result already indicates the high reactivity of this central enone system in **5** toward nucleophiles. Interestingly, no tricyclodecadienones **1** and **13** were observed showing that nucleophilic addition to **5** is much more rapid than the enolization shown in Scheme 4.

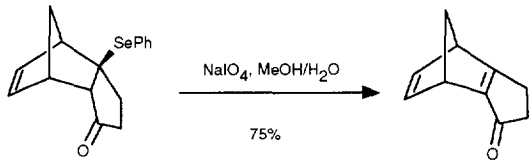
The oxidative deselenylation is a *syn*-elimination reaction which generally proceeds at moderate

Scheme 5



temperatures and in high yields[9]. Oxidation of selenide **7c** with sodium periodate at 5 °C using standard conditions fully conformed to this general picture. After 20 min. the reaction was already complete to give tricyclodecadienone **5** as a single product in 75% isolated yield (Scheme 6). No tricyclodecadienones **1** and

Scheme 6

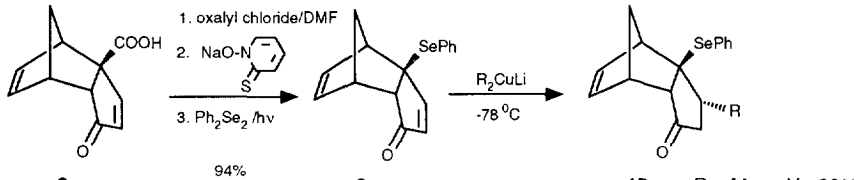


13 were detected in the reaction mixture, confirming that base is needed for the isomerization of **5** to these compounds.

It should be possible to extend the scope of the above methodology to the synthesis of derivatives of **5**. One way to do so would be to use the enone system in either carboxylic acid **2a** or 6-substituted tricyclodecadienones **3** as a handle for derivatization. After the desired enone transformation, elimination of an appropriate leaving group at C_6 would then give the desired C_2-C_6 enone moiety.

Tricyclic phenylselenide **3c** was selected to verify this approach as this compound is readily available in high yield from acid **2a**[4] (Scheme 7). In view of the previous experiences with conjugate

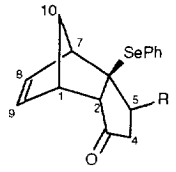
Scheme 7



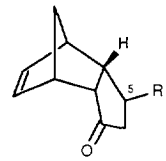
cuprate additions to tricyclodecadienones **1**[10], this reaction was investigated for **3c** using four different cuprates.

The addition of dimethyl- and di-n-butylcuprate to **3c** proceeded smoothly and in both cases afforded a single addition product in excellent yield. Based on their spectral data which will be discussed below, structures **15a** and **15b** were assigned to these addition products (Scheme 7). Increasing the steric bulk of the nucleophile by using di-t-butylcuprate led again to a single addition product *viz.* **15c** in a modest yield which is most likely due to the instability of the cuprate reagent. Subjecting **3c** to diphenylcuprate gave again a single 1,4-addition product, **15d**, and also a small amount of the 1,2-addition product.

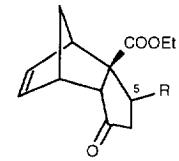
The gross structures of the products **15a-d** were all deduced from their mass, IR, and NMR data. However, the unequivocal assignment of the configuration (*endo* or *exo*) of the newly introduced substitutent at C_5 in **15** required a more detailed ^{1}H-NMR analysis. Comparison of the ^{1}H-NMR spectra of structures **15a-d** with related tricyclodecenones *viz.* **16** and **17**[10] revealed unambiguously the stereochemistry at C_5 in **15** (Table 2). All tricyclodecenones **16** and **17** having C_5 *endo*-protons exhibit



15



16



17

Table 2. chemical shift of selected protons in **15**, **16** and **17**

	δ (ppm)			
compound	$H_{5\text{-exo}}$	$H_{5\text{-endo}}$	H_8 and H_9	
15 a R = *endo* - Me	2.76		6.11	6.31
b *endo* - n-Bu	2.60		6.09	6.27
c *endo* - t -Bu	2.77		6.13	6.35
d *endo* - Ph	3.99		5.69	6.05
16 a R = *exo* - Me		1.86	6.12	6.16
b *exo* - n-Bu		1.68	6.14	6.15
c *exo* - Ph		2.92	6.26	6.30
d *endo* - Me	2.40		6.01	6.21
17 a R = *exo* - Me		2.04	6.20	6.30
b *exo* - n-Bu		1.86	6.18	6.30
c *exo* - Ph		3.26	6.42	6.42
d *endo* - Me	2.44		6.16	6.35
e *endo* - n-Bu	2.31		6.14	6.32
f *endo* - Ph	3.97		5.79	6.12

proton signals at a considerably higher field (lower shift value) than the C_5 *exo*-protons in the related structures. This phenomenon is the result of effective shielding of the *endo*-C_5 protons by the C_8-C_9 double bond. The observation that for **15a-d** the C_5 protons are found at relatively lower field (higher shift value) proves their *endo*-stereochemistry (*endo*-R). Additional evidence for the correctness of this assignment is derived from the strong shielding effect exhibited by the C_5 *endo*-phenyl group on the C_8 and C_9 olefinic

protons in **17f** and **15d**. In **17c** which contains an C_5-*exo*-phenyl substituent these olefinic protons absorb at considerably lower field (higher shift value). At a later stage of this project definite proof of the correctness of this ^{1}HNMR analysis was obtained from an X-ray diffraction analysis of **15a** the result of which is depicted in figure 1[11].

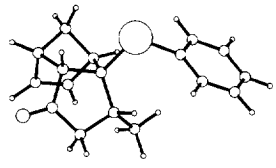
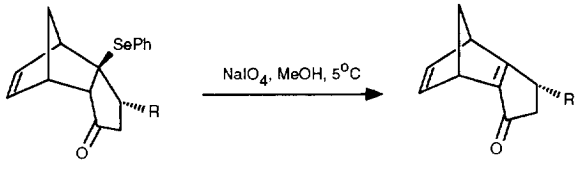


Figure 1. X-ray structure of **15a**

The complete *endo*-selectivity in combination with the high yields and relatively fast reaction rates observed for the cuprate addition to **3c** is quite surprising as the *endo*-face of the *endo*-tricyclodecadienone system is severely hindered by the C_8-C_9 ethene bridge which generally results in predominant *exo*-addition. It is evident that the bulky phenylselenyl group at C_6 may severely hinder or even block conjugate addition from the *exo*-face of **3c** but this should at least be reflected in lower reaction rates and lower yields. Detailed studies to uncover the true nature of this cuprate addition to **3c** are currently underway and will be reported in due course. From a synthetic point of view this directing effect of the phenylselenyl group is highly rewarding.

The oxidative deselenation of **15** was carried out as described above for the synthesis of **5** from **7c**. By stirring **15a**-**d** with sodium periodate in methanol a smooth elimination was observed in all cases to afford the corresponding tricyclodecadienones **18a**-**d** in yields of *ca.* 80% (Scheme 8).

Scheme 8



15

18	**a**.	R=Me	82%
	b.	n-Bu	81%
	c.	t-Bu	76%
	d.	Ph	90%

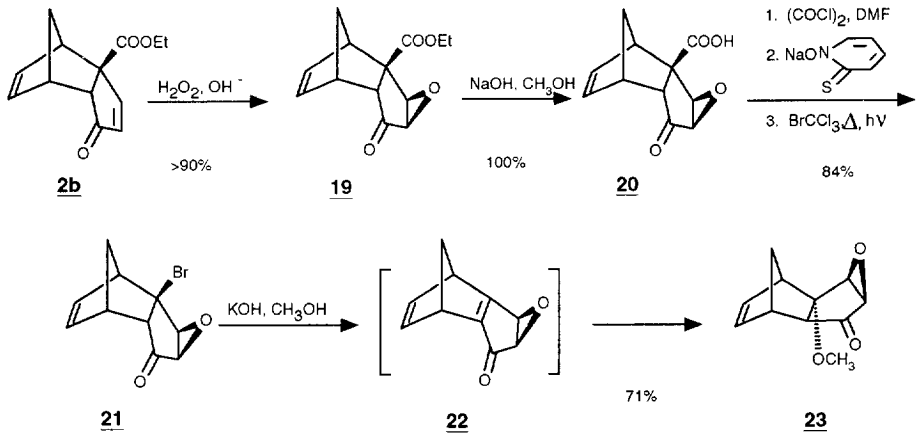
The successful synthesis of norbornene-annulated cyclopentenones **5** and **18** was a reason to consider this methodology for the preparation of norbornene-annulated cyclopentenone epoxide **22** (Scheme 9). Cyclopentenone epoxide **22** is a fascinating compound for which an unusual chemical reactivity is expected on basis of the unique combination of an epoxide ring, a vinyl system and a ketone function within in a compact, small ring system. In recent papers, a first general synthesis of some simply substituted cyclopentadienone epoxides and their reactions with nucleophilic reagents was reported[12]. The

synthetic potential of these epoxides for natural product synthesis was demonstrated by the preparation of *epi*-pentenomycin[1f,13].

A direct route to **22** would be the regioselective epoxidation of the enone moiety in tricyclic bromide **3a** to give epoxy bromide **21** followed by dehydrobromination. However, attempts to obtain **21** by alkaline epoxidation of tricyclic bromide **3a** using standard methods did not give satisfactory results. Epoxide **21** was obtained in only 40% yield due to the base sensitivity of bromide **3a**. As oxidation of selenium by hydrogen peroxide is a fast process we did not try such an epoxidation for **3c**.

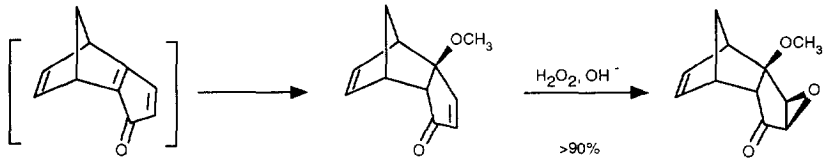
An alternative route to epoxy bromide **21** starts from tricyclic epoxide ester **19** which is produced from ester **2b** in more than 90% yield by alkaline epoxidation[1a,g] (Scheme 9). Basic hydrolysis using

Scheme 9



sodium hydroxide in methanol afforded epoxy acid **20** in quantitative yield. Barton halodecarboxylation of **20** using essentially the same procedure as described earlier for the synthesis of **7b**, gave **21** in 84% yield. Applying triethylamine as the base to effect dehydrobromination of **21** under a variety of conditions led only to complex mixtures. No cyclopentadienone epoxide **22** was detected among the products. When a more nucleophilic reagent was applied, such as potassium hydroxide in methanol, a methoxy substituted epoxide was isolated in 71% yield. Again there were no indications of the presence of **22** in the reaction mixture showing that this annulated cyclopentadienone epoxide is apparently too reactive to be isolated under these nucleophilic conditions[14]. Analysis of the ^{1}HNMR spectra suggested structure **23** for the newly formed epoxy ketone. The formation of this *endo*-6-methoxy-*exo*-tricyclodecenone epoxide from *exo*-6-bromo-*endo*-tricyclodecenone epoxide **21** proves the intermediacy of norbornene-annulated cyclopentenone epoxide **22** which under the reaction conditions rapidly undergoes stereospecific conjugate addition of methanol at its *endo*-face. In the preceding paper, it was reported that methanol addition to norbornene annulated cyclopentadienone **4** is also a stereospecific process to give exclusively *exo*-6-methoxy-*endo*-tricyclodecenone **24** (Scheme 10)[4]. This observation shows that in **4** the methylene bridge exerts less steric hindrance to the incoming nucleophile than the C_8-C_9 ethylene bridge. The complete inversion of stereochemistry observed for the methoxylation to epoxide **22** illustrates the subtlety of this 'bridge effect' on the facial stereoselectivity of conjugate addition reactions to these

Scheme 10



4 **24** **25**

tricyclodecadienones. The presence of a relative small epoxide function at the *exo*-face as in **22** exerts enough steric bulk to completely outweigh the directing effect of the bridges.

Unambiguous proof for the correctness of structure **23** was obtained from the alkaline epoxidation of **24**[4] which gave *exo*-6-methoxy-*endo*-tricyclodecadienone epoxide **25** in almost quantitative yield (Scheme 10). This epoxide, which structure was unequivocally established by comparison of its ^{1}HNMR-data with those of tricyclic *exo*-epoxides **19**, **20** and **21**[15], was *not* identical with tricyclic epoxide **23**.

The results described above indicate that the synthesis of norbornene annulated cyclopentenones including parent tricyclodeca-2(6),8-dien-3-one **5** can be accomplished starting from readily available carboxylic acid **2a**.

Experimental

General remarks

Melting points were measured with a Reichert Thermopan microscope and are uncorrected. IR spectra were recorded on a Perkin-Elmer 298 infrared spectrophotometer. ^{1}H and ^{13}C-NMR spectra were recorded on a Bruker AM-400 spectrophotometer, using TMS as an internal standard. For mass spectra a double focussing VG 7070E mass spectrometer was used. Capillary GC analyses were performed using a Hewlett-Packard 5890A gas chromatograph, containing a cross-linked methyl silicone column (25m). Flash chromatography were carried out at a pressure of ca. 1.5 bar, a column length of 15-25 cm and a column diameter of 1-4 cm, using Merck Kieselgel 60H. Elemental analyses were performed on a Carlo Erba Instruments CHNS-O 1108 Elemental analyzer. All solvents used were dried and distilled according to the standard procedures.

6-Bromo-endo-*tricyclo[5.2.1.0^{2,6}]deca-8-en-3-one* **7b**

A solution of acid **11** (192 mg, 1 mmole) in benzene (5 ml) was treated with oxalyl chloride (0.3 ml) and a drop of dimethylformamide. After stirring for 2 hrs at room temp. with protection from moisture, the solvent and excess oxalyl chloride were evaporated and the residual acid chloride was used as such.

A solution of acid chloride (1 mmole) in benzene (5 ml) was added dropwise (15 min.) to a dried, stirred suspension of N-hydroxypyridin-2-thione sodium salt (190 mg, 1.2 mmole) in refluxing bromotrichloromethane while irradiating with a 250 w tungsten lamp in an inert atmosphere. After completion of the addition, the reaction mixture was cooled to room temp. and evaporated to dryness. The crude product was purified by flash chromatography over silica gel to give pure **7b** (200 mg, 90 %) as a

colorless oil.

7b: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.25-6.20 (m, 2H, H_8 and H_9), 3.41 (brs, 1H, H_1 or H_7), 3.32 (d, $J_{1,2}$=4.5 Hz, 1H, H_2), 3.25 (brs, 1H, H_1 or H_7), 2.73-2.65, 2.61-2.52, 2.35-2.25 and 2.15-1.91 (4 x m, 4H, H_4 and H_5), 2.26 A of AB (d, $J_{10a,10s}$=8.9 Hz, 1H, H_{10s}), 1.91 B A of AB (d, $J_{10a,10s}$=8.9 Hz, 1H, H_{10a}). ^{13}C-NMR (100 MHz, H-dec., $CDCl_3$): δ 216.5 (quat.), 138.0/134.5 (tert.), 71.1 (quat.), 66.0/57.9 (tert.), 52.7 (sec.), 47.0 (tert.), 41.8/37.4 (sec.). IR (CH_2Cl_2): ν 3100-3020 (C-H, unsat.), 3010-2820 (C-H, sat.), 1730 (C=O) cm^{-1}. CI/MS: m/e (%) 229/227 (0.1/0.1, M^++1), 163/161 (12/13, M^++1-Br), 147 (12, M^+-C_5H_6), 66 (29, $C_5H_6^+$). EI/HRMS m/e: 227.0071 [calc.for $C_{10}H_{12}O^{79}Br(M^+$+1): 227.0072].

6-Phenylselenyl-endo-*tricyclo[5.2.1.0^{2,6}]deca-8-en-3-one* **7c**

A solution of acid **11** (192 mg, 1 mmole) in benzene (5 ml) was treated with oxalyl chloride (0.3 ml) and a drop of dimethylformamide. After stirring for 2 hrs at room temp. with protection from moisture, the solvent and excess oxalyl chloride were evaporated and the residual acid chloride used as such.

A solution of acid chloride (1 mmole) in toluene (5 ml) was added dropwise (15 min.) to a dried, stirred suspension of N-hydroxypyridin-2-thione sodium salt (190 mg, 1.2 mmole) in refluxing toluene (10 ml) containing 2 mmol of diphenyl diselenide while irradiating with a 250 w tungsten lamp in an inert atmosphere. After completion of the addition, the reaction mixture was cooled to room temp. and evaporated to dryness. The crude product was purified by flash chromatography (n-hexane /EtOAc = 9 /1) over silica gel to give pure **7c** (260 mg, 84 %) as a white solid.

7c: m.p.: 101-103 °C (diisopropyl ether). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.68-7.32 (m, 5H, Ph-H), 6.20-6.16 (m, 2H, H_8 and H_9), 3.24 and 3.19 (2 x brs, 2H, H_1 and H_7), 2.91 (d, $J_{1,2}$=4.5 Hz, 1H, H_2), 2.46-2.26 (m, 2H, H_4), 2.24 A of AB (d, $J_{10a,10s}$=8.7 Hz, 1H, H_{10s}), 2.08-2.00 and 1.94-1.76 (2 x m, 2H, H_5), 1.77 B A of AB (d, $J_{10a,10s}$=8.7 Hz, 1H, H_{10a}). ^{13}C-NMR (100 MHz, H-dec., $CDCl_3$): δ 218.5 (quat.), 137.0/136.6/135.9/129.2 (tert.), 128.9 (quat.), 128.7/62.4 (tert.), 58.0 (quat.), 53.8 (tert.), 52.4 (sec.), 47.0 (tert.), 41.5/33.3 (sec.). IR (CH_2Cl_2): ν 3100-3020 (C-H, unsat.), 3010-2820 (C-H, sat.), 1725 (C=O) cm^{-1}. CI/MS: m/e (%) 304 (0.5, M^+), 238 (44, M^+-C_5H_6), 66 (10, $C_5H_6^+$). EI/HRMS m/e: 304.0366 [calc.for $C_{16}H_{16}O^{80}Se(M^+)$: 304.0366].

endo-*Tricyclo[5.2.1.0^{2,6}]deca-2(6),8-dien-3-one* **5** and endo- and exo-*tricyclo[5.2.1.0^{2,6}]deca-4,8-dien-3-one* **1** and **13**[17]

A solution of **7b** (60 mg) in methanol (8 ml) and Et_3N (2 ml) was refluxed for 30 min. Removal of the solvent followed by dissolution of the residue in n-hexane/ethyl acetate (3/1) and subsequent filtration gave, after drying ($MgSO_4$) and concentration, a mixture (40 mg) of **5**, **1** and **13** in 12:4:1 ratio (according to GC and NMR). Pure **5** was obtained by flash chromatography (n-hexane /EtOAc = 6 /1).

5: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.88 A of AB (dd, $J_{8,9}$=5.0 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.2 Hz, 1H, H_8 or H_9), 6.79 B of AB (dd, $J_{8,9}$=5.0 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.3 Hz, 1H, H_8 or H_9), 3.76 and 3.61 (2 x brs, 2H, H_1 and H_7), 2.84-2.50 (m, 4H, H_4 and H_5), 2.47 and 2.39 AB x 2 (2 x d, $J_{10s,10a}$=6.8 Hz, 2H, H_{10}). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 203.2/199.4/159.4 (quat.), 144.6/141.6 (tert.), 74.6 (sec.), 51.1/44.9 (tert.), 41.2/26.3 (sec.). IR (CH_2Cl_2): υ 3010-2860 (C-H, sat.), 1675 (C=O) cm^{-1}. EI/MS: m/e (%) 146 (100, M^+), 66 (21, $C_5H_6^+$). EI/HRMS m/e: 146.0732 [calc.for $C_{10}H_{10}O(M^+)$: 146.0732].

1: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.38 (dd, $J_{4,5}$=5.7 Hz, $J_{5,6}$=2.6 Hz, 1H, H_5), 5.96 (d, $J_{4,5}$=5.7 Hz, 1H,

H_4), 5.94 A of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=2.9 Hz, 1H, H_8 or H_9), 5.78 B of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.0 Hz, 1H, H_8 or H_9), 3.42 and 3.22 and 2.97 (3 x brs, 3H, H_1, H_6 and H_7), 2.80 (dd, $J_{1,2}$= $J_{2,6}$=5.1 Hz, 1H, H_2), 1.74 and 1.63 AB x 2 (2 x d, $J_{10a,10s}$=8.4 Hz, 2H, H_{10a} and H_{10s}). GCEI/MS: m/e (%) 146 (84, M^+), 118 (33, M^+-CO), 81 (13, M^++1-C_5H_6), 66 (100, $C_5H_6^+$).

13: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.57 (dd, $J_{4,5}$=5.7 Hz, $J_{5,6}$=2.6 Hz, 1H, H_5), 6.29 A of AB (dd, $J_{8,9}$=5.5 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.1 Hz, 1H, H_8 or H_9), 6.27 (dd, $J_{4,5}$=5.7 Hz, $J_{4,6}$=1.5 Hz, 1H, H_4), 6.22 B of AB (dd, $J_{8,9}$=5.5 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.0 Hz, 1H, H_8 or H_9), 2.93 (brs, 1H, H_1), 2.87 (brs, 1H, H_6), 2.72 (brs, 1H, H_7), 2.27 (d, $J_{2,6}$=5.0 Hz, 1H, H_2), 1.41 (dt, $J_{a,b}$=9.4 Hz, J=1.5 Hz, 1H, H_{10a} or H_{10s}), 1.30 (d, 1H, H_{10a} or H_{10s}). GCEI/MS: m/e (%) 146 (64, M^+), 118 (19, M^+-CO), 81 (7, M^++1-C_5H_6), 66 (100, $C_5H_6^+$).

endo-Tricyclo[5.2.1.0^{2,6}]deca-2(6),8-dien-3-one **5** *by oxidative elimination of* **7c**

A solution of **7c** (180 mg, 0.6 mmol) in methanol (30 ml) was treated with a solution of sodium periodate (180 mg in 2 ml H_2O) at ca. 5 °C (ice water) with stirring. After 20 min., the solution was filtered and the remaining solid washed with ethyl acetate. The combined organic phase were evaporated and subjected to flash chromatography (n-hexane /EtOAc = 4 /1) to give pure **5** (65 mg, 75 %) as a colorless oil.

Rearrangement of **5** *to* **1** *and* **13**

A solution of **5** (30 mg) in THF (1 ml) was treated with DBU (5 drops) and stirred at room temp. for 3 days. The reaction mixture was poured into ether (50 ml) and washed with brine. Drying ($NaSO_4$) and concentration gave a product mixture (30 mg). GC (comparison with known compounds **1** and **13**) showed that starting material **5** had disappeared and rearranged quantitatively to a mixture of **1** and **13** in a 8:3 ratio. Further evidence for the formation of **1** and **13** was obtained from ^{1}H-NMR and GC-MS analyses.

General procedure A for cuprate addition to **3c**:

A solution of RLi (ca. 1.5 mmol) in hexane was gradually added to a suspension of dry CuI (200 mg, 1 mmol) in dry ether at temp. below 0 °C (ice-salt) in a nitrogen atmosphere. After stirring for 15 min. at this temp., the mixture was cooled to -78 °C. A solution of **3c** (0.5 mmol) in ether was then added. The mixture was stirred at -78 °C until the reaction was complete according to TLC (ca. 30 min.), then quenched with aqueous ammonium chloride and the aqueous phase extracted with ether (3x). The combined organic phases were washed with water (3x), dried (Na_2SO_4) and the solvent evaporated under reduced pressure. Analytical samples were obtained by flash chromatography and/or crystallization.

endo-*5-Methyl*-exo-*6-phenylselenyl*-endo-*tricyclo[5.2.1.0^{2,6}]deca-8-en-3-one* **15a**

Following the general procedure A [MeLi (1 ml of 1.6 M solution in hexane, 1.6 mmol), CuI (200 mg, 1 mmol), **3c** (150 mg, 0.5 mmol)], gave, after work-up and flash chromatography (n-hexane /EtOAc= 20/1), 140 mg (89 %) of **15a** as a white solid.

15a: m.p.: 61-62 °C (diisopropylether). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.66- 7.29 (m, 5H, Ph-H), 6.31 A of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.0 Hz, 1H, H_8 or H_9), 6.12 B of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=2.9 Hz, 1H, H_8 or H_9), 3.27 and 3.12 (2 x brs, 3H, H_1, H_2 and H_7), 2.81-2.71 (m, 1H, H_5), 2.39 A of AB (d, $J_{10a,s}$=8.6 Hz, 1H, H_{10s}), 2.08 A of AB (dd, $J_{4x,4n}$=18.4 Hz, $J_{4x,5}$=9.5 Hz, 1H, H_{4x}), 1.78 B of AB

(dd, $J_{4x,4n}$=18.4 Hz, $J_{4n,5}$=12.5 Hz, H_{4n}), 1.76 B of AB (d, $J_{10a,s}$=8.6 Hz, 1H, H_{10a}), 0.98 (d, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 218.8 (quat.), 137.7/137.5/136.0/129.2/129.1 (tert.), 128.2/63.6 (quat.), 62.8 (tert.), 53.4 (sec.), 52.4 (tert.), 49.4 (sec.), 48.3 (tert.), 39.7 (tert.), 14.6 (prim.). IR (CH_2Cl_2): υ 3080-3020 (C-H, unsat.), 3010-2860 (C-H, sat.), 1730 (C=O) cm^{-1}. EI/MS: m/e (%) 318 (9, M^+), 252 (77, M^+-C_5H_6), 161 (45, M^+-SePh), 133 (59, M^+-SePh-CO), 95 (100, M^+-SePh-C_5H_6), 66 (53, $C_5H_6^+$). EI/HRMS m/e: 318.0524 [calc.for $C_{17}H_{18}O^{80}Se$ (M^+): 318.0523].

endo-*5-n-Butyl*-exo-*6-phenylselenyl*-endo-*tricyclo[5.2.1.0^{2,6}]deca-8-en-3-one* **15b**

Following the general procedure A [n-BuLi (1 ml of 1.6 M solution in hexane, 1.6 mmol), CuI (200 mg, 1 mmol), **3c** (150 mg, 0.5 mmol)], gave, after work-up and flash chromatography (n-hexane /EtOAc= 20/1), 155 mg (86 %) of **15b**.

15b: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.66- 7.29 (m, 5H, Ph-H), 6.27 A of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.1 Hz, 1H, H_8 or H_9), 6.09 B of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=2.9 Hz, 1H, H_8 or H_9), 3.25 and 3.14 (2 x brs, 2H, H_1 and H_7), 3.11 (d, $J_{1,2}$=4.9 Hz, 1H, H_2), 2.63-2.55 (m, 1H, H_5), 2.37 A of AB (d, $J_{10a,s}$=8.6 Hz, 1H, H_{10s}), 2.11 A of AB (dd, $J_{4x,4n}$=18.4 Hz, $J_{4x,5}$=9.5 Hz, 1H, H_{4x}), 1.70 B of AB (dd, $J_{4x,4n}$=18.4 Hz, $J_{4n,5}$=12.0 Hz, 1H, H_{4n}), 1.75 B of AB (d, $J_{10a,s}$=8.6 Hz, 1H, H_{10a}), 1.58-1.00 (m, 6H, -$(CH_2)_3$-), 0.84 (t, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 218.7 (quat.), 137.7/137.2/136.2/129.1 (tert.), 128.2/63.2 (quat.), 62.5 (tert.), 53.3 (sec.), 52.6 (tert.), 48.0 (tert.), 47.7 (sec.), 45.4 (tert.), 31.1/30.3/22.7 (sec), 14.0 (prim.). IR (CH_2Cl_2): υ 3080-3020 (C-H, unsat.), 3010-2860 (C-H, sat.), 1720 (C=O) cm^{-1}. EI/MS: m/e (%) 360 (3, M^+), 294 (100, M^+-C_5H_6), 203 (55, M^+-SePh), 175 (37, M^+-SePh-CO), 137 (68, M^+-SePh-C_5H_6), 66 (51, $C_5H_6^+$). EI/HRMS m/e: 360.0991 [calc.for $C_{20}H_{24}O^{80}Se$ (M^+): 360.0992].

endo-*5-t-Butyl*-exo-*6-phenylselenyl*-endo-*tricyclo[5.2.1.0^{2,6}]deca-8-en-3-one* **15c**

Following the general procedure A [t-BuLi (1 ml of 1.6 M solution in hexane, 1.6 mmol), CuI (200 mg, 1 mmol), **3c** (150 mg, 0.5 mmol)], gave, after work-up and flash chromatography (n-hexane /EtOAc= 20/1), 45 mg (25 %) of **15c**.

15c: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.66- 7.29 (m, 5H, Ph-H), 6.36 A of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.0 Hz, 1H, H_8 or H_9), 6.13 B of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=2.9 Hz, 1H, H_8 or H_9), 3.34 (brs, 1H, H_1 or H_7), 3.18 (d, $J_{1,2}$=5.1 Hz, 1H, H_2), 3.12 (brs, 1H, H_1 or H_7), 2.77 (dd, $J_{4n,5}$=12.9 Hz, $J_{4x,5}$=10.3 Hz, 1H, H_5), 2.63 A of AB (d, $J_{10a,s}$=8.6 Hz, 1H, H_{10s}), 1.97 (d, $J=_{4x,5}$10.3 Hz, 1H, H_{4x}), 1.96 (d, $J_{4n,5}$=12.9 Hz, 1H, H_{4n}), 1.79 B of AB (d, $J_{10a,s}$=8.6 Hz, 1H, H_{10a}), 1.13 (s, 9H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 218.7 (quat.), 137.7/137.1 (tert.), 129.5 (quat.), 129.3/129.0 (tert.), 62.8 (quat.), 62.2 (tert.), 54.8 (sec.), 54.1/53.6/46.8 (tert.), 44.6 (sec.), 33.7 (quat.), 45.4 (tert.), 30.7 (prim.). IR (CH_2Cl_2): υ 3080-3020 (C-H, unsat.), 3010-2860 (C-H, sat.), 1720 (C=O) cm^{-1}. EI/MS: m/e (%) 360 (4, M^+), 294 (7, M^+-C_5H_6), 203 (66, M^+-SePh), 137 (35, M^+-SePh-C_5H_6), 66 (11, $C_5H_6^+$). EI/HRMS m/e: 360.0991 [calc.for $C_{20}H_{24}O^{80}Se$ (M^+): 360.0992].

endo-*5-Phenyl*-exo-*6-phenylselenyl*-endo-*tricyclo[5.2.1.0^{2,6}]deca-8-en-3-one* **15d** *and* exo-*3-phenyl-6-phenylselenyl*-endo-*tricyclo[5.2.1.0^{2,6}]deca-4,8-dien-3-ol*

Following the general procedure A [PheLi (1.5 ml of 2 M solution in hexane, 3 mmol), CuI (200 mg, 1

mmol), **3c** (150 mg, 0.5 mmol)], gave, after work-up and flash chromatography (n-hexane /EtOAc= 20/1), 170 mg (89 %) of a mixture of **15d** and **1,2-product** in 4:1 ratio.

15d: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.66- 7.29 (m, Ph-H), 6.05 A of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=2.9 Hz, 1H, H_8 or H_9), 5.69 B of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.2 Hz, 1H, H_8 or H_9), 3.99 (dd, J=9.5 Hz, J=12.1 Hz, 1H, H_5), 3.42 (d, $J_{1,2}$=3.61 Hz, 1H, H_2), 3.30 and 3.02 (2 x brs, 2H, H_1 and H_7), 2.54 A of AB (dd, $J_{4x,4n}$=18.1 Hz, $J_{4x,5}$=12.1 Hz, 1H, H_{4x}), 2.35 A of AB (d, $J_{10a,s}$=8.6 Hz, 1H, H_{10s}), 2.25 B of AB (dd, $J_{4x,4n}$=18.1 Hz, $J_{4n,5}$=9.5 Hz, 1H, H_{4n}), 1.63 B of AB (d, $J_{10a,s}$=8.6 Hz, 1H, H_{10a}).

1,2-product: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.66- 7.29 (m, Ph-H), 6.31 A of AB (dd, $J_{8,9}$=5.4 Hz, $J_{1,9}$ resp. $J_{7,8}$=2.9 Hz, 1H, H_8 or H_9), 5.91 B of AB (dd, $J_{8,9}$=5.4 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.4 Hz, 1H, H_8 or H_9), 5.77 and 5.56 AB (2 x d, $J_{4,5}$=5.5 Hz, 2H, H_4 and H_5), 3.15 and 3.05 (2 x brs, 2H, H_1 and H_7), 2.97 (d, $J_{1,2}$=4.1 Hz, 1H, H_2), 2.21 A of AB (d, $J_{10a,s}$=8.5 Hz, 1H, H_{10s}), 1.77 B of AB (d, $J_{10a,s}$=8.5 Hz, 1H, H_{10a}), 1.61 (s, 1H, OH).

General procedure B for the synthesis of **18** *by oxidative elimination of* **15**

A solution of **15** (100 mg, 0.3 mmol) in methanol (5 ml) was treated with a solution of sodium periodate (100 mg, 0.5 mmol in 1 ml water) at ca. 5 ^{0}C (ice water) with stirring. After 20 min., the solid was filtered and washed with ethyl acetate. The combined organic phases were evaporated and purified by chromatography.

5-endo-*Methyl-tricyclo[5.2.1.0^{2,6}]deca-2(6),8-en-3-one* **18a**

Following the general procedure B and applying **15a** gave, after flash chromatography (n-hexane /EtOAc = 4 /1), pure **18a** (40 mg, 82 %) as a colorless oil.

18a: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.88 A of AB (dd, $J_{8,9}$=4.9 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.2 Hz, 1H, H_8 or H_9), 6.77 B of AB (dd, $J_{8,9}$=4.9 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.3 Hz, 1H, H_8 or H_9), 3.74 and 3.59 (2 x brs, 2H, H_1 and H_7), 3.17-3.10 (m, 1H, H_5), 2.99 A of AB (dd, $J_{4x,n}$=18.0 Hz, $J_{4x,5}$=5.7 Hz, 1H, H_{4x}), 2.44 and 2.37 AB x 2 (2 x d, $J_{10s,10a}$=6.7 Hz, 2H, H_{10}), 2.20 B of AB (d, $J_{4x,n}$=18.0 Hz, 1H, H_{4n}), 1.06 (d, J=7.2 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 206.9/198.9/158.5 (quat.), 144.8/141.6 (tert.), 74.1/49.9 (sec.), 49.9/45.0/33.3 (tert.), 17.4 (prim.). IR (CH_2Cl_2): υ 3010-2860 (C-H, sat.), 1675 (C=O) cm^{-1}. EI/MS: m/e (%) 160 (64, M^+), 105 (100), 94 (29, M^+-C_5H_6), 66 (41, $C_5H_6^+$). EI/HRMS m/e: 160.0888 [calc.for $C_{11}H_{12}O(M^+)$: 160.0882].

5-endo-*n-Butyl-tricyclo[5.2.1.0^{2,6}]deca-2(6),8-en-3-one* **18b**

Following the general procedure B and applying **15b** gave, after flash chromatography (n-hexane /EtOAc = 4 /1), pure **18b** (44 mg, 81 %) as a colorless oil.

18b: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.82 A of AB (dd, $J_{8,9}$=4.9 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.1 Hz, 1H, H_8 or H_9), 6.68 B of AB (dd, $J_{8,9}$=4.9 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.2 Hz, 1H, H_8 or H_9), 3.66 and 3.54 (2 x brs, 2H, H_1 and H_7), 3.0-2.95 (m, 1H, H_5), 2.82 A of AB (dd, $J_{4x,n}$=18.0 Hz, $J_{4x,5}$ resp. $J_{4n,5}$=5.7 Hz, 1H, H_{4x} or H_{4n}), 2.37 and 2.30 AB x 2 (2 x d, $J_{10s,10a}$=6.7 Hz, 2H, H_{10}), 2.21 B of AB (d, $J_{4x,n}$=18.0 Hz, 1H, H_{4x} or H_{4n}), 1.43 (m, 1H, one of $C\underline{H}_2CH_2CH_2CH_3$), 1.29-1.14 (m, 5H), 0.82 (d, J=7.0 Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 206.0/198.9/158.9 (quat.), 144.8/141.6 (tert.), 74.6 (sec.), 50.6 (tert.), 48.0 (sec.), 44.8/39.0 (tert.), 32.5/29.7/22.6 (sec.), 13.9 (prim.). IR (CH_2Cl_2): υ 3010-2860 (C-H, sat.), 1670 (C=O) cm^{-1}. EI/MS: m/e

(%) 202 (27, M^+), 91 (100), 66 (17, $C_5H_6^+$). EI/HRMS m/e: 202.1357 [calc.for $C_{14}H_{18}O(M^+)$: 202.1358].

5-endo-*t-Butyl-tricyclo[5.2.1.0^{2,6}]deca-2(6),8-en-3-one* **18c**

Following the general procedure B and applying **15c** gave, after flash chromatography (n-hexane /EtOAc = 6 /1), pure **18c** (30 mg, 76 %) as a white solid.

18c: m.p.: 63.5-65.5 ^{0}C (diisopropyl ether). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.87 A of AB (dd, $J_{8,9}$=5.0 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.1 Hz, 1H, H_8 or H_9), 6.81 B of AB (dd, $J_{8,9}$=5.0 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.1 Hz, 1H, H_8 or H_9), 3.73 and 3.69 (2 x brs, 2H, H_1 and H_7), 2.92 (d, $J_{4x,5}$ resp. $J_{4n,5}$=5.8 Hz, 1H, H_5), 2.72 A of AB (dd, $J_{4x,n}$=18.2 Hz, $J_{4x,5}$ resp. $J_{4n,5}$=5.9 Hz, 1H, H_{4x} or H_{4n}), 2.44 B of AB (dd, $J_{4x,n}$=18.2 Hz, 1H, H_{4x} or H_{4n}), 2.45 and 2.37 AB x 2 (2 x d, $J_{10s,10a}$=6.8 Hz, 2H, H_{10}), 0.87 [s, 9H, $C(CH_3)_3$]. ^{13}C-NMR (100 MHz, $CDCl_3$): δ 204.1/199.0/160.2 (quat.), 144.2/141.2 (tert.), 75.6 (sec.), 52.8/50.6/44.6 (tert.), 44.5 (sec.), 34.4 (quat.), 27.9 (prim.). IR (CH_2Cl_2): υ 3010-2860 (C-H, sat.), 1670 (C=O) cm^{-1}. EI/MS: m/e (%) 203 (26, M^++1), 146 (100, M^++1-CMe_3), 66 (5, $C_5H_6^+$), 57 (56, CMe_3^+). EI/HRMS m/e: 203.1435 [calc.for $C_{14}H_{19}O(M^+$+1): 203.1436].

5-endo-*Phenyl-tricyclo[5.2.1.0^{2,6}]deca-2(6),8-en-3-one* **18d**

Following the general procedure B and applying **15d** (150 mg, purity is 80%) gave, after flash chromatography (n-hexane /EtOAc = 4 /1), pure **18d** (43 mg, 90 %) as a white solid.

18d: m.p.: 107-109 ^{0}C (diisopropyl ether). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.31-6.88 (2 x m, 5H, Ph-H), 6.86 A of AB (dd, $J_{8,9}$=5.0 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.1 Hz, 1H, H_8 or H_9), 6.36 B of AB (dd, $J_{8,9}$=5.0 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.3 Hz, 1H, H_8 or H_9), 4.25 (dd, J=6.3 Hz, J=1.7 Hz, 1H, H_5), 3.85 and 3.39 (2 x brs, 2H, H_1 and H_7), 3.28 A of AB (dd, J=18.2 Hz, J=6.3 Hz, 1H, one of H_4), 2.58 B of AB (dd, J=18.2 Hz, J=1.7 Hz, 1H, one of of H_4), 2.44 (s, 2H, H_{10}). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 203.6/198.7/158.9 (quat.), 142.8/142.5 (tert.), 139.9 (quat.), 128.8/127.6/127.0 (tert.), 74.4/51.8 (sec.), 50.3/45.2/44.7 (tert.). IR (CH_2Cl_2): υ 3010-2860 (C-H, sat.), 1680 (C=O) cm^{-1}. EI/MS: m/e (%) 222 (100, M^+), 156 (7, M^+-C_5H_6), 66 (5, $C_5H_6^+$). EI/HRMS m/e: 222.1044 [calc.for $C_{16}H_{14}O(M^+)$: 222.1045].

exo-3,4-Epoxy-endo-*tricyclo[5.2.1.0^{2,6}]deca-8-en-5-one-2-carboxylic acid* **20**

Ester **19** (1.2g, 5mmol) in a solution of NaOH in methanol (10%, 15ml) was stirred at room temp. for 5 hrs. The mixture was neutralized and concentrated to dryness. Water (20ml) was added, followed by extraction with ethyl acetate (3x), then the extracts were washed with water and brine, and dried (Na_2SO_4). Concentration *in vacuo* gave **20** (1g, ~100%) as a white solid.

20: m.p. 144.5-146.5°C (diisopropylether/EtOAc). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 10.5 (bs, 1H, COOH), 6.24 A of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.1 Hz, 1H, H_8 or H_9) 6.19 B of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=2.8 Hz, 1H, H_8 or H_9), 3.89 (dd, $J_{3,4}$=2.2 Hz, $J_{4,6}$= 1.8 Hz, 1H, H_4), 3.40 (bs, 1H, H_1 or H_7), 3.37 (bs, 1H, H_1 or H_7), 3.34 (d, $J_{3,4}$=2.2 Hz, 1H, H_3), 2.25 (dd, $J_{6,7}$=4.8 Hz, $J_{4,6}$=1.8 Hz, 1H, H_6), 1.87 A of AB (d, $J_{10a,10s}$=9.1 Hz, 1H, H_{10s}), 1.64 B of AB (d, $J_{10a,10s}$=9.1 Hz, 1H, H_{10a}). IR (CH_2Cl_2): υ 3600-2300 (COOH), 3100-3020 (C-H, unsat.), 3010-2820 (C-H, sat.), 1740 and 1705 (C=O) cm^{-1}. EI/MS: m/e (%) 206 (2, M^+), 161 (1, M^+-CO_2H), 141 (72, M^++1-C_5H_6), 66 (93, $C_5H_6^+$). EI/HRMS m/e: 206.0580 [calc.for $C_{11}H_{10}O_4(M^+)$: 256.0579]. Found: C 64.08, H 4.81 (calc.for $C_{11}H_{10}O_4$: C 64.08, H 4.89).

exo-*6-Bromo*-exo-*4,5-epoxy*-endo-*tricyclo[5.2.1.0^{2,6}]deca-8-en-3-one* **21**

A solution of acid **20** (208 mg, 1 mmole) in benzene (5 ml) was treated with oxalyl chloride (0.3 ml) and a drop of dimethylformamide. After stirring for 2 hrs at room temp. with protection from moisture, the solvent and excess oxalyl chloride were evaporated and the residual acid chloride was used as such.

A solution of acid chloride (1 mmole) in benzene (5 ml) was added dropwise (15 min.) to a dried, stirred suspension of N-hydroxypyridin-2-thione sodium salt (190 mg, 1.2 mmole) in refluxing bromotrichloromethane while irradiating with a 250 w tungsten lamp in an inert atmosphere. After completion of the addition, the reaction mixture was cooled to room temp. and evaporated to dryness. The crude product was purified by flash chromatography (n-hexane/EtOAc = 9/1) to give **21** (220 mg, 91%) as a white solid.

21: m.p.= 109 °C, decomposition (ether). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.17-6.12 (m, 2H, H_8 and H_9), 3.81 (dd, $J_{4,5}$=2.0 Hz, $J_{2,4}$= 1.6 Hz, 1H, H_4), 3.57 (d, $J_{4,5}$=2.0 Hz, 1H, H_5), 3.43 and 3.30 (brs, 2H, H_1 and H_7), 3.05 (dd, $J_{1,2}$=4.8 Hz, $J_{2,4}$=1.6 Hz, 1H, H_2), 2.30 A of AB (d, $J_{10a,10s}$=9.2 Hz, 1H, H_{10s}), 1.95 B of AB (dt, $J_{10a,10s}$=9.2 Hz, 1H, H_{10a}). IR (CH_2Cl_2): υ 3100-3020 (C-H, unsat.), 3010-2820 (C-H, sat.), 1740 (C=O) cm^{-1}. CI/MS: m/e (%) 242 (0.33) and 240 (0.35) (M^++1), 177 (13) and 175 (13) (M^++1-C_5H_6), 66 (100, $C_5H_6^+$). CI/HRMS m/e: 239.9786 [calc.for $C_{10}H_9O_2{}^{79}Br(M^+)$: 239.9786].

endo-*4,5-Epoxy*-endo-*6-methoxy*-exo-*tricyclo[5.2.1.0^{2,6}]deca-8-en-3-one* **23**

Crystalline bromide **21** (120 mg, 0.5 mmol) was added to a solution of KOH (20%, 10ml) in methanol with stirring under cooling (ice-water). Stirring was continued until crystalline **21** had dissolved. The mixture was then neutralized and concentrated to dryness. Water (10 ml) was added, the mixture extracted with ether (3x). The extracts were washed repeatedly with water and brine, dried (Na_2SO_4) and concentrated *in vacuo* to give a viscous oil (95 mg). Subsequent flash chromatography (n-hexane/EtOAc =5/1) gave pure **23** (75mg, 80%) as a colorless oil.

23: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.42 A of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=3.1 Hz, 1H, H_8 or H_9), 6.25 B of AB (dd, $J_{8,9}$=5.6 Hz, $J_{1,9}$ resp. $J_{7,8}$=2.9 Hz, 1H, H_8 or H_9), 3.94 (d, $J_{4,5}$=2.2 Hz, 1H, H_4), 3.49 (d, $J_{4,5}$=2.2 Hz, 1H, H_5), 3.39 (s, 3H, OCH_3), 3.28 and 3.04 (2 x bs, 2H, H_1 and H_7), 2.28 A of AB (d, $J_{10a,10s}$=9.3 Hz, 1H, H_{10s}), 2.16 (d, $J_{2,10a}$=2.6 Hz, 1H, H_2), 1.53 B of AB (ddt, $J_{10a,10s}$=9.3 Hz, $J_{10a,1}$= $J_{10a,7}$=1.7 Hz, $J_{10a,2}$=2.6 Hz, 1H, H_{10a},). IR (CH_2Cl_2): υ 3100-3020 (C-H, unsat.), 3010-2820 (C-H, sat.), 1735 (C=O) cm^{-1}. CI/MS: m/e (%) 192 (0.3, M^+), 161 (1, M^+-OCH_3), 127 (95, M^++1-C_5H_6), 66 (100, $C_5H_6^+$). EI/HRMS m/e: 192.0789 [calc.for $C_{11}H_{12}O_3(M^+)$: 192.0786].

exo-*4,5-Epoxy*-exo-*6-methoxy*-endo-*tricyclo[5.2.1.0^{2,6}]deca-8-en-3-one* **25**

A solution of **24**[4] (100 mg, 0.57 mmol) in dichloromethane (4 ml) and methanol (4 ml) was treated with NaOH aq. (0.2 N, 2ml) and H_2O_2 (35%, 2 ml) at room temp. The mixture was stirred for 4 hrs at room temp. Dichloromethane (50 ml) was added and washed with brine. After drying ($NaSO_4$) and concentration *in vacuo*, flash chromatography (n-hexane/EtOAc = 3/1) gave **25** (100mg, 90%).

25: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 6.12-6.10 (m, 2H, H_8 and H_9), 3.76-3.75 (m, 1H, H_4), 3.54 (s, 3H, OCH_3), 3.39 (d, $J_{4,5}$=2.4 Hz, 1H, H_5), 3.21-3.19 (m, 2H, H_1 and H_7), 2.57 (dd, $J_{1,2}$=5.2 Hz, $J_{2,4}$=1.7 Hz, 1H, H_2), 2.02 A of AB (d, $J_{10a,10s}$=8.7 Hz, 1H, H_{10s}), 1.78 B of AB (dt, $J_{10a,10s}$=8.7 Hz, $J_{10a,1}$= $J_{10a,7}$=1.6

Hz, 1H, H_{10a}). IR (CH_2Cl_2): υ 3100-3020 (C-H, unsat.), 3010-2820 (C-H, sat.), 1730 (C=O) cm^{-1}. CI/MS: m/e (%) 127 (100, M^++1-C_5H_6), 66 (100, $C_5H_6^+$). CI/HRMS m/e: 193.0865 [calc.for $C_{11}H_{13}O_3(M^+)$: 193.0865].

References and notes

1. (a) Klunder, A.J.H.; Bos, W.; Zwanenburg, B., *Tetrahedron Lett.*, **1981**, *22*, 4557. (b) Verlaak, J.M.J.; Klunder, A.J.H.; Zwanenburg, B., *ibid.*, **1982**, *23*, 5463. (c) Klunder, A.J.H.; Huizinga, W.B.; Sessink, P.J.M.; Zwanenburg, B., *ibid.*, **1987**, *28*, 357. (d) Klunder, A.J.H.; Houwen-Claassen, A.A.M.; Kooy, M.G.; Zwanenburg, B., *ibid.*, **1987**, *28*, 1329. (e) Lange, J.H.M.; Klunder, A.J.H.; Zwanenburg, B., *ibid.*, **1989**, *30*, 127. (f) Houwen-Claassen, A.A.M.; Klunder, A.J.H.; Zwanenburg, B., *Tetrahedron*, **1989**, *45*, 7134. (g) Klunder, A.J.H.; Zwanenburg, B.; Liu, Z-Y., *Tetrahedron Lett.*, **1991**, *32*, 3131. (h) Lange, J.H.M.; Klunder, A.J.H.; Zwanenburg, B., Zwanenburg, B., *Tetrahedron*, **1991**, *47*, 1509. (i) Zhu, J.; Klunder A.J.H.; Zwanenburg, B., *Tetrahedron*, **1994**, *50*, 10597.
2. (a) Grieco, P.A.; Abood, N., *J. Org. Chem.*, **1989**, *54*, 6008. (b) Takano, S.; Inomata, K.; Ogasawara, K., *J. Chem. Soc., Chem. Commun.*, **1989**, 271. (c) Garland, R.B.; Miyano, M.; Pireh, D.; Clare, M.; Finnegan, P.M.; Swenton, L., *J. Org. Chem.*, **1990**, *55*, 5854. (d) Grieco, P.A.; Abood, N., *J. Chem. Soc., Chem. Commun.*, **1990**, 410. (e) Takano, S.; Inomata, K.; Ogasawara, K., *ibid.*, **1990**, 1544. (f)(g) Takano, S.; Moriya, M.; Ogasawara, K., *Tetrahedron Lett.*, **1992**, *33*, 329 and 1909. (h) Liu, Z.Y.; He L.; Zheng, H., *Synlett.*, **1993**, 191. (i)(j) Liu, Z.Y.; Chu, X.J., *Tetrahedron Lett.*, **1993**, *34*, 349 and 3885. (k) Ogasawara, K., *Pure & Appl. Chem.*, **1994**, *66*, 2119.
3. Herz, W.; Iyer, V.S.; Nair, M.G., *J. Org. Chem.*, **1975**, *40*, 3519. For a modified and improved procedure, see: Klunder, A.J.H.; de Valk, W.C.G.M.; Verlaak, J.M.J.; Schellekens, J.W.M.; Noordik, J.H.; Parthasarathi, V.; Zwanenburg, B., *Tetrahedron*, **1985**, *41*, 963.
4. Zhu, J.; Klunder, A.J.H.; Zwanenburg, B., *Tetrahedron Lett.*, **1993**, *34*, 3335. Zhu, J.; Klunder, A.J.H.; Zwanenburg, B., *preceding paper.*
5. Kienzle, F.; Minder, R.E., *Helv. Chim. Acta*, **1987**, *70*, 1537.
6. Barton, D.H.R.; Crich, D.; Motherwell, W.B., *J. Chem. Soc., Chem. Commun.* **1983**, 939; Barton, D.H.R.; Lacher, B.; Zard, S.Z., *Tetrahedron Lett.* **1987**, *43*, 4321; Barton, D.H.R.; Crich D.; Motherwell, W., *Tetrahedron* **1985**, *41*, 3901.
7. Zhu, J.; Klunder, A.J.H.; Zwanenburg, B., *Tetrahedron Lett.*, **1994**, *35*, 2787.
8. Use of the services and facilities of the Dutch National NWO/SURF Expertise Center CAOS/CAMM, University of Nijmegen, The Netherlands, under grant numbers SON 326-052 and STW NCH99.1751, is gratefully acknowledged.
9. Larock, R.C., *Comprehensive Organic Transformations*, VCH Publishers.Inc., New York (1989).
10. Dols, P.M.M.A.; Verstappen, M.M.H.; Klunder, A.J.H.; Zwanenburg, B., *Tetrahedron*, **1993**, *49*, 11353.
11. Moers, F.G.; Beurskens, P.T.; Zhu, J.; Klunder, A.J.H., to be published.
12. Houwen-Claassen, A.A.M.; Klunder, A.J.H.; Zwanenburg, B., *Tetrahedron*, **1989**, *45*, 7134. Houwen-Claassen, A.A.M.; Klunder, A.J.H.; Zwanenburg, B., *Tetrahedron*, **1990**, *46*, 2593.
13. Houwen-Claassen, A.A.M.; Klunder, A.J.H.; Zwanenburg, B.; Beurskens, P.T.; Moers, F.G.; Beurskens, G., *Tetrahedron*, **1990**, *46*, 4283.
14. This result is consistent with an early report in which parent cyclopentadienone epoxide was shown to decompose in acidic or basic media, see: Chapmann, O.L.; Hess, T.C., *J. Org. Chem.*, **1979**, *44*, 962.
15. Comparison of the ^{1}HNMR-data of epoxide **25** with those of the tricyclic *exo*-epoxides **19**, **20** and **21** immediately revealed the *exo*-configuration of the epoxide function in **25**. In particular the striking correspondence in chemical shifts observed for the C_4-*endo*-protons is convincing. If the epoxide function would have been in the *endo*-position a significant upfield shift (> 0.6 ppm) of the C_4-*exo*-proton should have been observed[16].
16. Dols, P.P.M.A,; Arnouts, E.G.; Rohaan, J.; Klunder, A.J.H.,; Zwanenburg, B., *Tetrahedron* **1994**, *50*, *3473.*
17. Dols, P.P.M.A.; Klunder, A.J.H.; Zwanenburg, B., *Tetrahedron*, **1994**, *50*, 8515.

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