*Tetrahedron* Vol. 47, No. 8, pp 1495-1508, 1991
Printed in Great Britain

0040-4020/91 $3.00+.00


# SYNTHESIS, [3,3]-SIGMATROPIC REARRANGEMENT AND ELECTROPHILIC BEHAVIOR OF ANGULARLY ALKYLATED 2-CARBETHOXY-TRICYCLO[5.2.1.$0^{2,6}$]DECADIENONES

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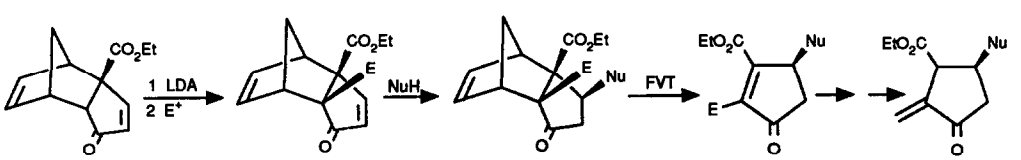
(*Received in UK* 8 *November* 1990)

*Abstract: The angular alkylation of tricyclodecadienone ester 1 with alkyl halides is described. A considerably diminished thermal stability is observed for the angularly alkylated tricyclic esters 7. Even at ambient temperature they rapidly undergo an unusually facile Cope rearrangement to bridge ketones 8. Both steric and electronic effects are held responsible for this unique behavior of 7. In contrast to ester 1, 6-alkyl esters 7 do not generally undergo conjugate addition. Instead, bridge ketone addition products are formed which may arise either from initial 1,2-nucleophilic addition to the $C_5$-ketone function in 7 followed by Cope rearrangement or from a stereoselective nucleophilic addition to the bridge ketone function in the Cope rearrangement compound 8. The remarkable stereoselectivity of the latter reaction is discussed in terms of Cieplak's model for the addition of nucleophiles to cyclic ketones.*

## Introduction

Tricyclo[5.2.1.$0^{2,6}$]decadienones are useful synthons for a variety of functionalized cyclopentenones, containing an endo-cyclic double bond, with defined stereochemistry and chirality[1,2]. The aim of the study presented in this paper is to extend the scope of the synthetic strategy based on these tricyclic systems to the preparation of cyclopentenones with an exo-cyclic olefinic moiety. Several naturally occurring cyclopentenoids contain an exo-cyclic enone function and therefore are appropriate targets for this study. Examples are sarkomycin[3], an antitumor compound, and the antibiotic methylenomycin B[4]. The proposed sequence of events is depicted in Scheme 1. Angular functionalization of the readily available[5] tricyclic ester 1, followed by a conjugate nucleophilic addition to the enone function, is expected to produce compound 3. Subsequent application of the technique of Flash Vacuum Thermolysis (FVT) will furnish cyclopentenone 4, which then in a series of transformations needs to be converted into the desired exo-cyclic product 5.

Scheme 1




1 2 3 4 5

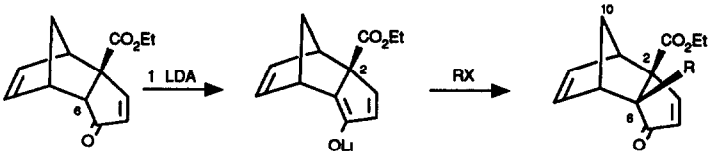
This report deals with the apparently simple angular alkylation, *viz.* the conversion of 1 into 2 with the

electrophile being an alkylating agent[6]. Furthermore, the chemical properties of the thus-prepared angularly alkylated tricyclic compounds, in particular their skeletal integrity will be discussed in detail.

**Angular alkylation of ethyl tricyclodecadienone 2-carboxylate 1**

For the angular deprotonation of tricyclic ester 1 a nonnucleophilic and strong base is most appropriate in order to avoid undesired reactions of both the enone- and carboethoxy group. With LDA in dry THF at -78 °C, a clean deprotonation at the 6-position of ester 1 was accomplished furnishing lithium enolate 6 (Scheme 2). The intermediacy of this anion was established by quenching with an excess of $D_2O$, which gave the corresponding 6-deuterated enone 1 in high yield. Alkylation of 1 was carried out by adding alkyl halides at -78 °C and slowly raising the temperature to 20 °C .

Scheme 2




1 6 7

| 7 | R | X | yield (%) |
|---|---|---|---|
| a | methyl | I | 88 |
| b | ethyl | I | 77 |
| c | allyl | I | 68 |
| d | n-heptyl | I | 47 |
| e | benzyl | Br | 28 |
| f | $CH_2I$ | I | 8 |

Electrophilic substitution of 6 with methyl iodide led stereospecifically to the corresponding 6-methylated enone ester 7a in 88 % yield. Addition of other primary alkyl halides, such as ethyl iodide, allyl bromide and *n*-heptyl iodide, similarly gave 7b-d. However, with benzyl bromide as the electrophile, a mixture of products was obtained, containing 6-benzyl ester 7e in a yield of only 28 %, together with 1,2-diphenyl-1-bromoethane and unreacted 1. The recovery of starting material 1 can readily be explained by assuming competitive proton exchange of enolate 6 with benzyl bromide, giving a benzyl carbanion that on coupling with another benzyl bromide produces 1,2-diphenyl-1-bromoethane. Most likely, the introduction of a relatively bulky benzyl group eclipsed with the ester function at $C_2$ will cause considerable steric interaction and consequently will retard the formation of the 6-substitution product 7e. To a certain extent, this steric interaction exists in all angularly substituted enones 7 and is directly dependent on the steric bulk exerted by the group introduced, as will be demonstrated later. Reaction of 1 with diiodomethane yielded a mixture of products consisting of iodide 7f, starting ester 1 and polymeric material. After flash chromatography pure 7f was obtained in a yield of 8 % only, implying that further annelation reactions[7] of 1, based on angular iodomethylations are not promising. The structures 7a-f were ascertained by their spectral data. Interestingly, their NMR-spectra differ markedly from 1, *e.g.* the *syn*-bridge proton at $C_{10}$ is considerably shifted to lower field (~0.4 ppm). This difference may be explained by assuming a Van der Waals interaction of this proton with the angular alkyl group. Structure 7a was unequivocally established by an X-ray diffraction analysis[8].

**Cope rearrangement of angularly 6-alkylated ethyl tricyclodecadienone 2-carboxylates**

During the synthesis of the angularly alkylated tricyclodecadienones 7 a considerable diminished chemical stability of the tricyclic enone system was observed. Alkylation of 1 with methyl iodide smoothly afforded 7a in a high yield as a single crystalline compound. Surprisingly, on standing at room temperature for some days, these crystals slowly liquified. $^1$H-NMR spectroscopy revealed the formation of a mixture containing 7a and its isomer 8a. The formation of 8a results from a sigmatropic [3,3] rearrangement (Cope rearrangement), as is

depicted in Scheme 3[9]. The observation of a high C=O absorption (1780 $cm^{-1}$) in the IR-spectrum of **8a** clearly indicates the presence of a strained carbonyl function.

Scheme 3


**7** **8**

| | R | 7(%) | 8(%) |
|---|---|---|---|
| | H | 100 | - |
| a | methyl | 65 | 35 |
| b | ethyl | 35 | 65 |
| c | allyl | 40 | 60 |
| d | n-heptyl | 35 | 65 |
| e | benzyl | 25 | 75 |
| f | $CH_2I$ | 40 | 60 |

After standing for approximately a week an equilibrium between **7a** and **8a** was reached with a molar ratio amounting to 65:35. Analogously, all other 6-alkyl enone esters **7** show this sigmatropic equilibration, however at a much higher rate and in favor of the rearranged product **8**. In contrast, ester **1** exhibits no Cope rearrangement, neither at room temperature nor at elevated temperatures. The position of the equilibria in these rearrangements could be easily determined from the corresponding $^1$H-NMR spectra in which several signals are well separated.

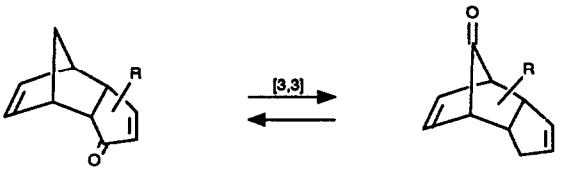
Apparently, angular substitution at $C_6$ in enone ester **1** leads to such highly congested structures **7** that [3,3]-sigmatropic rearrangement to **8** becomes thermodynamically favorable. It appeared that the equilibrium between **7** and **8** in these experiments is shifted in favor of **8** when the steric bulk of the 6-substituent is increasing. The rationale for this is the greater steric interaction between the group R and the 2-carboethoxy group in **7**, and as a consequence, raising their ground state energies. Force Field calculations using Allinger's MM2-program[10], seem to confirm this hypothesis. An increase in steric volume of the group R at $C_6$ in **7** enhances the total steric energy due to an increase of the Van der Waals repulsion between the group R and the adjacent ester function. In the rearranged structures **8a-f** such an interaction between the ester function and the 7-alkyl group affects the respective ground state energies to a lesser extent.

An effect of possible geometrical changes on this Cope rearrangement, situating the involved olefinic functions in a more favorable position, seems to be of minor importance[11] because the results of both MM2-calculations and X-ray diffraction studies[8,12] of the parent ester **1** and methylated ester **7** demonstrate that the orientation of the $C_3$-$C_4$ and $C_8$-$C_9$ bond hardly changes with the increasing steric volume of the 6-substituent.

Although Cope rearrangements are familiar processes in *endo*-tricyclodecadienones[13], these [3,3]-sigmatropic rearrangements seldom occur at ambient temperatures because the rearranged product **10** contains a rather strained bridged ketone function and there is loss of conjugative stabilization by disruption of the α,β-enone system in **9** (Scheme 4). As a result the ground state energy of the rearranged product **10** is generally much higher than that of **9**.

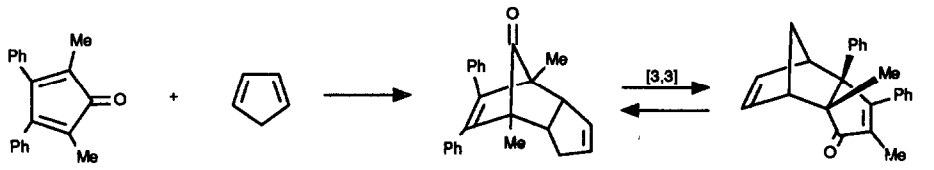
Hitherto, to our knowledge, only one case has been reported[14] in which a tricyclodecadienone and its rearranged bridged ketone are of comparable energy and, as a consequence, equilibrate in a Cope rearrangement. Reaction of 2,5-dimethyl-3,4-diphenylcyclopentadienone **11** with cyclopentadiene afforded *endo*-ketone **12** (Scheme 5). When **12** was heated at 105 °C, a rapid equilibrium with **13** was established, consisting of about 50 % of both **12** and **13**. Apparently, the energy effect of the strained carbonyl function in **12** and that of the steric hindrance of the 2-methyl and 6-phenyl group together with conjugative stabilization effects in both **12** and **13** are in balance. A similar explanation can be given for the equilibration between **7** and **8** (Scheme 3). In **7** there is

Scheme 4




9 10

Scheme 5



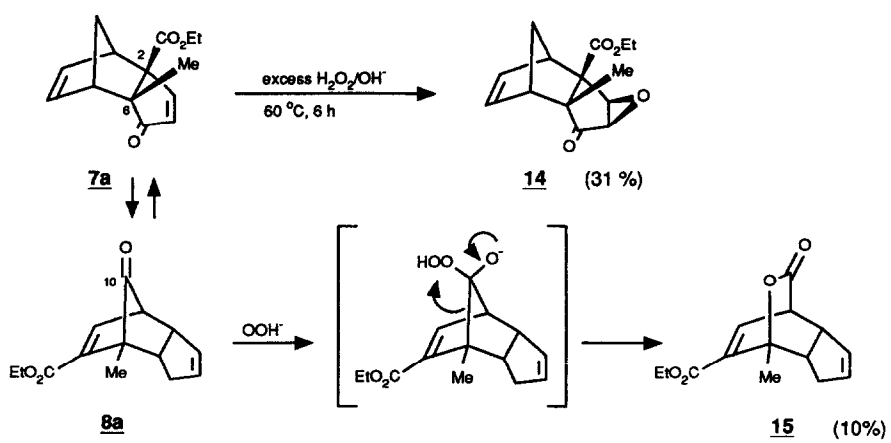

11 12 13

the steric effect of the 6-alkyl group and the 2-ester function, while 8 has a highly strained bridged carbonyl function. The loss of conjugative stabilization for the enone moiety in 7, however, is largely compensated by the α,β-unsaturated ester group in 8.

**Nucleophilic additions to ethyl 6-methyl-tricyclodecadienone 2-carboxylate**

In the preceding section it was shown that the introduction of an angular substituent at $C_6$ in ester 1 has a considerable effect on its skeletal stability, thereby facilitating the occurrence of a Cope rearrangement. The presence of a 6-alkyl group in enones 7 also has a notable influence on their aptitude to undergo conjugate nucleophilic addition. Alkaline epoxidation of 1 with $H_2O_2$ proceeds smoothly at room temperature to afford the corresponding epoxide in high yield[1b,c]; methyl enone 7a, however, could not be epoxidized at all under these conditions. Only after prolonged heating at 60 °C, epoxide 14 was obtained in a modest yield of 30 % and in a

Scheme 6



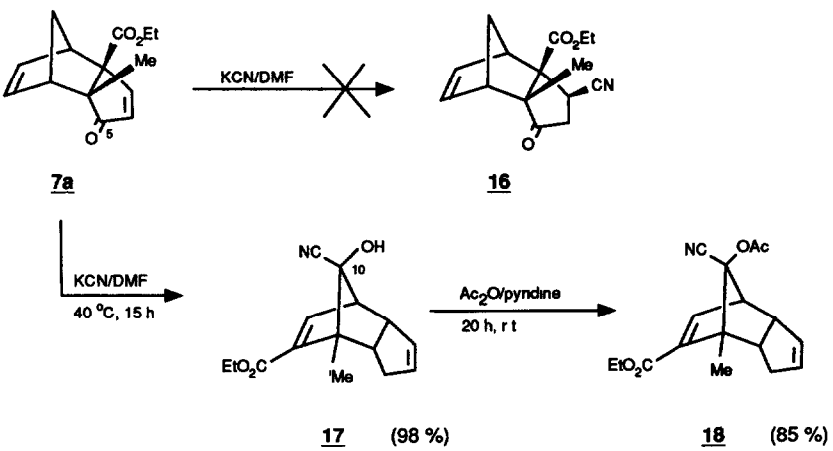

7a 14 (31 %)

8a 15 (10%)

poorly reproducible reaction (Scheme 6). In this epoxidation reaction lactone **15** was isolated as a by-product in 10 % yield. Its formation probably takes place by nucleophilic attack of the hydrogen peroxide anion ($OOH^-$) at the strained $C_{10}$-carbonyl group of **8a**, followed by a regio-selective Baeyer-Villiger type oxygen insertion (Scheme 6). This lactone **15** was independently prepared from **8a** in high yield by treatment with hydrogen peroxide in acetic acid[15].

The reluctance of the enone moiety in **7a** to undergo nucleophilic additions is also demonstrated by the results of hydrocyanation experiments. Using reaction conditions similar to those applied by Rouessac *et al*[1a] for the successful hydrocyanation of the parent tricyclodecadienone, no β-keto nitrile **16** was obtained at all. Instead, a cyanohydrol was isolated in excellent yield, to which structure **17** was tentatively assigned (Scheme 7). In order to establish the mechanistic pathway underlying its stereoselective formation, the configuration at $C_{10}$ in **17** was needed. Therefore, the corresponding acetate was prepared by reacting **17** with $Ac_2O$ in pyridine. This crystalline compound was subjected to an X-ray analysis[16] revealing structure **18**.

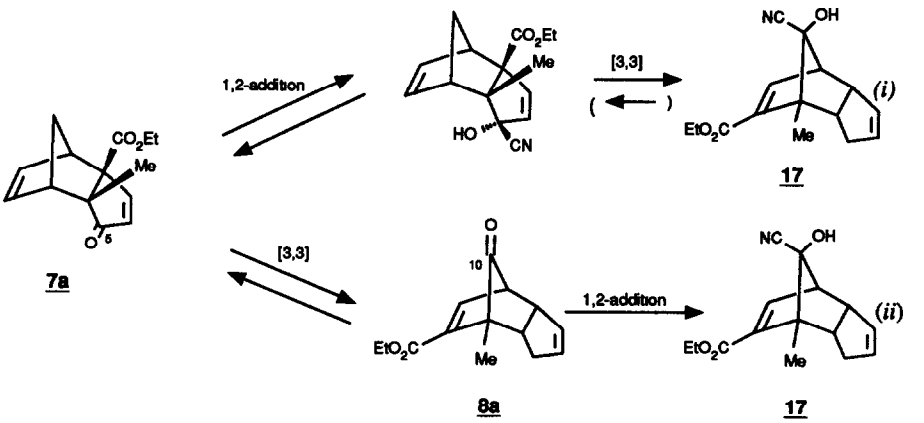
Scheme 7




The formation of **17** from **7a** can be rationalized in two ways: *(i)* initial stereoselective 1,2-addition of cyanide ion to the 5-carbonyl function in **7a**, followed by a fast [3,3]-sigmatropic rearrangement (Cope rearrangement) or *(ii)* initial [3,3]-sigmatropic rearrangement of **7a** into **8a** followed by a stereoselective cyanide addition to the strained $C_{10}$-keto function (Scheme 8). In an independent experiment it was shown that **8a** is converted completely into **17** within 1 h at r.t.. On the other hand, at that temperature **7a** is only partially transformed into **17** after 60 h of reaction (no **8a** was observed). These results suggest that **7a** itself either does not react with cyanide at all or only very slowly, while **8a**, as soon as it is formed from **7a**, is immediately converted into **17** in a stereoselective fashion, thereby shifting the Cope equilibrium between **7a** and **8a** toward the latter compound. Nevertheless, some formation of **17** from **7a** via route *(i)* cannot be excluded.

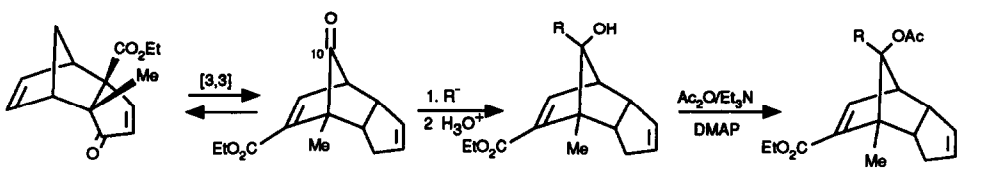
The diminished nucleophilic reactivity of the enone function of **7a** is also encountered when a 1,4-addition with methylmagnesium iodide in the presence of Cu(I)Cl[1] was attempted. Instead of undergoing conjugate addition with the Grignard reagent, formation of **19** was observed in 31% yield (with a recovery of 51% of **7a**) after a reaction of 4h at 0 °C and 15 h at r.t.(Scheme 9). The structure of **19** was unequivocally established by an X-ray diffraction analysis[17] of the corresponding acetate **20**. The formation of **19** can again be explained by either an initial 1,2-addition of the organometallic to **7a**, followed by a Cope rearrangement[18] or by a direct addi-

Scheme 8




tion to the $C_{10}$-carbonyl function of the rearranged product **8a**. Addition of MeLi to **8a** at -78 °C leads in 10 min to bridge alcohol **19** in 83% yield, which means that the reaction of **8a** with the Grignard reagent is very fast. Although a reaction via **7a** (1,2-addition at $C_5$ and subsequent rearrangement) is possible it seems that the formation of **19** from **7a** predominantly takes place via an initial Cope rearrangement to **8a** followed by a stereoselective addition to the $C_{10}$-carbonyl function.

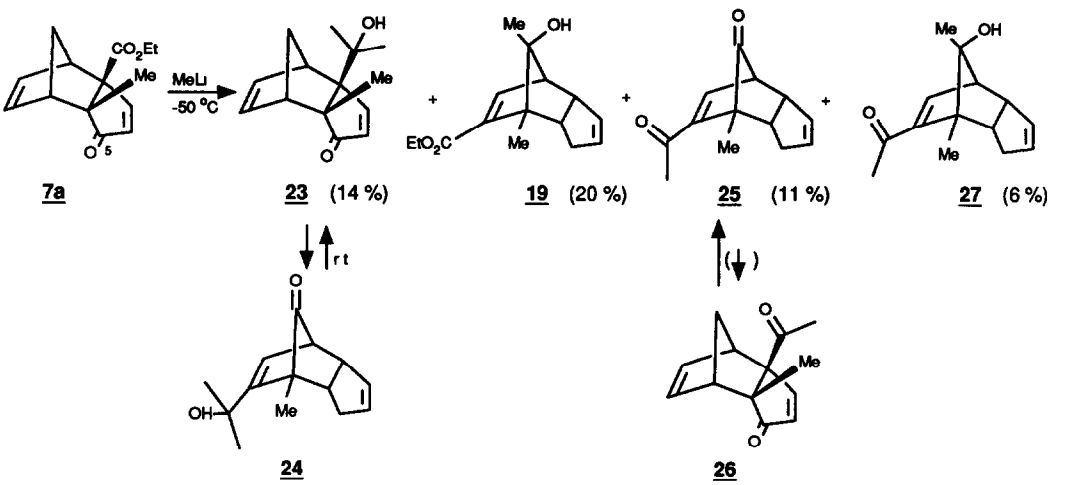
Scheme 9




Reaction of **7a** with an excess of MeLi at -50 °C for 10 min produces a series of compounds (Scheme 10). Carbinol **23** results from a double reaction of MeLi with the ester function of **7a**. It is of interest to note that **23** on standing at r.t., or when heated in refluxing chloroform for 15 min., equilibrates with its Cope isomer **24** (equilibrium ratio 1:1). Bridge alcohol **19** must be formed by a stereospecific addition of MeLi to the $C_5$-ketone function in **7a**, followed by a Cope rearrangement, because at the temperature of the reaction, rearrrangement of **7a** into **8a** does not take place. Product **25** is clearly the result of an initial formation of **26**, followed by a Cope rearrangement. Attempts to equilibrate compound **25** with **26** by heating in refluxing chloroform were not succesful. Hence, replacing the ester function in **7a** by an acetyl group as in **26** has a considerable influence on the position of the Cope equilibrium. Finally, ketone alcohol **27** arises from an attack of MeLi to both the ester and 5-ketone group in **7a**, followed by a Cope rearrangement.

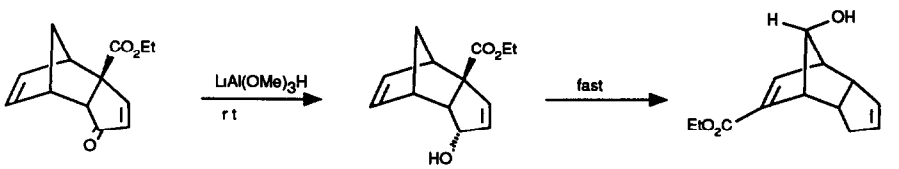
It is of interest to note that the formation of bridge alcohol **19** according to the reaction presented in Scheme 10 follows a pathway different from that given in Scheme 9. In this connection it is relevant to mention that the

Scheme 10




reduction of the parent ester **1** with lithium aluminum trimethoxy hydride at r.t. results in a 79% yield of bridge carbinol **29** (Scheme 11). This reaction must proceed via the primary reaction product **28**, which then undergoes

Scheme 11




a rapid sigmatropic rearrangement to **29**. Parent compound **1** does not show any Cope rearrangement at all at r.t.. At least a temperature of ca. 150 °C is required to enforce such a rerrangement[19]. Recently, the reduction of **1** and also of **7a**, with $NaBH_4$ in methanolic $CeCl_3.6H_2O$ has been described[18] to yield the products **29** and **21**, respectively, also via the the intermediacy of carbinol **28**. Reduction of **8a** with $NaBH_4$ in MeOH at r.t. rapidly gives alcohol **21** as the sole product, which on subsequent acetylation gives **22**.

The results described above show that the angularly substituted ester **7a** displays a very low tendency to undergo conjugate enone addition. This reluctance of **7a** to undergo 1,4-addition is probably due to severe steric interaction between the incoming nucleophile, the 2-ester group and the 6-alkyl substituent, because if this nucleophilic addition process would take place, all three groups would be positioned on the same *convex* face of the tricyclodecadienone system. At temperatures at which Cope rearrangement of **7a** into **8a** takes place, nucleophilic reactions preferably proceed via the rearranged species **8a** by a stereoselective addition to the strained $C_{10}$-ketone function. When a Cope rearrangement of **7a** is not feasible, product formation takes place via an initial addition to the $C_5$-ketone function of **7a** and a subsequent sigmatropic rearrangement.

The stereochemistry of the addition reactions to the $C_{10}$-ketone function of **8a** is the same in all cases studied. The stereochemical outcome of the cyanide addition to **8a** is in agreement with the result reported by Gassman

and Talley[20], who describe a highly stereoselective *syn*-addition of cyanide to bicyclo[2.2.1]hept-2-en-7-one using KCN in acetic acid. Other literature data available on nucleophilic additions to 7-norbornenone show that the general pattern involves predominantly *syn*-addition[21]. This observed predominance for *syn*-attack is not yet fully understood, although it is now been accepted that both steric and electronic features are involved. So far, it has been assumed that attack from the *anti*-side of the double bond in 7-norbornenone is slightly more hindered than from the olefinic side of the molecule, owing to steric repulsion between the *exo*-protons at $C_5$-$C_6$ and the incoming nucleophile. However, this has been opposed by recent calculations which suggest that *syn*-attack is actually less favorable than *anti*-addition, leading to the hypothesis that some chelating interaction of the double bond with the nucleophile may be responsible for the observed stereoselectivity rather than steric features. In our opinion an adequate explanation for the observed stereoselectivity in both 7-norbornenone and tricyclic ketone **8a** may be provided by Cieplak's transition state model for nucleophilic additions to cyclic ketones[23,24]. In this model, addition of the nucleophile preferably takes place from that face of the carbonyl function that allows the $\sigma^*$-orbital of the incipient C-Nu bond to effectively interact with the electron donating orbitals neighboring the carbonyl function. Both for 7-norbornenone and tricyclic ketone **8a** conceivable stabilizing orbital combinations are the $\pi,\sigma^*$ and $\sigma,\sigma^*$ interactions. Although the $\pi,\sigma^*$ interaction certainly contributes to the overall stereoelectronic features of these molecules[22,24], it is apparently outweighed by the $\sigma,\sigma^*$ hyperconjugative interaction, as the observed stereochemistry is just the opposite as would have been predicted on basis of such $\pi,\sigma^*$-stabilization. Considering $\sigma,\sigma^*$ hyperconjugative interaction of the incipient $\sigma^*$ orbital of the C-Nu bond with the electron-richest anti-periplanar $\alpha,\beta$-$\sigma$ bonds in both 7-norbornenone and ketone **8a**, *syn*-addition is here clearly preferred. In 7-norbornenone the $C_4$-$C_5$ and $C_1$-$C_6$ bonds are better electron donors than the $C_1$-$C_2$ and $C_3$-$C_4$ bonds because of the electron withdrawing effect of the $C_2$-$C_3$ $\pi$-electron system, whereas for the same reason, in **8a**, the $C_1$-$C_2$ and $C_6$-$C_7$ bonds are more electron-rich than the $C_1$-$C_9$ and $C_7$-$C_8$ bonds. As a consequence, a more effective hyperconjugative delocalization is attained when *syn*-addition takes place. Evidently, the presence of an electron withdrawing ester function connected to the $\pi$-system, as is the case in **8a** will further increase the *syn*-selectivity in these bridged ketones. This is nicely reflected in the observed high *syn*-selectivity of addition of nitrile, methyllithium and borohydride to tricyclic ketone **8a**.

In conclusion, angular alkylation of tricyclodecadienone ester **1** proceeds readily to give the corresponding 6-alkyl substituted esters **7**, which, due to a considerable increase of their steric energy, show a reduced skeletal stability and rapidly equilibrate with their Cope rearrangement products **8**, even at ambient temperature. These alkyl substituted esters **7** also show a considerably diminished propensity to undergo conjugate additions to the enone moiety. In all cases studied, such an addition could not be accomplished. Instead, a rapid stereospecific nucleophilic addition to the strained bridge ketone function in the Cope rearrangement product **8** is observed, provided that rearrangement to **8** is feasible at the temperature of the reaction. When the rearrangement to **8** is hampered, rearrangement of the initial carbonyl addition product of **7** may occur.

## Experimental

*General remarks*

$^1$H-NMR spectra were recorded on a Bruker WH-90 spectrometer in $CDCl_3$ solution with $SiMe_4$ as internal reference. $^{13}$C-NMR spectra were recorded on a Bruker WP-60 spectrometer or Bruker WM200 (in $CDCl_3$). Mass spectra were obtained using a double-focusing VG 7070E mass spectrometer. Melting points were determined using a Reichert melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 298 infrared spectrophotometer. UV spectra were measured on a Perkin-Elmer 555 spectrophotometer. Elemental analyses were carried out in the Microanalytical Department of the University of Nijmegen. Capillary GC

(CapGC) analyses were performed using a HP 5790 A, containing a cross-linked methyl silicone column; L=25 m, ID= 0.31 mm, film 0.17 µm applying a temperature program: 100 °C to 250 °C; 15 °C/min, unless indicated otherwise. Flash chromatographic purifications (pressure (p): 1.5-2 atm) were carried out using either silica gel (Kieselgel 60 H (Merck)) or $Al_2O_3$ (150 neutral typ T (Merck)).

*Ethyl* 5-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 2-*carboxylate* **1**

Ester **1** was prepared *via* a modified procedure[5], originally described by Herz and co-workers, in a yield of approximately 50 % from exo-4,5-*epoxy*-endo-*tricyclo*[6.2.1.$0^{2,7}$]*undec*-9-*en*-3,6-*dione*. $^{13}$C-NMR: δ 13.7 ($OCH_2CH_3$), 45.4, 49.3, 50.9, 53.8 ($C_1$, $C_6$, $C_7$, $C_{10}$), 61.4, 64.1 ($C_2$, $OCH_2$), 133.6, 134.8, 136.2 ($C_4$, $C_8$, $C_9$), 161.7 ($C_3$), 173.0 ($C_2CO$), 208.7 ($C_5$); UV (MeOH): $\lambda_{max}$ 229 nm.

*Ethyl* 6-*deuterio*-5-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 2-*carboxylate* 6-*D*-**1**

Monodeuterated **1** was prepared as described for **7a**, starting from diisopropylamine (0.11 g, 1.089 mmol), *n*-BuLi (0.7 ml, 1.6 M soln in *n*-hexane, 1.12 mmol), **1** (0.20 g, 0.917 mmol) and $D_2O$ (0.36 g, 18 mmol). After attaining r.t., $Et_2O$ (25 ml) was added, the yellow lithium salts were removed by filtration and the filtrate was concentrated *in vacuo*. Flash chromatography (silica gel, EtOAc /*n*-hexane = 1/10, Rf = 0.3) afforded 6-*D*-**1** (0.14 g, 70 %) as an oil. $^1$H-NMR: δ 1.30 (t, J=7.0 Hz, 3H, $OCH_2CH_3$), 1.73 A of AB (d, J=9.0 Hz, 1H, $H_{10}$), 1.96 B of AB (d, J=9.0 Hz, 1H, $H_{10}$), 3.16-3.33 (m, 2H, $H_1$, $H_7$ ), 4.22 (q, J=7.0 Hz, 2H, $OCH_2CH_3$), 5.83-6.02 (m, 3H, $H_4$, $H_8$, $H_9$), 7.29 (d, J=5.8 Hz, 1H, $H_3$); IR ($CCl_4$): ν 1725 (C=O, ester), 1705 (C=O, unsat.), 1585 (C=C, unsat.) $cm^{-1}$; EI/MS: m/e 219 ($M^+$), 66 ($C_5H_6$); Found 219.102. $C_{13}H_{13}DO_3$ requires 219.101.

*Ethyl* 6-*methyl*-5-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 2-*carboxylate* **7a**

To a stirred soln of diisopropylamine (0.17 g, 1.68 mmol) in dry THF (10 ml) was gradually added a 1.6 M soln of *n*-BuLi in *n*-hexane (1.0 ml, 1.6 mmol) at 0 °C. After 20 min the mixture was cooled to -78 °C and a soln of **1** (0.33 g, 1.514 mmol) in THF was gradually added using a syringe. After 15 min the mixture was quenched with MeI (0.30 g, 2.11 mmol) in 10 ml of THF. The yellow soln was then allowed to attain r.t. and stirred for 30 min. The resulting brown soln was treated with excess of $NH_4Cl$ (10 % aq) at 0 °C, extracted with diethyl ether (3x50 ml), washed with water (3x20 ml), dried over $MgSO_4$ and evaporated *in vacuo*, to give crude **7a**. Flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/10, Rf = 0.45) afforded **7a** (0.33 g, 88 %) as an oil which slowly solidified. Recrystallization, by cooling a saturated soln of **7a** in EtOH from 20 °C to -17 °C, yielded analytically pure **7a**; m.p. 74-76 °C; $^1$H-NMR: δ 1.26 (t, J=7.0 Hz, 3H, $OCH_2CH_3$), 1.30 (s, 3H, $C_6$-Me), 1.69-1.96 (m, 1H, $H_{10}$), 2.33-2.53 (m, 1H, $H_{10}$), 2.68-2.89 (m, 1H, $H_7$), 3.09-3.32 (m, 1H, $H_1$), 4.22 (q, J=7.0 Hz, 2H, $OCH_2CH_3$), 5.79-6.17 (m, 3H, $H_4$, $H_8$, $H_9$), 7.29 (d, J=5.8 Hz, 1H, $H_3$); IR (KBr): ν 3060, 2980, 1730 (C=O, ester), 1710 (C=O, enone), 1230, 1220 $cm^{-1}$; EI/MS: m/e 232 ($M^+$), 204 (M-CO), 159 (M-COOEt), 131 (M-CO-COOEt), 66 ($C_5H_6$); CI/MS: m/e 233 ($M^+$+1); UV (MeOH): $\lambda_{max}$ 227 nm; Found C, 72.27; H, 6.99. $C_{14}H_{16}O_3$ requires C, 72.39; H, 6.94.

*Ethyl* 6-*ethyl*-5-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 2-*carboxylate* **7b**

The procedure as described for **7a** was followed. Starting from diisopropylamine (0.56 g, 5.54 mmol), *n*-BuLi (4.0 ml, 6.4 mmol), **1** (1.0 g, 4.59 mmol) and EtI (1.45 g, 9.29 mmol) gave **7b** (1.291 g, crude yield). After flash chromatography ($Al_2O_3$, EtOAc / *n*-hexane = 1/10) pure **7b** (868 mg, 77%) was obtained as an oil. $^1$H-NMR: δ 0.81 (t, J=7.6 Hz, 3H, $C_6$-$CH_2CH_3$), 1.31 (t, J=7.0 Hz, 3H, $OCH_2CH_3$), 1.72 A of AB (J=9.0 Hz, 1H, $H_{10}$), 1.93 (q, J=7.6 Hz, 2H, $C_6$-$CH_2$), 2.65 B of AB (d, J=9.0 Hz, 1H, $H_{10}$), 2.86 (br s, 1H, $H_7$), 3.07 (br s, 1H, $H_1$), 4.23 (q, J=7 Hz, 2H, $OCH_2CH_3$), 5.75-5.89 (m, 1H, $H_8$ or $H_9$), 5.95-6.16 (m, 1H, $H_8$ or $H_9$), 5.96 (d, J=5.9 Hz, 1H, $H_4$), 7.44 (d, J=5.9 Hz, 1H, $H_3$); IR ($CCl_4$): ν 1725, 1710 $cm^{-1}$; EI/MS: m/e 246 ($M^+$), 228 ($M^+$-CO), 145 (M-CO-$CO_2$Et), 66 ($C_5H_6$); Found 246.1251. $C_{15}H_{18}O_3$ requires 246.1256.

*Ethyl* 6-*allyl*-5-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 2-*carboxylate* **7c**

The procedure as described for **7a** was followed. Starting from diisopropylamine (0.59 g, 5.84 mmol), *n*-BuLi (4.0 ml, 6.4 mmol), **1** (1.0 g, 4.59 mmol) and allyl iodide (1.15 g, 6.85 mmol) produced crude **7c** (1.151 g). Flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/20) yielded **7c** as an oil (810 mg, 68%) which was contaminated with some **8c**. $^1$H-NMR: δ 1.28 (t, J=7.0 Hz, 3H, $OCH_2CH_3$), 1.73 A of AB (d, J=9.0 Hz, 1H, $H_{10}$), 2.58-2.77 (m, 3H, $H_{10}$, $C_6$-$CH_2$), 2.89 (br s, 1H, $H_7$), 3.06 (br s, 1H, $H_1$), 4.16 (q,q, J=7.0 Hz, 2H, diastereotopic $OCH_2CH_3$), 4.88-5.12 (m, 2H, $C_6$-$CH_2CHCH_2$), 5.17-6.13 (m, 4H, $H_4$, $H_8$, $H_9$, $C_6$-$CH_2CHCH_2$), 7.40 (d, J=5.8 Hz, 1H, $H_3$); IR ($CCl_4$): ν 2980, 1725, 1710, 1590 (C=C, unsat.), 1230, 910 $cm^{-1}$; EI/MS: m/e 258 ($M^+$), 230 (M-CO), 157 (M-CO-COOEt), 115, 66 ($C_5H_6$); Found 258.1251. $C_{16}H_{18}O_3$ requires 258.1256.

*Ethyl* 6-n-*heptyl*-5-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 2-*carboxylate* **7d**

Diisopropylamine (0.69 g, 6.83 mmol), *n*-BuLi (4.5 ml, 7.2 mmol), **1** (1.20 g, 5.505 mmol) and *n*-heptyl iodide (1.4 g, 6.19 mmol) were reacted according to the procedure described for **7a**, to yield **7d** (810 mg, 47 %) after flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/20, Rf = 0.5) as an oil. $^1$H-NMR: δ 0.71-1.44 (m, 16H, $OCH_2CH_3$, $C_6$-$CH_2C_6H_{13}$), 1.69-1.98 (m, 3H, $H_{10}$, $C_6$-$CH_2$), 2.67 B of AB (d, J=9.4 Hz, 1H, $H_{10}$), 2.82 (br s, 1H, $H_7$), 3.02 (br s, 1H, $H_1$), 4.21 (q, J=7.0 Hz, 2H, $OCH_2CH_3$), 5.87 (dd, J=5.6 Hz, J=2.8 Hz, 1H, $H_8$ or $H_9$),

5.95 (d, J=6.0 Hz, 1H, $H_4$), 6.07 (dd, J=5.6 Hz, J=2.8 Hz, 1H, $H_8$ or $H_9$), 7.43 (d, J=6.0 Hz, 1H, $H_3$); IR ($CCl_4$): ν 2920, 1727, 1707, 1590, 1228 $cm^{-1}$; EI/MS: m/e 316 ($M^+$), 288 (M-CO), 243 (M-COOEt), 189 (M-CO-$C_7H_{15}$), 117, 66 ($C_5H_6$); Found 316.2030. $C_{20}H_{28}O_3$ requires 316.2038.

*Ethyl* 6-*benzyl*-5-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 2-*carboxylate* **7e**

The procedure as described for **7a** was followed. Starting from diisopropylamine (0.22 g, 2.18 mmol), *n*-BuLi (1.33 ml, 2.13 mmol), **1** (0.20 g, 0.917 mmol) and benzyl bromide (0.32 g, 1.87 mmol) furnished 0.27 g of a crude yellow oil which consisted of benzyl bromide, 1,2-diphenylbromoethane, **7e** and **8e**. Flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/10) gave 1,2-diphenylbromoethane (0.35 mg, Rf = 0.5) and a 1:3 molar mixture of **7e** and its Cope rearranged isomer **8e** (Rf = 0.25, 80 mg, 28 %). These compounds could not be isolated separately due to rapid equilibration. Therefore only the $^1$H-NMR- and MS-data of **7e** are relevant. **7e**: $^1$H-NMR: δ 1.07 (t, J=7.0 Hz, 3H, $OCH_2CH_3$), 5.83-6.15 (m, 3H, $H_4$, $H_8$, $H_9$), 7.04-7.84 (m, 6H, Ph, $H_3$). The other $^1$H-absorptions were not distinguishable from those of **8e**. EI/MS: m/e 308 ($M^+$), 280 (M-CO), 217 (M-benzyl), 117, 91 (benzyl), 66 ($C_5H_6$); Found 308.1417. $C_{20}H_{20}O_3$ requires 308.1412. *1,2-Diphenylbromoethane*: $^1$H-NMR: δ 3.52 (d, J=7.6 Hz, 2H, $H_2$), 5.13 (t, J= 7.6 Hz, 1H, $H_1$), 7.10 (s, 5H, Ph), 7.25 (s, 5H, Ph); IR ($CCl_4$): ν 3030, 1490, 1450 $cm^{-1}$; EI/MS: m/e 262, 260 ($M^+$), 181 ($M^+$-Br; $C_{14}H_{13}^+$); Found 181.1017. $C_{14}H_{13}$ ($M^+$-Br) requires 181.1018.

*Ethyl* 6-*iodomethyl*-5-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 2-*carboxylate* **7f**

Diisopropylamine (0.60 g, 5.94 mmol), *n*-BuLi (4.0 ml, 6.4 mmol), **1** (1.00 g, 4.587 mmol) and diiodomethane (1.60 g, 5.97 mmol) were reacted according to the procedure described for **7a** to yield 1.6 g of a mixture which contained **1**, **7f**, **8f** and polymeric material. Careful flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/10, Rf = 0.2) gave pure **7f** (125 mg, 8 %) as an oil. $^1$H-NMR: δ 1.36 (t, J=7 Hz, 3H, $OCH_2CH_3$), 1.64 A of AB (d, J=10.0 Hz, 1H, $H_{10}$), 1.84 B of AB (d, J=10.0 Hz, 1H, $H_{10}$), 2.82 (br s, 1H, $H_7$), 3.18 (br s, 1H, $H_1$), 3.60 A of AB (d, J=9.3 Hz, 1H, $C_6$-$CH_2$), 3.73 B of AB (d, J=9.3 Hz, 1H, $C_6$-$CH_2$), 4.31 (q, J=7 Hz, 2H, $OCH_2$), 5.85-6.29 (m, 3H, $H_4$, $H_8$, $H_9$), 7.56 (d, J= 6.0 Hz, 1H, $H_3$); IR ($CCl_4$): ν 1725 (C=O, ester), 1710 (C=O, enone), 1225 $cm^{-1}$; CI/MS: m/e 359 ($M^+$+1), 293 (M+1-$C_5H_6$), 231 (M-I), 203 (M-I-CO), 67 ($C_5H_6$+1); Found 359.0149. $C_{14}H_{16}IO_3$ requires 359.0144.

*Ethyl* 7-*methyl*-10-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **8a**

A stirred soln of **7a** (423 mg, 1.823 mmol) in $CHCl_3$ was refluxed for 15 min. After cooling to r.t. a mixture of **7a** and **8a** was obtained (molar ratio = 65:35, the average result of three $^1$H-NMR measurements). Flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/20, Rf = 0.25) yielded pure **8a** (128 mg, 30 %) as an oil. $^1$H-NMR: δ 1.30 (t, J=7.0 Hz, 3H, $OCH_2CH_3$), 1.48 (s, 3H, $C_7$-$CH_3$), 1.80-2.67 (m, 3H, $H_5$, $H_6$), 3.22 (t, J=4 Hz, 1H, $H_1$), 3.43-3.70 (m, 1H, $H_2$), 4.20 (q, J=7.0 Hz, 2H, $OCH_2CH_3$), 5.24-5.47 (m, 1H, $H_3$ or $H_4$), 5.67-5.83 (m, 1H, $H_3$ or $H_4$), 7.11 (d, J=4 Hz, 1H, $H_9$); IR ($CCl_4$): ν 3060, 2980, 1780 (C=O, bridged), 1710 (C=O, ester), 1270, 1230, 1185, 1085, 1045 $cm^{-1}$; EI/MS: m/e 232 ($M^+$), 204 (M-CO), 189 (M-CO-$CH_3$), 159 (M-COOEt), 131 (M-CO-COOEt), 66 ($C_5H_6$); Found 232.1090. $C_{14}H_{16}O_3$ requires 232.1099.

*Ethyl* 7-*ethyl*-10-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **8b**

Ester **7b** (513 mg, 2.085 mmol) was reacted as described for **8a** to produce a mixture of **7b** and **8b** (molar ratio = 35:65 ($^1$H-NMR)). Flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/20, Rf = 0.25-0.30) yielded pure **8b** (274 mg, 53 %) as an oil. $^1$H-NMR: δ 0.97 (t, J=7.4 Hz, 3H, $C_7$-$CH_2CH_3$), 1.31 (t, J=7.2 Hz, 3H, $OCH_2CH_3$), 1.62-2.73 (m, 5H, $H_5$, $H_6$, $C_7$-$CH_2$), 3.21 (t, J≅4 Hz, 1H, $H_1$), 3.44-3.71 (m, 1H, $H_2$), 4.22 (q, J=7.2 Hz, 2H, $OCH_2CH_3$), 5.31-5.46 (m, 1H, $H_3$ or $H_4$), 5.71-5.84 (m, 1H, $H_3$ or $H_4$), 7.11 (d, J=3.8 Hz, 1H, $H_9$); IR ($CCl_4$): ν 3050, 2980, 1780 (C=O, bridged), 1710 (C=O, ester), 1575 (C=C, unsat.), 1270, 1180, 1080 $cm^{-1}$; EI/MS: m/e 246 ($M^+$), 218 (M-CO), 189, 145 (M-CO-COOEt), 117 (M-CO-COOEt-Et), 66 ($C_5H_6$); Found 246.1252. $C_{15}H_{18}O_3$ requires 246.1256.

*Ethyl* 7-*allyl*-10-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **8c**

Ester **7c** (276 mg, 1.070 mmol) was reacted as described for **8a** to produce a mixture of **7c** and **8c** (molar ratio = 40:60 ($^1$H-NMR)). Flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/20, Rf = 0.25) yielded pure **8c** (153 mg, 55 %) as an oil. $^1$H-NMR: δ 1.31 (t, J=7.0 Hz, 3H, $OCH_2CH_3$), 2.16-2.43 (m, 2H, $H_5$), 2.45-3.11 (m, 3H, $H_6$, $C_7$-$CH_2$), 3.24 (t, J≅4 Hz, 1H, $H_1$), 3.47-3.71 (m, 1H, $H_2$), 4.22 (q,q, J=7.0 Hz, 2H, diastereotopic $OCH_2CH_3$), 4.88-5.28 (m, 2H, $C_7$-$CH_2CHCH_2$), 5.33-5.48 (m, 1H, $H_3$ or $H_4$), 5.66-6.18 (m, 2H, $H_3$ or $H_4$, $C_7$-$CH_2CHCH_2$), 7.10 (d, J=3.9 Hz, 1H, $H_9$); IR ($CCl_4$): ν 3050, 2980, 1784 (C=O, bridged), 1716 (C=O, ester), 1640 (C=C), 1575 (C=C, unsat.), 1270, 1095 $cm^{-1}$; EI/MS: m/e 258 ($M^+$), 230 (M-CO), 157, 115, 66 ($C_5H_6$); Found 258.1261. $C_{16}H_{18}O_3$ requires 258.1256.

*Ethyl* 7-n-*heptyl*-10-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **8d**

Ester **7d** (312 mg, 0.99 mmol) was reacted as described for **8a** to produce a mixture of **7d** and **8d** (molar ratio = 35:65 ($^1$H-NMR)). Flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/20, Rf = 0.6) yielded pure **8d** (152 mg, 49 %) as an oil. $^1$H-NMR: δ 0.71-1.98 (m, 18 H, $OCH_2CH_3$, $C_7$-*n*-$C_7H_{15}$), 1.98-2.73 (m, 3H, $H_5$, $H_6$), 3.20 (t,

J≅4 Hz, 1H, $H_1$), 3.40-3.69 (m, 1H, $H_2$), 4.22 (q, J=7.0 Hz, 2H, $OCH_2CH_3$), 5.31-5.45 (m, 1H, $H_3$ or $H_4$), 5.69-5.83 (m, 1H, $H_3$ or $H_4$), 7.11 (d, J=3.8 Hz, 1H, $H_9$); IR ($CCl_4$): ν 2920, 1780 (C=O, bridged), 1710 (C=O, ester), 1265, 1090 $cm^{-1}$; EI/MS: m/e 316 ($M^+$), 288 (M-CO), 189 (M-CO-$C_7H_{15}$), 117, 66 ($C_5H_6$); Found 316.2031. $C_{20}H_{28}O_3$ requires 316.2038.

*Ethyl* 7-*benzyl*-10-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **8e**

Ester **8e** was obtained as an equilibrium mixture with **7e** (molar ratio = 25:75 ($^1$H-NMR)). Although complete separation was impossible, **8e** was characterized by its spectral data: $^1$H-NMR: δ 1.16 (t, J=7 Hz, 3H, $OCH_2CH_3$), 2.27-3.67 (m, 7H, $H_1$, $H_2$, $H_5$, $H_6$, $C_7$-$CH_2$), 3.91-4.28 (m, 2H, diastereotopic $OCH_2CH_3$), 5.28-5.44 (m, 1H, $H_3$ or $H_4$), 5.69-5.87 (m, 1H, $H_3$ or $H_4$), 7.02 (d, J=3.9 Hz, 1H, $H_9$), 7.04-7.84 (m, 5H, Ph); IR ($CCl_4$): ν 1785 (C=O, bridged), 1712 (C=O, ester), 1280 $cm^{-1}$; EI/MS: m/e 308 ($M^+$), 280 (M-CO), 217 (M-benzyl), 117, 91 (benzyl), 66 ($C_5H_6$); Found 308.1417. $C_{20}H_{20}O_3$ requires 308.1412.

*Ethyl* 7-*iodomethyl*-10-*oxo*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **8f**

A mixture of **7f** and **8f** was obtained upon iodomethylation of **1** (*Cf.* the synthesis of **7f**). Although complete separation was impossible, **8f** was characterized by its spectral data: $^1$H-NMR: δ 1.36 (t, J=7 Hz, 3H, $OCH_2CH_3$), 2.00-2.82 (m, 3H, $H_5$, $H_6$), 3.22-3.38 (m, 1H, $H_1$), 3.49 A of AB (d, J=10 Hz, 1H, $C_7$-$CH_2$), 3.55-3.78 (m, 1H, $H_2$), 3.97 B of AB (d, J=10 Hz, 1H, $C_7$-$CH_2$), 4.21 (q, J=7 Hz, 2H, $OCH_2$), 5.34-5.47 (m, 1H, $H_3$ or $H_4$), 5.74-5.89 (m, 1H, $H_3$ or $H_4$), 7.13 (d, J=3.7 Hz, 1H, $H_9$); IR ($CCl_4$): ν 1790 (C=O, bridged), 1710 (C=O, ester), 1270, 1095 $cm^{-1}$; CI/MS: m/e 359 ($M^+$+1), 293 (M+1-$C_5H_6$), 231 (M-I), 203 (M-I-CO), 67 ($C_5H_6$+1); Found 359.0149. $C_{14}H_{16}IO_3$ requires 359.0144.

*Nucleophilic epoxidation of* **7a**

To a vigorously stirred soln of **7a** (2.0 g, 8.62 mmol) in MeOH (20 ml)/$CH_2Cl_2$ (20 ml) was added $H_2O_2$ (10 ml, 40 % aq) and NaOH (14 ml, 0.2 N). The temperature was raised to 65 °C and both $H_2O_2$ (10 ml, 40 % aq.) and NaOH (14 ml, 0.2 N) were added repeatedly after 30, 90 and 150 min reaction time, respectively. After 6 h the reaction mixture was allowed to attain r.t.. The organic layer was separated and the water layer was extracted with $CHCl_3$ (3 x 50 ml). The combined organic layers were washed with water (3 x 10 ml), dried and evaporated *in vacuo*. *Ca.* 50 % of **7a** had reacted ($^1$H-NMR). Two successive flash chromatographic purification steps (silica gel, EtOAc /*n*-hexane = 1/5, Rf = 0.25) yielded *ethyl* exo-3,4-*epoxy*-6-*methyl*-5-*oxo*-endo-*tricyclo*-[5.2.1.$0^{2,6}$]*dec*-8-*ene* 2-*carboxylate* **14** (0.66 g, 31 %) as a viscous oil which slowly solidified (m.p. 49-56 °C). $^1$H-NMR: δ 1.18-1.47 (m, 5H, $H_{10}$, $OCH_2CH_3$), 1.58 (s, 3H, $C_6$-Me), 2.70-2.87 (m, 1H, $H_7$), 3.08-3.22 (m, 1H, $H_1$), 3.33 (d, J=2.4 Hz, 1H, $H_3$), 3.79 (d, J=2.4 Hz, 1H, $H_4$), 4.27 (q, J=7.0 Hz, 2H, $OCH_2CH_3$), 6.01-6.27 (m, 2H, $H_8$, $H_9$); IR ($CCl_4$): ν 2980, 1744 (C=O), 1235, 910 $cm^{-1}$; EI/MS: m/e 248 ($M^+$), 233 (M-$CH_3$), 183 (M-$C_5H_6^+$), 66 ($C_5H_6$); Found 248.1054. $C_{14}H_{16}O_4$ requires 248.1049; Found C, 67.28; H, 6.48. $C_{14}H_{16}O_4$ requires C, 67.73; H, 6.50.

During the aforementioned separation also a small amount of **15** (260 mg, 75 % purity by CapGC) was isolated. **15** was purified by flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/5, Rf = 0.5) which finally gave 0.051 g (2 %) pure white solid. Ester **15** was also prepared[15] by dissolving **8a** (175 mg, 0.754 mmol) in HOAc (2.2 ml), adding $H_2O_2$ (0.2 g, 35 % aq, 2.06 mmol) and stirring for 20 h at 4 °C. After extraction with $Et_2O$ (3 x 50 ml), washing with $NaHCO_3$ (10 % aq), drying and concentrating *in vacuo*, pure *ethyl* 7-*methyl*-11-*oxo*-endo-10-*oxatricyclo*[5.2.2.$0^{2,6}$]*undeca*-3,8-*diene* 8-*carboxylate* **15** (115 mg, 61 %) was isolated as a white solid. M.p. 94-97 °C (after recrystallization from *n*-hexane). $^1$H-NMR: δ 1.29 (t, J=7.2 Hz, 3H, $OCH_2CH_3$), 1.84 (s, 3H, $C_7$-Me), 2.00-2.20 (m, 1H, $H_5$), 2.29-2.73 (m, 1H, $H_5$), 2.91 (ddd, J≅9.6 Hz, J≅8.4 Hz, J=4.0 Hz, 1H, $H_6$), 3.31-3.57 (m, 1H, $H_2$), 3.67 (dd, J=6.4 Hz, J=3.0 Hz, 1H, $H_1$), 4.20 (q, J=7.2 Hz, 2H, $OCH_2$), 5.34-5.49 (m, 1H, $H_3$ or $H_4$), 5.53-5.70 (m, 1H, $H_3$ or $H_4$), 7.14 (d, J=6.4 Hz, 1H, $H_9$); IR (KBr): ν 1750, 1725, 1710 (C=O), 1615 (C=C), 1265, 1075 $cm^{-1}$; EI/MS: m/e 249 ($M^+$+1), 204 (M-$CO_2$), 183 (M-$C_5H_6^+$), 131 (M-$CO_2$-COOEt), 66 ($C_5H_6$); Found C, 67.25; H, 6.57. $C_{14}H_{16}O_4$ requires C, 67.73; H, 6.50.

*Ethyl* syn-10-*cyano*-anti-10-*hydroxy*-7-*methyl*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **17**

Ester **7a** (1.00 g, 4.31 mmol), KCN (560 mg, 8.60 mmol) and $NH_4Cl$ (390 mg, 7.29 mmol) were added to a mixture of DMF (20 ml)/$H_2O$ (10 ml) and stirred for 15 h at 40 °C. Excess AcOH (5 ml) and $Et_2O$ (50 ml) were added, and the resulting mixture was thoroughly washed with water (8 x 5 ml) to remove DMF, dried and concentrated to afford **17** (1.09 g, 98 %). Crystallization from *n*-hexane gave an analytically pure sample; m.p. 92-93 °C. **17** was also synthesized starting from **8a** (33 mg, 0.142 mmol). After stirring for 1 h at r.t., pure **17** (37 mg, 99 %) was obtained. $^1$H-NMR: δ 1.32 (t, J=7 Hz, 3H, $OCH_2CH_3$), 1.58 (s, 3H, $C_7$-Me), 1.71-2.53 (m, 2H, $H_5$), 2.60-2.98 (m, 1H, $H_6$), 3.20 (t, J=3.8 Hz, 1H, $H_1$), 3.38-3.83 (m, 2H, $H_2$, OH), 4.21 (q, J=7 Hz, 2H, $OCH_2$), 5.36-5.65 (m, 2H, $H_3$, $H_4$), 6.88 (d, J=3.8 Hz, 1H, $H_9$); IR (KBr): ν 3400 (OH), 1680 (C=O, unsat.), 1585 (C=C, unsat.), 1060 $cm^{-1}$; CI/MS: m/e 260 ($M^+$+1), 242 (M+1-$H_2O$), 233 (M-CN), 187 (M+1-COOEt), 66 ($C_5H_6$); UV (MeOH): $\lambda_{max}$ 224 nm, (6500); MS: Found 260.1280. $C_{15}H_{18}O_3N$ requires 260.1287; Found C, 69.12; H, 6.54; N, 5.37. $C_{15}H_{17}O_3N$ requires C, 69.48; H, 6.61; N, 5.40.

*Ethyl* anti-10-*acetoxy*-syn-10-*cyano*-7-*methyl*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **18**

Alcohol **17** (1.09 g, 4.209 mmol) was added to a mixture of $Ac_2O$ (3.0 g, 29.4 mmol) in pyridine (10 ml) and stirred for 40 h at r.t.. Excess of $NaHCO_3$ aq was added. After extraction with $Et_2O$ (3 x 30 ml), the combined organic layers were washed with water (5 x 10 ml), dried and concentrated to yield pure **18** (1.10 g, 85 %). M.p. 123-125 °C (after recrystallization from *n*-hexane /EtOAc = 10/1). $^1$H-NMR: δ 1.34 (t, J=7 Hz, 3H, $OCH_2CH_3$), 1.65 (s, 3H, $C_7$-Me), 1.70-2.58 (m, 5H, $H_5$, OAc), 2.67-2.96 (m, 1H, $H_6$), 3.20-3.49 (m, 1H, $H_2$), 3.80 (t, J=3.8 Hz, 1H, $H_1$), 4.21 (q, J=7 Hz, 2H, $OCH_2$), 5.33-5.47 (m, 1H, $H_3$ or $H_4$), 5.51-5.67 (m, 1H, $H_3$ or $H_4$), 6.84 (d, J=4.0 Hz, 1H, $H_9$); $^{13}$C-NMR: δ 12.3 (q, $OCH_2CH_3$), 13.9 (q, $C_7$-$CH_3$), 20.4 (q, $OCOCH_3$), 32.5 (t, $C_5$), 43.9 (d, $C_6$), 50.5 (d), 51.7 (d, $C_1$, $C_2$), 60.1 (s, $C_7$), 60.3 (t, $OCH_2$), 87.8 (s, $C_{10}$), 116.5 (s, CN), 127.6 (d), 134.7 (d, $C_3$, $C_4$), 137.3 (s, $C_8$), 143.6 (d, $C_9$), 163.4 (s, $C_8$-CO), 168.5 (q, J=3.6 Hz, $OCOCH_3$); IR (KBr): ν 2245 (CN), 1755 (C=O, acetate), 1705 (C=O), 1590 (C=C, unsat.), 1370, 1220 cm$^{-1}$; CI/MS: m/e 302 ($M^+$+1), 256 (M+1-HOEt), 242 (M+1-HOAc), 67 ($C_5H_6$+1); UV (MeOH): $\lambda_{max}$ 219 nm, (6000); Found C, 67.93; H, 6.46; N, 4.63. $C_{17}H_{19}O_4N$ requires C, 67.76; H, 6.36; N, 4.65.

*Cu(I)-catalyzed Grignard addition of MeMgI to* **7a**.

Mg (50 mg, 2.06 mmol) was added to dry $Et_2O$ (10 ml) in a $N_2$ atmosphere at 0 °C. Then MeI (300 mg, 2.11 mmol) in $Et_2O$ was added using a syringe. The resulting mixture was stirred for 30 min and oven-dried Cu(I)Cl (12 mg, 0.12 mmol) was added. After addition of **7a** (363 mg, 1.565 mmol) in $Et_2O$ (10 ml), stirring was continued for 4 h. The reaction mixture was allowed to attain r.t. and stirred for another 15 h. An excess of $NH_4Cl$ aq was added. After extraction with $Et_2O$ (3 x 30 ml), the combined organic layers were washed with water (5 x 10 ml), dried and concentrated, to yield a 3:2 molar mixture of **19** and **7a** (360 mg, $^1$H-NMR). Flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/5) finally gave pure **19** (122 mg, 31 %) and **7a** (185 mg, 51 %).

*Reaction of* **8a** *with MeLi*

To a soln of **8a** (100 mg, 0.431 mmol) in dry $Et_2O$ at -78 °C was added MeLi (0.41 ml, 1.6 M soln in *n*-hexane, 0.66 mmol) using a syringe. After stirring for 10 min at -78 °C, an excess of HCl (3 % aq) was added and the mixture was allowed to attain r.t., extracted with $Et_2O$ (3 x 25 ml), washed with $H_2O$ (3 x 10 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/10, Rf = 0.10-0.15) to yield **19** as a pure oil (89 mg, 83 %, 99 % purity by CapGC).

*Ethyl* anti-10-*acetoxy*-7-syn-10-*dimethyl*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **20**

Alcohol **19** (100 mg, 0.403 mmol) was dissolved in an excess of $Et_3N$ (1.0 g, 9.90 mmol)/$CH_2Cl_2$ (5 ml). After addition of an excess of $Ac_2O$ (0.5 g, 4.90 mmol) and 4-(dimethylamino)-pyridine (DMAP) (96 mg, 0.76 mmol), the resulting mixture was stirred for 5 h at r.t and worked up as described for the preparation of **18**, to afford crude **20** (150 mg). Flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/10, Rf = 0.5) gave pure **20** (90 mg, 77 %). M.p. 87-88 °C (after recrystallization from *n*-pentane). $^1$H-NMR: δ 1.28 (t, J=7 Hz, 3H, $OCH_2CH_3$), 1.28 (s, 3H, $C_7$-Me), 1.37 (s, 3H, $C_{10}$-Me), 1.69-2.47 (m, 5H, $H_5$, OAc), 2.81 (ddd, J=9.4 Hz, J=8 Hz, J=4 Hz, 1H, $H_6$), 3.16-3.42 (m, 1H, $H_2$), 3.57 (t, J≅4 Hz, 1H, $H_1$), 4.18 (q, J=7 Hz, 2H, $OCH_2$), 5.31-5.60 (m, 2H, $H_3$, $H_4$), 6.81 (d, J=3.8 Hz, 1H, $H_9$); IR (KBr): ν 2900, 1737 (C=O, acetate), 1706 (C=O), 1595 (C=C, unsat.) cm$^{-1}$; EI/MS: m/e 290 ($M^+$), 245 (M-$OEt^+$), 230 (M-HOAc), 224 (M-$C_5H_6$), 182, 108; Found 290.1515. $C_{17}H_{22}O_4$ requires 290.1518. Found C, 70.13; H, 7.66. $C_{17}H_{22}O_4$ requires C, 70.32; H, 7.64.

*Ethyl* anti-10-*hydroxy*-7-*methyl*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **21**

Ester **8a** (200 mg, 0.862 mmol) was dissolved in EtOH (10 ml) and $NaBH_4$ (101 mg, 2.67 mmol) was added. The resulting mixture was stirred for 30 min at r.t. The soln was successively acidified with HCl (1 % aq), washed with $NaHCO_3$ aq, extracted twice with $Et_2O$ and concentrated, to produce crude **21** (189 mg). After flash chromatography (silica gel, EtOAc /*n*-hexane = 1/1, Rf = 0.4) pure **21** (130 mg, 64 %) was isolated as an oil. $^1$H-NMR: δ 1.27 (t, J=7 Hz, 3H, $OCH_2CH_3$), 1.41 (s, 3H, $C_7$-Me), 1.71-2.93 (m, 5H, $H_1$, $H_5$, $H_6$, $C_{10}$-OH), 3.40-3.71 (m, 2H, $H_2$, $H_{10}$), 4.16 (q, J=7 Hz, 2H, $OCH_2$), 5.48 (m, 2H, $H_3$, $H_4$), 6.79 (d, J=3.8 Hz, 1H, $H_9$); IR ($CCl_4$): ν 3620 (OH), 1710 (C=O), 1585 (C=C, unsat.), 1050 cm$^{-1}$; EI/MS: m/e 234 ($M^+$); Found 234.1245. $C_{14}H_{18}O_3$ requires 234.1256.

*Ethyl* anti-10-*acetoxy*-7-*methyl*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **22**

Alcohol **21** (123 mg, 0.53 mmol) was acylated as described for the preparation of **18**, using $Ac_2O$ (0.51 g, 5.0 mmol), pyridine (2 ml) and $CH_2Cl_2$ (10 ml) to give crude **22** (145 mg). Flash chromatography (silica gel, EtOAc /*n*-hexane = 1/3, Rf = 0.4) afforded pure **22** (126 mg, 87 %) as an oil. $^1$H-NMR: δ 1.20 (t, J=7 Hz, 3H, $OCH_2CH_3$), 1.33 (s, 3H, $C_7$-Me), 1.71-2.40 (m, 5H, $H_5$, OAc), 2.65 (ddd, J=9 Hz, J=8 Hz, J=4 Hz, 1H, $H_6$), 2.96 (td, J=3.8 Hz, J=1.6 Hz, 1H, $H_1$), 3.29-3.58 (m, 1H, $H_2$), 4.09 (q, J=7 Hz, 2H, $OCH_2$), 4.30 (d, J=1.6 Hz, 1H, $H_{10}$), 5.34-5.65 (m, 2H, $H_3$, $H_4$), 6.77 (d, J=3.8 Hz, 1H, $H_9$); IR ($CCl_4$): ν 1740 (C=O, acetate), 1710 (C=O), 1590 (C=C, unsat.), 1235, 1040 cm$^{-1}$; EI/MS: m/e 276 ($M^+$), 216 (M-HOAc), 210 (M-$C_5H_6$), 168; Found 276.1363. $C_{16}H_{20}O_4$ requires 276.1362.

*Reaction of* **7a** *with MeLi*

To a soln of **7a** (480 mg, 2.07 mmol) in dry THF at -78 °C was added MeLi (1.7 ml, 1.6 M soln in $Et_2O$, 2.72

mmol) using a syringe. The mixture was allowed to attain -50 °C (10 min) and subsequently treated with an excess of HCl (3 % aq), extracted with $Et_2O$ (3 x 25 ml), washed with water (3 x 20 ml), dried and concentrated *in vacuo*. The resulting crude oil was further purified by flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/10) to yield successively: **23**, **19**, **27** and a mixture of **25** and **7a**. 6-{2-*(2-Hydroxypropyl)*}-2-*methyl*-endo-*tricyclo*-[5.2.1.$0^{2,6}$]*deca*-4,8-*dien*-3-*one* **23** (65 mg, 14 %, Rf = 0.10-0.15, $Al_2O_3$, EtOAc /*n*-hexane=1/10). $^1$H-NMR: δ 1.42 (s, 6H, $C_2$-Me, $C_6$-C(OH)($CH_3$)$CH_3$), 1.56 (s, 3H, $C_6$-C(OH)($CH_3$)$CH_3$), 1.64 A of AB (br d, J≅8.8 Hz, 1H, $H_{10}$), 2.31 B of AB (br d, J≅8.8 Hz, 1H, $H_{10}$), 2.67 (br s, 1H, $H_1$), 3.00 (br s, 2H, $H_7$, OH), 5.96 (br s, 2H, $H_8$, $H_9$), 5.98 (d, J=6.2 Hz, 1H, $H_4$), 7.40 (d, J=6.2 Hz, 1H, $H_5$); IR ($CCl_4$): ν 3620 (OH), 3540-3300 (OH), 2970, 1700 (C=O), 1590 (C=C, unsat.) $cm^{-1}$; EI/MS: m/e 218 ($M^+$), 203 (M-Me), 66 ($C_5H_6$); Found 218.1284. $C_{14}H_{18}O_2$ requires 218.1307. *Ethyl* 7-syn-10-*dimethyl*-anti-10-*hydroxy*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **19** (130 mg, 20 % yield; 80 % purity by CapGC). $^1$H-NMR: δ 1.13 (s, 3H, $C_{10}$-Me), 1.24 (t, J=7 Hz, 3H, $OCH_2CH_3$), 1.27 (s, 3H, $C_7$-Me), 1.77 (s, 1H, OH), 1.80-2.43 (m, 2H, $H_5$), 2.60-2.93 (m, 2H, $H_1$, $H_6$), 3.50-3.77 (m, 1H, $H_2$), 4.18 (q, J=7 Hz, 2H, $OCH_2$), 5.38-5.57 (m, 2H, $H_3$, $H_4$), 6.82 (d, J=3.8 Hz, 1H, $H_9$); IR ($CCl_4$): ν 3620, 3500 (OH), 3040, 1710, (C=O), 1585 (C=C, unsat.), 1260, 1230, 1060 $cm^{-1}$; CI/MS: m/e 249 ($M^+$+1), 231 (M+1-$H_2O$), 217, 203 (M+1-HOEt), 183 (M+1-$C_5H_6$), 67 ($C_5H_6$+1); EI/MS: m/e 248 ($M^+$), 230 (M-$H_2O$), 202 (M-HOEt), 136 (M-HOEt-$C_5H_6$); Found 249.1487. $C_{15}H_{21}O_3$ requires 249.1491. 8-*Acetyl*-7-syn-10-*dimethyl*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*dien*-anti-10-*ol* **27** (26 mg, 6 %). M.p. 78-81 °C (after recrystallization from *n*-hexane), $^1$H-NMR: δ 1.11 (s, 3H, $C_{10}$-Me), 1.31 (s, 3H, $C_7$-Me), 1.53-2.42 (m, 3H, $H_5$, $C_{10}$-OH), 2.20 (s, 3H, $C_8$-$COCH_3$), 2.60-2.91 ( m, 2H, $H_1$, $H_6$), 3.53-3.78 (m, 1H, $H_2$), 5.34-5.54 (m, 2H, $H_3$, $H_4$), 6.76 (d, J=3.9 Hz, 1H, $H_9$); IR ($CCl_4$): ν 3620 (OH), 1670 (C=O, unsat.), 1575 (C=C, unsat.) $cm^{-1}$; EI/MS: m/e 218 ($M^+$), 175 (M-$CH_3CO$), 152 (M-$C_5H_6$), 43 ($CH_3CO$); Found 218.1301. $C_{14}H_{18}O_2$ requires 218.1307. The mixture of **25** and **7a** (165 mg, ratio 3:1, $^1$H-NMR) was separated by repeated (2x) flash chromatography ($Al_2O_3$, toluene/$CH_2Cl_2$ = 2/1, Rf = 0.45), to yield 8-*acetyl*-7-*methyl*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*dien*-10-*one* **25** (45 mg, 11 %) as a pure white solid. M.p. 57-62 °C (after recrystallization from *n*-pentane). $^1$H-NMR: δ 1.47 (s, 3H, $C_7$-Me), 2.27 (s, 3H, $C_8$-$COCH_3$), 1.78-2.56 (m, 3H, $H_5$, $H_6$), 3.28 (t, J=4.0 Hz, 1H, $H_1$), 3.47-3.78 (m, 1H, $H_2$), 5.34-5.45 (m, 1H, $H_3$ or $H_4$), 5.69-5.83 (m, 1H, $H_3$ or $H_4$), 7.03 (d, J=4.0 Hz, 1H, $H_9$); IR (KBr): ν 2920, 1780 (bridged C=O), 1660 (C=O, unsat.), 1560 (C=C, unsat.), 1270 $cm^{-1}$; EI/MS: m/e 202 ($M^+$), 174 (M-CO), 159 (M-$CH_3CO$), 131 (M-CO-$CH_3CO^+$), 43; Found 202.0990. $C_{13}H_{14}O_2$ requires 202.0944.

8-*(2-(2-Hydroxypropyl))*-7-*methyl*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*dien*-10-*one* **24**

Carbinol **23** (42 mg, 0.19 mmol) was refluxed in $CHCl_3$ for 15 min to afford an equilibrium mixture of **23** and **24** (ratio 1:1 ($^1$H-NMR)). This mixture was separated by flash chromatography ($Al_2O_3$, EtOAc /*n*-hexane = 1/3, Rf = 0.2-0.25) to give **24** (15 mg, 36 %) as a pure oil. $^1$H-NMR: δ 1.42 (s, 6H, $C_8$-$C(CH_3)_2$), 1.48 (s, 3H, $C_7$-$CH_3$), 2.29-2.60 (m, 3H, $H_5$, $H_6$), 3.01 (t, J=4.1 Hz, 1H, $H_1$), 3.33-3.62 (m, 2H, $H_2$, OH), 5.28-5.45 (m, 1H, $H_3$ or $H_4$), 5.67-5.85 (m, 1H, $H_3$ or $H_4$), 6.03 (d, J=4.1 Hz, 1H, $H_9$); IR ($CCl_4$): ν 3620 (OH), 2930, 1775 (bridged C=O) $cm^{-1}$; EI/MS: m/e 218 ($M^+$), 200 (M-$H_2O$), 190 (M-CO), 172 (M-CO-$H_2O$), 59 ($(CH_3)_2COH^+$); Found 218.1280. $C_{14}H_{18}O_2$ requires 218.1307.

*Ethyl* anti-10-*hydroxy*-endo-*tricyclo*[5.2.1.$0^{2,6}$]*deca*-3,8-*diene* 8-*carboxylate* **29**

Ester **1** (290 mg, 1.330 mmol) was added to a soln of freshly prepared $LiAlH(OMe)_3$ (330 mg, 2.58 mmol) in 10 ml of THF and stirred for 6 h. After 10 min, an excess of acetone was added to the mixture, followed by 3 % HCl aq. Extraction with $Et_2O$ (3x), several washings ($H_2O$), drying ($MgSO_4$) and concentration *in vacuo* produced **29** (230 mg, 79 %) was obtained as a crude oil. $^1$H-NMR: δ 1.29 (t, J=7.1 Hz, 3H, $OCH_2CH_3$), 1.49-1.56 (m, 3H, $H_5$, $H_6$), 2.80-3.31 (m, 3H), 3.38-3.72 (m, 1H), 3.87 (br s, 1H, $H_1$, $H_2$, $H_7$, $H_{10}$, $C_{10}$-OH), 4.18 (q, J=7 Hz, 2H, $OCH_2$), 5.50 (s, 2H, $H_3$, $H_4$), 6.77 (d, J=3.7 Hz, 1H, $H_9$); IR ($CCl_4$): ν 3620 (OH), 3480 (OH), 3040, 2980, 1710 (C=O), 1590 (C=C, unsat.), 1265, 1070 $cm^{-1}$; CI/MS: m/e 221 ($M^+$+1), 203 (M+1-$H_2O$), 155 (M+1-$C_5H_6$), 67, 66 ($C_5H_6$); Found 221.1177. $C_{13}H_{17}O_3$ requires 221.1178.

**Acknowledgement**

This research was supported by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organization for Scientific Research (NWO). Use of the services and facilities of the Dutch National NWO/SURF Expertise center CAOS/CAMM, under grant numbers SON 326-052 and STW NCH99-1751, is gratefully acknowledged.

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