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Stereocontrolled Syntheses of (−)-Cubebol and (−)-10-Epicubebol Involving Intramolecular Cyclopropanation of α-Lithiated Epoxides

David M. Hodgson,*[,†] Saifullah Salik,[†] and David J. Fox[‡]

[†]*Department of Chemistry, University of Oxford, Chemistry Research Laboratory, Mansfield Road, Oxford, OX1 3TA, United Kingdom and* [‡]*Department of Chemistry, University of Warwick, Gibbet Hill Road, Coventry, CV4 7AL, United Kingdom*

david.hodgson@chem.ox.ac.uk

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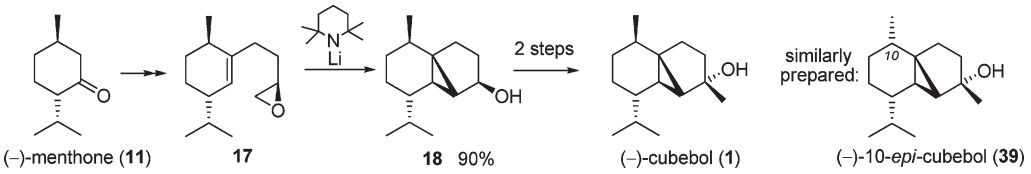

Formylation of (−)-menthone (**11**) with LDA and $HCO_2CH_2CF_3$ avoids loss of configurational integrity at the isopropyl group, giving hydroxymethylenementhone **12**. Lithium 2,2,6,6-tetramethylpiperidide-induced intramolecular cyclopropanation of derived unsaturated terminal epoxide **17** (and chlorohydrin **16**), efficiently generates a substituted tricyclo[4.4.0.0^{1,5}]decan-4-ol **18**, which is used in a concise synthesis of (−)-cubebol (**1**). In contrast, isopropyl group inversion during formylation of menthone with NaOMe and HCO_2Et led, by a similar strategy, to syntheses of 7-epicubebol (**33**) and (from (+)-menthone) of naturally occurring (−)-10-epicubebol (**39**), confirming the original structural assignment. Computational studies support the origin of the inversion as being rate-determining formylation of *cis*-enolate **27** from a mixture of rapidly interconverting enolates. In the synthesis of 7-epicubebol (**33**), allylic tertiary C−H insertion is observed as a significant competing reaction in the intramolecular cyclopropanation of unsaturated terminal epoxide **22**.

Introduction

Sesquiterpenes constitute a rich pool of structurally diverse synthetic challenges, and are often selected as targets to illustrate the advantages and examine the limits of newly developed methodology.[1] (−)-Cubebol (**1**) (Scheme 1) is principally found as one of the major constituents of cubeb oil, the latter being obtained from the berries of cubeb (*Piper cubeba*) grown in the Indonesian archipelago.[2] Cubeb has long found medicinal and culinary uses, and more recently Firmenich patented the use of cubebol as a sustained cooling and refreshing agent in the field of flavors.[3] The gross structure of cubebol was originally proposed by Sorm and co-workers in 1960,[4] with the structure and full stereochemistry subsequently being supported by the first total synthesis of (−)-cubebol by Yoshikoshi and co-workers in 1969.[5] The early syntheses of cubebol[5,6] and closely related, by formal dehydration, α- and *β*-cubebenes[5,7,8] proceed by way of norcubebanone (**2**)[9] as a common late stage intermediate. In all these syntheses, an unsaturated α-diazoketone (eg, **3**) was used to generate the embedded cyclopropane; however, cyclopropanation yields were moderate, and the diastereofacial selectivities were poor and in favor of undesired isomer. Recently, in 2006, independent syntheses of cubebol

(1) (a) Pirrung, M. C.; Morehead, A. T., Jr. In *The Total Synthesis of Natural Products*; Goldsmith. D., Ed.; Wiley: New York, 1997; Vol. 10, pp 1−160. (b) Pirrung, M. C.; Morehead, A. T., Jr.; Young, B. G. In *The Total Synthesis of Natural Products*; Goldsmith. D., Ed.; Wiley: New York, 2000; Vol. 11, pp 1−1455.

(2) Gunther, E. *The Essential Oils*; Van Nostrand: London, UK, 1952; Vol. 5, pp 148−157.

(3) Velazco, M. I.; Wuensche, L.; Deladoey, P. U.S. Patent, 6214788, **2001**; *Chem. Abstr.* **2000**, *133*, 265959.

(4) Vonasek, F.; Herout, V.; Sorm, F. *Collect. Czech. Chem. Commun.* **1960**, *25*, 919–926.

(5) (a) Tanaka, A.; Tanaka, R.; Uda, H.; Yoshikoshi, A. *Chem. Commun.* **1969**, 6365–6370. (b) Tanaka, A.; Tanaka, R.; Uda, H.; Yoshikoshi, A. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1721–1727.

(6) Torri, T.; Okamoto, T. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 771–774.

(7) (a) Piers, E.; Britton, R. W.; de Wall, W. *Tetrahedron Lett.* **1969**, 1251–1253. (b) Piers, E.; Britton, R. W.; de Wall, W. *Can. J. Chem.* **1971**, *49*, 12–19.

(8) Vig, O. P.; Bhatia, M. S.; Verma, A. K.; Matta, K. L. *J. Indian Chem. Soc.* **1970**, *47*, 277–281.

(9) Thiessen, W. E. *Acta Crystallogr.* **1977**, *B33*, 3838–3842.

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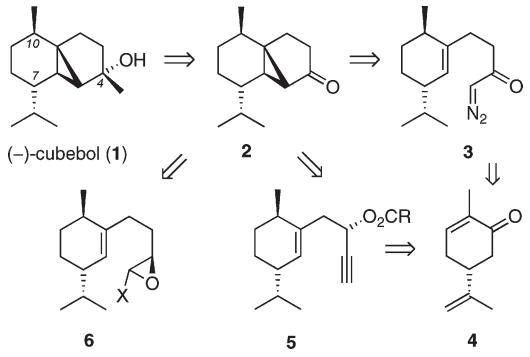
SCHEME 1. Synthetic Approaches to (−)-Cubebol (1)

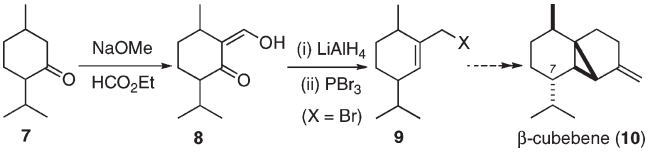


were reported by Fürstner[10] and by Fehr[11] in 14 and 13 steps, respectively, similarly starting from (*R*)-carvone (**4**). In these latter syntheses, the key cyclopropanation involved metal-catalyzed cycloisomerization of propargylic esters **5** (R = Me, *t*-Bu) and facial selectivity was controlled by the configuration at the propargylic stereocenter. In the present paper, we describe an alternative stereocontrolled and more concise synthesis of (−)-cubebol (**1**) using a lithiated epoxide **6** (X = Li) to effect cyclopropanation,[12−14] together with strategically related syntheses of 7- and 10-epicubebol.

Results and Discussion

All but one of the previous syntheses of (−)-cubebol (**1**) and α- and *β*-cubebenes noted above start from (*R*)-carvone (**4**), and all involve relatively lengthy sequences of transformations to generate a side chain suitable for intramolecular cyclopropanation. In seeking a more concise approach to our cyclopropanation substrate, epoxide **6** (Scheme 1, X = H), we were attracted to the synthesis of *β*-cubebene (**10**) claimed (but see below) by Vig and co-workers (Scheme 2),[8] in which allylic bromide **9** (X = Br, stereochemistry not indicated in Vig's work) was prepared in three steps by formylation of ketone **7**. We anticipated copper-catalyzed reaction of a corresponding Grignard reagent **9** (X = MgHal) with epichlorohydrin[15,16] should allow a comparatively short access to our desired epoxide substrate **6** (X = H).

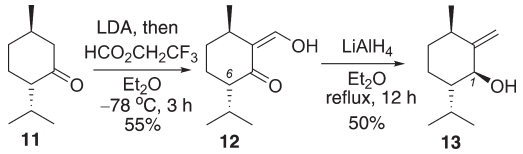
SCHEME 2. Vig's Approach to *β*-Cubebene (10)[8]



(10) Fürstner, A.; Hannen, P. *Chem.—Eur. J.* **2006**, *12*, 3006–3019.
(11) (a) Fehr, C.; Galindo, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 2901–2904. (b) Fehr, C.; Winter, B.; Magpantay, I. *Chem.—Eur. J.* **2009**, *15*, 9773–9784.
(12) (a) Hodgson, D. M.; Chung, Y. K.; Paris, J.-M. *J. Am. Chem. Soc.* **2004**, *126*, 8664–8665. (b) Hodgson, D. M.; Chung, Y. K.; Nuzzo, I.; Freixas, G.; Kulikiewic, K. K.; Cleator, E.; Paris, J.-M. *J. Am. Chem. Soc.* **2007**, *129*, 4456–4462.
(13) Preliminary communication: Hodgson, D. M.; Salik, S. *Synlett* **2009**, 1730–1732.
(14) For a recent example in natural product synthesis, see: Tashiro, T.; Mori, K. *Tetrahedron: Asymmetry* **2008**, *19*, 1215–1223.
(15) Hodgson, D. M.; Chung, Y. K.; Paris, J.-M. *Synthesis* **2005**, 2264–2266.
(16) Linstrumelle, G.; Lorne, R.; Dang, H. P. *Tetrahedron Lett.* **1978**, 4069–4072.

Although commercially available, (−)-menthone (**11**) (Scheme 3) was conveniently synthesized, without loss of configuration at the *i*-Pr bearing stereocenter, by oxidation (93%) of inexpensive (−)-menthol (99% ee) with $Ca(OCl)_2$.[17] Formylation of menthone, under now standard alkoxide/formate ester conditions, was originally reported by Claisen,[18] and was also initially examined in the first synthesis of (−)-cubebol by Yoshikoshi, but the approach was abandoned due to the formation of "an inseparable mixture of epimers".[5b] Subsequently, Tolman[19] noted the generation of a 7:93 epimeric mixture during formylation of menthone using NaOMe/HCO_2Et and, in a key study, Kashima and co-workers found an identical ratio to Tolman with the (currently undesired) cis-isomer predominating, when starting with menthone (or isomenthone) and using NaH/HCO_2Et.[20] However, Kashima also observed that the use of LDA (−78 °C) followed by HCO_2Et led to a 75:25 mixture in favor of the trans isomer. The latter result could be improved in our hands to give hydroxymethylenementhone (**12**) (55%, *S*:*R* = 98:2 at C-6, Scheme 3) by using $HCO_2CH_2CF_3$, which was introduced by Zayia for "kinetic formylation".[21]

SCHEME 3. Synthesis of Allylic Alcohol 13



Aware that the subsequent steps from hydroxymethylenementhone (**12**) to an allylic halide **9** (X = Hal) might not parallel Vig's study (Scheme 2), since the cis isomer was likely carried through in Vig's sequence (ultimately resulting in a synthesis of 7-epi-*β*-cubebene), we carried out the reduction of **12** using $LiAlH_4$ as described and were pleased to obtain a desired allylic alcohol **13** in 50% yield, after chromatography. The structure of allylic alcohol **13** was established by X-ray crystallographic analysis of the 3,5-dinitrobenzoate derivative **14** (Figure 1).[22] The reduction of hydroxymethylenementhone (**12**) likely[23] proceeds by exocyclic hydride delivery to deprotonated **12**, followed by *β*-elimination of an (aluminum-complexed) oxygen and finally 1,2-hydride delivery in an axial[24] manner to the resulting enone.

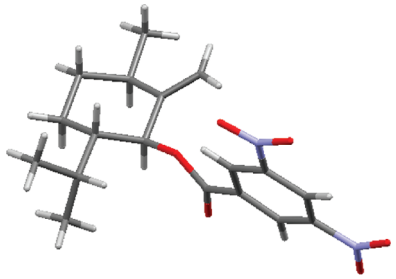
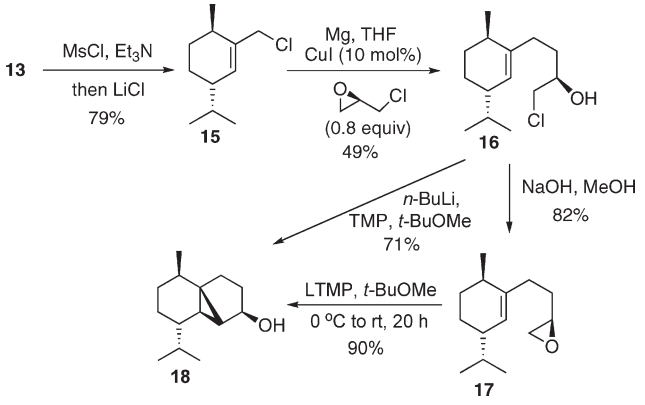


FIGURE 1. Crystal structure representation of 3,5-dinitrobenzoate derivative **14**.

(17) (a) Nwaukwa, S. O.; Keehn, P. M. *Tetrahedron Lett.* **1982**, *23*, 35–38. (b) Malkov, A. V.; Baxendale, I. R.; Bella, M.; Langer, V.; Fawcett, J.; Russel, D. R.; Mansfield, D. J.; Valko, M.; Kocovsky, P. *Organometallics* **2001**, *20*, 673–690.
(18) Bishop, A. W.; Claisen, L.; Sinclair, W. *Liebigs Ann. Chem.* **1894**, *281*, 314–398.

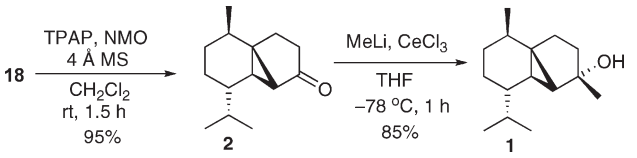
Conversion of the allylic alcohol **13** to the allylic chloride **15** (79%) was achieved in a one-flask operation with use of $MsCl/Et_3N$ followed by addition of LiCl (Scheme 4);[25] use of $SOCl_2$[26] or AcCl in EtOH[27] was less satisfactory. Allylic transposition was observed, despite the orthogonal disposition of the π-system and C−O bond evident in the all-equatorial 3,5-dinitrobenzonate derivative **14** (Figure 1) of allylic alcohol **13**. Reaction of the Grignard reagent from allylic chloride **15** with commercially available (*R*)-epichlorohydrin under copper catalysis[15,16] gave the unsaturated chlorohydrin **16** (49%), which was then ring-closed to epoxide **17** (82%, Scheme 4).

SCHEME 4. Synthesis and Intramolecular Cyclopropanation of Epoxide 17



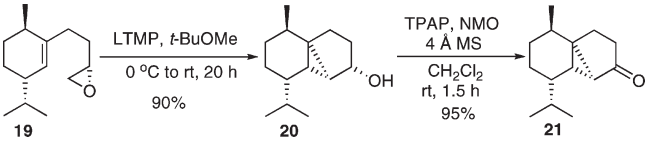
Lithium 2,2,6,6-tetramethylpiperidide (LTMP)-induced intramolecular cyclopropanation of epoxide **17** under our previously developed conditions[12] gave a single cyclopropyl alcohol **18** in excellent yield (90%, Scheme 4). Cyclopropyl alcohol **18** could also be obtained from epoxide **17** with use of *n*-BuLi (2 equiv) and a catalytic[12b] amount of 2,2,6,6-tetramethylpiperidine (TMP, 0.5 equiv), in 86% yield, and more directly[15] from chlorohydrin **16** in 71% yield, using *n*-BuLi (3.5 equiv) and TMP (2.5 equiv, Scheme 4). Oxidation of cyclopropyl alcohol **18** with 5 mol % TPAP-NMO (2 equiv) gave norcubebanone (**2**) (95%, Scheme 5); the spectral data for **2** were in full accord with the literature,[10,11] which confirms the facial selectivity in the cyclopropanation to be that shown in Scheme 4. The origin of the facial selectivity from the intermediate α-lithiated epoxide **6** (X = Li) likely parallels that previously discussed for simpler systems.[12] Reaction of $MeLi/CeCl_3$ with norcubebanone (**2**) according to Fürstner[10] and Fehr[11] gave (−)-cubebol (**1**) (85%).

SCHEME 5. Synthesis of (−)-Cubebol (1)



To establish that the configuration of the epoxide was the sole factor determining facial selectivity during cyclopropanation, the intramolecular cyclopropanation of epoxide **19** [available from allylic chloride **15** and (*S*)-epichlorohydrin][22] was carried out, which gave cyclopropyl alcohol **20** (90%, Scheme 6). Oxidation of cyclopropyl alcohol **20** gave known ketone **21**, which possessed data consistent with the literature.[10] The identical yields obtained for the intramolecular cyclopropanations of epoxides **17** and **19** also indicate that the presence of the isopropyl group on the same face of the alkene which undergoes cyclopropanation in epoxide **19** does not reduce the efficiency of this transformation.

SCHEME 6. Intramolecular Cyclopropanation of Epoxide 20



The unsaturated epoxides **22** and **23** (Figure 2) were next examined to further probe the effect on intramolecular cyclopropanation of tethered alkenes bearing additional stereocenters.

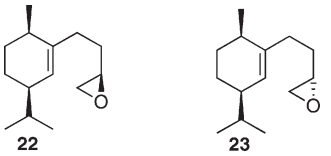


FIGURE 2. Further cyclopropanation substrates.

Following the discussion earlier on the formylation of (−)-menthone (**11**), it was anticipated that reaction under classical conditions (alkoxide/formate ester) would lead predominantly by *i*-Pr epimerization to the cis configuration required in the cyclohexene portion of epoxides **22** and **23**. In our hands, formylation gave mainly hydroxymethyleneisomenthone (**28**) (83%, 93:7 inseparable mixture with hydroxymethylenementhone (**12**), Scheme 7), in agreement with the prior observations of Tolman[19] and of Kashima.[20] The origin of the almost complete *i*-Pr epimerization during the formylation of menthone with alkoxide and a formate ester (also observed during Claisen−Schmidt condensations)[28] is not obvious; indeed, several applications of this chemistry erroneously assume the configuration is unchanged during this process.[17b,23c,29] Subjecting hydroxymethylenementhone

(19) (a) LeCloux, D. D.; Tolman, W. B. *J. Am. Chem. Soc.* **1993**, *115*, 1153–1154. (b) LeCloux, D. D.; Tokar, C. J.; Osawa, M.; Houser, R. P.; Keyes, M. C.; Tolman, W. B. *Organometallics* **1994**, *13*, 2855–2866.

(20) Kashima, C.; Miwa, Y.; Shibata, S.; Nakazono, H. *J. Heterocycl. Chem.* **2002**, *39*, 1235–1240.

(21) Zayia, G. H. *Org. Lett.* **1999**, *1*, 989–991.

(22) See the Supporting Information.

(23) (a) Dreiding, A. S.; Hartman, J. A. *J. Am. Chem. Soc.* **1953**, *75*, 939–943. (b) Searles, S., Jr.; Mortensen, H. E. *J. Org. Chem.* **1962**, *27*, 1979–1983. (c) See also: Murphy, R.; Prager, R. F. *Aust. J. Chem.* **1976**, *29*, 617–626.

(24) (a) Kasai, H. F.; Tsubuki, M.; Matsumoto, Y.; Shirao, M.; Takahashi, K.; Honda, T.; Ueda, H. *Chem. Pharm. Bull.* **2004**, *52*, 311–315. (b) Hedin-Dahlström, J.; Shoravi, S.; Wikman, S.; Nicholls, I. A. *Tetrahedron: Asymmetry* **2004**, *15*, 2431–2436.

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(27) Yadav, V. K.; Babu, G. K. *Tetrahedron* **2003**, *59*, 9111–9116.

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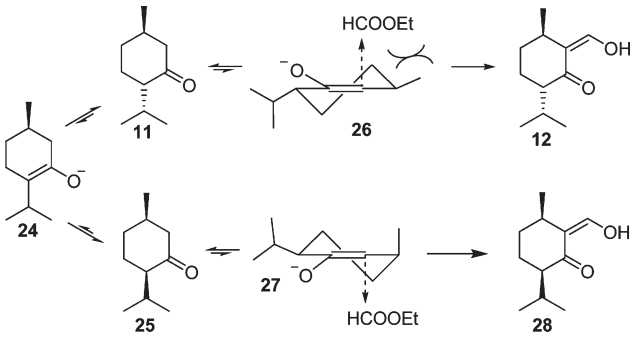
(29) (a) Shanmugam, P.; Srinivasan, R.; Rajagopalan, K. *Tetrahedron* **1997**, *53*, 6085–6096. (b) Srinivasan, R.; Rajagopalan, K. *Tetrahedron Lett.* **1998**, *39*, 4133–4136. (c) Oesterreich, K.; Spitzner, D. *Tetrahedron* **2002**, *58*, 4331–4334. (d) Oesterreich, K.; Klein, I.; Spitzner, D. *Synlett* **2002**, 1712–1714.

SCHEME 7. Overview Analysis of Alkoxide-Induced Formylation of Menthone (11)

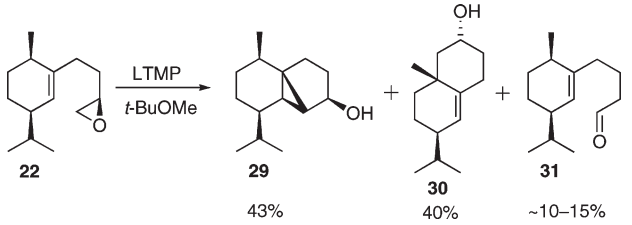


(**12**) to the classical formylation conditions for 3 days returned, as expected, mainly starting material (**12**:**28**, 80:20). This experiment shows that epimerization following formylation is not the origin of hydroxymethyleneisomenthone (**28**) from (−)-menthone. Under the classical formylation conditions, alkoxide-induced epimerization at the *i*-Pr group will occur to give isomenthone (**25**) (Scheme 7); however, it is well-known that menthone is preferred (though not strongly) over isomenthone at equilibrium (∼70:30).[30] This analysis indicates that the activation energy barrier for formylation of the isomenthone-derived enolate **27** will be less than that for menthone-derived enolate **26**, and this may be due to stereoelectronically preferred axial formylation occurring away from the Me group in enolate **27**.[31]

This explanation proposed above for the preferential formation of the *cis*-menthone derivative **28** was investigated by DFT calculations at the B3LYP/6-31G(d) level[32] with use of PC-GAMESS/Firefly.[33] Making the reasonable assumption[20] (see above) that *cis*- and *trans*-menthone (**11** and **25**) are in pre-equilibrium, then the relative rates of cis and trans product formation will be controlled by the relative energies of the cis and trans product forming transition states. Four anionic transition states were calculated with methyl formate. In all cases the two oxygens of the formate are oriented away from the enolate oxygen, mimicking the conformation expected for an "open" aldol-like transition structure stabilized by numerous hydrogen bonds to the solvent. In addition, all transition states involve axial attack onto the halfchair-like enolate with the isopropyl group occupying a pseudoequatorial position. This requirement forces the different enolate diastereoisomers to be attacked from different faces. For the isomenthone-derived *cis*-enolate **27**, attack occurs *anti* to the methyl substituent (Figure 3, *cis*-**TS1** and *cis*-**TS2**), but for the trans isomer attack must occur *syn* to the ring methyl group resulting in unfavorable steric interactions with the ester (*trans*-**TS2**). The methoxy group of the ester can attempt to swing out of the way to reduce this steric clash (*trans*-**TS1**), but this orientation is less favorable on stereoelectronic grounds:[34] the ground state conformational preference of methyl formate (20 kJ/mol) is reflected in the reaction transition state (6.2 kJ/mol for the *cis*-enolate). The more stable ester geometry seen in transition structure *trans*-**TS2** also has the most significant steric interactions between the enolate and ester methyl groups, raising its energy. Overall, assuming non-rate-determining enolate isomerization, it can be seen that the cis product forming reactions will be faster than the trans product forming reactions, consistent with the results observed experimentally. By using the four calculated transition state energies, the relative rate of formation of cis to trans product was determined to be 94:6 at 298 K, in good agreement with that observed experimentally.

Epoxides **22** and **23** were synthesized from hydroxymethyleneisomenthone (**28**) without incident by analogous application of the chemistry shown in Schemes 3 and 4, and epoxide **23** was found to undergo LTMP-induced intramolecular cyclopropanation in excellent yield (89%, 87% with catalytic (0.5 equiv) TMP and *n*-BuLi (2 equiv)).[22] However, in contrast to the smooth intramolecular cyclopropanation of epoxides **17**, **19**, and **23**, reaction of epoxide **22** (epimeric to **17** at the *i*-Pr group) reproducibly led to a mixture of the anticipated cyclopropyl alcohol **29** together with an approximately equal amount of bicyclic alcohol **30** and lesser quantities of aldehyde **31** (Scheme 8). In this case, intramolecular cyclopropanation is likely retarded by the presence of substituents at two allylic sites on the same face of the alkene which undergoes cyclopropanation, thus allowing intramolecular C−H insertion[35] at a tertiary allylic position to compete. The aldehyde very likely arises from hydrolysis of the corresponding 2,2,6,6-tetramethylpiperidinylenamine, the latter being generated from interception of the lithiated epoxide intermediate by LTMP.[36]

SCHEME 8. Reaction of Epoxide 22 with LTMP



As the cooling effect of almost odorless cubebol is sensitive to the precise stereochemistry of the tricyclic alcohol (for example, 4-epicubebol has a very bitter taste),[3,11] it was of interest to examine 7-epicubebol (**33**), prepared from

(30) (a) Rickborn, B. *J. Am. Chem. Soc.* **1962**, *84*, 2414–2417. (b) Takahashi, O.; Yamasaki, K.; Kohno, Y.; Kurihara, Y.; Ueda, K.; Umezawa, Y.; Suezawa, H.; Nishio, M. *Tetrahedron* **2008**, *64*, 2433–2440. Corrigendum: *Tetrahedron* **2009**, *65*, 5443.

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(36) (a) Hodgson, D. M.; Bray, C. D.; Kindon, N. D. *J. Am. Chem. Soc.* **2004**, *126*, 6870–6871. (b) Hodgson, D. M.; Bray, C. D.; Kindon, N. D.; Reynolds, N. J.; Coote, S. J.; Um, J. M.; Houk, K. N. *J. Org. Chem.* **2009**, *74*, 1019–1028.

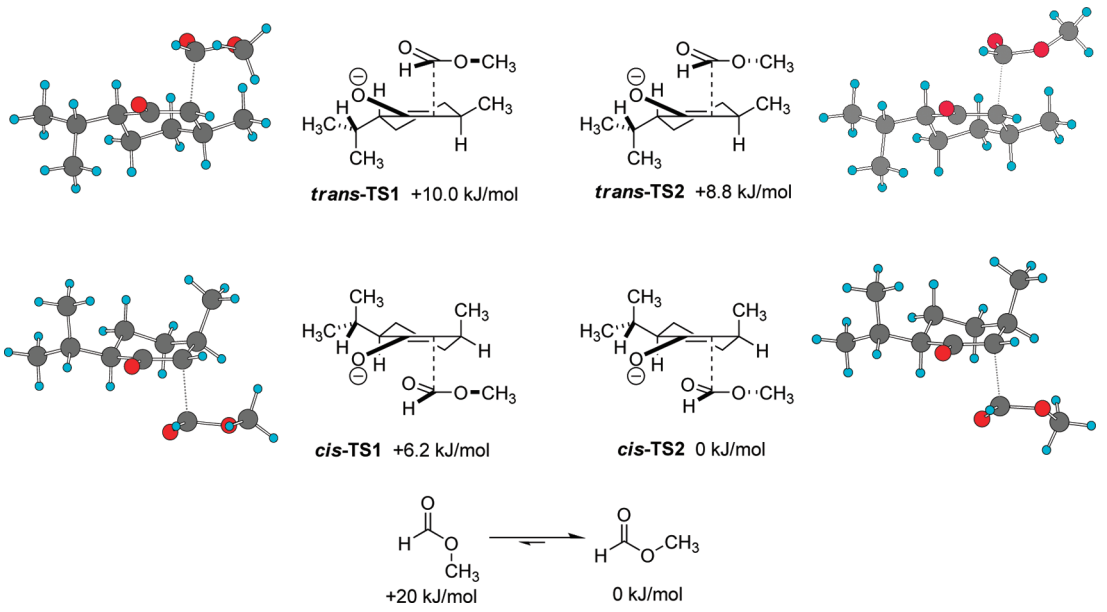
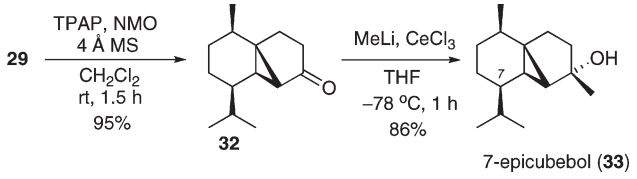


FIGURE 3. Computational analysis of formylation of menthone and isomenthone enolates, and conformational preference of methyl formate.

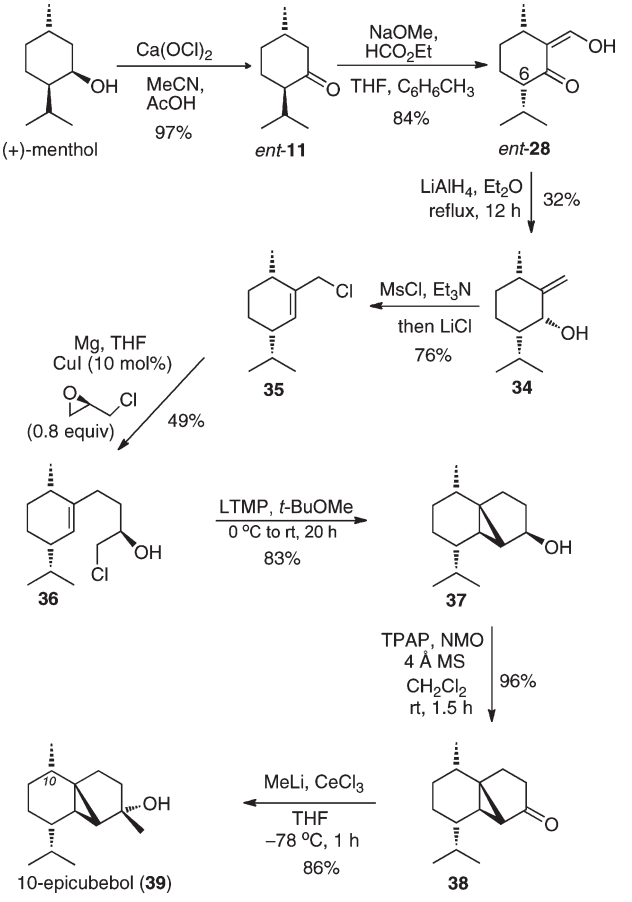
cyclopropyl alcohol **29** by way of ketone **32** as shown in Scheme 9. 7-Epicubebol (**33**) (structure confirmed by X-ray crystallographic analysis)[22] was examined at Firmenich, but was found to be bitter, terpenic, and without much of a cooling effect compared with cubebol.

SCHEME 9. Synthesis of 7-Epicubebol (33)



The successful intramolecular cyclopropanation of unsaturated epoxide **23** prompted us to work in the enantiomeric series, starting from commercially available (+)-menthol, so as to confirm the structure proposed for (−)-10-epicubebol (**39**) (Scheme 10; note: stereochemical assignment of alcohol **34** is discussed in the Experimental Section). (−)-10-Epicubebol (**39**) was identified in 1996[37] in the leaf oil of *Chamaecyparis obtuse*, an important timber tree in Japan, and assigned the structure shown on the basis of similar spectral data to the aglycon of 10-epicubebolxyloside,[38] with the latter structure being assigned by NOE studies and spectral comparisons with cubebol and 4-epicubebol. The ^{1}H and ^{13}C data for synthetically obtained (−)-10-epicubebol (**39**) were in perfect agreement with the literature data[37] for the natural isolate.[22] Analysis of the taste of 10-epicubebol at Firmenich found it to be slightly bitter.

SCHEME 10. Synthesis of (−)-10-Epicubebol (39)



Conclusions

Embedded cyclopropanes fused to 5- and 6-membered carbocycles are widely found in natural products, and there has been considerable interest in the synthesis of such

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systems, especially in a stereocontrolled manner. The above work has described an efficient intramolecular cyclopropanation strategy of unsaturated terminal epoxides to the stereocontrolled syntheses of cubebols. These applications of our cyclopropanation methodology exemplify the latter's utility as a fundamentally important alternative to classical intramolecular cyclopropanation of unsaturated α-diazocarbonyl compounds, because of the relative ease of construction of the highly enantioenriched epoxide substrates, and the experimentally straightforward protocol with use of commercially available reagents. Significantly, despite stereochemistry variation in the tethered alkene, in all these syntheses the facial selectivity of cyclopropanation is controlled solely by the epoxide stereochemistry. Aside from the most concise synthesis of cubebol reported to date, this Article also discloses the first synthesis of naturally occurring (−)-10-epicubebol, confirming the original structural assignment. Furthermore, arising out of these studies, the origins of the unusual and almost complete *i*-Pr epimerization during the formylation of menthone with alkoxide and a formate ester (a reaction originally reported by Claisen, in 1894) have been clarified with supporting computational studies, and a method established to formylate menthone with preservation of the original stereocenter.

Experimental Section

General Experimental Information. Details can be found in the Supporting Information.

General Procedure 1 (Ring-Opening of Epichlorohydrin with Grignard Reagents). Mg turnings (486 mg, 20 mmol) were activated by rapid stirring overnight under argon.[39] To a suspension of the activated Mg in THF (8 mL) at rt was added 1,2-dibromoethane (3 drops), followed by syringe pump addition of the allylic chloride (935 mg, 5.0 mmol) in THF (7 mL) over a period of 2 h. On completion of the addition, the mixture was stirred for a further 2 h at rt, and afterward the solids were allowed to settle for 30 min. The resulting Grignard reagent was added dropwise within 30 min to a mixture of CuI (95 mg, 0.5 mmol) and epichlorohydrin (0.31 mL, 4 mmol) in dry THF (7 mL) at −78 °C. The resulting solution was gradually warmed to 0 °C over 90 min and then stirred at 0 °C for a further 90 min. The reaction was then quenched with saturated aq NH_4Cl solution (3 mL) and extracted with Et_2O (2 × 25 mL). The combined organic layers were dried ($MgSO_4$), evaporated under reduced pressure, and purified by column chromatography (18% Et_2O in light petrol) to give the unsaturated chlorohydrin.

General Procedure 2 (Intramolecular Cyclopropanation of Unsaturated Terminal Epoxides with LTMP). *n*-BuLi (1.6 M in hexanes, 3.75 mL, 6.0 mmol) was added to a stirred solution of 2,2,6,6-tetramethylpiperidine (1.0 mL, 6.0 mmol) in *t*-BuOMe (30 mL) at −78 °C. The resulting pale yellow solution of LTMP was stirred at rt for 10 min and then cooled to 0 °C in an ice bath. To a stirred solution of the unsaturated terminal epoxide (593 mg, 2.85 mmol) in *t*-BuOMe (14 mL) at 0 °C was added the above LTMP solution dropwise via cannula over 2 h. The resulting mixture was stirred at rt for 16 h, then quenched with MeOH (3 mL) and concentrated under reduced pressure. The residue was dry-loaded onto a small amount of silica and purified by column chromatography (SiO_2, gradient elution, 20% to 35% Et_2O in light petrol) to give the cyclopropyl alcohol.

General Procedure 3 (Intramolecular Cyclopropanation of Unsaturated Terminal Epoxides with Catalytic TMP). *n*-BuLi (1.6 M in hexanes, 0.9 mL, 1.4 mmol) was added over 70 min to a stirred solution of the unsaturated terminal epoxide (148 mg, 0.71 mmol) and 2,2,6,6-tetramethylpiperidine (0.06 mL, 0.35 mmol) in *t*-BuOMe (4 mL) at 0 °C. The stirring was continued for 8 h and the mixture then quenched with MeOH (0.3 mL), and purified as in General Procedure 2 to give the cyclopropyl alcohol.

General Procedure 4 (Intramolecular Cyclopropanation of Unsaturated Chlorohydrins with LTMP). *n*-BuLi (1.6 M in hexanes, 2.2 mL, 3.5 mmol) was added over 5 min to a stirred solution of the unsaturated chlorohydrin (245 mg, 1.0 mmol) and 2,2,6,6-tetramethylpiperidine (0.42 mL, 2.5 mmol) in *t*-BuOMe (8 mL) at −78 °C. The solution was warmed to rt over 4 h and then left at rt for a further 16 h. The mixture was then quenched with MeOH (0.5 mL), and purified as in General Procedure 2 to give the cyclopropyl alcohol.

General Procedure 5 (Oxidation of Cyclopropyl Alcohol to Ketone). To a stirred solution of the cyclopropyl alcohol (521 mg, 2.5 mmol) in dry CH_2Cl_2 (20 mL) were added oven-dried powdered MS 4 Å (500 mg), *N*-methylmorpholine *N*-oxide (585 mg, 5.0 mmol, 2 equiv), and tetra-*n*-propylammonium perruthenate (47 mg, 0.13 mmol, 0.05 equiv) at rt. The mixture was then stirred at rt for 90 min, diluted with Et_2O (30 mL) and filtered through a pad of silica to give the crude ketone, which was purified by column chromatography (25% Et_2O in light petrol).

Synthesis of (−)-Cubebol (1). (2*S*,5*R*)-2-Isopropyl-5-methylcyclohexanone (11). L-Menthol (5.0 g, 32 mmol) was dissolved in MeCN:AcOH (3:2, 42 mL) and added dropwise over a period of 30 min to a cooled (0 °C) and stirred solution of calcium hypochlorite (4.0 g, 28 mmol) in water (65 mL). The stirring was continued for 3 h, then water (65 mL) was added in one portion. The solution was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic layers were washed with 10% aq $NaHCO_3$ (2 × 50 mL), dried ($MgSO_4$), and concentrated under reduced pressure. (−)-Menthone (**11**) (4.6 g, 93%) was obtained as a colorless oil, which was used in the next step without further purification; R_f 0.4 (4% ether in light petrol); $[\alpha]^{25}_D$ −27.9 (*c* 1.0, $CHCl_3$) (lit.[40] $[\alpha]^{25}_D$ −28.5) ; IR (cm^{-1}) 2961 s, 2931 s, 2872 m, 1712 s, 1455 w, 1369 w, 1315 w, 750 w; ^1H NMR (400 MHz) 2.30 (ddd, J = 12.5, 3.5, 2.0 Hz, 1 H), 2.15−2.07 (m, 1 H), 2.05−1.98 (m, 2 H), 1.94−1.75 (m, 3 H), 1.39−1.25 (m, 2 H), 0.96 (d, J = 6.0 Hz, 3 H), 0.87 (d, J = 6.5 Hz, 3 H), 0.81 (d, J = 6.5 Hz, 3 H); ^{13}C NMR (100 MHz) 212.3 (C-1), 55.8 (C-2), 50.8 (C-6), 35.4 (C-5), 33.9 (C-4), 27.8 (C-3), 25.8 (CMe_2), 22.2 (CMe), 21.2 (CMe*Me*), 18.7 (C*Me*Me); HRMS (CI^+) m/z $[MH]^+$ calcd for $C_{10}H_{19}O$ 155.1436, found 155.1436.

(3*R*,6*S*,*Z*)-2-(Hydroxymethylene)-6-isopropyl-3-methylcyclohexanone (12). To a solution of diisopropylamine (0.43 mL, 3.0 mmol) in Et_2O (4 mL) at −40 °C was added *n*-BuLi (1.6 M in hexanes, 2.25 mL, 3.6 mmol) dropwise over 2 min. After 30 min, the solution was cooled to −78 °C and then a solution of (−)-menthone (**11**)[22] (462 mg, 3.0 mmol) in Et_2O (3 mL) was added dropwise over 30 min. The solution was stirred at −78 °C for an additional 2 h, then $HCO_2CH_2CF_3$ (1.75 mL, 18 mmol, 6 equiv) was added in one portion and the mixture was stirred at −78 °C for a further 3 h. The reaction was quenched with H_2SO_4 (550 mg, 5.6 mmol) and water (15 mL) was added. The organic phase was extracted with Et_2O (3 × 25 mL) and the combined organic layers were washed with saturated aq NH_4Cl (20 mL) and extracted with 1% aq NaOH (4 × 25 mL). The combined basic extracts were cooled to 0 °C (ice bath), acidified to pH 1 by dropwise addition of 10% aq HCl, and then extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give hydroxymethylenementhone

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12 (300 mg, 55%, **12**:**28** = 98:2 by integration of =C*H*OH ^{1}H NMR signals[22]) as an orange oil, which was used in the next step without further purification; R_f 0.4 (5% Et_2O in light petrol); $[\alpha]^{26}_D$ −96.0 (*c* 1.5, $CHCl_3$); IR (cm^{-1}) 2961 s, 2931 m, 2873 w, 1734 w, 1703 m, 1633 br, 1466 m, 1388 w, 1181 w; ^{1}H NMR (400 MHz) 15.44 (d, *J* = 4.0 Hz, 1 H, =CHO*H*), 8.56 (d, 1 H, *J* = 4.0 Hz, =C*H*OH), 2.5−2.45 (m, 1 H, C*H*Me), 2.34−2.32 (m, 1 H, C*H*Me$_2$), 1.83−1.76 (m, 2 H, CH_2), 1.53−1.44 (m, 1 H, C*H*-*i*-Pr), 1.32−1.21 (m, 2 H, CH_2), 1.15 (d, *J* = 6.5 Hz, 3 H, Me), 0.11 (d, *J* = 7.0 Hz, 3 H, CH*Me*Me), 0.82 (d, *J* = 7.0 Hz, 3 H, CHMe*Me*); discernible data for **28**: 8.73 (br s, =C*H*OH); discernible data for aldehyde tautomer: 9.71 (d, *J* = 4 Hz, CHO), 2.81 (dd, *J* = 11.5 Hz, 4, C*H*CHO); ^{13}C NMR (100 MHz) 191.6 (C=O), 183.7 (*C*H-OH), 115.2 (C), 47.6 (C-*i*-Pr), 31.3 (CH_2), 29.1 (*C*Me$_2$), 28.2 (*C*Me), 21.4 (C*Me*), 20.5 (CH_2), 20.3 (C*Me*Me), 17.7 (CMe*Me*); discernible data for aldehyde tautomer: 210.0, 201.1, 69.2, 56.5, 36.0, 33.1, 28.0, 25.7, 21.1, 18.6; HRMS (CI^+) *m*/*z* $[MH]^+$ calcd for $C_{11}H_{19}O_2$ 183.1385, found 183.1383.

(*1S*,3*R*,6*S*)-6-Isopropyl-3-methyl-2-methylenecyclohexanol (13). Hydroxymethylenementhone **12** (219 mg, 1.2 mmol) was added dropwise to a stirred solution of $LiAlH_4$ (90 mg, 2.4 mmol, 2 equiv) in dry Et_2O (10 mL) at rt. The solution was heated to gentle reflux overnight, then cooled and carefully quenched with 20% aq Na_2CO_3 (3 mL). The organic phase was extracted with Et_2O (3 × 15 mL), dried (Na_2SO_4), and evaporated under reduced pressure. Purification of the residue by column chromatography gave the allylic alcohol **13** (101 mg, 50%) as a colorless oil; R_f 0.4 (6% Et_2O in light petrol); $[\alpha]^{25}_D$ −100.9 (*c* 1.4, $CHCl_3$); IR (cm^{-1}) 3480 br, 3067 w, 2958 s, 2933 s, 2870 m, 1644 w, 1475 w, 1450 w, 1029 m, 948 m, 905 s; ^{1}H NMR (400 MHz) 5.02 (d, *J* = 1.0 Hz, 1 H, =C*H*$_2$), 4.73 (d, *J* = 1.5 Hz, 1 H, =C*H*$_2$), 3.83 (br s, 1 H, C*H*OH), 2.29−2.20 (m, 1 H, C*H*Me$_2$), 2.03−1.94 (m, 1 H, C*H*Me), 1.84−1.79 (m, 1 H, H-4a), 1.71−1.62 (m, 1 H, H-5a), 1.56 (d, *J* = 5.5 Hz, 1 H, OH), 1.29−1.17 (m, 2 H, H-5b, H-6), 1.09 (d, *J* = 6.5 Hz, 3 H, CH*Me*), 1.02−0.95 (m, 1 H, H-4b), 0.93 (d, *J* = 7.0 Hz, 3 H, CH*Me*Me), 0.87 (d, *J* = 7.0 Hz, 3 H, CHMe*Me*); ^{13}C NMR (100 MHz) 156.9 (=C), 100.6 (=CH_2), 74.3 (*C*OH), 51.9 (C-6), 36.7 (*C*HMe), 35.9 (C-4), 26.5 (*C*HMe$_2$), 23.0 (C-5), 20.9 (C*Me*Me), 18.1 (CH*Me*), 15.8 (CMe*Me*); HRMS (CI^+) *m*/*z* $[M - OH]^+$ calcd for $C_{11}H_{19}$ 151.1487, found 151.1488.

(1*S*,3*R*,6*S*)-6-Isopropyl-3-methyl-2-methylenecyclohexyl 3,5-dinitrobenzoate (14). To a stirred solution of allylic alcohol **13** (168 mg, 1.0 mmol) and 3,5-dinitrobenzoyl chloride (230 mg, 1.0 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added dry pyridine (0.16 mL, 2 equiv) dropwise. The reaction mixture was warmed to rt and stirred overnight, before quenching with H_2O (5 mL). The solution was neutralized with 1 N HCl, extracted with CH_2Cl_2 (3 × 15 mL), dried ($MgSO_4$), and evaporated under reduced pressure to give yellowish brown crystals (300 mg, 80%). These crystals were washed twice with CH_2Cl_2 and Et_2O, then dried under reduced pressure; mp 162 °C; $[\alpha]^{25}_D$ −17.6 (*c* 0.6, $CHCl_3$); IR (cm^{-1}) 2950 m, 2831 m, 2870 m, 2401 w, 1710 s, 1575 s, 1354 s, 1012 w; ^{1}H NMR (400 MHz) 9.27−9.26 (m, 1 H, *p*-Ar), 9.25−9.24 (m, 2 H, *o*-Ar), 5.44 (d, *J* = 5.5 Hz, 1 H, C*H*-O), 4.74 (t, *J* = 1.5, 1 H, C*H*=C), 4.7 (br s, 1 H, C*H*=C), 2.22−2.13 (m, 1 H, C*H*-Me), 1.96−1.89 (m, 2 H, CH_2-CHMe, C*H*-Me$_2$), 1.86−1.76 (m, 2 H, CH_2CHMe, CH_2-CH-*i*-Pr), 1.45−1.34 (m, 1 H, CH_2-CH-*i*-Pr), 1.14 (d, *J* = 6 Hz, 3 H, CH-*Me*), 1.11−1.04 (m, 1 H, C*H*-*i*-Pr), 0.96 (d, *J* = 7 Hz, 3 H, CH(*Me*)$_2$), 0.85 (d, *J* = 7 Hz, 3 H, CH(*Me*)$_2$); ^{13}C NMR (100 MHz) 161.6 (*C*=O), 150.8 (2 × *m*-Ar), 148.8 (*C*=CH_2), 133.9 (*C*-C=O), 129.5 (2 × *o*-Ar), 122.5 (*p*-Ar), 102.1 (CH_2=C), 78.8 (C-O), 49.2 (C-*i*-Pr), 36.8 (*C*-Me), 35.4 (CH_2), 27.1 (*C*Me$_2$), 23.1 (CH_2), 20.7 (C*Me*), 17.9 (CMe*Me*), 16.1 (C*Me*Me); HRMS (FI^+) *m*/*z* $[M]^+$ calcd for $C_{18}H_{22}N_2O_6$ 362.1478, found 362.1476.

(3*S*,6*R*)-1-(Chloromethyl)-3-isopropyl-6-methylcyclohex-1-ene (15). To a stirred solution of allylic alcohol **13** (504 mg, 3.0 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added Et_3N (0.84 mL, 6 mmol), then MsCl (0.47 mL, 6 mmol) dropwise over 5 min. The reaction mixture was allowed to stir for 30 min at 0 °C, before addition of anhyd LiCl (1.3 g, 10 equiv) in dry acetone (20 mL) over 2 min. The reaction mixture was stirred overnight, then quenched with H_2O (20 mL), washed with 2 M aq NaOH (20 mL), and extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure, and purified by column chromatography (pentane) to give the allylic chloride **15** (407 mg, 79%) as a colorless oil; R_f 0.9 (pentane); IR (cm^{-1}) 2959 s, 2870 s, 1712 w, 1662 m, 1384 m, 1366 m, 1206 s, 1017 w; ^{1}H NMR (400 MHz) 5.73 (br s, 1H, CH=C), 4.24 (d, *J* = 11.0 Hz, 1 H, CH_2-Cl), 3.94 (d, *J* = 12.0 Hz, 1 H, CH_2-Cl), 2.44−2.35 (m, 1 H), 2.32−2.21 (m, 2 H), 2.18−2.13 (m, 1 H), 1.98−1.87 (m, 3 H), 1.06 (d, *J* = 7 Hz, 3 H, CH*Me*), 0.90 (dd, *J* = 12, 7 Hz, 6 H, C*Me*$_2$); ^{13}C NMR (100 MHz) 138.6 (C), 131.9 (*C*H=C), 48.8 (CH_2-Cl), 42.3 (*C*H-*i*-Pr), 32.1 (*C*HMe$_2$), 31.8 (*C*Me), 30.2 (CH_2), 24.5 (CH_2), 19.8 (C*Me*), 19.4 (C*Me*Me), 18.9 (CMe*Me*); HRMS $[M]^+$ found 186.1175, $C_{11}H_{19}Cl$ requires 186.1187.

(*R*)-1-Chloro-4-((3*S*,6*R*)-3-isopropyl-6-methylcyclohex-1-enyl)-butan-2-ol (16). Allylic chloride **15** (934 mg, 5 mmol) was reacted according to General Procedure 1 to give the unsaturated chlorohydrin **16** (479 mg, 49%) as a colorless oil; R_f 0.4 (18% Et_2O in light petrol); $[\alpha]^{25}_D$ +20.4 (*c* 0.7, $CHCl_3$); IR (cm^{-1}) 3584 br, 2978 s, 2871 s, 1714 m, 1470 s, 1366 m, 1255 m, 1050 s, 906 s, 740 s; ^{1}H NMR (400 MHz) 5.34 (br s, 1 H, C*H*=C), 3.86−3.80 (m, 1 H, C*H*OH), 3.67 (dd, *J* = 11.0, 3.0 Hz, 1 H, CH_2Cl), 3.52 (dd, *J* = 11.0, 6.5 Hz, CH_2Cl), 2.25−2.04 (m, 3 H, C*H*Me, CH_2,), 1.94−1.81 (m, 2 H, C*H*-*i*-Pr, CH_2), 1.75−1.51 (m, 4 H, C*H*Me$_2$, CH_2), 1.25−1.14 (m, 2 H, =C-CH_2, CH_2-CHOH), 0.99 (d, *J* = 7.0 Hz, 3 H, CH*Me*), 0.88 (d, *J* = 7.0 Hz, 3 H, C*Me*Me), 0.84 (d, *J* = 7.0 Hz, 3 H, CMe*Me*); ^{13}C NMR (100 MHz) 141.2 (C), 126.3 (*C*H=C), 71.5 (*C*H-OH), 50.1 (*C*H$_2$-Cl), 42.1 (*C*H-*i*-Pr), 32.4 (CH_2), 32.3 (*C*HMe), 32.2 (=C-*C*H$_2$), 32.1 (*C*HMe$_2$), 31.2 (CH_2), 24.6 (CH_2), 19.75 (C*Me*), 19.7 (C*Me*Me), 19.3 (CMe*Me*); HRMS (CI^+) *m*/*z* $[MH]^+$ calcd for $C_{14}H_{26}OCl$ 245.1672, found 245.1683.

(*R*)-2-(2-((3*S*,6*R*)-3-Isopropyl-6-methylcyclohex-1-enyl)ethyl)-oxirane (17). Powdered NaOH (91 mg, 2.27 mmol) was added to a stirred solution of unsaturated chlorohydrin **16** (464 mg, 1.9 mmol) in MeOH (2.5 mL) at 0 °C. The resulting mixture was stirred at rt for 90 min, then diluted with Et_2O (20 mL) and washed with water (20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification of the residue by column chromatography (8% Et_2O in light petrol) gave epoxide **17** (323 mg, 82%) as a colorless oil; R_f 0.4 (8% Et_2O in light petrol); $[\alpha]^{25}_D$ +26.8 (*c* 1.6, $CHCl_3$); IR (cm^{-1}) 2955 s, 2929 s, 2851 m, 1463 w, 1367 w, 918 w, 836 w; ^{1}H NMR (500 MHz) 5.32 (br s, 1H, C*H*=C), 2.95−2.91 (m, 1 H, C*H*OH), 2.75 (dd, *J* = 5.0, 4.0 Hz, 1 H, CH_2−O), 2.48 (dd, *J* = 5.0, 2.5 Hz, 1 H, CH_2-O), 2.24−2.10 (m, 3 H, C*H*Me, =C-CH_2, CH_2-CH-O), 1.94−1.89 (m, 2 H, C*H*-*i*-Pr, CH_2), 1.67−1.60 (m, 3 H, =C-CH_2, CH_2), 1.58−1.52 (m, 1 H, C*H*Me$_2$), 1.26−1.16 (m, 2 H, CH_2), 0.99 (d, *J* = 7.0 Hz, 3 H, CH*Me*), 0.87 (d, *J* = 7.0 Hz, 3 H, C*Me*Me), 0.84 (d, *J* = 7.0 Hz, 3 H, CMe*Me*); ^{13}C NMR (125 MHz) 141.0 (C), 125.8 (*C*H=C), 52.3 (*C*H-O), 47.1 (CH$_2$-Cl), 42.1 (*C*H-*i*-Pr), 32.35 (*C*HMe), 32.3 (*C*Me$_2$), 32.2 (=C-*C*H$_2$), 31.2 (CH_2), 31.1 (CH_2), 24.6 (CH_2), 19.7 (C*Me*), 19.65 (CMe*Me*), 19.3 (C*Me*Me); HRMS (CI^+) *m*/*z* $[MH]^+$ calcd for $C_{14}H_{25}O$ 209.1905, found 209.1907.

(1*R*,4*R*,5*R*,6*R*,7*S*,10*R*)-7-Isopropyl-10-methyltricyclo[4.4.0.0^{1,5}]-decan-4-ol (18). Unsaturated terminal epoxide **17** (593 mg, 2.85 mmol) was reacted according to General Procedure 2 to give cyclopropyl alcohol **18** (534 mg, 90%) as a white solid; R_f 0.4 (40% Et_2O in light petrol); mp 74−76 °C; $[\alpha]^{25}_D$ −10.7 (*c* 0.33, $CHCl_3$); IR (cm^{-1}) 3608 w, 3447 br, 3018 m, 2958 m, 2928 m, 2870 m, 1385 w, 1371 w, 1216 s; ^{1}H NMR (400 MHz) 4.22 (br s, 1 H, C*H*OH), 2.07−2.00 (m, 1 H, H-2a,), 1.88−1.79 (m, 1 H, H-10), 1.65−1.60 (m, 1 H, H-9a), 1.59−1.50 (m, 2 H, C*H*Me$_2$, H-3a), 1.45−1.38 (m, 3 H, H-2b, H-3b, H-8a), 1.20 (d, *J* = 4.5 Hz, 1 H,

−OH), 1.09−1.02 (m, 1 H, H-7), 1.00 (d, J = 6.5 Hz, 3 H, CH*Me*), 0.93−0.91 (m, 1H, H-5), 0.91 (d, J = 7.0 Hz, 3 H, C*Me*Me), 0.87 (d, J = 7.0 Hz, 3 H, CMe*Me*), 0.85−0.82 (m, 1 H, H-8b), 0.60−0.52 (m, 1 H, H-9b), 0.38 (t, J = 3.0 Hz, 1 H, H-6); ^{13}C NMR (100 MHz) 75.1 (C-4), 44.1 (C-7), 35.4 (C-5), 34.5 (C-1), 33.5 (C-10), 31.6 (C-3), 31.4 (C-9), 29.9 (*C*HMe$_2$), 28.6 (C-2), 26.5 (C-8), 24.6 (C-6), 19.9 (CH*Me*), 19.6 (C*Me*Me), 19.1 (CMe*Me*); HRMS-CI: m/z [M − OH]$^+$ calcd for $C_{14}H_{23}$ 191.1800, found 191.1811.

Cyclopropyl alcohol **18** was also prepared (129 mg, 86%, data as above) from unsaturated terminal epoxide **17** (149 mg, 0.71 mmol) following General Procedure 3.

Cyclopropyl alcohol **18** was also prepared (141 mg, 71%, data as above) from unsaturated chlorohydrin **16** (244 mg, 1 mmol) following General Procedure 4.

(1*R*,5*R*,6*R*,7*S*,10*R*)-7-Isopropyl-10-methyltricyclo[4.4.0.0^{1,5}]-decan-4-one (2). Following General Procedure 5, cyclopropyl alcohol **18** (521 mg, 2.5 mmol) gave norcubebanone **2** (495 mg, 95%) as a white crystalline solid; R_f 0.4 (25% Et$_2$O in light petrol); mp 58−59 °C (lit.[10] mp 58.5−60 °C); $[\alpha]^{25}_D$ −22.3 (c 0.62, CHCl$_3$) (lit.[10] $[\alpha]^{25}_D$ −21.8 (c 0.72, CH$_2$Cl$_2$)); IR (cm^{-1}) 2956 m, 2929 m, 2872 w, 1721 s, 1459 w, 1295 w, 1221 m, 913 w; ^{1}H NMR (500 MHz) 2.13−2.11 (m, 1 H, H-3a), 2.10−2.04 (m, 1 H, H-2a), 2.02−1.96 (m, 1 H, H-3b), 1.84−1.77 (m, 1 H, H-10), 1.79−1.63 (m, 2 H, H-2b, H-9a), 1.6 (oct, J = 6.0 Hz, 1 H, H-11), 1.49−1.37 (m, 2 H, H-5, H-6a), 1.24 (t, J = 2.5 Hz, 1 H, H-6), 1.15−1.13 (m, 1 H, H-7), 0.95 (d, J = 6.0 Hz, 3 H, C*Me*Me), 0.91 (m, 4 H, H-8b, CH*Me*), 0.87 (d, J = 6.0 Hz, 3 H, CMe*Me*), 0.55 (ddt, J = 2.5, 11.0, 13.0 Hz, 1 H, H-9b); ^{13}C NMR (125 MHz) 214.6 (C-4), 43.3 (C-7), 40.3 (C-1), 39.7 (C-5), 33.3 (C-3), 33.2 (C-11), 32.5 (C-6), 31.3 (C-10), 30.8 (C-9), 26.6 (C-2), 26.0 (C-8), 19.9 (C*Me*Me), 19.4 (CMe*Me*), 18.9 (CH*Me*); HRMS (CI$^+$) m/z [MH]$^+$ calcd for $C_{14}H_{23}O$ 207.1749, found 207.1767.

(1*R*,4*S*,5*R*,6*R*,7*S*,10*R*)-7-Isopropyl-4,10-dimethyltricyclo-[4.4.0.0^{1,5}]decan-4-ol (1) [(−)-Cubebol]. Anhyd $CeCl_3$ (740 mg, 3 mmol) was obtained by dehydrating $CeCl_3 \cdot 7H_2O$ (1.1 g, 3 mmol) under high vacuum (< 0.1 mbar) at 165 °C (oil bath) for 2 h.[41] To this anhyd $CeCl_3$ was added THF (15 mL) and the suspension was stirred for 2 h at rt. MeLi (1.6 M in Et$_2$O, 1.87 mL, 3 mmol) was then added to the above suspension at −78 °C, followed after 30 min by a solution of ketone **9** (310 mg, 1.5 mmol) in THF (10 mL) over 10 min. After 90 min, the reaction was quenched with aq NH_4Cl (3 mL) and then warmed to rt. The reaction mixture was extracted with Et$_2$O (2 × 20 mL) and the combined organic layers were dried (MgSO$_4$) and concentrated under reduced pressure. Purification of the residue by column chromatography (20% Et$_2$O in light petrol) gave (−)-cubebol (**1**) (283 mg, 85%, 97:3 mixture[11]) as a crystalline solid; mp 60−61 °C (lit.[10] mp 59−60.4 °C); $[\alpha]^{25}_D$ −59.6 (c 0.6, CHCl$_3$) (lit.[10] $[\alpha]^{25}_D$ −48.3 (c 1.0, CHCl$_3$)); IR (cm^{-1}) 3350 br, 2951 m, 2860 m, 1490 w, 1142 m, 910 w; ^{1}H NMR (400 MHz): 1.82−1.8 (m, 1 H, H-2a), 1.32−1.26 (m, 1 H, H-10), 1.62−1.59 (m, 1 H, H-11), 1.58−1.55 (m, 1 H, H-9a), 1.53−1.49 (m, 2 H, H-3a, H-2b), 1.4 (s, 1 H, H-16), 1.35−1.32 (m, 2 H, H-8a, H-3b), 1.25 (d, J = 1.0 Hz, 3 H, H-15), 0.96−0.93 (m, 10 H, H-7, CH*Me*, C*Me*Me, CMe*Me*), 0.80−0.77 (m, 3 H, H-10, H-6, H-8b), 0.49−0.46 (m, H-9b); ^{13}C NMR (100 MHz) 80.3 (C-4), 44.1 (C-7), 39.0 (C-5), 36.3 (C-3), 33.6 (C-11), 33.4 (C-1), 31.7 (C-9), 30.8 (C-10), 29.5 (C-2), 27.9 (C-15), 26.4 (C-8), 22.6 (C-6), 20.1 (C*Me*Me), 19.6 (CMe*Me*), 18.7 (CH*Me*), discernible data for 4-epi-(**1**): 80.8, 44.6, 39.9, 36.6, 34.9, 31.8, 30.2, 29.7, 27.1, 25.3, 25.0, 20.1, 19.2; HRMS (CI$^+$) m/z [MH]$^+$ calcd for $C_{15}H_{27}O$ 223.2062, found 223.2069.

(*S*)-1-Chloro-4-((3*S*,6*R*)-3-isopropyl-6-methylcyclohex-1-enyl)-butan-2-ol (40). Allylic chloride **15** (1.1 g, 6.0 mmol) was reacted according to General Procedure 1 to give unsaturated chlorohydrin **40** (574 mg, 49%) as a colorless oil; R_f 0.4 (18% ether in light petrol); $[\alpha]^{25}_D$ +18.8 (c 0.78, CHCl$_3$); IR (cm^{-1}) 3470 br, 2957 s, 2933 s, 2871 m, 1713 m, 1464 m, 1384 w, 1167 m, 1049 m; ^{1}H NMR (400 MHz) 5.33 (br s, 1 H, C*H*═C), 3.79 (tt, J = 8.0, 3.9 Hz, 1 H, C*H*−OH), 3.63 (dd, J = 10.0 Hz, 1 H, C*H*$_2$-Cl), 3.52−3.48 (m, 1 H, C*H*$_2$-Cl), 2.33−2.25 (m, 1 H, ═C-C*H*$_2$−), 2.02 (br s, 1 H, −OH), 2.10−2.00 (m, 2 H, C*H*Me, C*H*$_2$), 1.95−1.88 (m, 1 H, C*H*-*i*-Pr), 1.87−1.80 (m, 1 H, C*H*$_2$), 1.70−1.52 (m, 4 H, C*H*$_2$, C*H*$_2$, C*H*Me$_2$), 1.24−1.15 (m, 2 H, C*H*$_2$-CHMe), 0.98 (d, J = 7.0 Hz, 3 H, CH*Me*), 0.88 (d, J = 7.0 Hz, 3 H, C*Me*Me), 0.85 (d, J = 7.0 Hz, 3 H, CMe*Me*); ^{13}C NMR (100 MHz) 140.9 (C), 126.5 (*C*H═C), 71.0 (*C*H-OH), 50.6 (*C*H$_2$-Cl), 42.1 (*C*H-*i*-Pr), 32.35 (*C*HMe), 32.3 (CH$_2$), 32.2 (CH$_2$), 32.0 (*C*Me$_2$), 30.8 (CH$_2$), 24.6 (CH$_2$), 19.7 (C*Me*), 19.6 (C*Me*Me), 19.3 (CMe*Me*); HRMS (CI$^+$) m/z [M]$^+$ calcd for $C_{14}H_{25}OCl$ 244.1594, found 244.1606.

(*S*)-2-(2-((3*S*,6*R*)-3-Isopropyl-6-methylcyclohex-1-enyl)ethyl)-oxirane (19). Powdered NaOH (96 mg, 2.4 mmol, 1.2 equiv) was added to a stirred solution of unsaturated chlorohydrin **40** (488 mg, 2.0 mmol) in MeOH (4 mL) at 0 °C. The resulting mixture was stirred at rt for 90 min, then diluted with Et$_2$O (20 mL) and washed with water (25 mL). The organic layer was dried (MgSO$_4$), filtered, and concentrated under reduced pressure. Purification of the residue by column chromatography (8% Et$_2$O in light petrol) gave the epoxide **19** (324 mg, 78%) as a colorless oil; R_f 0.4 (8% Et$_2$O in petrol); $[\alpha]^{25}_D$ +28.0 (c 0.6, CHCl$_3$); IR (cm^{-1}) 2957 s, 2934 s, 2824 m, 1464 w, 1348 w, 1115 w, 917 w, 734 w; ^{1}H NMR (400 MHz) 5.34 (br s, 1 H, C*H*═C), 2.96−2.90 (m, 1 H, C*H*-OH), 2.76 (dd, J = 5.0, 4.0 Hz, 1 H, C*H*$_2$-O), 2.49 (dd, J = 5.0, 3.0 Hz, 1 H, C*H*$_2$-O), 2.30−2.22 (m, 1 H, C*H*$_2$CHMe), 2.11−2.03 (m, 2 H, C*H*Me, CH$_2$), 1.94−1.87 (m, 1 H, CH$_2$), 1.85−1.80 (m, 1 H, C*H*-*i*-Pr), 1.68−1.56 (m, 4 H, C*H*Me$_2$, CH$_2$), 1.24−1.13 (m, 2 H, CH$_2$), 0.97 (d, J = 7.0 Hz, 3 H, CH*Me*), 0.84 (dd, J = 12.0, 7.0 Hz, 6 H, CH*Me*$_2$); ^{13}C NMR (100 MHz) 140.8 (C), 126.1 (*C*H═C), 52.1 (*C*H-O), 47.3 (*C*H$_2$-O), 42.1 (*C*H-*i*-Pr), 32.3 (*C*HMe), 32.2 (*C*HMe$_2$), 32.1 (═C-*C*H$_2$), 31.2 (CH$_2$), 30.8 (*C*H$_2$-CHMe), 24.6 (CH$_2$), 19.6 (C*Me*), 19.6 (C*Me*Me), 19.2 (CMe*Me*); HRMS (CI$^+$) [M − H]$^+$ calcd for $C_{14}H_{23}O$ 207.1749, found 209.1760.

(1*S*,4*S*,5*S*,6*S*,7*S*,10*R*)-7-Isopropyl-10-methyltricyclo[4.4.0.0^{1,5}]-decan-4-ol (20). Unsaturated terminal epoxide **19** (304 mg, 1.46 mmol) was reacted according to General Procedure 2. The crude product was purified by flash column chromatography (SiO$_2$, gradient elution, 20−35% Et$_2$O−light petrol) to give cyclopropyl alcohol **20** (273 mg, 90%) as a colorless oil; R_f 0.4 (40% Et$_2$O−petroleum ether); $[\alpha]^{25}_D$ +28.0 (c 1.0, CHCl$_3$); IR (cm^{-1}) 3310 br, 2954 s, 2971 s, 2844 m, 1470 m, 1443 w, 1383 w, 1327 w, 1057 w, 974 s; ^{1}H NMR (400 MHz) 4.21 (d, J = 5.0 Hz, 1 H, C*H*OH), 2.03−1.95 (m, 1 H, H-2a), 1.94−1.88 (m, 1 H, H-10), 1.69−1.72 (m, 1 H, H-3a), 1.62−1.46 (m, 3 H, H-7, H-8a, H-9a), 1.43−1.32 (m, 3 H, C*H*Me$_2$, H-2b, H-3b), 1.08 (d, J = 7.0 Hz, 3 H, CH*Me*), 1.01 (d, J = 3.5 Hz, 1 H, H-5), 0.92 (d, J = 6.5 Hz, 3 H, CH*Me*Me), 0.89 (d, J = 6.5 Hz, 3 H, CHMe*Me*), 0.88−0.86 (m, 1 H, H-9b), 0.84−0.71 (m, 1 H, H-8b), 0.68 (t, J = 4.0 Hz, 1 H, H-6); ^{13}C NMR (100 MHz) 75.6 (C-4), 40.3 (C-7), 33.1 (C-10), 33.0 (C-3), 32.8 (C-5), 32.4 (C-1), 31.4 (C-2), 31.2 (*C*HMe$_2$), 28.6 (C-9), 23.55 (C-6), 23.5 (C-8), 20.8 (C*Me*Me), 20.7 (CMe*Me*), 20.4 (C*Me*); HRMS (CI$^+$) m/z [M − OH]$^+$ calcd for $C_{14}H_{23}$ 191.1800, found 191.1806.

(1*S*,5*S*,6*S*,7*S*,10*R*)-7-Isopropyl-10-methyltricyclo[4.4.0.0^{1,5}]-decan-4-one (21). Following General Procedure 5, cyclopropyl alcohol **20** (166 mg, 0.8 mmol) gave ketone **21** (158 mg, 95%) as a colorless oil; R_f 0.4 (25% Et$_2$O in light petrol); $[\alpha]^{25}_D$ −1.0 (c 0.54, CHCl$_3$); IR (cm^{-1}) 2972 m, 2872 m, 1725 s, 1471 w, 1420 w, 1285 w, 1187 w, 915 m; ^{1}H NMR (500 MHz) 2.15−2.11 (m, 1 H, H-2a), 2.08−2.05 (m, 1 H, H-3a), 2.04−1.99 (m, 1 H, H-2b), 1.99−1.95 (m, 2 H, H-3b, H-10), 1.65−1.59 (m, 1 H, H-9a), 1.58−1.53 (m, 4 H, H-5, H-8a, H-6, H-7), 1.45−1.37 (m, 1 H, H-11), 1.10 (d, J = 7.0 Hz, 3 H, CH*Me*), 1.00−0.95 (m, 1 H, H-9b), 0.94 (d, J = 7.0 Hz, 3 H, CH*Me*Me), 0.90 (d, J = 6.5 Hz, 3 H, CMe*Me*), 0.78−0.69 (m, 1 H, H-8b); ^{13}C NMR (125 MHz) 215.2 (C-4), 40.5 (C-7), 37.6

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(C-1), 37.5 (C-5), 32.9 (C-3), 32.8 (C-11), 32.2 (C-6), 32.1 (C-9), 30.6 (C-10), 26.8 (C-2), 23.1 (C-8), 20.6 (C*Me*Me), 20.5 (CMe*Me*), 18.7 (C*Me*); HRMS (CI^+) m/z $[MH]^+$ calcd for $C_{14}H_{23}O$ 207.1749, found 207.1762.

(3*R*,6*R*, *Z*)-2-(Hydroxymethylene)-6-isopropyl-3-methylcyclohexanone (28). A solution of ethyl formate (47.1 g, 636 mmol) in toluene (96 mL) was added to a vigorously stirred cooled (0 °C) solution of NaOMe (34.4 g, 636 mmol) in dry toluene (192 mL) over a period of 1 h. A solution of menthone **11** (32.7 g, 212 mmol) in a 1:3 toluene−THF mixture (135 mL) was added dropwise to the above cooled solution over 1 h. The solution was allowed to warm to room temperature and then stirring was continued for 72 h. The solution was then neutralized with ice-cooled 15% (w/v) H_2SO_4, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried (Na_2SO_4) and evaporated to give a pale red oil, which was distilled (15 mbar, 125 °C) to give a yellow oil hydroxymethylene ketone **28** (31.7 g, 82%, **12**:**28** = 7:93 by integration of ^1H NMR signals for =C*H*OH); R_f = 0.4 (5% ether in light petrol); $[\alpha]^{26}_D$ +26.8 (*c* 1.6, $CHCl_3$); IR (cm^{-1}) 3165 br, 3103 br, 2961 s, 2874 s, 1709 s, 1633 w, 1587 w, 1464 m, 1370 m, 1167 br; ^1H NMR (400 MHz) 14.81 (br s, 1 H, =CHO*H*), 8.72 (br s, 1 H, =C*H*OH), 2.70−2.59 (m, 1 H, C*H*Me), 2.54−2.39 (m, 1 H, C*H*Me_2), 2.32−2.27 (m, 1 H, C*H*-*i*-Pr), 1.63−1.51 (m, 4 H, 2 × CH_2), 1.16−1.04 (m, 3 H, CH*Me*Me), 1.01−0.92 (3 H, CHMe*Me*), 0.86−0.72 (m, 3 H, CH*Me*), discernible data 15.44 (br s, 1 H, =CHO*H*), 8.55 (br s, 1 H, =C*H*OH); ^{13}C NMR (100 MHz) 188.8 (C=O), 186.7 (*C*H-OH), 115.1 (C), 46.1 (C-*i*-Pr), 28.5 (CH_2), 27.7 (*C*Me_2), 27.6, 23.0 (C*Me*), 20.2 (C*Me*Me), 17.2 (CMe*Me*), 16.3 (CH_2); discernible data for **12**: 183.8, 47.5, 31.3; HRMS (CI^+) m/z $[MH]^+$ calcd for $C_{11}H_{19}O_2$ 183.1385, found 183.1383.

(1*S*,3*R*,6*R*)-6-Isopropyl-3-methyl-2-methylenecyclohexanol (*ent*-34). Hydroxymethylene ketone **28** (6.38 g, 35 mmol) was added dropwise to a stirred solution of $LiAlH_4$ (2.65 g, 70 mmol) in dry Et_2O (210 mL) at rt. The solution was heated to gentle reflux overnight, then cooled and carefully quenched with 20% Na_2CO_3 solution (20 mL). The organic phase was extracted with Et_2O (3 × 50 mL), dried (Na_2SO_4), and evaporated under reduced pressure. Purification of the residue by column chromatography gave the allylic alcohol *ent*-**34** (3.0 g, 51%) as a colorless oil; R_f 0.4 (5% ether in petrol); $[\alpha]^{25}_D$ −10.4 (*c* 1.2, $CHCl_3$); IR (cm^{-1}) 3165 br, 2961 s, 2874 s, 1633 w, 1587 w, 1464 m, 700 w; ^1H NMR (400 MHz) 4.88−4.86 (d, *J* = 2.0 Hz, 1 H, =CH_2), 4.8 (dd, *J* = 2.0 Hz, 1 H, =CH_2), 4.3 (br s,1 H, C*H*-OH), 2.48−2.42 (m, 1 H, C*H*Me), 1.73−1.62 (m, 2 H, CH_2), 1.57−1.49 (m, 3 H), 1.4 (s, 1 H, C*H*-*i*-Pr), 1.2 (d, *J* = 7.0 Hz, 3 H, CH*Me*), 1.15−1.06 (m, 1 H, C*H*-*i*-Pr), 0.1 (d, *J* = 6.5 Hz, 3 H, CH*Me*Me), 0.9 (d, *J* = 6.5 Hz, 3 H, CHMe*Me*); ^{13}C NMR(100 MHz) 154.6 (C), 110.0 (=*C*H_2), 74.9 (*C*OH), 49.4 (CH), 36.0 (CH), 32.7 (CH_2), 28.2 (CH_3), 21.3 (C*Me*Me), 21.3, 21.0 (CMe*Me*), 20.2 (CH_2); HRMS (CI^+) m/z $[MH^+]$ found 169.1589, $C_{11}H_{20}O$ requires 169.1592.

(1*S*,3*R*,6*R*)-6-Isopropyl-3-methyl-2-methylenecyclohexyl 3,5-dinitrobenzoate (41). To a stirred solution of allylic alcohol *ent*-**34** (168 mg, 1.0 mmol), 3,5-dinitrobenzoyl chloride (230 mg, 1.0 mmol), and DMAP (15 mg, 0.12 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added anhydrous Et_3N (0.28 mL, 2 equiv) dropwise. The reaction mixture was warmed to rt and stirred overnight, before quenching with aq $NaHCO_3$ solution (5 mL). The solution was washed with brine (20 mL), extracted with CH_2Cl_2 (3 × 15 mL), dried ($MgSO_4$), and evaporated under reduced pressure. Purification by column chromatography (3% Et_2O in light petrol) gave colorless oil **41** (225 mg, 62%); R_f 0.4 (4% Et_2O in light petrol); $[\alpha]^{25}_D$ + 52.6 (*c* 1.54, $CHCl_3$); IR (cm^{-1}) 3104 w, 2962 m, 2932 m, 2871 w, 1729 s, 1629 w, 1547 s, 1344 s, 1272 s, 1167 s, 777 m; ^1H NMR (500 MHz) 9.22 (br s, 1 H, *p*-Ar), 9.13 (d, *J* = 2.0 Hz, 2 H, *o*-Ar), 5.82 (d, *J* = 2.5 Hz, 1 H, C*H*-O), 5.17 (s, 1 H, C*H*=C), 5.04 (s, 1 H, C*H*=C), 2.63−2.56 (m, 1 H, C*H*-Me), 1.87−1.76 (m, 2 H, CH_2), 1.73−1.62 (m, 3 H, CH_2, C*H*Me_2), 1.41−1.36 (m, 1 H, C*H*-*i*-Pr), 1.13 (d, *J* = 7.0 Hz, 3 H, CH*Me*), 0.97 (dd, *J* = 11.0, 6.5 Hz, 6 H, CHMe_2); ^{13}C NMR (125 MHz) 161.6 (C=O), 148.7 (*C*=CH_2), 148.2 (2 × *o*-Ar), 134.5, 129.2 (2 × C-NO_2), 122.2 (*p*-Ar), 114.8 (C=*C*H_2), 79.2 (C-O), 48.5 (C-*i*-Pr), 35.7 (*C*-Me), 32.0 (CH_2), 28.7 (*C*HMe_2), 21.1 (C*Me*), 20.9 (C*Me*Me), 20.8 (CMe*Me*), 20.7 (CH_2); HRMS (FI^+) m/z $[M]^+$ calcd for $C_{18}H_{22}N_2O_6$ 362.1478, found 362.1476.

Comparison of **14** $J_{1,6}$ (5.5 Hz) with **41** $J_{1,6}$ (2.5 Hz) for 3,5-DNB derivatives of allylic alcohols **13** and *ent*-**34**, respectively, led to assignment of the cis configuration for 3,5-DNB derivative of *ent*-**34**.

(3*R*,6*R*)-1-(Chloromethyl)-3-isopropyl-6-methylcyclohex-1-ene (*ent*-35). To a stirred solution of allylic alcohol *ent*-**34** (1.5 g, 9 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added Et_3N (2.5 mL, 18 mmol), then MsCl (1.4 mL, 18 mmol) was added dropwise over 5 min. The reaction mixture was allowed to stir for 30 min at 0 °C, before the addition of anhyd LiCl (3.8 g, 10 equiv) in dry acetone (25 mL) over 2 min. The reaction mixture was stirred overnight, then quenched with H_2O (20 mL), washed with 2 M aq NaOH (40 mL), and extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried ($MgSO_4$), concentrated under reduced pressure, and purified by column chromatography (pentane) to give the allylic chloride *ent*-**35** (1.27 mg, 76%) as a colorless oil; R_f 0.9 (pentane); IR (cm^{-1}) 2959 s, 2870 s, 1712 w, 1662 m, 1384 m, 1366 m, 1206 s, 1017 w; ^1H NMR (400 MHz) 5.70 (br s, 1 H, CH=C), 4.18 (d, *J* = 11.0 Hz, 1 H, CH_2−Cl), 3.97 (d, *J* = 11.0 Hz, 1 H, CH_2-Cl), 2.49−2.45 (m, 1 H), 2.37−2.22 (m, 1 H), 2.03−1.93 (m, 1 H), 1.82−1.56 (4 H), 1.04 (d, *J* = 6.5 Hz, 3 H, CH*Me*), 0.89 (dd, *J* = 11.0, 6.5 Hz, 6 H, CHMe_2); (100 MHz) 139.2 (C), 131.5 (*C*H=C), 49.0 (CH_2-Cl), 42.4 (*C*H-*i*-Pr), 31.9 (*C*HMe), 29.6 (CH_2), 28.4 (*C*Me_2), 20.4 (CH_2), 19.7 (C*Me*), 19.3 (C*Me*Me), 19.2 (CMe*Me*); HRMS (Cl^+) m/z $[M]^+$ calcd for $C_{11}H_{19}Cl$ 186.1175, found 186.1171.

(*R*)-1-Chloro-4-((3*R*,6*R*)-3-isopropyl-6-methylcyclohex-1-enyl)-butan-2-ol (42). Allylic chloride *ent*-**35** (930 mg, 5 mmol) was reacted according to General Procedure 1 to give unsaturated chlorohydrin **42** (488 mg, 2 mmol, 50%) as a colorless oil; R_f 0.4 (18% ether in light petrol); $[\alpha]^{25}_D$ +32.9 (*c* 2.4, $CHCl_3$); IR (cm^{-1}) 3429 br, 2957 s, 2870 s, 1711 m, 1462 m, 1383 w, 1061 br, 487 w; ^1H NMR (400 MHz) 5.20−5.18 (m, 1 H, C*H*=C), 3.85−3.8 (m, 1 H, C*H*-OH), 3.66 (dd, *J* = 3.5, 1 H, CH_2-Cl), 3.51 (dd, *J* = 11.0, 6.5 Hz, 1 H, CH_2-Cl), 2.2−2.0 (m, 5 H), 1.85−1.95 (m, 1 H, C*H*-*i*-Pr), 1.75−1.45 (m, 4 H, 2 × CH_2), 1.39−1.31 (m, 1 H), 1.26 (s, 1 H), 1.0 (d, *J* = 7.0 Hz, 3 H, CH*Me*), 0.9 (d, *J* = 7.0 Hz, 3 H, CH*Me*Me), 0.85 (d, *J* = 7.0 Hz, 3 H, CHMe*Me*); ^{13}C NMR (100 MHz) 141.8 (C), 125.3 (*C*H=C), 71.6 (*C*H-OH), 50.3 (*C*H_2Cl), 42.2 (*C*H-*i*-Pr), 32.6 (CH_2), 32.2 (CH_2), 31.5 (CH_2), 31.2 (*C*HMe_2), 30.1 (CH_2), 20.5 (CH_2), 19.7 (CMe), 19.6 (C*Me*Me), 19.2 (CMe*Me*); HRMS (CI^+) m/z $[MH]^+$ calcd for $C_{14}H_{26}OCl$ 245.1672, found 245.1683.

(*R*)-2-(2-((3*R*,6*R*)-3-Isopropyl-6-methylcyclohex-1-enyl)ethyl)-oxirane (22). Powdered NaOH (91 mg, 2.4 mmol) was added to a stirred solution of unsaturated chlorohydrin **42** (488 mg, 2.0 mmol) in MeOH (3.5 mL) at 0 °C. The resulting mixture was stirred at rt for 90 min, then diluted with Et_2O (20 mL) and washed with water (20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification of the residue by column chromatography (8% Et_2O in petrol) gave the epoxide **22** (316 mg, 1.52 mmol, 76%) as a colorless oil; R_f 0.4 (8% Et_2O in light petrol); $[\alpha]^{25}_D$ +47.4 (*c* 0.7, $CHCl_3$); IR (cm^{-1}) 3381 br, 3046 w, 2959 s, 2872 m, 1713 w, 1659 m, 1462 m, 1409 m, 1257 w; ^1H NMR (400 MHz) 5.27 (br s, 1 H, C*H*=C), 2.95−2.90 (m, 1 H, C*H*-O), 2.75 (t, *J* = 4.5 Hz, 1 H, CH_2-O), 2.49 (dd, *J* = 4.5, 2.5 Hz, 1 H, CH_2-O), 2.20−2.07 (m, 3 H), 1.93−1.89 (m, 1 H, C*H*Me), 1.71−1.48 (m, 6 H), 1.38−1.22 (m, 1 H, C*H*-*i*-Pr), 1.00 (d, *J* = 7.0 Hz, 3 H, CH*Me*), 0.87 (dd, *J* = 16.5, 6.0 Hz, 6 H, CHMe_2); ^{13}C NMR (100 MHz) 141.5 (C), 124.9 (*C*H=C), 52.3 (*C*H-O), 47.2 (*C*H_2-O), 42.2 (*C*H-*i*-Pr), 32.2 (*C*HMe), 31.6 (CH_2), 31.4 (*C*H-*i*-Pr), 31.2 (CH_2), 30.1 (CH_2), 20.5 (CH_2), 19.7 (C*Me*), 19.6

(C*Me*Me), 19.2 (CMe*Me*); HRMS (CI^+) m/z $[MH]^+$ cald for $C_{14}H_{25}O$ 209.1907, found 209.1905.

(1*R*,4*R*,5*R*,6*R*,7*R*,10*R*)-7-Isopropyl-10-methyltricyclo[4.4.0.0^{1,5}]-decan-4-ol (29). Unsaturated epoxide **22** (707 mg, 3.4 mmol) was subjected to General Procedure 2. The crude product was purified by flash column chromatography (SiO_2, gradient elution, 20−35% Et_2O in light petrol) to give cyclopropyl alcohol **29** (304 mg, 1.74 mmol, 43%) as an orange oil; R_f 0.3 (40% Et_2O in light petrol); $[\alpha]^{25}_D$ −32.0 (*c* 0.6, $CHCl_3$); IR (cm^{-1}) 3326 br, 2953 s, 2870 m, 2360 w, 2341 w, 1457 w, 1382 w, 1057 w, 974 w; ^1H NMR (400 MHz) 4.20 (d, *J* = 4.5 Hz, 1 H, C*H*−OH), 2.12−2.09 (m, 1 H), 1.91−1.89 (m, 1 H), 1.64 (dd, *J* = 12.0, 8.0 Hz, 1 H), 1.54−1.49 (m, 1 H), 1.44−1.30 (m, 6 H), 1.26 (br s, 1 H), 1.17−1.13 (m, 1 H), 0.99 (d, *J* = 6.0 Hz, 3 H), 0.90 (dd, *J* = 4.5 Hz, 6 H, 2 × Me), 0.81−0.76 (m, 2 H); ^{13}C NMR (100 MHz) 75.8 (*C*−OH), 40.6 (*C*H-*i*-Pr), 34.6 (C), 32.7, 31.2 (CH_2), 30.6 (CH_2), 29.9 (CH_2), 28.5, 27.2, 23.8, 21.5 (CH_2), 20.9 (C*Me*), 20.8 (C*Me*Me), 18.5 (CMe*Me*); HRMS (CI^+) m/z $[M]^+$ calcd for $C_{14}H_{24}O$ 208.1827, found 209.1815.

(2*R*,6*R*,8a*R*)-6-Isopropyl-8a-methyl-1,2,3,4,6,7,8,8a-octahydro-naphthalen-2-ol (30). The unsaturated alcohol **30** (282 mg, 40%) was obtained as a major byproduct during the cyclopropanation of epoxide **22**; R_f 0.4 (40% Et_2O in light petrol); $[\alpha]^{26}_D$ + 44.6 (*c* 0.56, $CHCl_3$); IR (cm^{-1}) 3336 br, 2956 s, 2930 s,2870 m, 2360 w, 2341 w, 1463 w, 1384 w, 1045 m; ^1H NMR (500 MHz) 5.23 (s, 1 H, H-5), 3.97−3.91 (m, 1 H, H-2), 2.25 (tt, *J* = 14, 4.5 Hz, 1 H, H-8b), 2.11−2.02 (m, 2 H, H-4a, H-8a), 1.95−1.92 (m, 1 H, H-6), 1.84 (ddd, 1 H, *J* = 12, 4, 2.5 Hz, H-1a), 1.58−1.51 (m, 3 H, H-3b, H-7b, CHMe), 1.40−1.30 (m, 2 H, H-3a, H-7a), 1.27−1.18 (m, 2 H, H-4b, −OH), 1.13−1.09 (m, 1 H, H-1a), 1.05 (s, 3 H, Me), 0.86 (dd, *J* = 15.5, 6.5 Hz, 6 H, CH*Me*$_2$); ^{13}C NMR (125 MHz) 141.2 (C-4a), 124.3 (C-5), 67.6 (C-2), 51.0 (C-1), 42.7 (C-6), 39.6 (C-3), 37.3 (C-4), 35.4 (C-8a), 32.1 (*C*HMe$_2$), 30.9 (C-8), 25.1 (Me), 21.2 (C-7), 19.6 (C*Me*Me), 19.1 (CMe*Me*); HRMS (CI^+) m/z $[MH]^+$ calcd for $C_{14}H_{25}O$ 209.1905, found 209.1909.

4-((3*R*,6*R*)-3-Isopropyl-6-methylcyclohex-1-enyl)butanal (31). The unsaturated aldehyde **31** (10−15%) was obtained as a minor byproduct during the cyclopropanation of epoxide **22**; R_f 0.4 (10% Et_2O in light petrol); IR (cm^{-1}) 3421 br, 2956 s, 2932 s, 2861 m, 1715 w, 1466 w, 1147 m, 949 w; ^1H NMR (400 MHz) 9.77 (s, 1 H, CHO), 5.25 (br s, 1 H, CH=C), 2.44−2.39 (m, 1 H, C=C*H*$_2$), 2.08−2.05 (m, 2 H, CH_2-CHO, CHMe), 1.98−1.90 (m, 2 H, CH_2), 1.84−1.69 (m, 1 H, CH_2), 1.67−1.46 (m, 6 H, CH_2, CHMe$_2$), 1.22−1.21 (m, 1 H, CH-*i*-Pr), 0.99 (d, *J* = 7.0 Hz, 3 H, CHMe), 0.88 (d, *J* = 7.0 Hz, 3 H, CH*Me*Me), 0.84 (d, *J* = 7.0 Hz, 3 H, CHMe*Me*); ^{13}C NMR (100 MHz) 202.9 (C=O), 141.3 (C), 125.7 (*C*H=C), 43.5 (CH_2), 42.2 (CH-*i*-Pr), 34.7 (=C-CH_2), 32.2 (*C*H-Me), 30.9 (*C*HMe$_2$), 30.1 (CH_2), 20.5 (2 × CH_2), 19.7 (C*Me*), 19.6 (C*Me*Me), 19.2 (CMe*Me*); HRMS (CI^+) m/z $[MH]^+$ calcd for $C_{14}H_{25}O$ 209.1905, found 209.1898.

(1*R*,5*R*,6*R*,7*R*,10*R*)-7-Isopropyl-10-methyltricyclo[4.4.0.0^{1,5}]-decan-4-one (32). Following General Procedure 5, cyclopropyl alcohol **29** (256 mg, 1.23 mmol) gave ketone **32** (240 mg, 95%) as a colorless oil; R_f 0.4 (25% Et_2O in light petrol); $[\alpha]^{25}_D$ −46.4 (*c* 1.5, $CHCl_3$); IR (cm^{-1}) 2955 m, 2928 m, 2870 w, 1721 s, 1460 w, 1322 w, 1220 w,1043 w; ^1H NMR (400 MHz) 2.16−1.97 (m, 5 H), 1.67−1.64 (m, 1 H), 1.57 (d, *J* = 3.0 Hz, 1 H), 1.51−1.42 (m, 3 H), 1.41−1.35 (1 H), 1.21−1.18 (m, 1 H), 0.94 (d, *J* = 6.5 Hz, 3 H, Me), 0.89 (dd, *J* = 10, 6.5 Hz, 6 H, 2 × Me), 0.75−0.73 (m, 1 H); ^{13}C NMR (100 MHz) 215.3 (C-4), 41.0 (C-7), 40.5 (C-1), 33.3 (C-5), 33.1 (C-3), 32.4 (C-11), 32.3 (C-6), 29.4 (C-10), 29.1 (C-9), 28.8 (C-2), 21.1 (C-8), 20.7 (C*Me*), 20.6 (C*Me*Me), 18.2 (CMe*Me*); HRMS (CI^+) m/z $[M]^+$ calcd for $C_{14}H_{22}O$ 206.1671, found 206.1669.

(1*R*,4*S*,5*R*,6*R*,7*R*,10*R*)-7-Isopropyl-4,10-dimethyltricyclo-[4.4.0.0^{1,5}]decan-4-ol (33) [(−)-7-Epicubebol]. Anhyd $CeCl_3$ (493 mg, 2.0 mmol) was obtained by dehydrating $CeCl_3 \cdot 7H_2O$ (745 mg, 2 mmol) under high vacuum (< 0.1 mbar) at 165 °C (oil bath) for 2 h.[41] To this anhyd $CeCl_3$ was added THF (10 mL) and the suspension was stirred for 2 h at rt. MeLi (1.6 M in Et_2O, 1.25 mL, 2 mmol) was then added to the above suspension at −78 °C, followed after 30 min by a solution of ketone **32** (206 mg, 1.0 mmol) in THF (7 mL) over 10 min. After 90 min, the reaction was quenched with aq NH_4Cl (3 mL) and then warmed to rt. The reaction mixture was extracted with Et_2O (2 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. Purification by column chromatography (20% Et_2O in light petrol) gave the crystalline white solid, alcohol **33** (191 mg, 86%); R_f 0.4 (25% Et_2O in light petrol); mp 87−89 °C; $[\alpha]^{25}_D$ −9.8 (*c* 0.6, $CHCl_3$); IR (cm^{-1}) 3273 br, 2953 s, 2916 s, 2877 m, 2850 m, 1460 w, 1370 w, 1299 w, 1199 w, 1149 w; ^1H NMR (400 MHz) 1.95−1.89 (m, 1 H, H-10), 1.74−1.64 (m, 2 H, H-2a, H-3a), 1.56−1.49 (m, 2 H, H-9), 1.41−1.32 (m, 8 H, H-8a, H-2b, H-3b, H-11, H-5, H-15), 1.21 (t, *J* = 3.5 Hz, 1 H, H-6), 1.14−1.10 (m, 1 H, H-8b), 1.02 (d, *J* = 6.5 Hz, 3 H, Me), 0.93−0.91 (m, 4 H, H-7, C*Me*Me), 0.84 (d, *J* = 7.0 Hz, 3 H, CMe*Me*), 0.78−0.71 (m, 1 H, H-6); ^{13}C NMR (100 MHz) 80.2 (C-4), 40.6 (C-5), 35.9 (C-3), 33.7 (C-1), 32.6 (C-11), 31.7 (C-7), 31.6 (C-2), 29.9 (C-9), 28.4 (C-15), 28.2 (C-10), 21.9 (C-6), 21.3 (C-8), 21.0 (CH*Me*), 20.7 (CH*Me*Me), 18.0 (CHMe*Me*); HRMS (CI^+) m/z $[MH]^+$ calcd for $C_{15}H_{27}O$ 223.2062, found 223.2052.

(*S*)-1-Chloro-4-((3*R*,6*R*)-3-Isopropyl-6-methylcyclohex-1-enyl)-butan-2-ol (*ent*-36). Allylic chloride *ent*-**35** (1.12 g, 6.0 mmol) was subjected to General Procedure 1 to give unsaturated chlorohydrin *ent*-**36** (585 mg, 50%) as a colorless oil; R_f 0.4 (18% Et_2O in light petrol); $[\alpha]^{25}_D$ +40.0 (*c* 0.5, $CHCl_3$); IR (cm^{-1}) 3390 br, 2957 s, 2933 s, 2871 m, 1731 m, 1464 w, 1384 w, 1366 w, 1167 w, 1106 w, 1150 w,740 w; ^1H NMR (400 MHz) 5.28 (br s, 1 H, C*H*=C), 3.79−3.73 (m, 1 H, C*H*OH), 3.64−3.60 (m, 1 H, C*H*$_2$-Cl), 3.51−3.46 (m, 1 H, C*H*$_2$-Cl), 2.33 (br s, I H, −O*H*), 2.19−2.11 (m, 1 H, C*H*$_2$-CHOH), 2.07−2.03 (m, 2 H, C*H*Me, =C-C*H*$_2$), 1.94−1.86 (m, 1 H, C*H*-*i*-Pr), 1.71−1.44 (m, 5 H, C*H*Me$_2$, 2 × CH_2), 1.37−1.29 (m, 2 H), 0.99 (d, *J* = 7.0, 3 H, CH*Me*), 0.85 (d, *J* = 7.0, 3 H, CH*Me*Me), 0.82 (d, *J* = 7.0, 3 H, CHMe*Me*); ^{13}C NMR (100 MHz) 141.5 (C), 125.4 (*C*H=C), 71.0 (*C*HOH), 50.5 (*C*H$_2$-Cl), 42.2 (*C*H-*i*-Pr), 32.4 (*C*HMe), 32.2 (*C*H$_2$-CHOH), 31.1 (CH_2), 30.9 (*C*Me$_2$), 30.1 (CH_2), 20.5 (CH_2), 19.7 (C*Me*), 19.5 (C*Me*Me), 19.2 (CMe*Me*); HRMS (CI^+) m/z $[MH]^+$ calcd for $C_{14}H_{26}OCl$ 245.1672, found 245.1662.

(*S*)-2-(2-((3*R*,6*R*)-3-Isopropyl-6-methylcyclohex-1-enyl)ethyl)-oxirane (23). To a stirred solution of unsaturated chlorohydrin *ent*-**36** (585 mg, 2.4 mmol) in MeOH (3 mL) at 0 °C was added powdered NaOH (115 mg, 2.9 mmol). The resulting mixture was stirred at rt for 90 min, then diluted with Et_2O (25 mL) and washed with water (30 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification of the residue by column chromatography (8% Et_2O in light petrol) gave the epoxide **23** (383 mg, 1.84 mmol, 77%) as a colorless oil; R_f 0.4 (8% Et_2O in light petrol); $[\alpha]_D^{25}$ +33.7 (*c* 1.0, $CHCl_3$); IR (cm^{-1}) 3042 w, 2957 s, 2934 s, 2870 m, 1663 w, 1384 w, 1365 w, 774 w; ^1H NMR (400 MHz) 5.27 (br s, 1 H, C*H*=C), 2.93−2.88 (m, 1 H, C*H*-O), 2.73 (t, *J* = 4.5 Hz, 1 H, C*H*$_2$-O), 2.46 (dd, *J* = 5.0, 3.9 Hz, 1 H, C*H*$_2$-O), 2.20−2.04 (m, 3 H, C*H*Me, CH_2), 1.92−1.85 (m, 1 H, C*H*-*i*-Pr), 1.67−1.57 (m, 3 H, C*H*$_2$-CH-*i*-Pr, C*H*$_2$-CH-O), 1.55−1.45 (m, 3 H, C*H*Me$_2$, C*H*$_2$-CHMe), 1.39−1.28 (m, 1 H, C*H*$_2$), 0.99 (d, *J* = 7.0 Hz, 3 H, CH*Me*), 0.87 (d, *J* = 6.5 Hz, 3 H, CH*Me*$_2$), 0.83 (d, *J* = 7.0 Hz, 3 H, CH*Me*$_2$); ^{13}C NMR (100 MHz) 141.3 (C), 125.1 (*C*H=C), 52.1 (*C*H-O), 47.3 (*C*H$_2$-O), 42.2 (*C*H-*i*-Pr), 32.2 (*C*HMe), 31.5 (=C-*C*H$_2$), 31.1 (*C*HMe$_2$), 31.0 (CH_2), 30.1 (CH_2), 20.5 (CH_2), 19.7 (C*Me*), 19.5 (C*Me*Me), 19.2 (CMe*Me*); HRMS (CI^+) m/z $[MH]^+$ calcd for $C_{14}H_{25}O$ 209.1905, found 209.1905.

(1*S*,4*S*,5*S*,6*S*,7*R*,10*R*)-7-Isopropyl-10-methyltricyclo[4.4.0.0^{1,5}]-decan-4-ol (*ent*-37). Unsaturated epoxide **23** (304 mg, 1.46 mmol) was reacted according to General Procedure 2. The crude product

was purified by flash column chromatography (SiO_2, gradient elution, 20−35% Et_2O−petrol) to give cyclopropyl alcohol *ent*-**37** (270 mg, 89%) as a colorless oil; R_f 0.4 (40% Et_2O in light petrol); $[\alpha]^{25}_D$ +25.5 (*c* 3.0, $CHCl_3$); IR(cm^{-1}) 3350 br, 2974 s, 2851 s, 1470 m, 1385 m, 1264 w, 1072 w, 906 w, 740 m; ^1H NMR (400 MHz) 4.23 (d, *J* = 4.5 Hz, 1 H, H-4), 2.11−2.06 (m, 1 H, H-10), 1.82−1.74 (m, 1 H, H-2a), 1.65−1.60 (m, 1 H, H-9a), 1.58−1.50 (m, 2 H, H-3a, H-11), 1.42−1.23 (m, 4 H, H-3b, H-7, H-2b, H-8a), 1.20−1.13 (m, 1 H, H-9b), 1.11−1.08 (m, 1 H, H-8b), 1.04 (d, *J* = 7.0 Hz, 3 H, CH*Me*), 0.99 (d, *J* = 2.5 Hz, 1 H, H-5), 0.89 (d, *J* = 7.0 Hz, 3 H, CH*Me*Me), 0.86 (d, *J* = 7.0 Hz, 3 H, CHMe*Me*), 0.29 (br s, 1H, H-6); ^{13}C NMR (100 MHz) 75.3 (C-4), 42.4 (C-7), 37.5 (C-10), 33.9 (C-1), 33.6 (C-5), 31.6 (C-3), 29.9 (C-9), 29.3 (C-2), 29.3 (C-11), 22.6 (C-6), 19.8 (C-8), 19.7 (C*Me*Me), 19.2 (CMe*Me*), 18.6 (C*Me*); HRMS (CI^+) *m*/*z* $[M - OH]^+$ calcd for $C_{14}H_{23}$ 191.1800, found 191.1808.

From epoxide **23** (244 mg, 1 mmol), following General Procedure 3, the cyclopropyl alcohol *ent*-**37** was also prepared in 87% yield.

Synthesis of (−)-10-Epicubebol (39). (2*R*,5*S*)-2-Isopropyl-5-methylcyclohexanone (*ent*-11). *d*-Menthol (5.0 g, 32.0 mmol) was dissolved in MeCN:AcOH (3:2, 42 mL) and added dropwise over a period of 30 min to a cooled (0 °C) and stirred solution of calcium hypochlorite (4.0 g, 28.0 mmol) in water (65 mL). The stirring was continued for 3 h, and then water (65 mL) was added in one portion. The reaction mixture was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic layers were washed with 10% aq $NaHCO_3$ (2 × 50 mL), dried ($MgSO_4$), and concentrated under reduced pressure to give *d*-menthone (*ent*-**11**) (4.8 g, 97%) as a colorless oil; R_f 0.4 (4% ether in petrol); $[\alpha]_D^{25}$ +29.4 (*c* 0.4, $CHCl_3$) (lit.[42] $[\alpha]^{20}_D$ +19.0 (*c* 10.0, EtOH)). Other data as *l*-menthone **11**, see above.

(3*S*,6*R*,*Z*)-2-(Hydroxymethylene)-6-Isopropyl-3-methylcyclohexanone (*ent*-28). A solution of ethyl formate (7.1 g, 96.0 mmol) in toluene (15 mL) was added to a vigorously stirred cooled (0 °C) solution of NaOMe (5.2 g, 96.0 mmol) in dry toluene (30 mL) over a period of 1 h. A solution of *d*-menthone (*ent*-**11**) (5.0 g, 32.0 mmol) in a 1:3 toluene−THF mixture (20 mL) was added dropwise to the above cooled solution over 1 h. The solution was allowed to warm to room temperature and then stirring was continued for 72 h. The solution was neutralized with ice-cooled 15% (w/v) H_2SO_4, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under vacuum and distilled (15 mbar, 125 °C) to give a yellow oil hydroxymethylene ketone *ent*-**28** (5.0 g, 84%, 93:7 cis:trans by ^1H NMR analysis of signals of =C*H*); $[\alpha]^{25}_D$ +9.0 (*c* 1.9, $CHCl_3$); other data as **28**.

(3*S*,6*R*)-6-Isopropyl-3-methyl-2-methylenecyclohexanol (34). Hydroxymethylene ketone *ent*-**28** (5.0 g, 27 mmol) was added dropwise to a stirred solution of $LiAlH_4$ (2 g, 54 mmol), in dry Et_2O (160 mL) at rt. The solution was heated to gentle reflux overnight and then cooled and carefully quenched with 20% aq $NaHCO_3$. The organic phase was extracted with Et_2O (4 × 50 mL), dried (Na_2SO_4), and evaporated under reduced pressure. Purification of the residue by column chromatography gave the allylic alcohol **34** (1.47 g, 32%) as a colorless oil; $[\alpha]^{25}_D$ +6.1 (*c* 0.3, $CHCl_3$); other data as *ent*-**34**.

(3*R*,6*S*)-1-(Chloromethyl)-3-isopropyl-6-methylcyclohex-1-ene (35). To a stirred solution of allylic alcohol **34** (1.0 g, 6 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added Et_3N (1.7 mL, 12 mmol), then MsCl (0.94 mL, 12 mmol) dropwise over 5 min. The reaction mixture was then stirred for 30 min at 0 °C, before addition of anhyd LiCl (2.6 g, 10 equiv) in dry acetone (25 mL) over 2 min. The reaction mixture was stirred overnight and then quenched with 20 mL of H_2O, washed with 2 M aq NaOH (35 mL), and extracted with CH_2Cl_2 (3 × 60 mL). The combined organic layers were dried under reduced pressure and purified by column chromatography (pentane) to give the allylic chloride **35** as a colorless oil (815 mg, 76%); other data as *ent*-**35**.

(*R*)-1-Chloro-4-((3*S*,6*S*)-3-isopropyl-6-methylcyclohex-1-enyl)-butan-2-ol (36). Allylic chloride **35** (1.1 g, 5.94 mmol) was reacted according to General Procedure 1 to give the unsaturated chlorohydrin **36** (568 mg, 49%) as a colorless oil; $[\alpha]^{25}_D$ −38.1 (*c* 0.6, $CHCl_3$); other data as *ent*-**36**.

(1*R*,4*R*,5*R*,6*R*,7*S*,10*R*)-7-Isopropyl-10-methyltricyclo[4.4.0.0^{1,5}]-decan-4-ol (37). Unsaturated chlorohydrin **36** (427 mg, 1.75 mmol) was reacted according to General Procedure 4. The crude product was purified by flash column chromatography (SiO_2, gradient elution, 20−35% Et_2O in light petrol) to give cyclopropyl alcohol **37** (302 mg, 83%) as a colorless oil; $[\alpha]^{25}_D$ −28.8 (*c* 1.9, $CHCl_3$); other data as *ent*-**37**.

(1*R*,5*R*,6*R*,7*S*,10*R*)-7-Isopropyl-10-methyltricyclo[4.4.0.0^{1,5}]-decan-4-one (38). Following General Procedure 5, the cyclopropyl alcohol **37** (187 mg, 0.9 mmol) gave ketone **38** (178 mg, 96%) as a colorless oil; R_f 0.4 (25% Et_2O in light petrol); $[\alpha]^{25}_D$ +7.76 (*c* 1.0, $CHCl_3$); IR (cm^{-1}) 2956 s, 2929 s, 2872 m, 1719 s, 1459 w, 1387 w, 1248 w, 1185 m, 936 w; ^1H NMR (400 MHz) 2.16−2.07 (m, 2 H, H-10, H-3a), 2.05−1.97 (m, 2 H, H-3b, H-9a), 1.90−1.82 (m, 1 H, H-2a), 1.68−1.60 (m, 1 H, H-11), 1.56 (d, *J* = 2.0 Hz, 1 H, H-5), 1.43−1.36 (m, 2 H, H-9b, H-8a), 1.26−1.15 (m, 4 H, H-8b, H-7, H-2b, H-6), 1.07−1.05 (m, 3 H, H-14), 0.93−0.89 (m, 6 H, CH*Me*$_2$); ^{13}C NMR (100 MHz) 214.6 (C-4), 42.1 (C-7), 41.5 (C-5), 39.6 (C-1), 33.3 (C-11), 33.3 (C-3), 30.9 (C-6), 29.1 (C-10), 28.2 (C-9), 28.1 (C-2), 19.6 (C*Me*Me), 19.1 (C-8), 18.9 (CMe*Me*), 16.5 (C*Me*); HRMS (CI^+) *m*/*z* $[M]^+$ calcd for $C_{14}H_{22}O$ 206.1671, found 206.1680.

(1*R*,4*S*,5*R*,6*R*,7*S*,10*S*)-7-Isopropyl-4,10-dimethyltricyclo-[4.4.0.0^{1,5}]decan-4-ol (39) [(−)-10-Epicubebol]. Anhyd $CeCl_3$ (333 mg, 1.35 mmol) was obtained by dehydrating $CeCl_3 \cdot 7H_2O$ (503 mg, 1.35 mmol) under high vacuum (< 0.1 mbar) at 165 °C (oil bath) for 2 h.[41] To this anhyd $CeCl_3$ was added THF (7 mL) and the suspension was stirred for 2 h at rt. MeLi (1.6 M in Et_2O, 0.85 mL, 1.35 mmol) was then added to the above suspension at −78 °C, followed after 30 min by a solution of ketone **38** (140 mg, 0.67 mmol) in THF (2 mL) over 20 min. After 90 min, the reaction was quenched with aq NH_4Cl (3 mL) and then warmed to rt. The reaction mixture was extracted with Et_2O (2 × 15 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Purification by column chromatography (20% Et_2O in light petrol) gave the (−)-10-epicubebol (**39**) (130 mg, 86%) as a white solid, mp 99−100 °C (lit.[37a] mp 100 °C); $[\alpha]^{25}_D$ −64.6 (*c* 0.175, $CHCl_3$) (lit.[37a] $[\alpha]^{25}_D$ −72.3 (*c* 3.3, $CHCl_3$)); IR (cm^{-1}) 3390 br, 2956 s, 2935 s, 2862 w, 1447 w, 1368 w, 1320 w, 1193 w, 1151 w, 946 w, 931 w; ^1H NMR (500 MHz) 1.96−1.90 (m, 1 H, H-10), 1.76−1.71 (m, 1 H, H-3a), 1.68−1.59 (oct, 1 H, H-11), 1.56−1.49 (m, 2 H, H-9a, H-3b), 1.45 (br s, −OH), 1.36−1.31 (m, 2 H, H-9b, H-2a), 1.27 (d, *J* = 1.0 Hz, 3 H, H-15), 1.26−1.13 (m, 3 H, H-2b, H-8a, H-8b), 1.9−1.04 (m, 1 H, H-5), 0.98 (d, *J* = 7.0 Hz, 3 H, CH*Me*), 0.95 (d, *J* = 6.5 Hz, 3 H, CH*Me*Me), 0.93−0.91 (m, 1 H, H-7), 0.92 (d, *J* = 6.5 Hz, 3 H, CHMe*Me*), 0.77 (t, *J* = 3.0 Hz, 1 H, H-6); ^{13}C NMR (125 MHz) 80.1 (C-4), 42.4 (C-7), 41.1 (C-5), 36.5 (C-3), 33.7 (C-11), 32.8 (C-1), 30.8 (C-9), 29.3 (C-2), 29.3 (C-10), 28.0 (C-15), 20.7 (C-6), 19.9 (C*Me*Me), 19.7 (C-8), 19.2 (CMe*Me*), 17.4 (C*Me*); HRMS (CI^+) *m*/*z* $[M - OH]^+$ calcd for $C_{15}H_{25}$ 205.1956, found 205.1962.

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Supporting Information Available: General experimental details, additional reactions schemes, a comparison of synthetic and natural product spectroscopic data for **39**, X-ray data, calculated transition states energies and coordinates, and ^{1}H and ^{13}C NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.