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Regio- and Stereoselective Functionalization of Deltacyclenes: A Route to the Synthesis of Optically Active (+)-Deltacyclan-8-one

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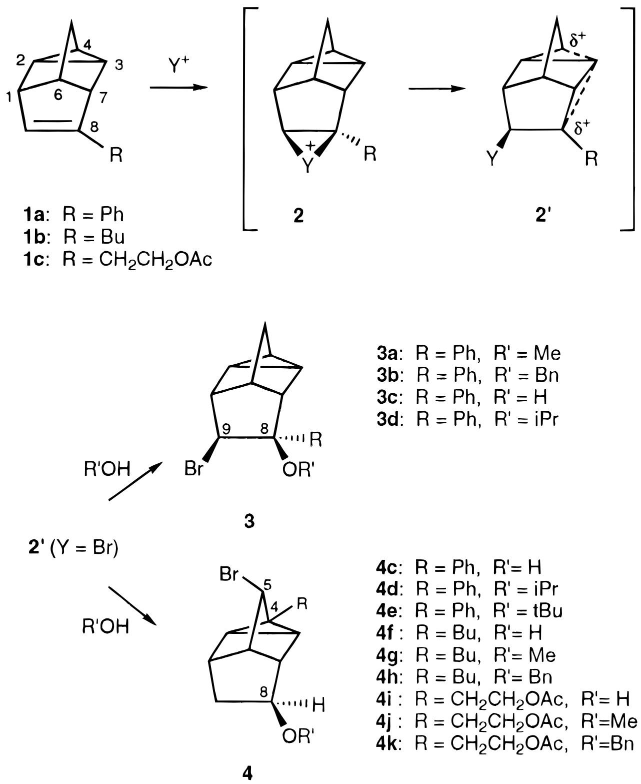
Due to their unique highly strained tetracyclic skeleton, deltacyclanes, which are readily available in a single step by the homo Diels−Alder (HDA) reaction[1] of norbornadiene and electron-deficient alkenes, have been used as synthetically valuable precursors for the synthesis of brexane and brendane derivatives.[2] They are also interesting substrates for mechanistic studies.[3] We have recently shown that brendane derivatives can be easily transformed to the trifunctionalized diquinane framework with high control of five stereogenic centers.[4]

Synthesis of functionalized deltacyclanes occurs with low stereoselectivity.[5] However, in the metal-catalyzed version of these HDA reactions,[6] higher stereoselectivity can be achieved depending on the functionality of the dienophile and the catalytic system involved. We recently reported a Co/Zn-mediated synthesis of functionalized deltacyclenes and an enantioselective reaction which affords up to 96% ee when (*S*)-(+)-ValNOP[7] is used as ligand.[6n] We describe now the direct and stereocontrolled functionalization of 8-substituted deltacyclenes **1** via an electrophilic activation leading to 8,9- or 5,8-difunctionalized deltacyclanes, i.e., **3** or **4**.

Scheme 1. Reaction of 8-Alkyldeltacyclenes with NBS and Protic Species



Carbonium ion rearrangements are frequently observed in the deltacyclane ring system, especially when *exo*-8-substituted deltacyclanes are solvolyzed.[3b] We became interested in exploiting the direct functionalization of 8-alkyl deltacyclenes **1** via deltacyclylcarbonium ion **2**. This could be a route to the stereoselectively substituted deltacyclanes. Previous reports on disubstituted deltacyclanes involve acid-promoted ring-opening of the very sensitive deltacyclene epoxides with hydrobromic acid,[8ab] acetic acid,[8b] or methanol in the presence of $BF_3{\cdot}OEt_2$.[8c] We chose deltacyclenes **1a**−**c** as starting materials since (i) these compounds are readily available from the cobalt-catalyzed [2 + 2 + 2] cycloaddition reaction of norbornadiene and 1-alkynes,[6g−j] circumventing the problem of stereoisomers, (ii) electrophilic addition of an onium species Y^+ to 8-alkyl (or aryl) deltacyclene can generate primarily a tertiary carbonium ion which is expected to delocalize to a deltacyclyl carbonium ion **2′** with positive charge spread largely between the C(4) and C(8) carbon atoms, and (iii) these highly reactive intermediates could be trapped with an appropriate nucleophile to afford the *syn*-8,9-difunctionalized **3** and/or 5,8-difunctionalized **4** deltacyclane derivatives according to the nature of the nucleophile and the charge delocalization in **2′** (Scheme 1).

Firstly, the reaction of 8-phenyldeltacyclene **(1a)** was examined with *N*-bromosuccinimide (NBS, 1 equiv) as a bromonium ion source together with alcohols (2−3 equiv)

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Table 1. Reaction of 8-Phenyldeltacyclene (1a) with NBS/R′OH[a]

entry	R′	reaction condns	product(s) (ratio)[b]	yield[c] (%)
1	Me	CH_3CN, 5 min	**3a**	85
2	Bn	CH_3CN, 5 min	**3b**	60
3	H	CH_3CN, 5 min	**3c**:**4c** (49:51)	88
4	H	$(CH_3)_2CO$, 5 min	**3c**:**4c** (47:53)	81
5	iPr	CH_3CN, 5 min	**3d**:**4d** (33:67)	76
6	tBu	CH_3CN, 5 min	**4e**	58

[a] All reactions were performed at 0 °C. [b] Ratio determined on the crude mixture by ^1H NMR integration of signals of H(9) and H(8) for compounds **3** and **4**, respectively. [c] Isolated yield.

Table 2. Reaction of 8-Alkyldeltacyclenes 1b and 1c with NBS/R′OH[a]

deltacyclene	reaction condns	R′	product	yield[b] (%)
1b	$(CH_3)_2CO$, 50 min	H	**4f**	73
	dioxane, 2 h	H	**4f**	40
	CH_3CN, 2 h	Me	**4g**	54
	CH_3CN, 2 h	Bn	**4h**	55
	$(CH_3)_2CO$, 5 min	*i*-Pr	**5b**	51
	CH_3CN, 5 min	*i*-Pr	**5b**	54
	$(CH_3)_2CO$, 5 min	*t*-Bu	**5b**	51
	CH_3CN, 5 min	*t*-Bu	**5b**	53
1c	CH_3CN, 5 min	H	**4i**	62
	dioxane, 2 h	H	**4i**	58
	CH_3CN, 10 min	Me	**4j**	80
	CH_3CN, 10 min	Bn	**4k**	57
	CH_3CN, 5 min	*i*-Pr	**5c**	52

[a] All reactions were performed at 0 °C. [b] Isolated yield.

or water (20 equiv) as nucleophiles. The reaction occurs readily in acetonitrile at temperatures between −20 and +20 °C, but were preferably performed at 0 °C (Table 1). Acetonitrile can be replaced by acetone without any significant differences (entries 3 and 4). Primary alcohols selectively afford sterically congested products of type **3**, whereas water or 2-propanol give a mixture of the tetracyclic isomers **3** and **4**. The bulkier 2-methyl-2-propanol affords only rearranged deltacyclane of type **4**. These results show that stabilization of the tertiary benzylic carbonium ion followed by nucleophilic attack competes efficiently with the transposition process and that the outcome of the reaction highly depends on nucleophilicity and/or steric demand of the protic species (entry 5 and 6). For instance, 2-methyl-2-propanol attacks exclusively in position 4 (Scheme 1) to produce **4e** due to severe steric interaction in *syn* periplanar attack with respect to the C−Br bond in the 8 position. In the reaction of **1a** with NBS and water, it is not clear at that time why water led to rearranged product **4c**.[9]

The reaction of 8-alkyldeltacyclenes **1b** or **1c** with NBS in the presence of alcohol (2−3 equiv) affords compounds **4** selectively as a single diastereomer (Table 2). Satisfactory yields are obtained with primary alcohols or a poor nucleophile such as water which is able to produce 4-alkyl-5-bromodeltacyclan-8-ols **4f** or **4i**. In sharp contrast to the reaction of **1a**, secondary or tertiary alcohols are not able to trap the intermediate deltacyclyl ion **2b′** or **2c′** efficiently, which in these cases readily releases a proton to give the highly sensitive allylic bromides **5b** and **5c**, in 54% and 52% yield, respectively, as a 1:1 mixture (determined by ^1H NMR) of *E* and *Z* stereomers. Ozonolysis affords subsequently the *exo*-9-bromodeltacyclan-8-one (**6a**).

Allylic bromides **5b** and **5c** have been detected as byproducts (<5%) in the reactions involving deltacyclenes **1b** and **1c**. They are also directly obtained in fair yields when **1b** or **1c** are reacted with NBS in the absence of nucleophiles.

Scheme 2

5b: R = Pr
5c: R = CH_2OAc

6a: X = Br
6b: X = H

We assume that 9-bromodeltacyclic ion **2′** (Y = Br) is trapped efficiently at C-8 with nucleophiles with low steric demand, even with water. Since these bromo ethers (or alcohols) are obtained as a single stereoisomer, the mechanism depicted in Scheme 1 parallels the one proposed for the acid-promoted ring opening of deltacyclene epoxides with carboxylic or hydrobromic acid.[8] Efficient trapping of the secondary carbocation centers (C-4) instead of the tertiary ones (C-8) suggests a process under kinetic control.

The *exo* orientation of the alkoxy group in bromo ethers and bromo alcohols **4** was assigned on the basis of the coupling constant of *endo* H-8 as a doublet of doublets ($J_{8-9x} \sim 2.2-2.5$ Hz, $J_{8-9n} \sim 6.8$ Hz) whereas H-9 appears with $J_{gem} \sim 13.2-13.6$ Hz, in agreement with those reported for related cycloadducts.[6c] Structural determination for compound **3c** was established by X−H COORD, COSY, and HMBC experiments, and the syn relationship between Br and the hydroxyl group was secured by NOESY experiment.

As an extension of this study, we have investigated a short route to optically active (+)-deltacyclan-8-one (**6b***)[1b,2b,3a] from (+)-*n*-butyldeltacyclene (**1b***) (ee 97.0 ± 0.3%)[6n] whose absolute configuration has been assigned using the Mosher correlations of the MPTA derivatives. Oxidation of **1b*** with NBS (CH_3CN, 0 °C, 5 min) afforded allylic bromide **5b*** (as a 1:1 mixture of *E* and *Z* stereoisomers) which was converted to the single bromoketone **6a*** upon ozonolysis (O_3, CH_2Cl_2, −78 °C then Me_2S) in 55% overall yield from **1b***. Reductive debromination (Zn, HOAc, reflux, 5 h, 93%) of **6a*** leads to (+)-deltacyclan-8-one (**6b***) with 97.1 ± 0.3% ee[10] whose (1*R*,2*R*,3*R*,4*R*,6*S*,7*R*) absolute configuration was attributed. This assignment is in agreeement with the one reported by Nakazaki,[11] based on the positive Cotton Effect and correlations with related compounds. This is the first practical enantioselective synthesis of the tetracyclic ketone **6b** which was accomplished in four steps from norbornadiene with an overall yield of 41%.

Experimental Section

General. All solvents and reagents were purchased from commercial sources and were used without purification unless otherwise indicated. See also ref 6n.

NBS-Promoted Functionalization of Deltacyclenes: General Procedure. To a cooled (0 °C) suspension of $CaCO_3$ (100 mg, 1 mmol), deltacyclene **1** (1 mmol), and water (20 mmol, 360

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[9] This results perhaps that water is extensively hydrogen bonded and acts as a "large" nucleophile, as suggested by a reviewer.

[10] Determined by GC analysis with a 25 m 2,4,6-perpentyled γ-cyclodextrin column (Lipodex E); 75 °C, carrier gas: He, pressure 1.7 bar, $t_{R(-)} = 78.9$ min, $t_{R(+)} = 79.9$ min; the major enantiomer of **6b** depicted in Scheme 2, which was eluted in second position, displays a positive rotatory power.

[11] (−)-Deltacyclan-8-one (**6b**) was previously obtained by partial resolution from its morpholiminium perchlorate salt, see ref 3b, or kinetic resolution using reduction with microorganisms: Nakazaki, M.; Chikamatzu, H.; Fujii, T.; Nakatsuji, T. *J. Org. Chem.* **1981**, *46*, 585.

μL) or alcohol (2−3 mmol) in CH_3CN (6 mL) was added NBS (178 mg, 1 mmol) portionwise. The mixture was stirred at 0 °C for a period of time indicated in Table 1 or 2, filtered through a Celite pad, and concentrated in vacuo. The crude product was purified by medium pressure liquid chromatography (MPLC) on a silica gel column.

(1*S,2*S**,3*R**,4*S**,6*R**,7*R**,8*R**,9*S**)-8-Phenyl-9-bromo-8-methoxytetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (3a)** was obtained by MPLC (petroleum ether/ether 99/1) as a white solid: yield 85%; mp 41−42 °C; IR (neat) ν 3060, 2940, 2870, 2830, 1495, 1450, 1350, 1300, 1265, 1185, 1160, 1085, 1060, 950, 910, 890, 825, 800, 765, 730, 705 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.85 (m, 1H), 0.98 (m, 1H), 1.32 (m, 1H), 1.62 (br s, 2H), 2.39 (t, J = 1.9 Hz, 1H), 2.58 (br s, $w/2$ = 6.1 Hz, 1H), 2.69 (m, 1H), 2.91 (s, 3H), 4.67 (s, 1H), 7.34 (m, 3H), 7.47 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 12.58, 16.57, 16.67, 30.98, 38.66, 49.68, 52.03, 53.41, 61.69, 86.84, 126.68, 127.91 (two CH), 128.18 (two CH), 140.27. Anal. Calcd for $C_{16}H_{17}BrO$: C, 62.96; H, 5.61. Found: C, 62.62; H, 5.57.

(1*S,2*S**,3*R**,4*S**,6*R**,7*R**,8*R**,9*S**)-8-Phenyl-9-bromo-8-(benzyloxy)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (3b)** was obtained by MPLC (petroleum ether/ether 99/1) as a white solid: yield 60%; mp 79−80 °C; IR (neat) ν 3065, 3040, 2940, 2870, 1950, 1875, 1810, 1750, 1600, 1495, 1380, 1300, 1265, 1215, 1190, 1160, 1090, 1030, 945, 910, 840, 825, 800, 775, 750, 735, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (m, 1H), 1.02 (m, 1H), 1.34 (m, 1H), 1.62 (br s, 2H), 2.44 (br s, 1H), 2.69 (br s, 1H), 2.77 (br s, 1H), 4.13 (s, 2H), 4.76 (br s, 1H), 7.27 (m, 7H), 7.58 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 12.70, 16.68, 16.84, 31.04, 38.93, 50.54, 53.54, 62.06, 65.74, 86.77, 126.61 (two CH), 126.69, 127.87, 127.90 (two CH), 128.09 (two CH), 128.28 (two CH), 139.20, 140.66. Anal. Calcd for $C_{22}H_{21}BrO$: C, 69.30; H, 5.55. Found: C, 69.22; H, 5.57.

(1*S,2*S**,3*R**,4*S**,6*R**,7*R**,8*R**,9*S**)-8-Phenyl-9-bromotetracyclo [4.3.0.0^{2,4}.0^{3,7}]nonan-8-ol (3c)** was obtained by MPLC (petroleum ether/ether 95/5) as a colorless oil: yield 43%; IR (neat) ν 3540, 3065, 2950, 2870, 1600, 1495, 1445, 1300, 1280, 1265, 1250, 1185, 1160, 1070, 1035, 1000, 990, 965, 910, 890, 830, 800, 770, 760, 730, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.86 (m, 1H), 1.13 (m, 1H), 1.39 (m, 1H), 1.62 (br s, 2H), 2.43 (m, w/2 = 8.4 Hz, 2H), 2.55 (br, 1H, OH), 2.66 (br s, 1H), 4.92 (s, 1H), 7.30 (m, 3H), 7.54 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 12.15, 16.28, 16.95, 30.99, 40.09, 53.16, 55.25, 65.19, 81.68, 126.07, 127.40 (two CH), 128.19 (two CH), 143.67. Anal. Calcd for $C_{15}H_{15}BrO$: C, 61.87; H, 5.19. Found: C, 61.49; H, 5.17.

(1*S,2*S**,3*R**,4*S**,6*R**,7*R**,8*R**,9*S**)-8-Phenyl-9-bromo-8-(isopropyloxy)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (3d)** was obtained by MPLC (petroleum ether/ether 98/2) as a colorless oil: yield 25%; IR (neat) ν 3060, 2968, 2866, 1959, 1886, 1812, 1750, 1655, 1495, 1448, 1366, 1297, 1262, 1183, 1121, 1069, 1048, 946, 891, 804, 766 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.60 (d, J = 6.1 Hz, 3H), 0.98 (m, 2H), 1.00 (d, J = 6.1 Hz, 3H), 1.33 (dt, J = 1.2, 4.8 Hz, 1H), 1.60 (m, 2H), 2.35 (br s, 1H), 2.60 (br s, 1H), 2.64 (br s, 1H), 3.55 (hept, J = 6.1 Hz, 1H), 4.52 (s, 1H), 7.31 (m, 3H), 7.52 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 12.88, 16.82, 17.27, 23.45, 24.55, 30.97, 38.81, 50.23, 53.45, 63.34, 66.06, 86.09, 127.60, 127.78 (two CH), 128.44 (two CH), 142.27. Anal. Calcd for $C_{18}H_{21}BrO$: C, 64.87; H, 6.35. Found: C, 64.71; H, 6.36.

(1*R,2*R**,3*R**,4*R**,5*S**,6*S**,7*S**,8*S**)-4-Phenyl-5-bromotetracyclo [4.3.0.0^{2,4}.0^{3,7}]nonan-8-ol (4c)** was obtained by MPLC (petroleum ether/ether 3/7) as white crystals: yield 45%; mp 99−100 °C; IR (neat) ν 3605, 3430, 3060, 3000, 2960, 2870, 1610, 1500, 1450, 1385, 1330, 1315, 1270, 1205, 1155, 1070, 1020, 980, 960, 925 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.35 (ddd, J = 1.1, 1.9, 5.8 Hz, 1H), 1.54 (ddd, J = 2.3, 4.1, 13.5 Hz, 1H), 1.76 (dd, J = 1.6, 5.8 Hz, 1H), 1.96 (br s, 1H), 2.22 (dd, J = 6.8, 13.5 Hz, 1H), 2.38 (m, 1H), 2.53 (br s, 1H), 2.95 (m, 1H), 4.19 (dd, J = 2.2, 6.8 Hz, 1H); 4.51 (s, 1H), 7.22 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 25.01, 26.93, 37.47, 38.10, 43.35, 48.45, 49.49, 58.00, 73.25, 126.26, 127.40 (two CH), 128.13 (two CH), 137.02. Anal. Calcd for $C_{15}H_{15}BrO$: C, 61.87; H, 5.19. Found: C, 61.40; H, 5.20.

(1*R,2*R**,3*R**,4*R**,5*S**,6*S**,7*S**,8*S**)-4-Phenyl-5-bromo-8-(isopropyloxy)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (4d)** was obtained by MPLC (petroleum ether/ether 98/2) as a white solid: yield 51%; mp 49−50 °C; IR (neat) ν 3058, 2967, 2931, 2887, 1943, 1886, 1807, 1744, 1606, 1502, 1465, 1447, 1376, 1366, 1336, 1267, 1232, 1201, 1141, 1123, 1077, 1034, 936, 910, 878, 758 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.18 (d, J = 6.12 Hz, 3H), 1.22 (d, J = 6.1 Hz, 3H), 1.31 (m, 1H), 1.58 (ddd, J = 2.5, 4.1, 13.3 Hz, 1H), 1.74 (dd, J = 1.6, 5.8 Hz, 1H), 2.10 (dd, J = 6.8, 13.3 Hz, 1H), 2.42 (m, 1H), 2.50 (br s, 1H), 2.90 (m, 1H), 3.59 (hept, J = 6.1 Hz, 1H), 3.88 (dd, J = 2.5, 6.8 Hz, 1H), 4.48 (br s, 1H), 7.23 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 23.40, 22.63, 25.28, 27.01, 36.08, 37.23, 43.09, 47.05, 48.79, 58.11, 68.91, 77.64, 126.04, 127.28 (two CH), 127.98 (two CH), 137.14. Anal. Calcd for $C_{18}H_{21}BrO$: C, 64.87; H, 6.35. Found: C, 64.63; H, 6.36.

(1*R,2*R**,3*R**,4*R**,5*S**,6*S**,7*S**,8*S**)-4-Phenyl-5-bromo-8-(*tert*-butyloxy)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (4e)** was obtained by MPLC (petroleum ether/ether 99/1) as a white solid: yield 58%; mp 83−84 °C; IR (neat) ν 3058, 2967, 2931, 2887, 1943, 1886, 1807, 1744, 1606, 1502, 1465, 1447, 1376, 1366, 1336, 1267, 1232, 1201, 1141, 1123, 1077, 1034, 936, 910, 878, 758 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 9H), 1.13 (m, 1H), 1.57 (m, 1H), 1.71 (m, 1H), 2.12 (dd, J = 7.0, 13.3 Hz, 1H), 2.26 (m, 1H), 2.52 (br s, 1H), 2.87 (m, 1H), 3.90 (dd, J = 2.6, 7.0 Hz, 1H), 4.46 (br s, 1H), 7.24 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 25.22, 27.38, 28.41 (three CH_3), 37.28, 38.70, 43.25, 49.06, 49.18, 58.45, 72.74, 73.23, 126.11, 127.40 (two CH), 128.07 (two CH), 137.33. Anal. Calcd for $C_{19}H_{23}BrO$: C, 65.71; H, 6.68. Found: C, 65.28; H, 6.70.

(1*R,2*R**,3*S**,4*R**,5*S**,6*S**,7*R**,8*S**)-4-Butyl-5-bromotetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonan-8-ol (4f)** was obtained by MPLC (petroleum ether/ether 3/1) as a colorless oil: yield 73%; IR (neat) ν 3360, 3060, 2965, 2935, 2880, 2860, 1470, 1370, 1345, 1240, 1200, 1160, 1070, 1020, 980, 925, 905, 850, 725 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.86 (t, J = 6.7 Hz, 3H), 0.98 (m, 2H), 1.23 (m, 5H), 1.42 (ddd, J = 2.3, 4.1, 13.5 Hz, 1H), 1.54 (br, 1H, OH), 1.86 (m, 1H), 2.11 (dd, J = 6.8, 13.5 Hz, 1H), 2.16 (br s, 1H), 2.31 (br s, 1H), 2.67 (m, 1H), 4.11 (dd, J = 2.3, 6.8 Hz, 1H), 4.13 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.97, 20.52, 22.68, 22.79, 26.39, 29.39, 33.66, 38.36, 42.58, 47.76, 49.16, 59.45, 73.45. Anal. Calcd for $C_{13}H_{19}BrO$: C, 57.58; H, 7.06. Found: C, 57.43; H, 7.14.

(1*R,2*R**,3*S**,4*R**,5*S**,6*S**,7*R**,8*S**)-4-Butyl-5-bromo-8-methoxytetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (4g)** was obtained by MPLC (petroleum ether/ether 95/5) as a colorless oil: yield 54%; IR (neat) ν 3060, 2970, 2940, 2880, 2830, 1470, 1455, 1360, 1240, 1200, 1105, 1050, 1005, 970, 920, 905 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, J = 6.7 Hz, 3H), 0.97 (m, 2H), 1.24 (m, 5H), 1.48 (ddd, J = 2.5, 4.0, 13.3 Hz, 1H), 1.87 (m, 1H), 1.99 (dd, J = 6.8, 13.3 Hz, 1H), 2.24 (m, 1H), 2.30 (m, 1H), 2.65 (m, 1H), 3.22 (s, 3H), 3.60 (dd, J = 2.5, 6.8 Hz, 1H), 4.12 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.98, 20.46, 22.69, 23.05, 26.42, 29.42, 33.55, 35.38, 42.36, 45.51, 48.08, 55.92, 59.45, 82.69. Anal. Calcd for $C_{14}H_{21}BrO$: C, 58.96; H, 7.42. Found: C, 58.71; H, 7.37.

(1*R,2*R**,3*S**,4*R**,5*S**,6*S**,7*R**,8*S**)-4-Butyl-5-bromo-8-(benzyloxy)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (4h)** was obtained by MPLC (petroleum ether/ether 98/2) as a colorless oil: yield 55%; IR (neat) ν 3070, 3030, 2965, 2935, 2875, 1495, 1455, 1350, 1290, 1265, 1250, 1165, 1095, 1075, 1045, 1030, 920, 905 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (m, 5H), 1.27 (m, 4H), 1.39 (m, 1H), 1.61 (ddd, J = 2.5, 4.1, 13.3 Hz, 1H), 1.89 (m, 1H), 2.02 (dd, J = 6.8, 13.3 Hz, 1H), 2.35 (br s, 1H), 2.67 (m, 1H), 3.82 (dd, J = 2.5, 6.8 Hz, 1H), 4.13 (br s, 1H), 4.43 (br s, 2H), 7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.03, 20.61, 22.76, 23.19, 26.50, 29.50, 33.68, 35.77, 42.52, 46.10, 48.32, 59.62, 70.28, 80.67, 127.43, 127.52 (two CH), 128.34 (two CH), 138.57. Anal. Calcd for $C_{20}H_{25}BrO$: C, 66.48; H, 6.97. Found: C, 66.45; H, 6.93.

(1*R,2*R**,3*S**,4*R**,5*S**,6*S**,7*R**,8*S**)-4-(Acetoxyethyl)-5-bromotetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonan-8-ol (4i)** was obtained by MPLC (petroleum ether/ether 8/2) as a colorless oil: yield 52%; IR (neat) ν 3430, 3060, 2970, 1740, 1390, 1370, 1245, 1085, 1040, 1025, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 2H), 1.50 (m, 3H), 2.03 (s, 3H), 2.08 (dd, J = 6.8, 13.6 Hz, 1H), 2.18 (m, 1H), 2.60 (m, 1H), 2.32 (m, 1H), 2.69 (m, 1H), 4.00 (dt, J = 6.5, 10.9 Hz, 1H), 4.15 (m, 2H), 4.20 (dt, J = 6.5, 10.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.40, 20.93, 22.86, 26.04, 31.31, 38.07, 42.32, 47.69, 49.12, 58.77, 62.73, 73.13, 171.03. Anal. Calcd for $C_{13}H_{17}BrO_3$: C, 51.84; H, 5.69. Found: C, 51.47; H, 5.67.

(1*R,2*R**,3*S**,4*R**,5*S**,6*S**,7*R**,8*S**)-4-(Acetoxyethyl)-5-bromo-8-methoxytetracyclo[4.3.0.0^{2,4}.0^{3,7}] nonane (4j)** was obtained by MPLC (petroleum ether/ether 8/2) as a colorless oil: yield 80%; IR (neat) ν 3050, 2960, 2825, 1735, 1445, 1385, 1365, 1235, 1100, 1040, 1005, 970, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.04 (m, 2H), 1.52 (m, 2H), 1.99 (dd, J = 6.8, 13.5 Hz, 1H), 2.03 (s, 3H), 2.22 (m, 1H), 2.28 (m, 2H), 2.66 (m, 1H), 3.22 (s, 3H), 3.59 (dd, J = 2.4, 6.8 Hz, 1H), 3.99 (dt, J = 6.6, 10.9 Hz, 1H), 4.14 (br s, 1H), 4.19 (dt, $J = 6.6, 10.9$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 20.18, 20.77, 22.99, 25.95, 31.12, 35.00, 41.99, 45.36, 47.90, 55.77, 58.69, 62.49, 82.28, 170.56. Anal. Calcd for $C_{14}H_{19}BrO_3$: C, 53.35; H, 6.08. Found: C, 52.82; H, 6.08.

(1*R,2*R**,3*S**,4*R**,5*S**,6*S**,7*R**,8*S**)-4-(Acetoxyethyl)-5-bromo-8-(benzyloxy)tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (4k)** was obtained by MPLC (petroleum ether/ether 85/15) as a colorless oil: yield 57%; IR (neat) ν 3059, 3029, 2957, 2862, 1739, 1452, 1386, 1364, 1235, 1093, 1076, 1039, 916 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.04 (m, 2H), 1.53 (m, 2H), 1.65 (m, 1H), 2.03 (s, 3H), 2.27 (m, 1H), 2.36 (br s, 2H), 2.69 (m, 1H), 3.82 (dd, $J = 2.5, 6.7$ Hz, 1H), 4.00 (dt, $J = 6.6, 11.0$ Hz, 1H), 4.16 (br s, 1H), 4.20 (dt, $J = 6.6, 11.0$ Hz, 1H), 4.43 (s, 2H), 7.29 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 20.24, 20.84, 23.11, 25.97, 31.19, 35.37, 42.11, 45.89, 48.09, 58.77, 62.57, 70.11, 80.26, 127.24, 127.30 (two CH), 128.13 (two CH), 136.32, 170.66. Anal. Calcd for $C_{20}H_{23}BrO_3$: C, 61.39; H, 5.92. Found: C, 61.02; H, 5.96.

(1*R*,2*R*,3*R*,4*S*,6*R*,7*R*,9*S*)-8-*exo*-bromo-9-butylidenetetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (5b) was obtained according to the general procedure without nucleophilic species. From **1b** (348 mg, 2 mmol) and NBS (356 mg, 2 mmol), 274 mg (1.08 mmol) (54%) of **5b** was obtained by bulb-to-bulb distillation [bp 130°C (0.01 mm Hg)] as a pale yellow oil: IR (neat) ν 3065, 3025, 2950, 2870, 1600, 1495, 1445 cm^{-1}; ^{1}H NMR ($CDCl_3$) (1:1 *E:Z* stereomers) δ 0.94 (m, 3H), 1.44 (m, 8H), 1.16 (m, 6H), 2.72 (m, 1H), 4,68 (br s, 1H), 5.41 (t, $J = 6.3$ Hz, 0.5H), 5.64 (t, $J = 6.3$ Hz, 0.5H); ^{13}C NMR ($CDCl_3$) δ 13.88, 14.49, 15.09, 17.80, 22.25, 22.73, 31.39, 31.70, 40.52, 44.01, 45.24, 48.71, 49.85, 50.73, 51.24, 52.16, 52.95, 58.08, 57.89, 58.02, 126.93, 128.13, 144.94, 146.14. Anal. Calcd for $C_{13}H_{17}Br$: C, 61.67; H, 6.77; Br, 31.56. Found: C, 61.82; H, 6.48; Br, 31.62.

(1*R*,2*R*,3*R*,4*S*,6*R*,7*R*,9*S*)-8-*exo*-bromo-9-(acetoxypropylidene)tetracyclo [4.3.0.0^{2,4}.0^{3,7}]nonane (5c) was prepared as for **5b**. From **1c** (204 mg, 1 mmol) and NBS (178 mg, 1 mmol), 199 mg (0.52 mmol) (52%) of **5c** was obtained as a colorless oil: IR (neat) ν 3061, 2939, 2866, 1738, 1444, 1368, 1232, 1027, 818 cm^{-1}; ^{1}H NMR ($CDCl_3$) (1:1 *E:Z* stereomers) δ 1.14 (m, 2H), 1.37 (m, 1H), 1.70 (m, 2H), 2.09 (s, 3H), 2.43 (m, 2H), 2.55 (br s, 0.5H), 2.83 (br s, 0.5H), 4.66 (m, 3H), 5.48 (t, $J = 7.1$ Hz, 0.5H), 5.72 (t, $J = 7.2$ Hz, 0.5H); ^{13}C NMR ($CDCl_3$) δ 14.46, 14.61, 16.29, 16.98, 17.59, 17.67, 20.98, 31.29, 40.51, 40.70, 45.63, 49.89, 50.30, 51.73, 52.79, 53.70, 61.81, 119.35, 120.80, 150.48, 152.28, 170.78. Anal. Calcd for $C_{13}H_{15}BrO_2$: C, 55.14; H, 5.34; Br, 28.22. Found: C, 55.01; H, 5.43; Br, 28.10.

(+)-(1*S*,2*S*,3*R*,4*S*,6*R*,7*R*,9*S*)-9-*exo*-Bromotetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonan-8-one (6a). Ozone was bubbled to a solution of **5b** (102 mg, 0.4 mmol) in CH_2Cl_2 (20 mL) at −78 °C until a pale blue color persisted. Nitrogen was bubbled for 5 mn, methyl sulfide (272 μL, 2.4 mmol) was added, and the mixture was allowed to reach room temperature. Concentration in vacuo afforded the crude product which was purified by MPLC (petroleum ether/ether 9/1) as a colorless oil: yield 84% (99.3% purity by GC); $[\alpha]^{20}_{589}$ +277° (*c* 1.4, MeOH), ee 97.1 ± 0.3%; IR (neat) ν 3067, 2938, 2867, 1753, 1149 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28 (m, 2H), 1.67 (m, 2H), 1.71 (br s, 1H), 2.45 (br s, 1H), 2.50 (m, 1H), 2.53 (m, 1H), 4.16 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.74, 14.94, 18.77, 31.73, 39.12, 48.42, 48.91, 52.49, 208.93. Anal. Calcd for C_9H_9BrO: C, 50.73; H, 4.26; Br, 37.50. Found: C, 50.69; H, 4.29; Br, 37.52.

(+)-(1*R*,2*R*,3*R*,4*R*,6*S*,7*R*)-Tetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonan-8-one (6b). 9-Bromodeltacyclan-8-one (**6a**) (170 mg, 0.797 mmol) and Zn powder (208 mg, 3.19 mmol) in AcOH (5 mL) were heated at reflux for 5 h. The mixture was poured into ether (20 mL) and ice (5g). The organic layer was washed with a 1 M solution of $NaHCO_3$ until neutrality with brine (3 mL) and dried over $MgSO_4$. On purification by MPLC (petroleum ether/ether 85/15), 100 mg (93.5%) of **6b** was obtained as a colorless oil (99.5% purity by GC): $[\alpha]^{20}_{589}$ +272° (*c* 0.2, MeOH), ee 97.1 ± 0.3% [lit.[9] **(−)-6b**: $[\alpha]^{30}_{D}$ −241° (*c* 0.46, $CHCl_3$), ee 83.2%]; IR (neat) ν 3056, 2938, 2866, 1708, 1169 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.09 (m, 2H), 1.50 (m, 1H), 1.58 (dt, $J = 1.2, 11.1$ Hz, 1H), 1.67 (dt, $J = 1.2, 11.1$ Hz, 1H), 2.09 (s, 1H), 2.12 (dd, $J = 1.7, 3.6$ Hz, 1H), 2.17 (s, 1H), 2.28 (m, 1H), 2.32 (t, $J = 2.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.6, 15.9, 16.0, 32.5, 39.9, 41.0, 41.3, 54.2, 216.6.

Supporting Information Available: Detailed data (C−H COORD, COSY, NOESY, and HMBC) for compound **3c** and copies of ^{1}H and ^{13}C NMR ($CDCl_3$) spectra for compounds **3d** and **4d** (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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