HETEROCYCLES, Vol. 99, No. 1, 2019, pp. 425 - 445. © 2019 The Japan Institute of Heterocyclic Chemistry
Received, 21st August, 2018, Accepted, 5th September, 2018, Published online, 15th October, 2018
DOI: 10.3987/COM-18-S(F)38

DESIGN AND SYNTHESIS OF CYCLOHEXENYL-*p*-CARBORANE DERIVATIVES AS A NEW CLASS OF PROGESTERONE RECEPTOR ANTAGONISTS

Shinya Fujii,[1,2] Naoki Yanagida,[1] Shuichi Mori,[1] Emiko Kawachi,[1] and Hiroyuki Kagechika[1]*

[1] Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, 2-3-10 Kanda-Surugadai, Chiyoda-ku, Tokyo 101-0062, Japan. [2] Institute for Quantitative Biosciences, The University of Tokyo, 1-1-1 Yayoi, Bunkyo-ku, Tokyo 113-0032, Japan. E-mail: kage.chem@tmd.ac.jp

Abstract – We report here the synthesis and structure-activity relationships of a series of *C*-cyclohexenyl-*p*-carborane derivatives, which we designed as candidates for a novel class of progesterone receptor (PR) antagonists. Biological evaluation using T47D alkaline phosphatase assay revealed that several compounds exhibited potent PR-antagonistic activity. We also examined the selectivity of these compounds for PR over androgen receptor (AR). Among them, **11b** functioned as a PR-selective antagonist, while other compounds, such as **13b**, acted as PR/AR dual antagonists. Notably, docking simulations indicated that **11b** and **13b** bind in similar orientations to the ligand-binding site of PR, but in opposite orientations to that of AR. These findings could helpful for developing more selective ligands for PR.

INTRODUCTION

Progesterone receptor (PR) is a member of the nuclear receptor superfamily of ligand-dependent transcription factors.[1] PR is regulated by an endogenous steroid, progesterone (P4, **1**), and plays a critical role in physiological functions related to the female reproductive system, including uterine cell proliferation and differentiation, the ovulation cycle, and mammary gland growth.[2] In addition to these sex hormonal functions, PR is involved in various cardiovascular, immune and nervous system functions.[3] Thus, PR is a promising target for drug discovery, and various synthetic PR ligands have been synthesized and evaluated. For instance, several steroidal PR agonists have been developed and used clinically for the treatment of gynecological disorders, for contraception, and for hormone replacement

therapy.[4] The steroidal PR antagonist mifepristone (**2**) and related PR antagonists are also used as contraceptive agents in some countries.[5] Development of nonsteroidal PR agonists has been also investigated, as exemplified by tanaproget (**4**),[6] which is being developed for clinical use. In addition, it has been suggested that PR antagonists might be effective in the treatment of uterine leiomyoma, endometriosis breast cancer, and some psychiatric disorders,[7] and thus there is increasing interest in the development of nonsteroidal PR antagonists (Figure 1).

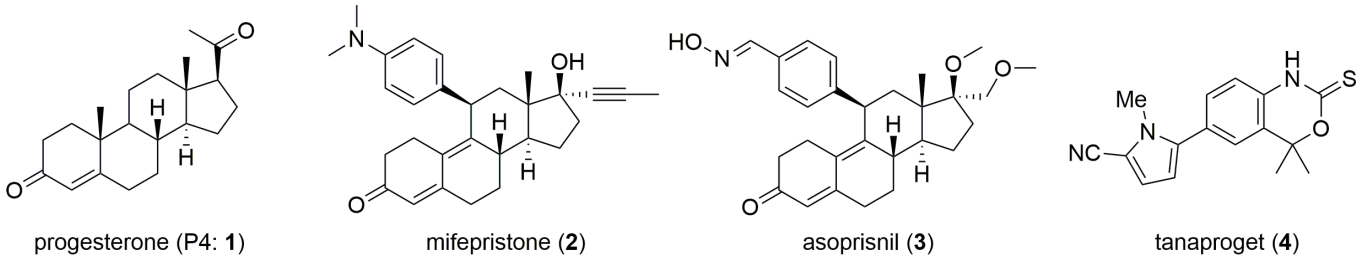


Figure 1. Structures of endogenous and synthetic PR ligands

We recently developed a series of novel PR antagonists bearing a phenylcarborane scaffold as a hydrophobic core structure, such as **8** and **9**.[8] Carboranes (more specifically, dicarba-*closo*-dodecaboranes, $C_2H_{12}B_{10}$) are carbon-containing icosahedral boron clusters with a bulky spherical surface, remarkable thermal and chemical stability, and high hydrophobicity, comparable to that of hydrocarbons.[9] We have shown that these properties of carboranes make them suitable for use as a hydrophobic pharmacophore of nuclear receptor modulators, including ligands for vitamin D receptor (VDR),[10] estrogen receptor (ER),[11] androgen receptor (AR),[12,13] and PR.[8] We have proposed that the *C*-phenylcarborane core structure as in compounds **8** and **9** is a privileged structure for developing modulators for these receptors. We also developed AR antagonists such as BA111 (**10**) based on the hypothesis that the hydrophobic carborane cage can function as an alternative to the CD-ring of the steroidal skeleton.[12] The cyclohexenone moiety functions as the key pharmacophore of steroid hormone receptor ligands, and therefore the *C*-cyclohexenyl-*p*-carborane skeleton of **10** is one possible option for design of novel steroid hormone receptor antagonists. In this work, we planned to develop a series of *C*-cyclohexenyl-*p*-carborane derivatives as candidates for a novel class of PR antagonists (Figure 2).

We designed compounds **11a-e** and **12a-e** bearing two carbonyl moieties as hydrophilic pharmacophores like those of **1**, together with a hydrophobic *p*-carborane cage instead of the CD-ring of **1**. We also designed the hydroxyl derivatives **13a-e** and **14a-e** in order to investigate the structure-activity relationship, since differences in the hydrophilic pharmacophore might influence the selectivity for PR over AR (Figure 3).

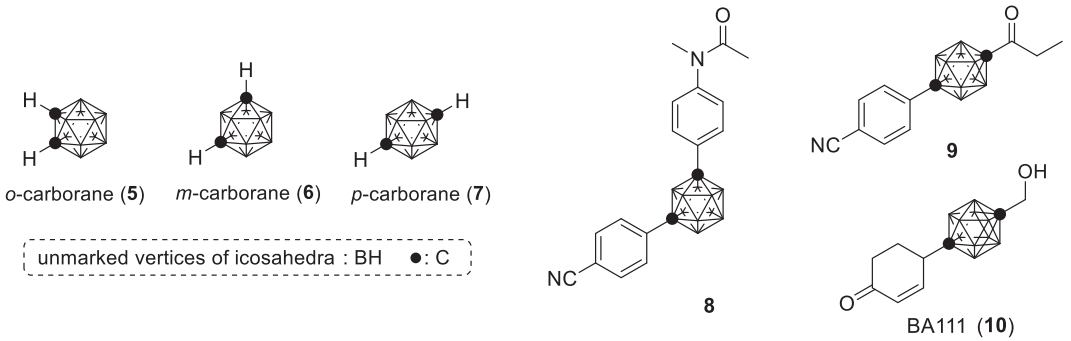


Figure 2. Structures of the three isomers of carborane and our developed carborane-based PR and AR antagonists

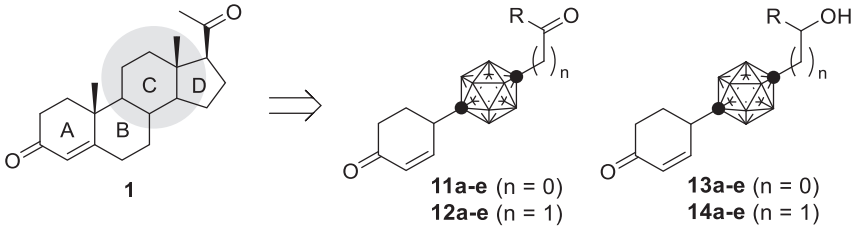
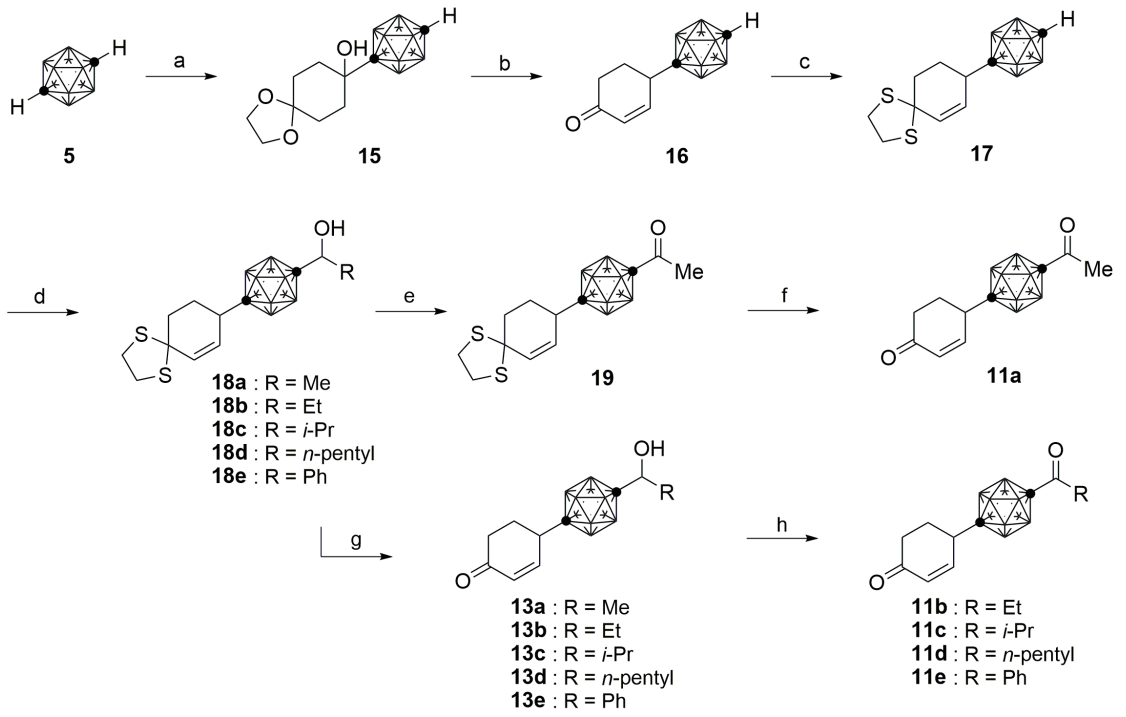


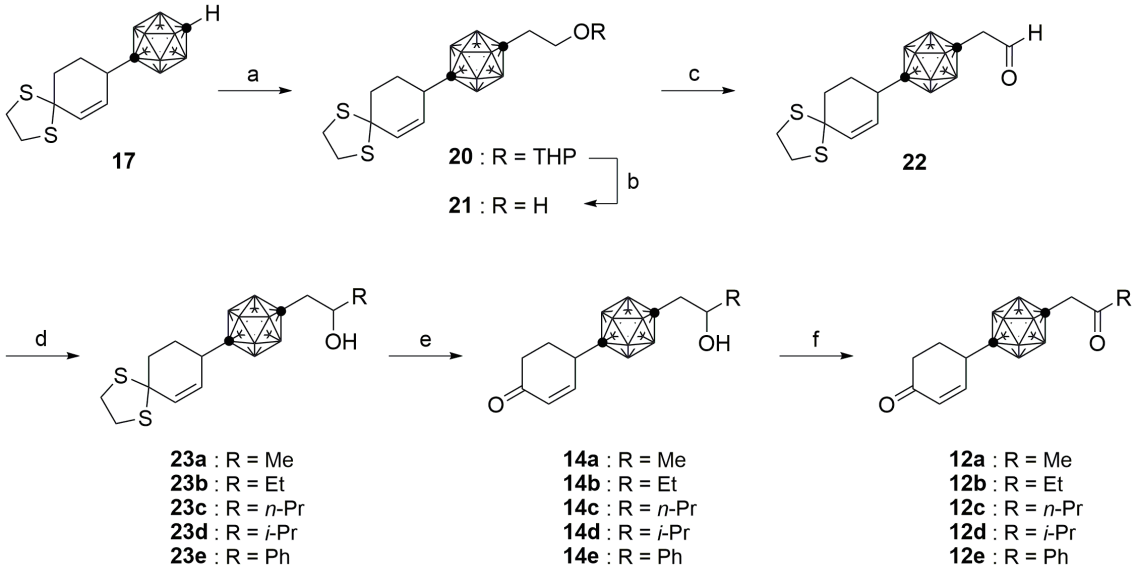
Figure 3. Design scheme for candidate PR antagonists bearing a cyclohexenyl-*p*-carborane core structure

RESULTS AND DISCUSSION

Synthesis. The synthesis of the designed compounds **11a-e** and **13a-e** is summarized in Scheme 1. Reaction of the lithiated form of *p*-carborane with 1,4-cyclohexanedione *mono*-ethylene ketal gave compound **15**, and then deprotection of the ketal and isomerization of the double bond by treatment with concentrated sulfuric acid afforded cyclohexenone derivative **16**. Our previous study revealed that the double bond of **16** is easily isomerized to the 1,3,4-trisubstituted (i.e., β,γ-position) form under the reaction conditions necessary to protect the carbonyl group with cyclic ketal, and therefore we had to make a synthetic detour.[12] In this study, we successfully protected the carbonyl group with 1,3-dithiolane, without isomerization of the double bond, to obtain dithiolane **17**. To introduce the hydroxylated moieties on the contralateral vertex of the carborane cage, reaction between lithiated **17** and various aldehydes was employed to afford alcohols **18a-e**. Oxidation of methyl analog **18a** using PDC gave methyl ketone **19**, and then removal of the dithiolane group using iodomethane afforded compound **11a**. Removal of the dithiolane group of **18a-e** under oxidative conditions afforded the corresponding hydroxyketones **13a-e**, respectively, and then oxidation of the hydroxyl group gave the dicarbonyl derivatives **11b-e**, respectively (Scheme 1).



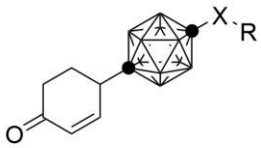
Scheme 1. Synthesis of the designed compounds **11a-e** and **13a-e**. Reagents and conditions: (a) *n*-BuLi, 1,4-cyclohexanedione *mono*-ethylene ketal, Et_2O, rt, 78%; (b) concd. H_2SO_4, 80 °C, 86%; (c) 1,2-ethanedithiol, $BF_3{\cdot}OEt_2$, 4A MS, $CHCl_3$, rt, 83%; (d) *n*-BuLi, RCHO, Et_2O, rt, 46-86%; (e) PDC, 4A MS, CH_2Cl_2, rt, 48%; (f) MeI, MeOH-THF-H_2O, 60 °C, 66%; (g) Dess-Martin periodinane, MeCN-THF-H_2O, rt, 52-79%; (h) Dess-Martin periodinane, CH_2Cl_2, rt, 75-89%.



Scheme 2. Synthesis of the designed compounds **12a-e** and **14a-e**. Reagents and conditions: (a) *n*-BuLi, $THPOCH_2CH_2Br$, Et_2O, rt, 56%; (b) $TsOH{\cdot}H_2O$, MeOH, CH_2Cl_2, rt, 92%; (c) TEMPO, $C_6H_5I(OAc)_2$, CH_2Cl_2, rt, 64%; (d) MeLi (for **23a**) or RMgX, THF, rt, 11-47%; (e) Dess-Martin periodinane, MeCN-THF-H_2O, rt, 47-85%; (f) Dess-Martin periodinane, CH_2Cl_2, rt, 35-94%.

Synthesis of compounds **12a-e** and **14a-e** by one-carbon elongation is illustrated in Scheme 2. The THP-protected 2-hydroxyethyl moiety was introduced into **17** to afford **20**, and removal of the THP group under acidic conditions gave alcohol **21**. Oxidation of **21** with TEMPO and (diacetoxy)iodobenzene gave aldehyde **22**, and reaction of **22** with lithium or Grignard reagents afforded the corresponding secondary alcohols **23a-e**. Removal of the dithiolane group of **23a-e** under oxidative conditions afforded the corresponding hydroxyketones **14a-e**, and oxidation of the hydroxyl group gave the dicarbonyl compounds **12a-e**, respectively (Scheme 2).

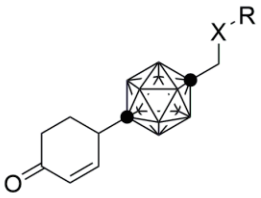
Table 1. PR-antagonistic activity of cyclohexenylcarborane derivatives **11a-e** and **13a-e** determined by means of T-47D alkaline phosphatase assay



Compound	X	R	IC_{50} (μM)[a]	Compound	X	R	IC_{50} (μM)[a]
11a	C=O	Me	0.27	**13a**	CH-OH	Me	0.28
11b	C=O	Et	0.37	**13b**	CH-OH	Et	0.42
11c	C=O	*i*-Pr	0.63	**13c**	CH-OH	*i*-Pr	0.56
11d	C=O	*n*-pentyl	4.95	**13d**	CH-OH	*n*-pentyl	1.18
11e	C=O	Ph	2.18	**13e**	CH-OH	Ph	1.33

[a] Expression of alkaline phosphatase was induced with 1 nM progesterone.

Table 2. PR-antagonistic activity of cyclohexenylcarborane derivatives **12a-e** and **14a-e** determined by means of T-47D alkaline phosphatase assay



Compound	X	R	IC_{50} (μM)[a]	Compound	X	R	IC_{50} (μM)[a]
12a	C=O	Me	0.65	**14a**	CH-OH	Me	0.32
12b	C=O	Et	0.91	**14b**	CH-OH	Et	0.63
12c	C=O	*n*-Pr	>10	**14c**	CH-OH	*n*-Pr	1.04
12d	C=O	*i*-Pr	>10	**14d**	CH-OH	*i*-Pr	0.38
12e	C=O	Ph	1.87	**14e**	CH-OH	Ph	1.55

[a] Expression of alkaline phosphatase was induced with 1 nM progesterone.

Biological evaluation. The PR agonistic and antagonistic activities of the synthesized carborane derivatives were evaluated by means of T47D alkaline phosphatase assay.[14] None of the synthesized compounds exhibited PR-agonistic activity (data not shown). Table 1 shows the PR antagonistic activities of compounds **11a-e** and **13a-e**. Among the diketone derivatives **11a-e**, compounds **11a** and **11b** bearing a small hydrophobic substituent exhibited potent PR-antagonistic activity, whereas the introduction of a larger substituent such as *n*-pentyl (**11d**) or phenyl (**11e**) significantly reduced the antagonistic activity. Compound **11a** bearing a methyl group exhibited the most potent antagonistic activity among the diketones. The same tendency was observed in the case of hydroxyketone derivatives **13a-e**, namely, methyl and ethyl derivatives **13a** and **13b** exhibited significant activity, comparable to those of the corresponding diketone derivatives, whereas the introduction of a larger hydrophobic substituent decreased the potency, and the *n*-pentyl (**13d**) and phenyl (**13e**) derivatives exhibited comparatively low activity (Table 1). Table 2 shows the activities of compounds **12a-e** and **14a-e** with a one-carbon-elongated side chain. The structure–activity relationship of these compounds was similar to that of the above-mentioned compounds, namely a small hydrophobic substituent was preferable to a large substituent (Table 2). The results summarized in Tables 1 and 2 indicate that only cyclohexylcarborane derivatives bearing a small or short substituent, such as methyl, ethyl or isopropyl, can enter the hydrophobic cavity in the ligand-binding pocket, while differences in the polar functionality, namely the position and type (carbonyl or hydroxyl), did not significantly affect the activity.

Table 3. AR-antagonistic activity of selected compounds determined by means of cell-proliferation inhibitory activity toward androgen-dependent SC-3 cells

Compound	AR IC_{50} (μM)[a]	Compound	AR IC_{50} (μM)[a]
11a	4.6	**13a**	3.4
11b	>10	**13b**	7.1
12a	4.2	**14a**	3.2
12b	>10	**14b**	5.3

[a] SC-3 cell proliferation was promoted with 1 nM DHT.

In order to investigate the PR selectivity of the compounds, we examined the AR-antagonistic activity of selected methyl and ethyl derivatives by assay of cell proliferation activity toward androgen-dependent SC-3 cells.[15] Whereas most of the compounds exhibited moderate AR-antagonistic activity, ethyl ketone derivatives **11b** and **12b** did not exhibit AR antagonistic activity in the concentration range below 10 μM. The corresponding hydroxyl derivatives **13b** and **14b** showed AR-antagonistic activity, so the nature of the polar functionality influences the anti-androgenic activity and PR selectivity (Figure 3).

Docking simulation. In order to understand the structure-activity and the structure-selectivity relationships, we next simulated the binding modes of selected compounds using docking software AutoDock4.[16] We focused on ethyl ketone **11b** because of its significant potency and selectivity, together with the corresponding alcohol **13b**. Figure 4A shows the calculated structure of (*S*)-**11b** bound to PR-LBD, superimposed on the crystal structure of the PR-LBD complexed with progesterone (**1**). In the calculated structure, the carborane moiety of (*S*)-**11b** binds at the hydrophobic region of the PR-LBD, where the CD ring of **1** is located. Our previous studies suggested the increased bulkiness of the carborane moiety compared to the CD ring is one possible reason why the carborane derivatives act as PR and AR antagonists.[8,13] The carbonyl group at the cyclohexyl ring interacts with Gln725 and Arg766, which are residues are interacting with the 3-carbonyl group of **1**. On the other hand, the carbonyl group of the ethyl ketone moiety of (*S*)-**11b** did not form a hydrogen bond with Thr894, which interacts with the 20-carbonyl group of **1**. We had selected (*S*)-**11b** for the initial docking study because the stereochemistry of cyclohexyl moiety is the same as that of the A-ring of **1**, so next we conducted docking simulation using (*R*)-**11b**. Figure 4B shows the superimposition of the two isomers; there is no significant difference between the docking conformations of the two isomers. This study suggested that compound **11b** functions as a PR antagonist in the designed manner, even though the second carbonyl group, which was expected to have the same functional role as the 20-carbonyl group of **1**, does not serve as a H-bond anchor. We also conducted docking simulation of the corresponding alcohol **13b**. Figure 4C shows the superimposition of the calculated binding structures of all four isomers of **13b**. The calculated binding forms were essentially the same as those of **11b**, namely, the carbonyl group at the cyclohexane ring interacts with Gln725 and Arg766, and the carborane cage occupies the hydrophobic cavity of PR-LBD, like the CD ring of **1**. The results of docking simulation are consistent with the observed biological activities. There is little room around the Cys891 and Thr894 residues, and therefore small substituents are preferable at this position. Hydrogen bonding does not occur between the carbonyl or the hydroxy group and Thr894, and this may be the reason why the cyclohexylcarborane derivatives were less potent than the phenylcarborane derivatives, which are considered to form a hydrogen bond to this residue.[8]

Next, we conducted a docking simulation using the X-ray structure of AR-LBD. Figure 4D shows the calculated structure of (*S*,*S*)-**13b** bound to AR-LBD, superimposed on the crystal structure of AR-LBD complexed with dihydrotestosterone. Interestingly, the calculated binding form was entirely different from that in the case of PR. In the docked structure in AR-LBD, compound (*S*,*S*)-**13b** is positioned in the opposite direction, namely the carbonyl group at the cyclohexyl ring interacts with Thr877, which interacts with the 17β-hydroxy group of DHT, while the carborane cage is located in the hydrophobic legion where the B ring of DHT is located. We also examined the docking of the other stereoisomers, and all isomers of **13b** gave similar binding forms (Figure 4E). Docking simulation of compound **11b**, which

has only weak potency toward AR, suggested that this diketone derivative binds to AR in the opposite orientation to alcohol **13b** (Figure 4F), and thus, the binding mode indicated in Figure 4E may be required for significant activity toward AR. These findings could helpful for developing selective ligands for PR and AR.

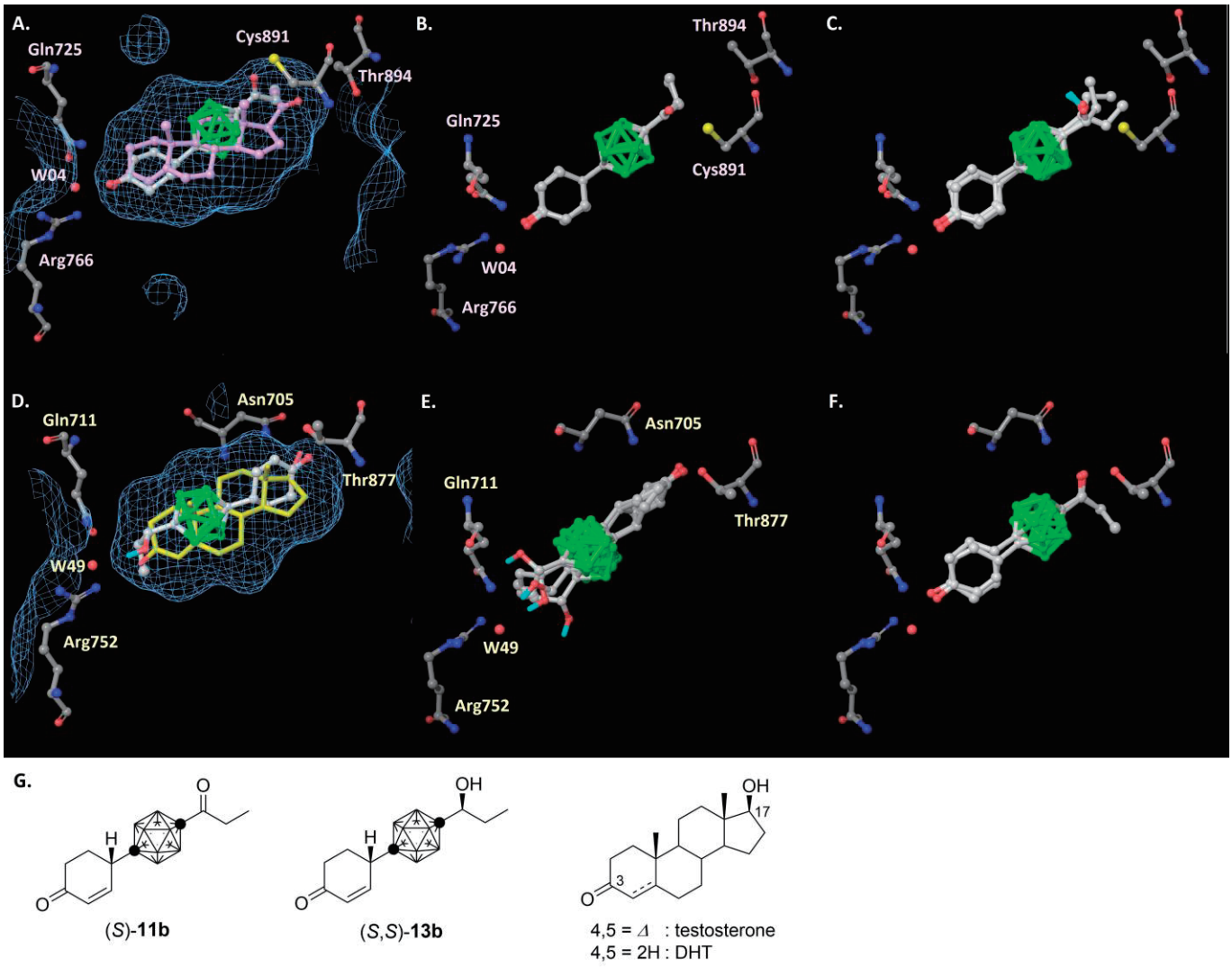


Figure 4. Docking simulations of synthesized compounds. A) The docking model of (*S*)-**11b** is superimposed on the hPR LBD bound to progesterone (**1**: pink, PDB ID: 1A28)[17]. The protein surface is indicated as a light blue mesh. B) Overlay of the docking structures of two isomers of **11b** in hPR LBD. C) Overlay of the docking structures of four isomers of **13b** in hPR LBD. D) The docking model of (*S*,*S*)-**13b** is superimposed on the hAR LBD bound to DHT (yellow, PDB ID: 1I37)[18]. E) Overlay of the docking structures of four isomers of **13b** in hPAR LBD. F) Overlay of the docking structures of two isomers of **11b** in hAR LBD. G) Structures of compounds used in the docking studies.

CONCLUSION

We designed and synthesized a series of cyclohexenyl-*p*-carborane derivatives as candidates for a new class of PR antagonists. Biological evaluation using T47D alkaline phosphatase assay revealed that

several compounds including **11a**,**b** and **13a**,**b** exhibited potent PR-antagonistic activity. We also examined activity toward AR, and found compound **11b** functions as a PR-selective antagonist, whereas several other compounds including **13b** function as PR/AR dual antagonists. Notably, the results of docking simulations of the compounds with the X-ray structures of the PR-LBD and AR-LBD suggest that **11b** and **13b** bind in similar orientations to the ligand-binding site of PR, but in opposite orientations to that of AR. The information and insights obtained in this study are expected to contribute not only to the development and application of more selective PR ligands, but also to extending the medicinal application of carboranes.

EXPERIMENTAL

Synthesis

General: All reagents were purchased from Sigma-Aldrich Chemical Co., Tokyo Kasei Kogyo Co., Wako Pure Chemical Industries, or Kanto Chemical Co., Inc. Silica gel for column chromatography was purchased from Kanto Chemical Co., Inc. ^{1}H NMR spectra were recorded on at 500 MHz on a Bruker AVANCE 500 spectrometer. ^{13}C NMR spectra were recorded on at 125 MHz on a Bruker AVANCE 500 spectrometer. Chemical shifts are reported as parts per million (ppm). Data are reported as follows: chemical shift, multiplicity (s, singlet; d, doublet; t, triplet; br, broad; m, multiplet), coupling constants (Hz), integration. The purity of the final compounds was determined by elemental analysis or ^{1}H NMR, and was ≥95% in all cases. Elemental analyses were carried out on a Yanaco MT-6 CHN CORDER.

8-(1,12-Dicarba-*closo*-dodecaboran-1-yl)-1,4-dioxaspiro[4.5]decan-8-ol (15): To a solution of *p*-carborane (1.05 g, 6.94 mmol) in Et_2O (20 mL) was added dropwise a solution of *n*-BuLi in *n*-hexane (1.55 mol/L, 4.9 mL, 7.52 mmol) at 0 °C under Ar. The mixture was stirred at rt for 30 min, and 1,4-cyclohexanedione *mono*-ethylene ketal (1.56 g, 10.0 mmol) was added in one portion at 0 °C. The mixture was stirred at rt for 1.5 h, then poured into ice water, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. Purification of the residue by silica gel flash column chromatography (eluent: hexane/AcOEt, 5:1) gave **15** (78%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (m, 4H), 2.90-1.50 (br m, 10H), 2.80 (br s, 1H), 1.77 (m, 2H), 1.60-1.50 (m, 6H), 1.26 (s, 1H).

4-(1,12-Dicarba-*closo*-dodecaboran-1-yl)-2-cyclohexen-1-one (16): To concentrated H_2SO_4 (19 mL) was added **15** (1.63 g, 5.41 mmol) in one portion at 0 °C. The mixture was stirred at 80 °C for 45 min, then poured into ice water, and extracted with Et_2O. The organic layer was washed with aqueous $NaHCO_3$, water and brine, dried over Na_2SO_4, then concentrated. Purification of the residue by silica gel column chromatography (eluent: hexane/AcOEt, 10:1) gave **16** (86%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.68 (ddd, 1H, J = 11, 2.4, 2.1 Hz), 5.88 (ddd, 1H, J = 11.0, 2.8, 0.8 Hz), 2.80-1.70 (br m,

10H), 2.78 (br s, 1H), 2.61 (dddd, 1H, *J* = 10.0, 4.2, 2.9, 2.5 Hz), 2.44 (ddd, 1H, *J* = 17.0, 4.2, 4.2 Hz), 2.19 (ddd, 1H, *J* = 17.0, 13.0, 4.7 Hz), 2.02 (ddddd, 1H, *J* = 13.0, 4.7, 4.7, 4.7, 1.8 Hz), 1.70 (dddd, 1H, *J* = 13.0, 13.0, 10.3, 4.2 Hz).

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-1,12-dicarba-*closo*-dodecaborane (17): To a solution of **16** (100 mg, 0.427 mmol) in $CHCl_3$ (3.4 mL) were added BF_3 etherate (39.2 μL, 0.422 mmol), 4A molecular sieves (69.4 mg) and 1,2-ethanedithiol (39.2 μL, 0.470 mmol) under Ar. The mixture was stirred at rt for 6 h, then filtered. The filtrate was extracted with AcOEt. The organic layer was washed with aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. Purification by silica gel column chromatography (eluent: hexane/AcOEt, 50:1) gave **17** (83%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (d, 1H, *J* = 10 Hz), 5.39 (d, 1H, *J* = 9.8 Hz), 3.31 (m, 3H), 3.20 (m, 1H), 2.80-1.50 (br m, 10H), 2.72 (br s, 1H), 2.28 (m, 1H), 2.17 (m, 1H), 1.92 (m, 1H), 1.78 (m, 1H), 1.51 (m, 1H).

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(1-hydroxyethyl)-1,12-dicarba-*closo*-dodecaborane (18a): To a solution of **17** (50.8 mg, 0.159 mmol) in Et_2O (1.5 mL) was added *n*-BuLi in *n*-hexane (135 μL, 0.207 mmol, 1.55 mol/L) at 0 °C under Ar. The mixture was stirred at rt for 30 min, and then acetaldehyde (200 μL, 3.56 mmol) in Et_2O (800 μL) was added at 0 °C under Ar. The mixture was stirred at rt for 2 h, poured into water and saturated aqueous NH_4Cl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. Purification of the residue by silica gel column chromatography (eluent: hexane/AcOEt, 10:1) gave **18a** (75%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.75 (ddd, 1H, *J* = 10.1, 2.6, 1.3 Hz), 5.38 (ddd, 1H, *J* = 10.1, 2.6, 1.4 Hz), 3.68 (qd, 1H, *J* = 10.1, 6.1 Hz), 3.34-3.28 (m, 3H), 3.22-3.16 (m, 1H), 2.90-1.70 (br m, 10H), 2.30 (dddd, 1H, *J* = 9.5, 5.6, 2.6, 2.5 Hz), 2.17 (dddd, 1H, *J* = 13.3, 6.2, 2.6, 1.3 Hz), 1.93 (ddd, 1H, *J* = 13.8, 11.6, 2.7 Hz), 1.78 (ddddd, 1H, *J* = 13.6, 6.3, 5.5, 2.7, 1.4 Hz), 1.58 (d, 1H, *J* = 5.8 Hz), 1.49 (dddd, 1H, *J* = 13.5, 11.9, 9.5, 2.6 Hz), 1.06 (d, 3H, *J* = 6.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.0, 128.5, 87.2, 85.3, 69.3, 63.6, 40.2, 40.2, 39.9, 39.8, 29.9, 23.0.

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(1-hydroxypropyl)-1,12-dicarba-*closo*-dodecaborane (18b): Compound **18b** was prepared from **17** in a similar manner to that used for the preparation of **18a**, but with propionaldehyde as a reagent. 58% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (ddd, 1H, *J* = 10.1, 2.6, 1.3 Hz), 5.38 (ddd, 1H, *J* = 10.1, 2.6, 1.3 Hz), 3.35-3.28 (m, 3H), 3.34-3.30 (m, 1H), 3.23-3.15 (m, 1H), 2.90-1.60 (br m, 10H), 2.30 (dddd, 1H, *J* = 9.5, 5.7, 2.6, 2.5 Hz), 2.17 (dddd, 1H, *J* = 13.8, 6.2, 2.6, 1.3 Hz), 1.93 (ddd, 1H, *J* = 13.8, 11.6, 2.5 Hz), 1.78 (ddddd, 1H, *J* = 13.5, 6.4, 5.6, 2.7, 1.4 Hz), 1.51-1.39 (m, 1H), 1.51-1.39 (m, 1H), 1.16-1.06 (m, 1H), 0.86 (t, 3H, *J* = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.4, 129.3, 89.5, 86.6, 75.0, 64.6, 41.4, 41.1, 41.0, 40.7, 31.0, 30.8, 11.6.

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(1-hydroxy-2-methylpropyl)-1,12-dicarba-*closo*-dodecaborane (18c): Compound **18c** was prepared from **17** in a similar manner to that used for preparation of **18a**, but with isobutylaldehyde as a reagent. 85% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (ddd, 1H, *J* = 10.0, 2.6, 1.3 Hz), 5.38 (ddd, 1H, *J* = 10.1, 2.6, 1.3 Hz), 3.35 (dd, 1H, *J* = 7.0, 1.4 Hz), 3.33-3.28 (m, 3H), 3.22-3.15 (m, 1H), 3.00-1.60 (br m, 10H), 2.30 (dddd, 1H, *J* = 9.5, 5.6, 2.6, 1.3 Hz), 2.16 (dddd, 1H, *J* = 13.8, 6.2, 2.6, 1.3 Hz), 1.92 (ddd, 1H, *J* = 13.8, 11.6, 2.5 Hz), 1.77 (ddddd, 1H, *J* = 13.5, 6.4, 5.6, 2.7, 1.4 Hz), 1.69 (sep d, 1H, *J* = 6.8, 1.4 Hz), 1.55 (d, 1H, *J* = 7.0 Hz), 1.48 (dddd, 1H, *J* = 13.4, 11.7, 9.5, 2.7 Hz), 0.87 (d, 3H, *J* = 6.9 Hz), 0.75 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.1, 128.6, 87.0, 86.0, 77.2, 63.7, 40.3, 40.2, 40.0, 39.9, 32.2, 29.9, 22.7, 14.2.

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(1-hydroxyhexyl)-1,12-dicarba-*closo*-dodecaborane (18d): Compound **18d** was prepared from **17** in a similar manner to that used for preparation of **18a**, but with 1-hexanal as a reagent. 46% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (ddd, 1H, *J* = 10.0, 2.6, 1.3 Hz), 5.38 (ddd, 1H, *J* = 10.1, 2.6, 1.3 Hz), 3.42-3.37 (m, 1H), 3.33-3.27 (m, 3H), 3.22-3.15 (m, 1H), 2.90-1.60 (br m, 10H), 2.29 (dddd, 1H, *J* = 9.5, 5.7, 2.6, 2.5 Hz), 2.16 (dddd, 1H, *J* = 13.8, 6.2, 2.6, 1.3 Hz), 1.92 (ddd, 1H, *J* = 13.8, 11.6, 2.5 Hz), 1.78 (ddddd, 1H, *J* = 13.5, 6.4, 5.6, 2.7, 1.4 Hz), 1.56 (d, 1H, *J* = 5.6 Hz), 1.48 (dddd, 1H, *J* = 13.4, 11.7, 9.5, 2.7 Hz), 1.43-1.06 (m, 8H), 0.83 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.1, 128.6, 87.4, 85.5, 73.0, 63.7, 40.3, 40.2, 40.0, 39.9, 36.9, 29.9, 26.3, 22.6, 14.1.

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(hydroxyl(phenyl)methyl)-1,12-dicarba-*closo*-dodecaborane (18e): Compound **18e** was prepared from **17** in a similar manner to that used for preparation of **18a**, but with benzaldehyde as a reagent. 86% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.26 (m, 3H), 7.15-7.11 (m, 2H), 5.72 (ddd, 1H, *J* = 10.1, 2.6, 1.3 Hz), 5.34 (ddd, 1H, *J* = 10.1, 2.2, 1.1 Hz), 4.60 (d, 1H, *J* = 3.2 Hz), 3.32-3.27 (m, 3H), 3.21-3.14 (m, 1H), 2.80-1.60 (br m, 10H), 2.26 (dddd, 1H, *J* = 9.5, 5.7, 2.6, 2.5 Hz), 2.17 (d, 1H, *J* = 3.7 Hz), 2.15 (dddd, 1H, *J* = 13.8, 6.2, 2.6, 1.3 Hz), 1.90 (ddd, 1H, *J* = 13.8, 11.6, 2.5 Hz), 1.75 (ddddd, 1H, *J* = 13.5, 6.4, 5.6, 2.7, 1.4 Hz), 1.45 (dddd, 1H, *J* = 13.4, 11.7, 9.5, 2.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.3, 133.1, 128.8, 128.6, 128.2, 126.9, 86.5, 85.9, 75.8, 63.7, 40.3, 40.2, 40.0, 39.9, 29.9.

1-Acetyl-12-(1,4-dithia-spiro[4.5]dec-6-en-8-yl)-1,12-dicarba-*closo*-dodecaborane (19): To a solution of **18a** (37.0 mg, 0.103 mmol) in CH_2Cl_2 (850 μL) was added 4A molecular sieves (powder, 100 mg) under Ar, followed by addition of PDC (116 mg, 0.310 mmol) at 0 °C. The mixture was stirred at rt for 4 h. Purification by silica gel column chromatography (eluent: hexane/AcOEt, 10:1) gave **19** (48%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.76 (ddd, 1H, *J* = 10.0, 2.6, 1.3 Hz), 5.35 (ddd, 1H, *J* = 10.0, 2.6, 1.5 Hz), 3.34-3.28 (m, 3H), 3.23-3.15 (m, 1H), 3.00-1.70 (br m, 10H), 2.29 (dddd, 1H, *J* = 9.5,

5.7, 2.6, 2.5 Hz), 2.16 (dddd, 1H, *J* = 13.8, 6.2, 2.6, 1.3 Hz), 2.06 (s, 3H), 1.93 (ddd, 1H, *J* = 13.8, 11.6, 2.5 Hz), 1.78 (ddddd, 1H, *J* = 13.5, 6.4, 5.6, 2.7, 1.4 Hz), 1.48 (dddd, 1H, *J* = 13.4, 11.7, 9.5, 2.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.2, 133.5, 128.1, 87.8, 84.5, 63.6, 40.3, 40.3, 40.2, 40.0, 29.8, 27.6.

4-(12-Acetyl-1,12-dicarba-*closo*-dodecaboran-1-yl)-2-cyclohexen-1-one (11a): To a solution of **19** (17.6 mg, 0.0494 mmol) in MeCN:THF:H_2O = 2:1:2 (1.95 mL) was added MeI (615 μL, 9.88 mmol) at 0 °C. The mixture was stirred at 60 °C for 3.5 h, poured into water and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. Purification of the residue by silica gel column chromatography (eluent: hexane/AcOEt, 10:1) gave **11a** (66%) as a brown solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.64 (ddd, 1H, *J* = 10.5, 2.6, 1.9 Hz), 5.89 (ddd, 1H, *J* = 10.4, 2.8, 0.9 Hz), 3.00-1.80 (br m, 10H), 2.63 (dddd, 1H, *J* = 10.2, 4.5, 2.6, 2.4 Hz), 2.44 (dddd, 1H, *J* = 16.9, 4.2, 4.2, 0.5 Hz), 2.19 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 2.07 (s, 3H), 2.01 (ddddd, 1H, *J* = 13.3, 4.7, 4.7, 4.7, 1.8 Hz), 1.69 (dddd, 1H, *J* = 13.2, 13.1, 10.3, 4.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 192.7, 149.6, 129.7, 85.9, 85.0, 41.6, 37.0, 29.7, 27.5; Anal. Calcd for $C_{10}H_{20}B_{10}O_2$: C, 42.84%; H, 7.19%. Found: C, 42.86%; H, 6.97%.

4-[12-(1-Hydroxyethyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (13a): To a solution of **18a** (94.2 mg, 0.263 mmol) in MeCN:THF:H_2O = 12:3:1 (1.3 mL) was added Dess-Martin periodinane (111 mg, 0.263 mmol) at 0 °C. The mixture was stirred at rt for 3 h, poured into water and saturated aqueous $NaHCO_3$ and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. Purification by silica gel column chromatography (eluent: hexane/AcOEt, 5:1) gave **13a** (79%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.67 (ddd, 1H, *J* = 10.4, 2.5, 1.9 Hz), 5.88 (ddd, 1H, *J* = 10.4, 2.8, 0.8 Hz), 3.70 (quint, 1H, *J* = 6.3 Hz), 3.00-1.70 (br m, 10H), 2.65 (m, 1H), 2.44 (dddd, 1H, *J* = 16.9, 4.2, 4.2, 0.6 Hz), 2.19 (ddd, 1H, *J* = 16.9, 12.9, 4.7 Hz), 2.05-1.98 (m, 1H), 1.74-1.65 (m, 1H), 1.62 (d, 1H, *J* = 5.9 Hz), 1.07 (d, 3H, *J* = 6.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 150.3, 129.5, 87.9, 83.7, 69.4, 41.3, 37.1, 29.9, 23.1; Anal. Calcd for $C_{10}H_{22}B_{10}O_2$: C, 42.53%; H, 7.85%. Found: C, 42.38%; H, 7.56%.

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(1-hydroxypropyl)-1,12-dicarba-*closo*-dodecaborane (13b): Compound **13b** was prepared from **18b** in a similar manner to that used for preparation of **13a**. 73% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.66 (ddd, 1H, *J* = 10.4, 2.1, 1.9 Hz), 5.86 (ddd, 1H, *J* = 10.4, 2.1, 0.5 Hz), 3.31 (m, 1H), 2.90-1.60 (br m, 10H), 2.63 (dddd, 1H, *J* = 10.2, 4.5, 2.6, 2.4 Hz), 2.42 (ddd, 1H, *J* = 16.9, 4.2, 4.2 Hz), 2.17 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 2.04-1.96 (m, 1H), 1.80 (br s, 1H), 1.68 (dddd, 1H, *J* = 13.2, 13.1, 10.3, 4.1 Hz), 1.46-1.37 (m, 1H), 1.16 (m, 1H), 0.85 (t, 3H, *J* = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.1, 150.4, 129.4, 88.0, 83.7, 74.4, 41.3, 37.0, 29.9, 29.8, 11.2; Anal. Calcd for $C_{11}H_{24}B_{10}O_2$: C, 44.57%; H, 8.16%. Found: C, 44.84%; H, 8.04%.

4-[12-(1-Hydroxy-2-methylpropyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (13c): Compound **13c** was prepared from **18c** in a similar manner to that used for preparation of **13a**. 67% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.67 (ddd, 1H, *J* = 10.4, 2.4, 2.0 Hz), 5.88 (dd, 1H, *J* = 10.4, 2.7 Hz), 3.38 (dd, 1H, *J* = 7.0, 1.1 Hz), 3.00-1.70 (br m, 10H), 2.64 (dddd, 1H, *J* = 10.2, 4.5, 2.6, 2.4 Hz), 2.44 (dddd, 1H, *J* = 16.9, 4.2, 4.2 Hz), 2.19 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 2.01 (ddddd, 1H, *J* = 13.3, 4.7, 4.7, 4.7, 1.8 Hz), 1.75 (m, 1H), 1.73-1.65 (m, 1H), 1.54 (d, 1H, *J* = 7.1 Hz) , 0.89 (d, 3H, *J* = 6.9 Hz), 0.76 (d, 3H, *J* = 6.6 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 150.3, 129.5, 87.7, 84.2, 77.2, 41.3, 37.0, 32.3, 29.9, 22.7, 14.2; Anal. Calcd for $C_{12}H_{26}B_{10}O_2$: C, 52.30%; H, 7.02%. Found: C, 46.58%; H, 8.19%.

4-[12-(1-Hydroxyhexyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (13d): Compound **13d** was prepared from **18d** in a similar manner to that used for preparation of **13a**. 57% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.67 (ddd, 1H, *J* = 10.5, 2.2, 2.1 Hz), 5.87 (dd, 1H, *J* = 10.4, 2.7 Hz), 3.41 (dd, 1H, *J* = 9.6, 6.0 Hz), 2.90-1.60 (br m, 10H), 2.63 (dddd, 1H, *J* = 10.2, 4.5, 2.6, 2.4 Hz), 2.43 (ddd, 1H, *J* = 16.9, 4.2, 4.2 Hz), 2.18 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 2.01 (ddddd, 1H, *J* = 13.3, 4.7, 4.7, 4.7, 1.8 Hz), 1.79 (br s, 1H), 1.69 (dddd, 1H, *J* = 13.2, 13.1, 10.3, 4.1 Hz), 1.45-1.07 (m, 8H), 0.83 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 150.4, 129.4, 88.1, 83.8, 73.0, 41.3, 37.0, 36.9, 31.4, 29.8, 26.2, 22.6, 14.1; Anal. Calcd for $C_{14}H_{30}B_{10}O_2$: C, 49.68%; H, 8.93%. Found: C, 49.49%; H, 8.65%.

4-[12-Hydroxy(phenyl)methyl-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (13e): Compound **13e** was prepared from **18e** in a similar manner to that used for preparation of **13a**. 52% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.26 (m, 3H), 7.15-7.10 (m, 2H), 6.63 (ddd, 1H, *J* = 10.4, 2.0, 2.0 Hz), 5.84 (dd, 1H, *J* = 10.5, 2.7 Hz), 4.60 (d, 1H, *J* = 3.2 Hz), 2.90-1.60 (br m, 10H), 2.60 (dddd, 1H, *J* = 10.2, 4.5, 2.6, 2.4 Hz), 2.47 (br s, 1H), 2.39 (ddd, 1H, *J* = 16.9, 4.2, 4.2 Hz), 2.14 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 1.97 (ddddd, 1H, *J* = 13.3, 4.7, 4.7, 4.7, 1.8 Hz), 1.64 (dddd, 1H, *J* = 13.2, 13.1, 10.3, 4.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.1, 150.4, 140.3, 129.4, 128.8, 128.2, 126.8, 87.2, 84.0, 75.7, 41.3, 37.0, 29.8; Anal. Calcd for $C_{15}H_{24}B_{10}O_2$: C, 52.30%; H, 7.02%. Found: C, 52.24%; H, 7.10%.

4-(12-Propionyl-1,12-dicarba-*closo*-dodecaboran-1-yl)-2-cyclohexen-1-one (11b): To a solution of **13b** (52.8 mg, 0.182 mmol) in CH_2Cl_2 (2.0 mL) was added Dess-Martin periodinane (111.2 mg, 0.272 mmol) at 0 °C under Ar. The mixture was stirred at rt for 22 h, poured into aqueous $Na_2S_2O_4$, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. Purification of the residue by silica gel column chromatography (eluent: hexane/AcOEt, 10:1) gave **11b** (89%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.62 (ddd, 1H, *J* = 10.4, 2.4, 2.1 Hz), 5.87 (ddd, 1H, *J* = 10.4, 2.7, 0.7 Hz), 3.00-1.70 (br m, 10H), 2.65-2.59 (m, 1H), 2.42 (ddd, 1H, *J* = 16.9, 4.4, 4.4 Hz), 2.36 (q, 2H, *J* = 7.1 Hz), 2.17 (ddd, 1H, *J* = 16.9, 12.9, 4.7 Hz), 2.03-1.96 (m, 1H), 1.72-1.63 (m, 1H),

0.88 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.6, 195.3, 149.6, 129.7, 85.9, 85.0, 41.6, 36.9, 32.9, 29.7, 7.8; Anal. Calcd for $C_{11}H_{22}B_{10}O_2$: C 44.88%; H, 7.53%. Found: C, 44.89%; H, 7.26%.

4-[12-Isobutyryl-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (11c): Compound **11c** was prepared from **13c** in a similar manner to that used for preparation of **11b**. 84% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.64 (ddd, 1H, *J* = 10.4, 2.3, 2.1 Hz), 5.88 (dd, 1H, *J* = 10.4, 2.7 Hz), 3.00-1.80 (br m, 10H), 2.86 (dddd, 1H, *J* = 10.2, 4.5, 2.6, 2.4 Hz), 2.43 (ddd, 1H, *J* = 16.9, 4.2, 4.2 Hz), 2.19 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 2.01 (ddddd, 1H, *J* = 13.3, 4.7, 4.7, 4.7, 1.8 Hz), 1.69 (dddd, 1H, *J* = 13.2, 13.1, 10.3, 4.1 Hz), 0.94 (d, 6H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.6, 197.7, 149.7, 129.7, 86.3, 85.2, 41.7, 37.1, 37.0, 29.7, 19.8; Anal. Calcd for $C_{12}H_{24}B_{10}O_2$: C, 46.73%; H, 7.84%. Found: C, 46.62%; H, 7.60%.

4-[12-Hexanoyl-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (11d): Compound **11d** was prepared from **13d** in a similar manner to that used for preparation of **11b**. 78% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.63 (ddd, 1H, *J* = 10.5, 2.2, 2.1 Hz), 5.88 (ddd, 1H, *J* = 10.4, 2.4, 0.4 Hz), 3.00-1.70 (br m, 10H), 2.65-2.60 (m, 1H), 2.43 (ddd, 1H, *J* = 16.9, 4.4, 4.4 Hz), 2.33 (t, 2H, *J* = 7.2 Hz), 2.18 (ddd, 1H, *J* = 16.9, 12.9, 4.7 Hz), 2.04-1.97 (m, 1H), 1.72-1.63 (m, 1H), 1.38 (quint, 2H, *J* = 7.4 Hz), 1.26-1.17 (m, 2H), 1.16-1.08 (m, 2H), 0.82 (t, 3H, *J* = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 194.8, 149.6, 129.7, 85.9, 85.3, 41.6, 39.3, 36.9, 30.9, 29.7, 23.3, 22.4, 13.9.

4-(12-Benzoyl-1,12-dicarba-*closo*-dodecaboran-1-yl)-2-cyclohexen-1-one (11e): Compound **11e** was prepared from **13e** in a similar manner to that used for preparation of **11b**. 75% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47-7.42 (m, 3H), 7.35-7.31 (m, 2H), 6.64 (ddd, 1H, *J* = 10.5, 2.6, 1.9 Hz), 5.89 (dd, 1H, *J* = 10.4, 2.4 Hz), 3.20-1.80 (br m, 10H), 2.68-2.62 (m, 1H), 2.43 (ddd, 1H, *J* = 16.9, 4.2, 4.2 Hz), 2.19 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 2.05-1.98 (m, 1H), 1.74-1.65 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.6, 189.6, 149.6, 136.4, 132.1, 129.7, 128.3, 128.1, 87.1, 84.7, 41.7, 36.9, 29.7; Anal. Calcd for $C_{15}H_{22}B_{10}O_2$: C, 52.61%; H, 6.48%. Found: C, 52.35%; H, 6.25%.

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-[2-(tetrahydro-2H-pyran-2-yloxy)ethyl]-1,12-dicarba-*closo*-dodecaborane (20): To a solution of **17** (798 mg, 2.54 mmol) in Et_2O (11 mL) was added *n*-BuLi in *n*-hexane (2.77 mol/L, 1.1 mL, 3.05 mmol) at 0 °C under Ar. The mixture was stirred at rt for 30 min, then *O*-tetrahydropyranyl-2-bromoethanol (789 mg, 3.82 mmol) was added at 0 °C under Ar. The mixture was stirred at rt for 72 h, poured into water, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. Purification by silica gel column chromatography (eluent: hexane/CH_2Cl_2, 1:1) gave **20** (56%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.78 (ddd, 1H, *J* = 10.0, 2.6, 1.3 Hz), 5.37 (ddd, 1H, *J* = 10.1, 2.6, 1.4 Hz), 4.45 (dd, 1H, *J* = 3.6, 3.5 Hz), 3.76 (ddd, 1H, *J* = 11.3, 8.2, 3.1 Hz), 3.49 (ddd, 1H, *J* = 9.4, 7.7, 7.0 Hz), 3.47-3.42 (m, 1H), 3.33-3.28 (m, 3H), 3.22-3.15 (m, 1H), 3.12 (ddd, 1H, *J* = 9.7, 8.0, 7.2 Hz), 2.90-1.60 (br m, 10H), 2.29-2.24 (m, 1H),

2.19-2.12 (m, 1H), 1.92 (dd, 2H, *J* = 8.1, 7.3 Hz), 1.91 (ddd, 1H, *J* = 14.0, 11.5, 2.6 Hz), 1.80-1.73 (m, 1H), 1.77-1.70 (m, 1H), 1.66-1.58 (m, 1H), 1.54-1.44 (m, 1H), 1.51-1.42 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.0, 128.7, 99.1, 83.5, 78.3, 66.1, 63.7, 62.5, 40.3, 40.3, 40.0, 39.8, 37.3, 30.7, 29.9, 25.5, 19.6.

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(2-hydroxyethyl)-1,12-dicarba-*closo*-dodecaborane (21): To a solution of **20** (588 mg, 1.33 mmol) in CH_2Cl_2 (5.0 mL) were added MeOH (10 mL) and *p*-TsOH monohydride (25.3 mg, 0.133 mmol). The mixture was stirred at rt for 2 h, poured into aqueous $NaHCO_3$, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. Purification by silica gel column chromatography (eluent: hexane/AcOEt, 3:1) gave **21** (92%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (ddd, 1H, *J* = 10.1, 2.6, 1.3 Hz), 5.36 (ddd, 1H, *J* = 10.1, 2.6, 1.4 Hz), 3.42 (td, 2H, *J* = 7.0, 5.8 Hz), 3.34-3.28 (m, 3H), 3.22-3.15 (m, 1H), 2.90-1.60 (br m, 10H), 2.30-2.24 (m, 1H), 2.19-2.13 (m, 1H), 1.92 (ddd, 2H, *J* = 13.8, 11.7, 2.7 Hz), 1.89 (t, 1H, *J* = 7.0 Hz), 1.80-1.73 (m, 1H), 1.51-1.42 (m, 1H), 1.25 (t, 1H, *J* = 5.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.1, 128.6, 83.7, 78.2, 63.7, 61.6, 40.3, 40.3, 40.0, 40.0, 39.8, 29.9.

2-[12-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-1,12-dicarba-*closo*-dodecaboran-1-yl]acetaldehyde (22): To a solution of **21** (373 mg, 1.04 mmol) in CH_2Cl_2 (4.2 mL) was added TEMPO (22.7 mg, 0.104 mmol) under Ar, followed by addition of iodobenzene diacetate (366 mg, 1.14 mmol) at 0 °C. The mixture was stirred at rt for 9 h, poured into aqueous $Na_2S_2O_3$, and extracted with AcOEt. The organic layer was washed with aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. Purification by silica gel column chromatography (eluent: hexane/AcOEt, 15:1) gave **22** (64%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 (t, 1H, *J* = 2.8 Hz), 5.74 (ddd, 1H, *J* = 10.0, 2.4, 1.1 Hz), 5.34 (ddd, 1H, *J* = 10.1, 2.4, 1.3 Hz), 3.33-3.27 (m, 3H), 3.21-3.14 (m, 1H), 3.00-1.70 (br m, 10H), 2.51 (d, 2H, *J* = 2.7 Hz), 2.31-2.25 (m, 1H), 2.19-2.12 (m, 1H), 1.91 (ddd, 2H, *J* = 13.8, 11.8, 2.6 Hz), 1.80-1.73 (m, 1H), 1.51-1.41 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.8, 133.2, 128.1, 84.9, 72.9, 63.4, 48.7, 40.2, 40.0, 39.8, 39.8, 29.8.

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(2-hydroxypropyl)-1,12-dicarba-*closo*-dodecaborane (23a): To a solution of **22** (95.1 mg, 0.280 mmol) in THF (2.0 mL) was added MeMgBr (0.93 mol/L, 0.33 mL, 0.309 mmol) at -78 °C under Ar. The mixture was stirred at 0 °C to rt for 3 h, then poured into saturated aqueous NH_4Cl, and extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. Purification by silica gel column chromatography (eluent: hexane/AcOEt, 15:1), twice, gave **23a** (32%) as a colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.73 (ddd, 1H, *J* = 10.1, 2.5, 1.2 Hz), 5.36 (ddd, 1H, *J* = 10.1, 2.5, 1.3 Hz), 3.62 (br s, 1H), 3.33-3.27 (m, 3H), 3.22-3.15 (m, 1H), 2.90-1.70 (br m, 10H), 2.30-2.25 (m, 1H), 2.19-2.13 (m, 1H), 1.92 (ddd, 2H, *J* = 13.8, 11.8, 2.6 Hz), 1.80-1.75 (m, 1H), 1.77 (d, 1H, *J* = 15.3 Hz), 1.73 (dd, 1H, *J* = 15.2, 3.3 Hz), 1.52 (br s, 1H), 1.51-1.42 (m, 1H), 1.02 (d, 3H,

J = 6.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.1, 128.6, 83.9, 79.0, 67.0, 63.7, 46.9, 40.3, 40.2, 40.0, 39.8, 29.9, 23.8.

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(2-hydroxybutyl)-1,12-dicarba-*closo*-dodecaborane (23b): Compound **23b** was prepared from **22** in a similar manner to that used for preparation of **23a**, but with EtMgBr as a reagent. 47% yield, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.72 (ddd, 1H, *J* = 10.1, 1.2, 1.2 Hz), 5.36 (ddd, 1H, *J* = 10.0, 1.2, 1.2 Hz), 3.36-3.27 (m, 1H), 3.34-3.26 (m, 3H), 3.21-3.14 (m, 1H), 2.90-1.60 (br m, 10H), 2.30-2.24 (m, 1H), 2.18-2.12 (m, 1H), 1.92 (ddd, 1H, *J* = 13.8, 11.9, 2.6 Hz), 1.80-1.72 (m, 1H), 1.76 (dd, 1H, *J* = 15.0, 1.8 Hz), 1.70 (dd, 1H, *J* = 15.4, 8.4 Hz), 1.51-1.41 (m, 1H), 1.30-1.22 (m, 2H), 0.81 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.0, 128.6, 83.7, 79.2, 72.1, 63.7, 45.1, 40.3, 40.2, 39.9, 39.8, 30.3, 29.9, 9.8.

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(2-hydroxy-3-methylbutyl)-1,12-dicarba-*closo*-dodecaborane (23c): Compound **23c** was prepared from **22** in a similar manner to that used for preparation of **23a**, but with *n*-PrMgBr as a reagent. 34% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.72 (dd, 1H, *J* = 10.1, 1.2 Hz), 5.36 (ddd, 1H, *J* = 10.1, 1.9, 1.4 Hz), 3.43-3.38 (m, 1H), 3.32-3.27 (m, 3H), 3.21-3.14 (m, 1H), 2.90-1.70 (br m, 10H), 2.30-2.24 (m, 1H), 2.18-2.12 (m, 1H), 1.91 (ddd, 1H, *J* = 13.8, 11.8, 2.6 Hz), 1.80-1.74 (m, 1H), 1.75 (dd, 1H, *J* = 15.1, 2.6 Hz), 1.70 (dd, 1H, *J* = 15.4, 8.3 Hz), 1.51-1.42 (m, 1H), 1.36-1.25 (m, 4H), 0.84 (t, 3H, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.0, 128.6, 83.8, 79.4, 70.6, 63.7, 45.4, 40.3, 40.2, 39.9, 39.8, 39.6, 29.9, 18.6, 14.0.

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(2-hydroxyheptyl)-1,12-dicarba-*closo*-dodecaborane (23d): Compound **23d** was prepared from **22** in a similar manner to that used for preparation of **23a**, but with *i*-PrMgBr as a reagent. 11% yield, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.73 (ddd, 1H, *J* = 10.1, 1.1, 1.1 Hz), 5.37 (d, 1H, *J* = 10.0 Hz), 3.33-3.27 (m, 3H), 3.23-3.18 (m, 1H), 3.23-3.15 (m, 1H), 2.90-1.60 (br m, 10H), 2.32-2.25 (m, 1H), 2.19-2.13 (m, 1H), 1.92 (ddd, 1H, *J* = 13.8, 11.7, 2.4 Hz), 1.81-1.73 (m, 1H), 1.76 (d, 1H, *J* = 14.9 Hz), 1.66 (dd, 1H, *J* = 15.3, 9.2 Hz), 1.52-1.43 (m, 1H), 1.51-1.44 (m, 1H), 0.78 (t, 3H, *J* = 6.8 Hz), 0.75 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.0, 128.7, 83.7, 79.6, 75.4, 63.7, 42.6, 40.3, 40.3, 40.0, 39.8, 33.8, 29.9, 18.5, 17.0

1-(1,4-Dithia-spiro[4.5]dec-6-en-8-yl)-12-(2-hydroxy-2-phenylethyl)-1,12-dicarba-*closo*-dodecaborane (23e): Compound **23e** was prepared from **22** in a similar manner to that used for preparation of **23a**, but with PhMgCl as a reagent. 33% yield, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.25 (m, 2H), 7.25-7.20 (m, 1H), 7.20-7.16 (m, 2H), 5.74 (ddd, 1H, *J* = 10.0, 2.3, 1.0 Hz), 5.39 (d, 1H, *J* = 10.1 Hz), 4.50 (d, 1H, *J* = 9.6 Hz), 3.34-3.28 (m, 3H), 3.22-3.15 (m, 1H), 3.00-1.60 (br m, 10H), 2.33-2.26 (m, 1H), 2.20-2.14 (m, 1H), 2.07 (dd, 1H, *J* = 15.5, 9.6 Hz), 1.94 (dd, 1H, *J* = 14.3, 2.1 Hz), 1.93 (ddd, 1H, *J* = 13.7, 12.1, 2.5 Hz), 1.88 (d, 1H, *J* = 3.2 Hz), 1.82-1.75 (m, 1H), 1.53-1.44 (m, 1H); ^{13}C

NMR (125 MHz, $CDCl_3$) δ 143.5, 133.1, 128.7, 128.6, 128.0, 125.7, 83.9, 78.9, 73.3, 63.7, 47.2, 40.3, 40.2, 40.0, 39.8, 29.9.

4-[12-(2-Hydroxypropyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (14a): Compound **14a** was prepared from **23a** in a similar manner to that used for preparation of **13a**. 85% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.65 (ddd, 1H, *J* = 10.4, 2.1, 2.0 Hz), 5.87 (dd, 1H, *J* = 10.4, 2.7 Hz), 3.66-3.58 (m, 1H), 2.90-1.60 (br m, 10H), 2.65-1.59 (m, 1H), 2.42 (ddd, 1H, *J* = 16.9, 4.4, 4.4 Hz), 2.17 (ddd, 1H, *J* = 16.9, 12.9, 4.7 Hz), 2.03-1.96 (m, 1H), 1.78 (dd, 1H, *J* = 15.3, 8.1 Hz), 1.73 (dd, 1H, *J* = 15.4, 3.3 Hz), 1.72-1.63 (m, 1H), 1.57 (br s, 1H), 1.03 (d, 3H, *J* = 6.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 150.3, 129.5, 82.1, 79.7, 67.0, 46.9, 41.2, 37.0, 29.8, 23.0.

4-[12-(2-Hydroxybutyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (14b): Compound **14b** was prepared from **23b** in a similar manner to that used for preparation of **13a**. 52% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.66 (ddd, 1H, *J* = 10.4, 2.1, 1.8 Hz), 5.86 (dd, 1H, *J* = 10.4, 2.7 Hz), 3.66-3.29 (m, 1H), 2.90-1.60 (br m, 10H), 2.64-2.59 (m, 1H), 2.42 (ddd, 1H, *J* = 16.9, 4.4, 4.4 Hz), 2.17 (ddd, 1H, *J* = 16.9, 12.9, 4.7 Hz), 2.03-1.96 (m, 1H), 1.77 (dd, 1H, *J* = 15.2, 2.3 Hz), 1.72 (dd, 1H, *J* = 15.0, 8.3 Hz), 1.72-1.63 (m, 1H), 1.33-1.21 (m, 2H), 0.81 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 150.4, 129.4, 82.0, 79.9, 72.1, 45.1, 41.2, 37.0, 30.4, 29.9, 9.7; Anal. Calcd for $C_{12}H_{26}B_{10}O_2$: C, 46.43%; H, 8.44%. Found: C, 46.25%; H, 8.31%.

4-[12-(2-Hydroxy-3-methylbutyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (14c): Compound **14c** was prepared from **23c** in a similar manner to that used for preparation of **13a**. 64% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.65 (ddd, 1H, *J* = 10.4, 2.1, 2.0 Hz), 5.86 (dd, 1H, *J* = 10.4, 2.7 Hz), 3.44-3.38 (m, 1H), 2.90-1.60 (br m, 10H), 2.64-2.59 (m, 1H), 2.42 (ddd, 1H, *J* = 16.9, 4.4, 4.3 Hz), 2.17 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 2.03-1.96 (m, 1H), 1.77 (dd, 1H, *J* = 15.4, 2.9 Hz), 1.72 (dd, 1H, *J* = 15.5, 8.1 Hz), 1.72-1.62 (m, 1H), 1.36-1.15 (m, 4H), 0.84 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 150.4, 129.4, 82.0, 79.9, 70.6, 45.4, 41.2, 39.7, 37.0, 29.8, 18.6, 14.0; Anal. Calcd for $C_{13}H_{28}B_{10}O_2$: C, 48.12%; H, 8.70%. Found: C, 47.84%; H, 8.50%.

4-[12-(2-Hydroxyheptyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (14d): Compound **14d** was prepared from **23d** in a similar manner to that used for preparation of **13a**. 61% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.66 (ddd, 1H, *J* = 10.4, 2.1, 2.0 Hz), 5.87 (dd, 1H, *J* = 10.5, 2.7 Hz), 3.21 (dd, 1H, *J* = 6.1, 4.4 Hz), 3.00-1.60 (br m, 10H), 2.65-2.60 (m, 1H), 2.43 (ddd, 1H, *J* = 16.7, 4.3, 4.2 Hz), 2.18 (ddd, 1H, *J* = 16.9, 12.8, 4.7 Hz), 2.04-1.97 (m, 1H), 1.78 (d, 1H, *J* = 15.2 Hz), 1.73-1.63 (m, 1H), 1.68 (dd, 1H, *J* = 15.6, 9.4 Hz), 1.53-1.43 (m, 1H), 0.79 (d, 3H, *J* = 6.8 Hz), 0.76 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 150.4, 129.5, 81.9, 80.3, 75.4, 42.6, 41.2, 37.0, 33.9, 29.9, 18.5, 16.9.

4-[12-(2-Hydroxy-2-phenylethyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (14e): Compound **14e** was prepared from **23e** in a similar manner to that used for preparation of **13a**. 47% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.25 (m, 2H), 7.25-7.20 (m, 1H), 7.20-7.16 (m, 2H), 6.67 (ddd, 1H, *J* = 10.4, 2.1, 2.0 Hz), 5.87 (dd, 1H, *J* = 10.4, 2.87 Hz), 4.50 (d, 1H, *J* = 9.5 Hz), 3.00-1.70 (br m, 10H), 2.66-2.61 (m, 1H), 2.43 (ddd, 1H, *J* = 16.9, 4.4, 4.4 Hz), 2.18 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 2.09 (dd, 1H, *J* = 15.5, 9.6 Hz), 2.05-1.98 (m, 1H), 1.94 (dd, 1H, *J* = 15.0, 1.7 Hz), 1.93 (br s, 1H), 1.74-1.64 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 150.4, 143.4, 129.4, 128.8, 128.1, 125.7, 82.2, 79.6, 73.3, 47.1, 41.2, 37.0, 29.9; Anal. Calcd for $C_{16}H_{26}B_{10}O_2$: C, 53.61%; H, 7.31%. Found: C, 53.33%; H, 7.16%.

4-[12-(2-Oxopropyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (12a): Compound **12a** was prepared from **14a** in a similar manner to that used for preparation of **11b**. 82% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.63 (ddd, 1H, *J* = 10.4, 2.1, 2.0 Hz), 5.87 (dd, 1H, *J* = 10.4, 2.8 Hz), 2.90-1.70 (br m, 10H), 2.63 (s, 2H), 2.63-2.58 (m, 1H), 2.43 (ddd, 1H, *J* = 16.9, 4.4, 4.4 Hz), 2.17 (ddd, 1H, *J* = 16.9, 12.9, 4.7 Hz), 2.06 (s, 3H), 2.03-1.96 (m, 1H), 1.71-1.61 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.9, 197.8, 150.0, 129.6, 82.6, 74.8, 49.6, 41.2, 37.0, 31.6, 29.8; Anal. Calcd for $C_{11}H_{22}B_{10}O_2$: C, 44.88%; H, 7.53%. Found: C, 44.63%; H, 7.28%.

4-[12-(2-Oxobutyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (12b): Compound **12b** was prepared from **14b** in a similar manner to that used for preparation of **11b**. 75% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.63 (ddd, 1H, *J* = 10.4, 1.8, 1.7 Hz), 5.86 (dd, 1H, *J* = 10.4, 2.7 Hz), 3.00-1.70 (br m, 10H), 2.64-2.58 (m, 1H), 2.60 (s, 2H), 2.42 (ddd, 1H, *J* = 16.9, 4.5, 4.4 Hz), 2.32 (q, 2H, *J* = 7.2 Hz), 2.17 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 2.03-1.95 (m, 1H), 1.71-1.61 (m, 1H), 0.96 (t, 3H, *J* = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.5, 197.9, 150.1, 129.5, 82.5, 75.2, 48.5, 41.2, 37.6, 37.0, 29.8, 7.3; Anal. Calcd for $C_{12}H_{24}B_{10}O_2$: C, 46.73%; H, 7.84%. Found: C, 46.65%; H, 7.93%.

4-[12-(2-Oxo-3-methylbutyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (12c): Compound **12c** was prepared from **14c** in a similar manner to that used for preparation of **11b**. 74% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.63 (ddd, 1H, *J* = 10.4, 1.8, 1.7 Hz), 5.87 (dd, 1H, *J* = 10.4, 2.7 Hz), 2.90-1.70 (br m, 10H), 2.64-2.58 (m, 1H), 2.59 (s, 2H), 2.42 (ddd, 1H, *J* = 16.9, 4.4, 4.4 Hz), 2.27 (t, 2H, *J* = 7.2 Hz), 2.17 (ddd, 1H, *J* = 16.9, 13.0, 4.6 Hz), 2.02-1.96 (m, 1H), 1.71-1.62 (m, 1H), 1.49 (sextet, 2H, *J* = 7.3 Hz), 0.86 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.0, 197.9, 150.1, 129.5, 82.5, 75.2, 48.5, 46.3, 41.2, 37.0, 29.8, 16.8, 13.7.

4-[12-(2-Oxoheptyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (12d): Compound **12d** was prepared from **14d** in a similar manner to that used for preparation of **11b**. 35% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.64 (ddd, 1H, *J* = 10.4, 2.2, 2.0 Hz), 5.87 (ddd, 1H, *J* = 10.4, 2.7, 0.7 Hz), 2.90-1.70 (br m, 10H), 2.67 (s, 2H), 2.64-2.59 (m, 1H) , 2.46 (septet, 1H, *J* = 6.9 Hz), 2.43 (ddd,

1H, *J* = 16.9, 4.3, 4.3 Hz), 2.18 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 2.03-1.96 (m, 1H), 1.72-1.62 (m, 1H), 0.98 (d, 6H, *J* = 6.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.5, 197.9, 150.2, 129.6, 82.6, 75.5, 46.5, 41.6, 41.2, 37.1, 29.9, 17.7.

4-[12-(2-Oxo-2-phenylethyl)-1,12-dicarba-*closo*-dodecaboran-1-yl]-2-cyclohexen-1-one (12e): Compound **12e** was prepared from **14e** in a similar manner to that used for preparation of **11b**. 94% yield, colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (dd, 2H, *J* = 8.2, 1.3 Hz), 7.57 (tt, 1H, *J* = 7.4, 1.1 Hz), 7.44 (dd, 2H, *J* = 8.1, 7.6 Hz), 6.62 (ddd, 1H, *J* = 10.5, 2.2, 1.9 Hz), 5.96 (ddd, 1H, *J* = 10.4, 2.8, 0.8 Hz), 3.17 (s, 2H), 3.00-1.70 (br m, 10H), 2.63-2.57 (m, 1H), 2.41 (ddd, 1H, *J* = 16.8, 4.4, 4.3 Hz), 2.16 (ddd, 1H, *J* = 16.9, 13.0, 4.7 Hz), 2.02-1.94 (m, 1H), 1.70-1.60 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.9, 194.1, 150.1, 136.6, 133.9, 129.5, 128.9, 128.9, 82.6, 75.6, 43.8, 41.2, 37.0, 29.8; Found: C, 53.89%; H, 6.64%. Calcd for C16H24: C, 53.91%; H, 6.79%.

Biology

Alkaline phosphatase assay: The human breast-carcinoma cell line T47D was routinely cultivated in RPMI 1640 medium with 10% FBS at 37 °C in an atmosphere of 5% CO_2 in humidified air. Cells were plated in 96-well plates and incubated overnight under the same conditions. The next day, cells were treated with fresh medium containing test compound in the presence or absence of 1 nM progesterone and further incubated for 24 h. The medium was aspirated, and the cells were fixed with 100 μL of 1.8% formalin in PBS. The fixed cells were washed with PBS, and 75 μL of assay buffer (1 mg/mL *p*-nitrophenol phosphate in diethanolamine water solution, pH 9.0, 2 mM $MgCl_2$) was added. The mixture was incubated at room temperature with shielding from light for 2 h. The absorbance at 405 nm was measured with DTX 880 Multimode Detector (Beckman Coulter).

SC-3 growth inhibition assay: SC-3 cells were cultured in the presence of MEMα supplemented with 2% FBS and 1 nM dihydrotestosterone at 37 °C in an atmosphere of 5% CO_2 in humidified air. All experiments were performed in triplicate. Cells were trypsinized and diluted to 20,000 cells/mL with MEMα supplemented with 2% stripped FBS. This cell suspension was seeded in 96-well plates at a volume of 100 μL and incubated at 24 h. Then 10 μL of medium from each well was removed and replaced with 10 μL of medium containing serial dilutions of test compound or DMSO as a dilution control in the presence or absence of 1 nM dihydrotestosterone. Incubation was continued under the same conditions for 3 days, and the cell number was determined using a Cell Counting Kit-8 (DOJINDO). A 10 μL aliquot of WST-8 was added to each well, and the cells were further incubated for 1 h. The absorbance at 450 nm was measured with a DTX 880 Multimode Detector (Beckman Coulter). This parameter is related to the number of living cells in the culture.

Docking simulation: The structures of the LBDs of hPR and hAR were prepared from the Protein Data Bank accession Nos. 1A28[17] and 1I37[18], respectively. Polar hydrogens and partial atomic charges were

assigned using AutoDockTools (ADT). Molecular docking was performed using AutoDock 4.2 with the Genetic Algorithm. AutoDock parameters for boron atom were Rii = 4.08 and eii = 0.180.

ACKNOWLEDGEMENTS

This work was partially supported by the Japan Society for the Promotion of Science (JSPS) Grants in-Aid for Scientific Research (Nos. 17H03887 and 16K15138 (S.F.)).

REFERENCES AND NOTES

1. D. J. Mangelsdorf, C. Thummel, M. Beato, P. Herrlich, G. Schuetz, K. Umesono, B. Blumberg, P. Kastner, and M. Mark, *Cell*, 1995, **83**, 835; R. M. Evans, *Science*, 1988, **240**, 889.
2. A. Psychoyos, *Vitam. Horm.*, 1973, **31**, 201; Z. Zhang, C. Funk, S. R. Glasser, and J. Mulholland, *Endocrinology*, 1994, **135**, 1256; S. K. Mani, J. M. C. Allen, J. H. Clark, J. D. Blaustein, and B. W. O'Malley, *Science*, 1994, **265**, 1246; J. P. Lydon, F. J. Demayo, C. R. Funk, S. K. Mani, A. R. Hughes, C. A. Montgomery, G. Shyamala, O. M. Conneely, and B. W. O'Malley, *Genes Dev.*, 1995, **9**, 2266.
3. M. Singh and C. Su, *Neuroscience*, 2013, **239**, 84; R. Guennoun, F. Labombarda, M. C. Gonzalez Deniselle, P. Liere, A. F. De Nicola, and M. Schumacher, *J. Steroid Biochem. Mol. Biol.*, 2015, **146**, 48.
4. R. A. Edgren and F. M. Sturtevant, *Am. J. Obstet. Gynecol.*, 1976, **125**, 1029; P. Vercellini, O. De Giorgi, S. Oldani, I. Cortesi, S. Panazza, and P. G. Crosgnani, *Am. J. Obstet. Gynecol.*, 1996, **175**, 396; D. J. Torgerson and S. E. Bell-Syer, *JAMA*, 2001, **285**, 2891.
5. G. Teutsch and D. Philibert, 'Human Reproduction,' Vol. 9, Suppl. 1, ed. by R. G. Edwards, Oxford University Press, Oxford, 1994, pp. 12–31.
6. A. Fensome, R. Bender, R. Chopra, J. Cohen, M. A. Collins, V. Hudak, K. Malakian, S. Lockhead, A. Olland, K. Svenson, E. A. Terefenko, R. J. Unwalla, J. M. Wilhelm, S. Wolfrom, Y. Zhu, Z. Zhang, P. Zhang, R. C. Winneker, and J. Wrobel, *J. Med. Chem.*, 2005, **48**, 5092.
7. H. N. Hilton, J. D. Graham, and C. L. Clarke, *Mol. Endocrinol.*, 2015, **29**, 1230; L. M. Kettel, A. A. Murphy, A. J. Morales, and S. S. Yen, *Am. J. Obstet. Gynecol.*, 1998, **178**, 1151.
8. S. Fujii, A. Yamada, E. Nakano, Y. Takeuchi, S. Mori, H. Masuno, and H. Kagechika, *Eur. J. Med. Chem.*, 2014, **84**, 264; S. Fujii, E. Nakano, N. Yanagida, S. Mori, H. Masuno, and H. Kagechika, *Bioorg. Med. Chem.*, 2014, **22**, 5329.
9. Carboranes, 3rd edn., ed. by R. N. Grimes, Academic Press, London, 2016; V. I. Bregadze, *Chem. Rev.*, 1992, **92**, 209.
10. S. Fujii, H. Masuno, Y. Taoda, A. Kano, A. Wongmayura, M. Nakabayashi, N. Ito, M. Shimizu, E.

Kawachi, T. Hirano, Y. Endo, A. Tanatani, and H. Kagechika, *J. Am. Chem. Soc.*, 2011, **133**, 20933; S. Fujii, R. Sekine, A. Kano, H. Masuno, C. Songkram, E. Kawachi, T. Hirano, A. Tanatani, and H. Kagechika, *Bioorg. Med. Chem.*, 2014, **22**, 5891.

11. Y. Endo, T. Iijima, Y. Yamakoshi, M. Yamaguchi, H. Fukasawa, and K. Shudo, *J. Med. Chem.*, 1999, **42**, 1501; Y. Endo, T. Iijima, Y. Yamakoshi, H. Fukasawa, C. Miyaura, M. Inada, A. Kubo, and A. Itai, *Chem. Biol.*, 2001, **8**, 341.
12. S. Fujii, Y. Hashimoto, T. Suzuki, S. Ohta, and Y. Endo, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 227.
13. S. Fujii, T. Goto, K. Ohta, Y. Hashimoto, T. Suzuki, S. Ohta, and Y. Endo, *J. Med. Chem.*, 2005, **48**, 4654; K. Ohta, T. Goto, S. Fujii, M. Kawahata, A. Oda, S. Ohta, K. Yamaguchi, S. Hirono, and Y. Endo, *Bioorg. Med. Chem.*, 2011, **19**, 3540; A. Kaise, K. Ohta, S. Fujii, A. Oda, T. Goto, and Y. Endo, *Bioorg. Med. Chem.*, 2018, **26**, 3805.
14. D. D. Lorenzo, A. Albertini, and D. Zava, *Cancer Res.*, 1991, **51**, 4470.
15. D. Hiraoka, N. Nakamura, Y. Nishizawa, N. Uchida, S. Noguchi, K. Matsumoto, and B. Sato, *Cancer Res.*, 1987, **47**, 6560.
16. G. M. Morris, R. Huey, W. Lindstrom, M. F. Sanner, R. K. Belew, D. S. Goodsell, and A. J. Olson, *J. Comput. Chem.*, 2009, **30**, 2785.
17. S. P. Williams and P. B. Sigler, *Nature*, 1998, **393**, 392.
18. J. S. Sack, K. F. Kish, C. Wang, R. M. Attar, S. E. Kiefer, Y. An, G. Y. Wu, J. E. Scheffler, M. E. Salvati, S. R. Krystek, Jr., R. Weinmann, and H. M. Einspahr, *Proc. Natl. Acad. Sci. U.S.A.*, 2001, **98**, 4904.