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SYNTHESIS OF *o*-CARBORANE-*C*-CARBOXYLATES OF CERTAIN NATURAL TERPENE ALCOHOLS, STEROLS, PHENOLS, AND CAMPHAR OXIME

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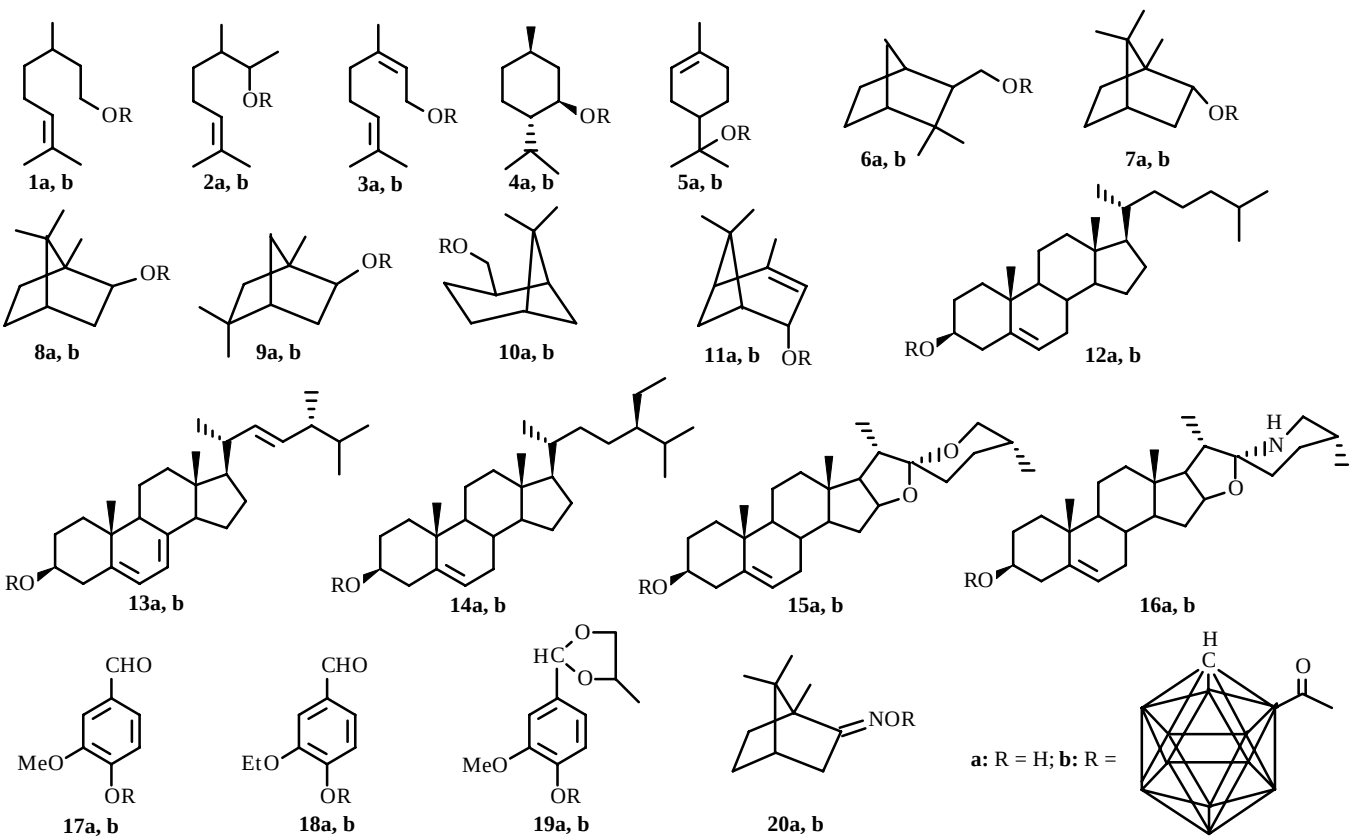
*Previously unreported esters **1b-20b** were synthesized from natural terpene alcohols, sterols, plant phenols, and camphar oxime (**1a-20a**) by reaction with* o-*carborane*-C-*carboxylic acid chloride.*

Key words: terpenols, sterols, alcohols, phenols, oximes, *o*-carborane-*C*-carboxylic acid, acid chloride, pyridine, esters, chemical modification.

Natural derivatives of polyhedral clusters are definitely interesting for pharmacokinetic studies of boron neutron capture therapy of oncologic diseases and radionuclidic diagnostics and therapy [1-4].



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The goal of our work was to prepare several new derivatives of terpene alcohols, sterols, plant phenols, and camphar oxime as esters of *o*-carborane-*C*-carboxylic acid (**1b**-**20b**) for further studies and screening as anti-tumor preparations. We selected the following natural compounds for chemical modification: citronellol (**1a**), elenol (**2a**), nerol (**3a**), (-)-1*R*,2*S*,5*R*-menthol (**4a**), terpineol (**5a**), 10-hydroxy-methylcamphene (**6a**), borneol (**7a**), isoborneol (**8a**), isofenchol (**9a**), nopol (**10a**), *trans*-verbenol (**11a**), cholesterol (**12a**), ergosterol (**13a**), *β*-sitosterol (**14a**), diosgenin (**15a**), solasodine (**16a**), vanillin (**17a**), vanillal (**18a**), vanillin 1,2-propyleneglycolacetal (**19a**), and D,L-camphar oxime (**20a**).

Esters of *o*-carborane-*C*-carboxylic acid **1b**-**20b** were prepared by reacting the corresponding hydroxy compounds **1a**-**20a** with the acid chloride of *o*-carborane-*C*-carboxylic acid in absolute benzene in the presence of pyridine. The optimal stoichiometric ratio was found to be 1:1:1. The yields of the esters were 80-90%.

The structures of the synthesized esters were confirmed by elemental analysis; PMR, IR, and UV spectra; and cryoscopic determination of molecular weights. According to PMR spectroscopy, the purity of the products was 98 ± 1%. The analyses and molecular weights of all synthesized compounds agreed with those calculated.

EXPERIMENTAL

IR spectra were recorded on a Protege-460 IR-Fourier spectrophotometer (Nicolet) in thin films or KBr; UV spectra, on a Specord UV Vis instrument as solutions ($1 \cdot 10^{-4}$ M) in CH_3OH. PMR spectra were recorded on a BS-587A spectrometer (100 MHz, Tesla) as solutions (5%) in $CDCl_3$. Chemical shifts were determined relative to TMS internal standard. Molecular weights were determined by cryoscopy in benzene. Column chromatogrpahy used silica gel L 5/40 μm and hexane eluent.

o-Carborane-*C*-carboxylic acid and its acid chloride were prepared as before [5].

Esters of *o*-Carborane-*C*-carboxylic Acid (1b-20b) (general method). The appropriate alcohol, phenol, or camphar oxime (5 mmol, **1a**-**20a**) was dissolved in absolute benzene (50 mL), treated with dry pyridine (5 mmol), cooled to 10°C and shaken, and treated with *o*-carborane-*C*-carboxylic acid chloride (5 mmol). The reaction mixture was left for 2-3 d at 20-23°C. The precipitate of pyridinium chloride was filtered off. The filtrate was thoroughly washed with water and aqueous sodium bicarbonate solution (5%) and dried with $CaCl_2$. The solvent was removed. The solid was purified by column chromatography over silica gel with hexane eluent (**1b**-**3b**, **5b**, **19b**) or by low-temperature crystallization from ethanol (96%) (**4b**, **6b**-**18b**, **20b**).

The following compounds were prepared by this method.

Citronellyl *o*-Carborane-*C*-carboxylate 1b. Yield 90%, d_{20}^{20} 0.9842, n_D^{20} 1.5140, $C_{13}H_{30}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3074 (CH_{carb}); 2965, 2927, 2874, 2854 (CH_{alk}); 2608, 2582 (BH); 1747 (C=O); 1670 (C=C); 1456 (CH_2); 1283 (C–O). UV spectrum (λ_{max}, nm, ε): 204 (4000). PMR spectrum (δ, ppm): 0.91 (d, CH_3 on C-3), 1.61 and 1.68 (s and s, $2CH_3$ on C-7), 4.03 (br.s, CH), 4.12 (t, 2H-1), 5.06 (m, H-6).

Elenyl *o*-Carborane-*C*-carboxylate 2b. Yield 88%, d_{20}^{20} 0.9822, n_D^{20} 1.5075, $C_{13}H_{30}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3075 (CH_{carb}); 2965, 2928, 2877, 2859 (CH_{alk}); 2607, 2582 (BH); 1742 (C=O); 1645 (C=C); 1453 (CH_2); 1281 (C–O). UV spectrum (λ_{max}, nm, ε): 204 (4000). PMR spectrum (δ, ppm): 0.93 (d, CH_3 on C-2), 1.33 (d, CH_3 on C-1), 1.60 and 1.68 (s and s, $2CH_3$ on C-6), 4.03 (br.s, CH), 4.62 (t, H-1), 5.12 (m, H-5).

Neryl *o*-Carborane-*C*-carboxylate 3b. Yield 90%, d_{20}^{20} 0.9895, n_D^{20} 1.5135, $C_{13}H_{28}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3074 (CH_{carb}); 2966, 2926, 2856 (CH_{alk}); 2608, 2582 (BH); 1745 (C=O); 1670, 1645 (C=C); 1447 (CH_2); 1278 (C–O). UV spectrum (λ_{max}, nm, ε): 204 (8000). PMR spectrum (δ, ppm): 1.60 and 1.70 (s and s, $2CH_3$ on C-7), 1.78 (br.s, CH_3 on C-3), 4.04 (br.s, CH), 4.56 (m, 2H-1), 4.93-5.42 (m, H-2, H-6).

(-)-1*R*,2*S*,5*R*-Menthyl *o*-Carborane-*C*-carboxylate 4b. Yield 86%, mp 94-95°C, $C_{13}H_{30}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3089 (CH_{carb}); 2958, 2920, 2900, 2870, 2846 (CH_{alk}); 2634, 2616, 2600, 2583, 2560 (BH); 1733 (C=O); 1465, 1451 (CH_2); 1290, 1278 (C–O). UV spectrum (λ_{max}, nm, ε): 206 (300), 220 (150), 245 (100). PMR spectrum (δ, ppm): 0.83 (d, CH_3 on C-3), 0.92 [d, $(CH_3)_2$ on C-6], 4.06 (br.s, CH), 4.75 (dt, H-1).

Terpinyl *o*-Carborane-*C*-carboxylate 5b. Yield 80%, d_{20}^{20} 0.9870, n_D^{20} 1.5015, $C_{13}H_{28}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3075 (CH_{carb}); 2966, 2928, 2879, 2859 (CH_{alk}); 2607, 2582 (BH); 1743 (C=O); 1647 (C=C); 1452 (CH_2); 1281 (C–O). UV spectrum (λ_{max}, nm, ε): 205 (4000). PMR spectrum (δ, ppm): 1.18 [s, $(CH_3)_2$ on C-4], 1.65 (s, CH_3 on C-1), 4.05 (br.s, CH), 5.45 (m, H-2).

10-Methylcamphenyl *o*-Carborane-*C*-carboxylate 6b. Yield 82%, mp 23-24°C, $C_{13}H_{28}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3073 (CH_{carb}); 2959, 2926, 2870 (CH_{alk}); 2606, 2582 (BH); 1745 (C=O); 1469 (CH_2); 1280 (C–O). UV spectrum (λ_{max},

nm, ε): 206 (300), 220 (150), 247 (100). PMR spectrum (δ, ppm): 1.02 (s, $2CH_3$ on C-2), 3.00 (br.s, H-3), 4.05 (br.s, CH), 5.66 (d, 2H-10).

Bornyl *o*-Carborane-*C*-carboxylate 7b. Yield 87%, mp 127-128°C, $C_{13}H_{28}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3072 (CH_{carb}); 2958, 2922, 2886, 2872 (CH_{alk}); 2603, 2585 (BH); 1739 (C=O); 1454 (CH_2); 1304, 1286 (C–O). UV spectrum (λ_{max}, nm, ε): 206 (300), 220 (150), 245 (100). PMR spectrum (δ, ppm): 0.83 (s, CH_3 on C-1), 0.88 and 0.90 (s and s, $2CH_3$ on C-7), 4.06 (br.s, CH), 4.92 (m, H-2).

Isobornyl *o*-Carborane-*C*-carboxylate 8b. Yield 84%, mp 131-132°C, $C_{13}H_{28}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3073 (CH_{carb}); 2957, 2920, 2874 (CH_{alk}); 2604, 2585 (BH); 1740 (C=O); 1455 (CH_2); 1299, 1282 (C–O). UV spectrum (λ_{max}, nm, ε): 206 (300), 220 (150), 245 (100). PMR spectrum (δ, ppm): 0.90 (s, CH_3 on C-1), 0.91 and 0.98 (s and s, $2CH_3$ on C-7), 4.06 (br.s, CH), 4.72 (m, H-2).

Isofenchyl *o*-Carborane-*C*-carboxylate 9b. Yield 86%, mp 104-105°C, $C_{13}H_{28}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3070 (CH_{carb}); 2963, 2945, 2928, 2871 (CH_{alk}); 2610, 2580 (BH); 1737 (C=O); 1451 (CH_2); 1285 (C–O). UV spectrum (λ_{max}, nm, ε): 206 (300), 220 (150), 245 (100). PMR spectrum (δ, ppm): 0.92 (s, CH_3 on C-1), 1.02 (s, $2CH_3$ on C-5), 4.06 (br.s, CH), 4.44 (m, H-2).

Nopyl *o*-Carborane-*C*-carboxylate 10b. Yield 88%, mp 32-33°C, $C_{13}H_{28}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3074 (CH_{carb}); 2984, 2951, 2918, 2880, 2833 (CH_{alk}); 2607, 2582 (BH); 1747 (C=O); 1465 (CH_2); 1281 (C–O). UV spectrum (λ_{max}, nm, ε): 205 (300), 220 (150), 244 (100). PMR spectrum (δ, ppm): 0.82 (s, CH_3), 1.28 (s, CH_3), 4.06 (br.s, CH), 4.14 (t, 2H-2).

***trans*-Verbenyl *o*-Carborane-*C*-carboxylate 11b.** Yield 80%, mp 57-58°C, $C_{13}H_{26}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3076 (CH_{carb}); 2990, 2960, 2926, 2871 (CH_{alk}); 2604, 2581 (BH); 1746 (C=O); 1635 (C=C); 1466, 1445 (CH_2); 1277 (C–O). UV spectrum (λ_{max}, nm, ε): 205 (4000). PMR spectrum (δ, ppm): 0.88 (s, CH_3), 1.35 (s, CH_3), 1.74 (br.s, CH_3 on C-4), 4.06 (br.s, CH), 4.74 (m, H-2), 5.30 (m, H-3).

Cholesteryl *o*-Carborane-*C*-carboxylate 12b. Yield 84%, mp 101-102°C, $C_{30}H_{56}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3075 (CH_{carb}); 2965, 2931, 2902, 2866, 2852 (CH_{alk}); 2607, 2584 (BH); 1743 (C=O); 1638 (C=C); 1466, 1442 (CH_2), 1278 (C–O). UV spectrum (λ_{max}, nm, ε): 204 (4000). PMR spectrum (δ, ppm): 0.69 (s, CH_3-18), 1.03 (s, CH_3-19), 4.06 (br.s, CH), 4.71 (m, H-3), 5.38 (m, H-6).

Ergosteryl *o*-Carborane-*C*-carboxylate 13b. Yield 81%, mp 132-133°C, $C_{31}H_{54}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3073 (CH_{carb}); 3040 (=CH); 2964, 2930, 2902, 2864, 2852 (CH_{alk}); 2607, 2580 (BH); 1744 (C=O); 1640 (C=C); 1466, 1444 (CH_2), 1278 (C–O). UV spectrum (λ_{max}, nm, ε): 205 (12000), 242 (5000), 264 (10000). PMR spectrum (δ, ppm): 0.64 (s, CH_3-18), 1.03 (s, CH_3-19), 4.06 (br.s, CH), 4.73 (m, H-3), 5.05-5.75 (m, H-6, H-7, H-22, H-23).

β-Sitosteryl *o*-Carborane-*C*-carboxylate 14b. Yield 83%, mp 118-119°C, $C_{32}H_{60}B_{10}O_2$. IR spectrum (ν, cm^{-1}): 3075 (CH_{carb}); 3040 (=CH); 2958, 2933, 2867, 2852 (CH_{alk}); 2604, 2581 (BH); 1742 (C=O); 1635 (C=C); 1464, 1445 (CH_2), 1290, 1281 (C–O). UV spectrum (λ_{max}, nm, ε): 204 (4000). PMR spectrum (δ, ppm): 0.68 (s, CH_3-18), 1.03 (s, CH_3-19), 4.06 (br.s, CH), 4.70 (m, H-3), 5.37 (m, H-6).

Diosgeninyl *o*-Carborane-*C*-carboxylate 15b. Yield 80%, mp 188-189°C, $C_{30}H_{52}B_{10}O_4$. IR spectrum (ν, cm^{-1}): 3072 (CH_{carb}); 3040 (=CH); 2949, 2940, 2907, 2870, 2854 (CH_{alk}); 2612, 2606, 2575 (BH); 1732 (C=O); 1630 (C=C); 1455 (CH_2); 1294 (C–O). UV spectrum (λ_{max}, nm, ε): 204 (4000). PMR spectrum (δ, ppm): 0.80 (s, CH_3-18), 1.04 (s, CH_3-19), 4.06 (br.s, CH), 4.40 (m, H-3), 5.39 (m, H-6).

Solasodinyl *o*-Carborane-*C*-carboxylate 16b. Yield 80%, mp 300°C (dec.), $C_{30}H_{53}B_{10}NO_3$. IR spectrum (ν, cm^{-1}): 3074 (CH_{carb}); 3042 (=CH); 2933, 2901, 2869, 2849 (CH_{alk}); 2528 (BH); 1735 (C=O); 1630 (C=C); 1457 (CH_2); 1288 (C–O). UV spectrum (λ_{max}, nm, ε): 205 (4000). PMR spectrum (δ, ppm): 0.80 (s, CH_3-18), 1.04 (s, CH_3-19), 4.06 (br.s, CH), 4.40 (m, H-3), 5.34 (m, H-6).

Vanillinyl *o*-Carborane-*C*-carboxylate 17b. Yield 83%, mp 53-54°C, $C_{11}H_{18}B_{10}O_4$. IR spectrum (ν, cm^{-1}): 3066 (CH_{carb}); 3010 (CH_{Ar}); 2977, 2940, 2930, 2855 (CH_{alk}); 2610, 2581 (BH); 1772 (C=O); 1703 (CHO); 1605, 1501, 1464, 1424, 1394 (Ar); 1280, 1260 (C–O); 800, 780, 732, 709 (CH_{Ar}). UV spectrum (λ_{max}, nm, ε): 206 (9000), 224 (12000), 260 (8000), 308 (4000). PMR spectrum (δ, ppm): 3.91 (s, CH_3O), 4.18 (br.s, CH), 7.07-7.60 (m, C_6H_3), 9.96 (s, CHO).

Vanillalyl *o*-Carborane-*C*-carboxylate 18b. Yield 81%, mp 86-87°C, $C_{12}H_{20}B_{10}O_4$. IR spectrum (ν, cm^{-1}): 3066 (CH_{carb}); 3010 (CH_{Ar}); 2987, 2938, 2927, 2903, 2850 (CH_{alk}); 2614, 2594 (BH); 1772 (C=O); 1697 (CHO); 1603, 1500, 1481, 1437, 1392 (Ar); 1279, 1260 (C–O); 800, 742, 729, 710 (CH_{Ar}). UV spectrum (λ_{max}, nm, ε): 206 (9000), 224 (13000), 260 (8000), 309 (4000). PMR spectrum (δ, ppm): 1.45 (t, CH_3), 4.08 (q, CH_2), 4.16 (br.s, CH), 7.04-7.55 (m, C_6H_3), 9.94 (s, CHO).

4-(4-Methyl-1,3-dioxolan-2-yl)-2-methoxyphenyl *o*-Carborane-*C*-carboxylate 19b. Yield 80%, d_{20}^{20} 1.1234, n_D^{20} 1.5520, $C_{14}H_{24}B_{10}O_5$. IR spectrum (ν, cm^{-1}): 3072 (CH_{carb}); 3010 (CH_{Ar}); 2975, 2940, 2879 (CH_{alk}); 2606, 2581 (BH); 1770 (C=O); 1607, 1507, 1465, 1424, 1394, 1381 (Ar); 1270 (C–O); 801, 780, 732, 711 (CH_{Ar}). UV spectrum (λ_{max}, nm, ε): 206 (9000), 220 (10000), 260 (4000), 278 (3000). PMR spectrum (δ, ppm): 1.20-1.45 (m, CH), 3.35-4.60 (m, CH and CH_2), 3.82 (s, CH_3O), 5.80 (s, CH), 6.78-7.60 (m, C_6H_3).

***E*-(*o*-Carborane-*C*-methanoyloxyimino)-1,7,7-trimethylbicyclo[2.2.1]-heptane 20b.** Yield 89%, mp 94-95°C, $C_{13}H_{27}B_{10}NO_2$. IR spectrum (ν, cm^{-1}): 3068 (CH_{carb}); 2963, 2925, 2890, 2870 (CH_{alk}); 2609, 2585 (BH); 1766 (C=O); 1658 (C=N); 1450 (CH_2); 1261 (C–O). UV spectrum (λ_{max}, nm, ε): 209 (5000). PMR spectrum (δ, ppm): 0.85 (s, CH_3 on C-1), 1.00 and 1.07 (s and s, $2CH_3$ on C-7), 4.07 (br.s, CH).

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