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Ferrocenyltriazoles from 3β,28-Diacylbetulin: Synthesis and Cytotoxic Activity

V. A. Glushkov[a,b,*], D. A. Shemyakina[b], N. K. Zhukova[b], L. V. Pavlogradskaya[a], M. V. Dmitriev[b], D. V. Eroshenko[a], A. R. Galeev[b], and I. G. Mokrushin[b]

[a] *Institute of Technical Chemistry, Perm Federal Research Centre, Ural Branch, Russian Academy of Sciences, ul. Akademika Koroleva 3, Perm, 614013 Russia*
**e-mail: glusha55@gmail.com*

[b] *Perm State National Research University, ul. Bukireva 15, Perm, 614990 Russia*

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Abstract—The reaction of 30-bromo-3β,28-diacylbetulin with sodium azide afforded 30-azido-3β,28-diacyloxylup-20(29)-enes. The products were subjected to a CuI/TMEDA-catalyzed click reaction with ethynylferrocene to obtain the corresponding ferrocene–betulin conjugates with a 1,2,3-triazole linker.

Keywords: betulin, ferrocene, 1,2,3-triazole

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Over the past years the click synthesis of triazoles from mono-, di-, and triterpenoids has gained wide popularity [1–3]. Most reactions of triterpenoids involve the functional groups bound with the C^{2} [4, 5], C^{3} [6–8], and C^{28} atoms of the triterpene core [9–15], as well as bound both to C^{3} and C^{28} [16]. Only a few examples of the triazole synthesis from lupane derivatives, where the functional group bound to C^{30} was involved, are available in the literature [17, 18]. On the other hand, today there is continuing search for biologically active compounds, including those with anticancer effects, among ferrocene derivatives [19–25]. Previously, we obtained by click chemistry conjugates of betulonic acid with ferrocene, bound by a 1,2,3-triazole bridge at C^{28} [26, 27].

The present study was undertaken as a continuation of our research into the synthesis of ferrocene-substituted triterpenoids. The aim of this work was to obtain ferrocene conjugates with a 1,2,3-triazole linker at C^{30} from 3β, 28-diacyl derivatives of betulin and to study their cytotoxic activity.

As the starting substrates we took 3β,28-diacetylbetulin (**1a**) [28–30], 3β,28-dipropionylbetulin (**1b**) [31, 32], and 3β,28-dibenzoylbetulin (**1c**) [33, 34]. Compounds **1b** and **1c** were synthesized by treating technical betulin with an acylating agent (propionic anhydride or benzoyl chloride) in pyridine in the presence of 4-(dimethylamino)pyridine. The structure of dipropionyl derivative **1b** was confirmed by X-ray diffraction (XRD) analysis (Fig. 1).

The radical allylic bromination of diacylbetulins **1a–1c** was performed with bromosuccinimide in a mixture of CCl_4 and CH_2Cl_2 under reflux in the presence of AIBN by a known procedure (Scheme 1) [35].

30-Bromo derivative of diacetylbetulin **2a** is described in [36]. By recrystallization of bromide **2a** from petroleum ether was obtained its single crystal. The XRD analysis confirmed the structure of compound **2a**, but the Br atom could not be localized exactly because of the poor quality of the crystal.

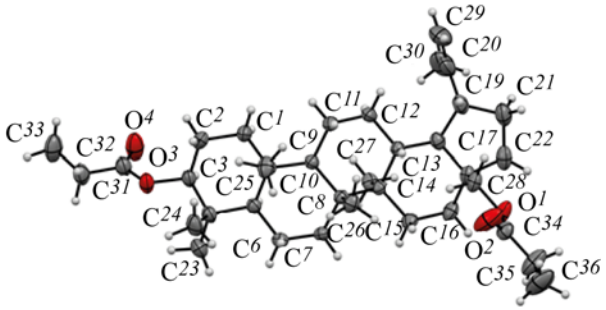
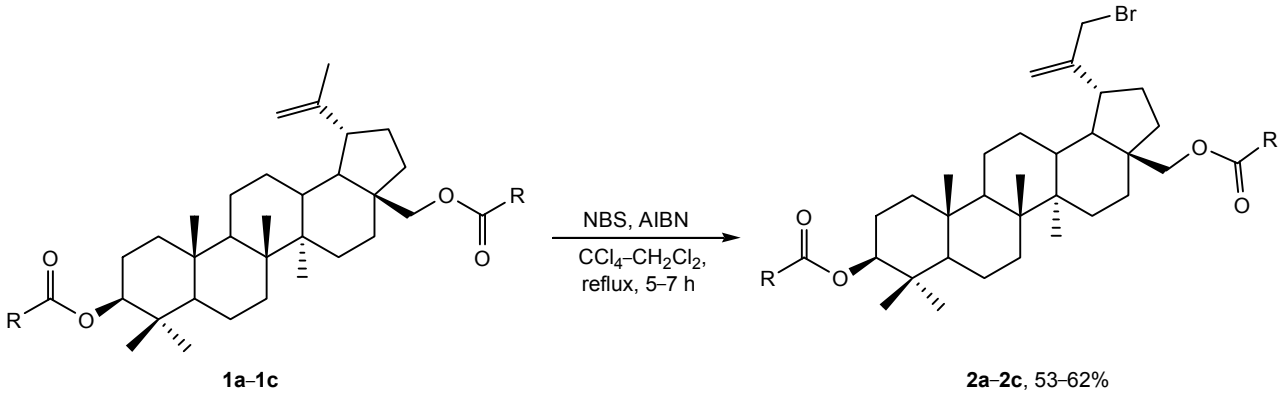


Fig. 1. General view of a molecule of compound **1b** by the XRD data (thermal ellipsoids are drawn at a 30% probability level).

Scheme 1.



1, **2**, R = Me (**a**), R = Et (**b**), R = Ph (**c**).

The ^{1}H NMR spectra of 3β,28-dipropionyl- (**2b**) and 3β,28-dibenziylbetulins (**2c**) no longer show the C$\underline{H}_3$C= at signals at 1.67–1.74 ppm, observed in the spectrum of starting diacylbetulins **1a–1c**, but contain a new singlet at 3.97–4.03 ppm assignable to the BrC$\underline{H}_2$ protons; the H^{29} proton signals of compounds **2b** and **2c** are shifted downfield compared to the respective signals of **1b** and **1c**: 5.02 and 5.12 ppm (**2b**) against 4.58 and 4.67 ppm (**1b**) and 5.10 and 5.19 ppm (**2c**) against 4.65 and 4.76 ppm (**1c**).

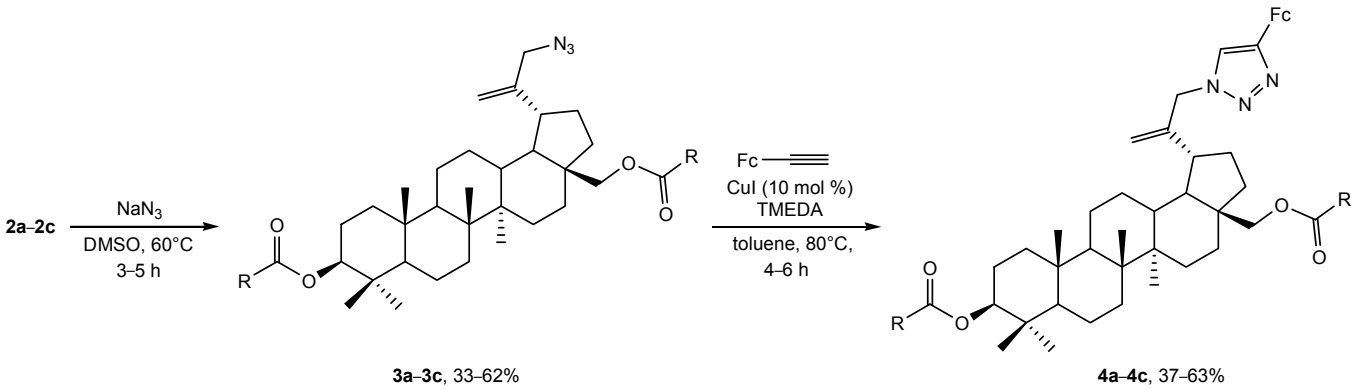
The reactions of bromides **2a–2c** with sodium azide in DMSO gave azido derivatives **3a–3c** (yields 54–62%). Evidence for the formation of these products is provided by the presence in their IR spectra of a band at 2099–2105 cm^{-1} characteristic of the azido group. Azides **3a–3c** were subjected to a Cu-catalyzed [3+2]-cycloaddition reaction (click chemistry) with ethynylferrocene (Scheme 2). As the catalyst we used CuI (10 mol %) doped with TMEDA, in view of the fact that this system showed a good performance in our previous studies [26, 27].

According to the ^{1}H NMR spectra, the reaction formed a single triazole isomer, specifically 4-substituted 1,2,3-triazole **4a–4c** (yields 37–63%), as evidenced by the observation of a characteristic signal of the triazole C^{5}H proton at 7.39–7.43 ppm and the corresponding C^5 signal at 119 ppm in the ^{13}C NMR spectra, which is consistent with published data for 1,4-disubstituted 1,2,3-triazoles [17, 37].

The structure of compounds **4b** and **4c** was confirmed by 2D correlation ^{1}H–^{13}C NMR spectroscopy (HMBC). The HMBC spectrum of compound **4c** clearly demonstrates long-range coupling between the H$_2$C^{30} protons with C$^{5'}$, C^{20}, and C^{29} (Fig. 2).

The *in vitro* cytotoxicity of the compounds was assessed against MS (melanoma), A549 (lung carcinoma) and RD (rhabdomyosarcoma) human tumor cell

Scheme 2.



3, **4**, R = Me (**a**), R = Et (**b**), R = Ph (**c**); Fc = ferrocene.

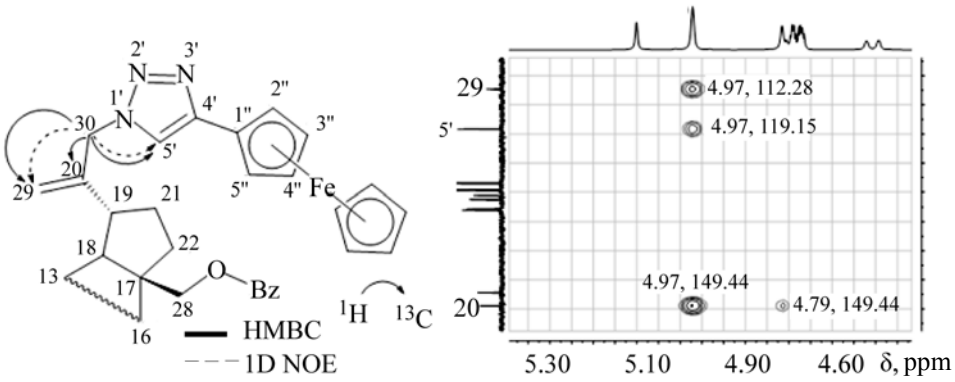


Fig. 2. Fragment HMBC NMR spectrum of compound **4c**.

lines. To this end, solutions of the test compounds in DMSO (1.6–100 μM) were added to cell monolayers formed in the wells of a 96-well plate. The wells with 0.1% DMSO were used as a control, and Camptothecin, as a reference drug.

Cell viability was assessed after 72-h incubation after adding the MTT solution by measuring the optical density of the formed formazane at 544 nm on a Labtech FLUOstar OPTIMA BMG spectrophotometer. The IC_{50} values were calculated from the dose–effect plots. It was found that the cytotoxic activity increases in the order **4b** < **4c** < **4a** (Table 1). Compound **4a** showed moderate activity against the MS line (IC_{50} = 48.71±3.55 μM).

EXPERIMENTAL

The IR spectra were recorded on a Bruker VERTEX 80v FTIR spectrometer in thin films obtained by evaporation of chloroform solutions of the analyzed compounds. The ^1H and ^{13}C NMR spectra were measured in $CDCl_3$ on a Bruker Avance III HD 400 spectrometer (400 and 100 MHz, respectively), using as internal references HMDS for the ^1H NMR spectra and $CDCl_3$ (δ_C 77.0 ppm) for the ^{13}C NMR spectra. Elemental analysis was performed on a Vario EL cube CHNOS analyzer. The melting points were determined on a PTP apparatus. The specific rotations were measured on a Perkin–Elmer 341 polarimeter in chemical grade chloroform containing 0.5% of ethanol and are reported in 10^{-1}·deg g^{-1} cm^2. Column chromatography was performed on Silicagel 60 (Alfa Aesar, 0.060–0.2 mm, 70–230 mesh), eluent petroleum ether (40–70°C)–ethyl acetate. The reaction progress was monored by TLC on Sorbfil plates, eluent petroleum ether (40–70°C)–ethyl acetate, 7 : 3; the spots were visualized by treatment with 20% H_2SO_4 followed by heating. Ethynylferrocene was synthesized as described in [39]. Sodium azide, Cu(I) iodide, 4-(dimethylamino)pyridine, benzoyl chloride, and *N*-bromosuccinimide were purchased from Alfa Aesar, propionic anhydride, from Aldrich, and pure grade petroleum ether and chemical grade ethyl acetate, propan-2-ol, DMSO, and pyridine, from Russian producers.

X-ray diffraction analysis of compound 1b. Compound **1b** crystallizes in a centrosymmetric space group of the rhombic system. The bond lengths and bond angles are normal values. All six-membered rings are in a *chair* conformation. The five-membered ring has an *envelope* conformation with the C^{17} atom

Table 1. Cyctotoxicity of diacylbetulin−ferrocene conjugates **4a–4c**

Compound no.	IC_{50}, μM		
	MS	RD	A549
4a	48.71±3.55	>200	131.00±7.54
4b	>200	>200	>200
4c	128.0±9.54	>200	107.3±1.53
Camptothecin	0.77±0.34	1.72±0.37	1.31±0.03

deviating from the plane formed by the other 4 atoms by 0.64 Å. No specific shortened contacts in the crystal were found.

The XRD analysis was performed on an Xcalibur Ruby diffractometer with a CCD detector by a standard procedure (MoK_α radiation, 295(2) K, ω scans, scan steps 1°). Empirical absorption corrections were applied SCALE3 ABSPACK [40]. Compound **1b** ($C_{36}H_{58}O_4$, *M* 554.82), rhombic crystal, space group $P2_12_12_1$, *a* 12.875(3) Å, *b* 15.786(4) Å, *c* 16.289(4) Å, *V* 3310.6(13) Å^3, *Z* 4, d_{calc} 1.113 g/cm^3, μ 0.070 mm^{-1}. The structure was solved using Superflip [41] and refined by full-matrix least squares on F^2 with anisotropic temperature factors for all non-hydrogen factors using SHELXL [42] with OLEX2 graphical user interface [43]. Hydrogen atoms were refined riding on their carrier atoms. Final refinement parameters: R_1 0.0652, wR_2 0.1517 [for 4063 reflections with $I > 2\sigma(I)$], R_1 0.1113, wR_2 0.1796 (on all 6689 unique reflections), *S* 1.022. The results of the XRD analysis of compound **1b** are deposited at the Cambridge Crystallographic Data Center (www.ccdc.cam.ac.uk/data_request/cif), CCDC 1910975.

Lup-20(29)-ene-3β,28-diyldipropionate (1b). A solution of 20 g (45 mmol) of technical betulin (purity ~ 90%), 17.5 mL (136 mmol, 17.7 g) of propionoc anhydride, and 0.55 g (4.5 mmol, 10 mol %) of 4-(dimethylamino)pyridine in 180 mL of pyridine was heated on a water bath for 1 h and left to stand overnight. The reaction mixture was then poured into a mixture of 300 mL of water, 200 mL of conc. HCl, and 100 g of crushed ice, the mixture was stirred, and the tar that formed was dissolved in 300 mL of dichloromethane. The solution was washed with water, 5% HCl, saturated $NaHCO_3$ and NaCl, dried over $MgSO_4$, the solvent was removed by distillation, and the residue was crystallized from 250 mL of propan-2-ol with a little of water to obtain 10.08 g (48%) of compound **1b** as nearly colorless prisms. The analytical sample was obtained by recrystallization from petroleum ether–ethyl acetate, coarse transparent prisms, mp 162–164°C (149°C [31]; 163.6°C [32]). R_f 0.63. The ^{1}H and ^{13}C NMR spectra are consistent with those reported in [31].

Lup-20(29)-ene-3β,28-diyldibenzoate (1c). Benzoyl chloride, 5.34 mL (6.47 g, 46 mmol), and 3.05 g (25 mmol) of 4-(dimethylamino)pyridine were added to 80 mL of pyridine and 80 mL of dioxane. The mixture was stirred, after which 10 g (23 mmol) of technical betulin was added. After 12-h stirring at room temperature, the reaction mixture was poured into 500 mL of cold water, and the precipitate that formed was filtered off, washed with 5% acetic acid and water, dried in air, and recrystallized from ethanol to obtain 10.7 g (72%) of compound **1c** as colorless fine crystals, mp 159–161°C (139–140°C [33]; colorless oil [34]). R_f 0.65. The ^{1}H and ^{13}C NMR spectra are consistent with those reported in [34].

30-Bromolup-20(29)-en-3β,28-diyldipropionate (2b). A mixture of 1.88 g (3.4 mmol) of compound **1b** and 0.6 g (3.4 mmol) of *N*-bromosuccinimide in 80 mL of CCl_4 containing 100 mg of AIBN (recrystallized from ethanol) was heated under reflux for 5 h, cooled, washed with cold water to separate succinimide, dried over $MgSO_4$, the solvent was removed by distillation, and the residue was subjected to column chromatography. Yield 1.15 g (53%), colorless crystals, mp 150–151°C, R_f 0.61, $[\alpha]_D^{24}$ +2.4 ($CHCl_3$, *c* 1). IR spectrum, cm^{-1}: 2944, 2874, 1733, 1462, 1390, 1356, 1275, 1188, 1082, 1015, 968, 757. ^{1}H NMR spectrum, δ, ppm: 0.83 s (6H, 2Me), 0.84 s (3H, Me), 0.98 s (3H, Me), 1.03 s (3H, Me), 1.13 t (3H, CH_3, ^3J 7.2 Hz), 1.15 t (3H, CH_3, ^3J 7.2 Hz), 2.33 q [2H, C(O)CH_2, ^3J 7.2 Hz], 2.34 q [2H, C(O)CH_2, ^3J 7.2 Hz], 3.83 d (1H, H^{28}, ^2J 10.8 Hz), 3.97 s (2H, CH_2Br), 4.27 d (1H, H^{28}, ^2J 10.8 Hz), 4.46 m (1H, H^3), 5.02 s (1H, H^{29}), 5.12 s (1H, H^{29}). ^{13}C NMR spectrum, δ, ppm: 9.12, 9.22, 14.66, 15.98, 16.04, 16.42, 18.08, 20.86, 23.61, 26.90, 26.99, 27.59, 27.86, 27.94, 29.57, 29.82, 32.45, 34.11, 34.24, 37.00, 37.41, 37.78, 38.33, 40.89, 42.61, 43.31, 46.43, 50.19, 50.27, 55.32, 62.22, 80.22 (C^3), 113.18 (C^{20}), 150.77 (C^{29}), 174.01 (C=O), 174.41 (C=O). Found, %: C 68.53; H 10.19; Br 12.47. $C_{36}H_{57}BrO_4$. Calculated, %: C 68.23; H 9.07; Br 12.31.

30-Bromolup-20(29)-ene-3β,28-diyldibenzoate (2c). A mixture of 4.28 g (7.41 mmol) of compound **1c** and 1.38 g (7.41 mmol) of *N*-bromosuccinimide in a mixture of 200 mL CCl_4 and 50 mL of CH_2Cl_2, containing 200 mg of AIBN was heated under reflux for 5 h, cooled, washed with water to separate succinimide, dried over $MgSO_4$, the solvent was removed by distillation, and the residue was subjected to column chromatography (eluent petroleum ether–ethyl acetate, 20 : 1). Yield 3.09 g (57%), colorless crystals, mp 148–151°C, R_f 0.63, $[\alpha]_D^{24}$ +26.2 ($CHCl_3$, s 1). IR spectrum, cm^{-1}: 2947, 2878, 1716 (C=O), 1451, 1390, 1315, 1274, 1215, 1176, 1114, 1070, 1026, 971, 757, 711. ^{1}H NMR spectrum, δ, ppm: 0.89 s (3H, Me), 0.90 s (3H, Me), 0.98 s (3H, Me), 1.01 s (3H, Me), 1.08 s (3H,

Me), 2.51 m (1H, H^{19}), 3.98 s (2H, $BrCCH_2$), 4.09 d (1H, H^{28}, ^2J 12.0 Hz), 4.53 d (1H, H^{28}, ^2J 12.0 Hz), 4.71 m (1H, H^3), 5.05 s (1H, H^{29}), 5.14 s (1H, H^{29}), 7.41 m ($4H_{arom}$), 7.51 m ($2H_{arom}$), 8.02 m ($4H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 14.81, 16.12, 16.14, 16.75, 18.19, 20.98, 23.74, 25.25, 27.02, 27.15, 28.10, 30.11, 32.60, 34.20, 34.51, 37.61, 38.19, 38.44, 41.01, 42.79, 43.47, 46.79, 50.30, 50.43, 55.47, 63.12, 81.52, 113.34, 128.26, 128.40, 129.49, 129.54, 130.44, 131.03, 132.62, 132.85, 150.84, 166.22 (C=O), 166.83 (C=O). Found, %: C 72.17; H 8.02; Br 10.79. $C_{44}H_{57}BrO_4$. Calculated, %: C 72.41; H 7.87; Br 10.95.

30-Azidolup-20(29)-ene-3β,28-diyldiacetate (3a) is described in [17].

30-Azidolup-20(29)-en-3β,28-diyldipropionate (3b). Solium azide, 120 mg (1.90 mmol), was added to a solution of 300 mg (0.476 mmol) of bromide **2b** in 20 mL of DMSO, and the mixture was stirred at 60–70°C for 5 h. After cooling, the mixture was poured into a mixture of 150 mL of water and 100 g of ice, acidified with 10 mL of conc. HCl, the precipitate that formed was filtered off, washed with water, dried in air, and the residue was subjected to column chromatography on silica gel (eluent petroleum ether–ethyl acetate, 10 : 1). Yield 175 mg (62%), pale yellow powder, mp 129–130°C, $[\alpha]_D^{25}$ +7.0 (*c* 0.5, $CHCl_3$), R_f 0.55. IR spectrum, cm^{-1}: 2944, 2874, 2099 (N_3), 1734 (C=O), 1462, 1390, 1356, 1275, 1216, 1187, 1082, 1016, 970, 887, 806, 757. ^1H NMR spectrum, δ, ppm: 0.83 s (6H, 2Me), 0.84 s (3H, Me), 0.97 s (3H, Me), 1.03 s (3H, Me), 1.13 t (3H, CH_3, ^3J 7.2 Hz), 1.15 t (3H, CH_3, ^3J 7.2 Hz), 2.33 q [2H, $C(O)CH_2$, ^3J 7.2 Hz], 2.34 q [2H, $C(O)CH_2$, ^3J 7.2 Hz], 3.75 s (2H CH_2N_3), 3.83 d (1H, H^{28}, ^2J 12.0 Hz), 4.26 d (1H, H^{28}, ^2J 12.0 Hz), 4.46 m (1H, H^3), 4.95 s (1H, H^{29}), 5.00 s (1H, H^{29}). ^{13}C NMR spectrum, δ, ppm: 9.17, 9.27, 14.71, 16.03, 16.10, 16.49, 18.14, 20.91, 23.68, 26.81, 27.04, 27.67, 27.93, 28.03, 29.83, 31.23, 34.16, 34.33, 37.07, 37.43, 37.87, 38.39, 40.95, 42.68, 44.17, 46.17, 46.49, 49.88, 50.24, 55.39, 62.20, 80.48, 111.61, 148.49, 174.36, 174.67. Found, %: C 72.55; H 7.04; N 6.87. $C_{36}H_{57}N_3O_4$. Calculated, %: C 72.57; H 9.64; N 7.05.

30-Azidolup-20(29)-ene-3β,28-diyldibenzoate (3c) was prepared in a similar way from 0.73 g (1 mmol) of bromide **2c** and 0.195 g (3 mmol) of sodium azide in 35 mL of DMSO. Yield 0.373 g (54%), colorless crystals, mp 129–131°C, $[\alpha]_D^{29}$ +27.6 (*c* 1, $CHCl_3$), R_f 0.57. IR spectrum, cm^{-1}: 2947, 2872, 2099 (N_3), 1715 (C=O), 1451, 1391, 1347, 1316, 1274, 1216, 1176, 1115, 1070, 1026, 972, 757, 711. ^1H NMR spectrum, δ, ppm (the multipletes of the lupane ring CH_2 and CH protons are not shown): 0.95 s (3H, Me), 0.96 s (3H, Me), 1.04 s (3H, Me), 1.07 s (3H, Me), 1.13 s (3H, Me), 2.50 m (1H, H^{19}), 3.82 s (2H, CH_2N_3), 4.12 d (1H, H^{28}, ^2J 12.0 Hz), 4.57 d (1H, H^{28}, ^2J 12.0 Hz), 4.75 m (1H, H^3), 5.03 s (1H, H^{29}), 5.08 s (1H, H^{29}), 7.45 m ($4H_{arom}$), 7.56 m ($2H_{arom}$), 8.07 m ($4H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 14.32, 15.63, 16.27, 17.72, 20.51, 22.10, 23.27, 26.39, 26.67, 27.63, 28.54, 29.56, 30.83, 33.73, 34.04, 36.68, 37.11, 37.65, 37.98, 40.46, 42.31, 43.68, 46.33, 49.45, 49.82, 62.47, 81.05, 111.22, 127.78, 127.87, 129.02, 129.05, 129.97, 130.59, 132.13, 132.38, 148.12, 165.75 (C=O), 166.35 (C=O). Found, %: C 76.25; H 8.28; N 5.96. $C_{44}H_{57}N_3O_4$. Calculated, %: C 76.38; H 8.30; N 6.07.

Click reaction (*general procedure*). Compound **3a–3c** (or **9a–9c**), 1 mmol, and 210 mg (1 mmol) of ethynylferrocene [39] were dissolved in 20 mL of toluene, after which 19.2 mg (0.1 mmol, 10 mol %) of CuI and 3 droplets of TMEDA were added to the solution, and the reaction mixture was stirred at 80°C for 3–4 h. The reaction progress was monitored by TLC. Toluene was removed by distillation, and the residue was subjected to column chromatography on silica gel in petroleum ether–ethyl acetate (the fraction of ethyl acetate in the eluent was gradually increased from 0 to 20%).

30-(4-Ferrocenyl[1,2,3]triazol-1-yl)lup-20(29)-ene-3β,28-diyldiacetate (4a). Yield 484 mg (63%), yellow foam, mp 143–146°C, R_f 0.21. IR spectrum, ν, cm^{-1}: 3094, 2947, 2873, 1731 (C=O), 1463, 1391, 1366, 1247, 1106, 1032, 979, 756. ^1H NMR spectrum, δ, ppm: 0.83 s (3H, Me), 0.84 s (6H, 2Me), 0.98 s (3H, Me), 1.01 s (3H, Me), 2.03 s [3H, $CH_3C(O)$], 2.04 s [3H, $CH_3C(O)$], 2.36 m (1H, H^{19}), 3.75 d (1H, H^{28}, ^2J 11.1 Hz), 4.08 s ($5H_{Fc}$), 4.23 d (1H, H^{28}, ^2J 11.1 Hz), 4.33 s ($2H_{Fc}$), 4.46 m (1H, H^3), 4.72 s (1H, H^{29}), 4.76 m (2H, NCH_2), 4.93 s ($2H_{Fc}$), 5.05 s (1H, H^{29}), 7.41 s (1H, $H^{5'}$). ^{13}C NMR spectrum, δ, ppm: 14.71, 16.00, 16.13, 16.45, 18.10, 20.89, 20.98, 21.28, 23.64, 26.96, 26.96, 27.90, 29.78, 31.27, 34.09, 34.28, 37.03, 37.40, 37.75, 38.37, 40.88, 42.67, 46.31, 49.85, 50.17, 55.32, 62.38, 66.52, 66.59, 68.61, 69.48, 75.30, 80.83, 112.04, 119.00, 149.25, 170.98. Found, %: C 69.05; H 8.02; N 5.37. $C_{45}H_{61}FeN_3O_5$. Calculated, %: C 69.31; H 7.88; N 5.39.

30-(4-Ferrocenyl[1,2,3]triazol-1-yl)lup-20(29)-en-3β,28-diyldipropionate (4b). Yield 298 mg (37%), yellow foam, does not have a well-defined melting point, plasticizes in the range 120–135°C, R_f 0.40. IR spectrum, cm^{-1}: 3004, 2943, 2873, 1732, 1462, 1391, 1356, 1276, 1217, 1189, 1106, 1083, 1047, 1017, 968, 878, 819, 756. ^1H NMR spectrum, δ, ppm: 0.83 s (3H, Me), 0.84 s (3H, Me), 0.85 s (3H, Me), 0.99 s (3H, Me), 1.03 s (3H, Me), 1.13 t (3H, CH_3, ^3J 7.2 Hz), 1.15 t (3H, CH_3, ^3J 7.2 Hz), 2.29 q [2H, C(O)CH_2, ^3J 7.2 Hz], 2.31 q [2H, C(O)CH_2, ^3J 7.2 Hz], 2.34 m (1H, H^{19}), 3.76 d (1H, H^{28}, ^2J 11.2 Hz), 4.05 s (5H_{Fc}), 4.26 d (1H, H^{28}, ^2J 11.2 Hz), 4.28 s (2H_{Fc}), 4.47 m (1H, H^3), 4.70 s (1H, H^{29}), 4.73 m ($C^{30}H_2$), 4.92 s (2H_{Fc}), 5.05 s (1H, H^{29}), 7.41 s (1H, $H^{5'}$). ^{13}C NMR spectrum, δ, ppm: 9.15, 9.28, 14.75, 16.02, 16.11, 16.49, 18.13, 20.94, 22.77, 23.69, 26.93, 27.02, 27.63, 27.93, 28.03, 29.39, 29.86, 31.32, 34.14, 34.30, 37.08, 37.45, 37.87, 38.41, 40.94, 42.72, 43.87, 46.47, 49.95, 50.22, 54.64, 55.38, 62.13, 66.67, 68.65, 69.53, 75.47, 80.55, 112.05, 119.01, 147.02, 149.32, 174.20, 174.67. Found, %: C 70.34; H 8.17; N 4.94. $C_{47}H_{65}FeN_3O_5$. Calculated, %: C 69.91; H 8.11; N 5.20.

30-(4-Ferrocenyl[1,2,3]triazol-1-yl)lup-20(29)-ene-3β,28-diyldibenzoate (4c). Yield 66%, orange crystals, does not have a well-defined melting point, melts with decomposition in the range 147–158°C, R_f 0.28. IR spectrum, cm^{-1}: 2947, 2872, 1715 (C=O), 1602, 1585, 1451, 1391, 1316, 1274, 1217, 1176, 1115, 1070, 1047, 1026, 1003, 970, 877, 819, 756, 712. ^1H NMR spectrum, δ, ppm (the multipletes of the lupane ring CH_2 and CH protons are not shown): 0.89 s (3H, Me), 0.95 s (3H, Me), 0.96 s (3H, Me), 1.04 s (3H, Me), 1.13 s (3H, Me), 2.51 m (1H, H^{19}), 4.05 d (1H, H^{28}, ^2J 11.2 Hz), 4.21 s (5H_{Fc}), 4.46 s (2H_{Fc}), 4.46 d (1H, H^{28}, ^2J 11.2 Hz), 4.78 m (3H, 2H_{Fc} + H^3), 4.90 br.s (2H, $C^{30}H_2$), 4.98 s (1H, H^{29}), 5.12 s (1H, H^{29}), 7.46 m (5H, 4H_{arom} + $H^5_{triazole}$), 7.56 m (2H_{arom}), 8.07 m (4H_{arom}). ^{13}C NMR spectrum, δ, ppm: 9.15, 9.28, 14.75, 16.02, 16.11, 16.49, 18.13, 20.94, 22.77, 23.69, 26.93, 27.02, 27.63, 27.93, 28.03, 29.39, 29.86, 31.32, 34.14, 34.30, 37.08, 37.45, 38.41, 40.94, 42.72, 43.87, 46.47, 49.47, 49.95, 50.22, 54.64, 55.38, 62.13, 66.61, 66.67, 68.65, 69.53, 75.47, 80.55, 112.05, 119.01, 147.02, 149.32, 174.20, 174.67. Found, %: C 72.77; H 7.32; N 4.61. $C_{55}H_{65}FeN_3O_5$. Calculated, %: C 73.08; H 7.25; N 4.65.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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