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Synthesis and Cytotoxic Evaluation of 2-*O*-alkyl Derivatives of L-Ascorbic Acid

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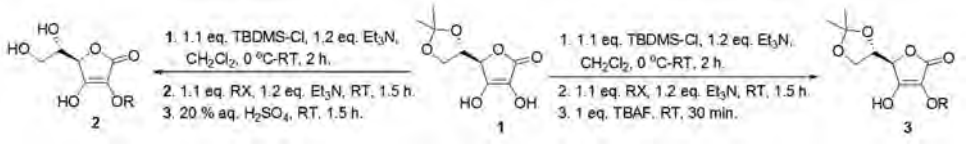
ABSTRACT A series of both 5,6-*O*-protected and unprotected 2-*O*-alkyl derivatives of L-ascorbic acid were synthesized using silylation-alkylation-desilylation sequence in a one-pot manner. These derivatives were screened for their anticancer activity against human breast cancer cell line (MCF-7) and exhibited decent cytotoxicity.



KEY WORDS Alkylation, L-Ascorbic acid derivatives, Cytotoxicity, Desilylation, One-pot synthesis, Silylation.

INTRODUCTION

Due to the intrinsic therapeutical and pharmacological potential of L-ascorbic acid (L-AA) and its derivatives, the study of L-AA in organic synthesis has gathered momentum which has resulted in the synthesis of various new molecules with prominent biological activity and chemotherapeutic significance.[1] As the basic core of L-AA is responsible for its importance in biological systems, therefore, the chemist is keen in designing various derivatives of L-AA without affecting the core structure of L-AA. The properties of L-AA such as antioxidant, redox, and α-amylase inhibition are closely associated with the 2,3-enediol moiety of the molecule,[2,3] hence its detailed structure-activity studies can be done only by selective functionalization of the 2-and 3-OH groups. In this context, various *O*-alkyl derivatives of L-AA have been synthesized and their biological study has been done.[4] The stability of organic compound has always been an important aspect while studying its biology. Due to the susceptibility of L-AA toward thermal and oxidative degradation, considerable efforts had been made in recent years to develop more stable L-AA derivatives. These derivatives have displayed improved biological activities.[4-6]

For example, 5,6-*O*-modified L-AA derivatives have shown anti-tumor activity against various human cancers by inducing apoptosis in tumor cells.[6] 2-*C* alkyl derivatives exhibit immunostimulant activity,[7] 2-*O* and 3-*O*-alkylated derivatives protect lipids of the bio-membranes against peroxidation.[8] Although 2-*O* and/or 3-*O*-alkylated derivatives of L-AA have shown ROS scavenging activity, their anticancer activity has not been evaluated. Recent study by our group has shown that 2,3-di-*O*-alkyl and C2-aryl derivatives of 5,6-*O*-isopropylidene-L-AA exhibit enhanced cytotoxic activity compared to L-AA.[4,5] As an ongoing project in our laboratory to develop new derivatives of L-AA, herein we report synthesis and cytotoxicity study of 2-*O*-alkyl derivatives of L-AA against human breast cancer cells line (MCF7).

RESULTS AND DISCUSSION

Chemistry

The various 5,6-*O*-protected and unprotected 2-*O*-alkyl derivatives of L-AA were synthesized using method developed in our laboratory, employing silylation-alkylation-desilylation sequence in a one-pot manner as shown in **Scheme 1**.[9] Thus, a variety of alkyl halides smoothly underwent alkylation of 5,6-*O*-isopropylidene L-AA under this reaction condition and gave 2-*O*-alkyl derivatives of 5,6-*O*-isopropylidene L-AA (**2a-f**) in overall good yields [**Table 1**]. Further, a minor modification of the above procedure furnished an efficient synthesis of

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5,6-*O*-protected 2-*O*-alkyl derivatives of L-AA. Thus, use of *tetra*-butylammonium fluoride (TBAF) instead of H_2SO_4 in the last step of the above procedure selectively removed *tert*-butyldimethylsilyl (TBDMS) group and gave various 2-*O*-alkyl derivatives of 5,6-*O*-isopropylidene L-AA **3a-g** [**Table 1**] in moderate to good yields.

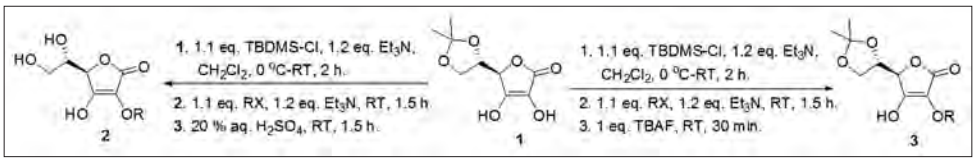
BIOLOGICAL INVESTIGATION

Newly synthesized compounds [**Table 1**] were screened for their cytotoxicity against the MCF-7 breast cancer cell line using (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide) colorimetric assay.

All the tested derivatives exhibited moderate inhibition of MCF-7 cell proliferation as compared to L-AA (half maximal inhibitory concentration [IC_{50}] = 128.54 µM) [**Table 1**]. In 5,6-*O*-unprotected series compound **2b** with benzyl group at *2-O* position showed moderate inhibition of MCF-7 cell proliferation (IC_{50} = 283.79 µM). Replacing the benzyl group with substituted 4-Cl-benzyl group **2c** resulted in increase in potency (IC_{50} = 158.52 µM), while 4-Br-benzyl group **2d** showed a decrease in potency with an IC_{50} value of 244.52 µM. 3 and 4-nitrobenzyl group (**2e** and **2f)** decreased activity further with an IC_{50} value of 327.79 and 303.61, respectively. Replacement of aromatic group by aliphatic one, e.g., isopropyl **2a** group resulted in decrease in potency (IC_{50} = 546.06). In 5,6-*O*-protected series, 2-*O*-methyl derivative **3a** showed IC_{50} value of 274.35 µM. Replacing methyl with ethyl group (derivative **3b**) decreased the activity to IC_{50} value of 459.22 µM. Derivative **3c** having 3-*O*-benzyl group exhibited moderate inhibition of MCF-7 cell proliferation (IC_{50} = 224.04 µM). Exchanging the benzyl group with substituted 4-Cl-Bn **3d**, 4-Br-benzyl **3e,** and 4-NO_2-Bn **3g** group resulted in decrease in potency (IC_{50} = 708.58, 255.13, and 620.92 µM, respectively), while 4-NO_2-Bn group **3f** showed improved potency with an IC_{50} value of 202.57 µM µM. In general, as the lipophilicity of alkyl group increases the antiproliferative activity of molecules decreases. Second, unsubstituted benzene ring shows better activity as compared to substituted benzene and aliphatic groups.

EXPERIMENTAL SECTION

Unless otherwise specified, all reagents and starting materials were purchased from commercial sources and used as received. Analytical thin-layer chromatography (TLC) was performed on precoated Merck silica gel plates (60F-254), visualized with a UV254 lamp, and stained with $KMnO_4$. ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were obtained as solutions in deuterated solvents. Standard ^1H NMR (300/400 MHz) and ^{13}C NMR (75/100 MHz) were recorded on a Varian Mercury spectrometer in $CDCl_3$ or dimethyl sulfoxide (DMSO)-d_6 solution and with tetramethylsilane as an internal standard. Chemical



Scheme 1

Table 1: One-pot synthesis of 2-*O*-alkyl derivatives of L-AA and 5,6-*O*-isopropylidene-L-AA

Entry	Compound	R	% yield[a]	Cytotoxic activity, IC_{50} (µM)[b]
				MCF-7 (SD±0.062)
1	**2a**	*i*-Pr	48	546.06
2	**2b**	Bn	44	283.79
3	**2c**	4-Cl-Bn	54	158.52
4	**2d**	4-Br-Bn	50	244.52
5	**2e**	3-NO_2-Bn	42	327.79
6	**2f**	4-NO_2-Bn	45	303.61
7	**3a**	Me	57	274.35
8	**3b**	Ethyl	51	459.22
9	**3c**	Bn	52	224.04
10	**3d**	4-Cl-Bn	44	708.58
11	**3e**	4-Br-Bn	40	255.13
12	**3f**	3-NO_2-Bn	43	202.57
13	**3g**	4-NO_2-Bn	47	620.92
14	**L-AA**	----	---	128.54

[a]Isolated yields. [b]Anticancer activity of 2-*O*-alkyl derivatives of L-AA at a concentration of 20 µM was screened. Against MCF-7 cell, cell proliferation is represented as relative cell numbers after treatment; A low percentage indicates potent anticancer activity for that compound. All data are normalized to the DMSO vehicle control. L-AA: L-ascorbic acid, SD: Standard deviation, IC_{50}: Half maximal inhibitory concentration, DMSO: Dimethyl sulfoxide

shifts (δ) in parts per million are reported relative to the residual signals of chloroform (7.26 ppm for ^{1}H and 77.16 ppm for ^{13}C). Multiplicities are described as s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet), and the coupling constants (*J*) are reported in Hertz. IR spectra were recorded on Perkin Elmer Model 1600 series FTIR instrument. Mass spectra were recorded on Liquid chromatography–mass spectrometry (ES-API) instrument. All the compounds synthesized are previously reported,[9] physical, and spectroscopic data [**Table 2**] are in agreement with reported values.

General procedure for one-pot synthesis of 2-*O*-alkyl derivatives of L-AA

A solution of 5,6-*O*-isopropylidene-L-AA (**1**) (2.0 g. 9.3 mmol) and triethylamine (1.55 mL, 11.1 mmol) in dry CH_2Cl_2 (10.0 mL) was cooled to 0°C. To this solution was added a solution of TBDMS-Cl (1.5 g, 10.2 mmol) in dry CH_2Cl_2 (5.0 mL). The reaction mixture was allowed to warm up to room temperature and stirred for 2 h. After completion of reaction (TLC check), reaction mixture was cooled to 0°C, and triethylamine (1.2 mL, 11.1 mmol) was added to the same reaction mixture followed by corresponding alkylating agent (1.1 eq. 10.2 mmol). Moreover, the mixture was stirred further at room temperature for 1–2 h. Next, the reaction mixture was treated with 20% aqueous H_2SO_4 (10.0 mL) and stirred at room temperature for another 1.5 h. After completion of reaction (TLC check), reaction mixture was neutralized with solid $NaHCO_3$ and filtered through celite pad. The filtrate was evaporated under vacuum to give the crude products **(2a-f)** which were purified by silica gel column chromatography using *n*-hexane:ethyl acetate solvent system.

Same experimental procedure was employed as above with minor modification. Selective deprotection of TBDMS group in the last step was achieved by addition of TBAF (1.0 eq., 9.3 mmol) instead of aqueous H_2SO_4. The reaction mixture was stirred at room temperature for 0.5 h. After completion of reaction (TLC check), the reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). Combined organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude products **(3a-g)** were purified by silica gel column chromatography using n-hexane: ethyl acetate solvent system.

2-*O*-isopropyl-L-AA (2a)

White Solid; m. p.: 100–103°C, Lit.[9] 100–102°C; $[\alpha]_D^{25}$ = +69.72 (c 0.5, MeOH); IR: 3423, 2987, 1749, 1681, 1373, 1074, 910 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (m, 6H), 2.90 (bs, 3H), 3.79–3.85 (m, 2H), 3.96 (dd, *J* = 6.2 and 2.4 Hz, 1H), 4.65 (d, *J* = 2.4 Hz, 1H), 5.10–5.18 (m, *J* = 5.7 Hz, 1H); ^{13}C NMR (75 MHz, DMSO) δ 23.3, 23.4, 62.1, 68.7, 73.1, 74.8, 118.1, 149.2, 170.8.

2-*O*-benzyl-L-AA (2b)

Viscous liquid; $[\alpha]_D^{25}$ = +7.88 (c 0.5, MeOH); IR: 3427, 2943, 1732, 1681, 1336, 1157, 758 cm^{-1}; ^{1}H NMR (400 MHz, DMSO) δ 3.77–3.84 (m, 2H), 4.03–4.09 (m, 1H), 4.78 (s, 1H), 5.18–5.19 (bs, 1H), 5.43–5.53 (AB quartet, *J* = 12 Hz, 2H), 7.36 (m, 5H), 8.75 (bs, 1H); ^{13}C NMR (100 MHz, DMSO) δ 61.8, 69.1, 71.1, 74.7, 119.6, 127.8, 136.3, 149.7, 170.5; MS (M^+ + Na): 288.97.

2-*O*-(4-chlorobenzyl)-L-AA (2c)

White Solid; m. p.: 110–112°C; $[\alpha]_D^{25}$ = +12.56 (c 0.5, MeOH); IR: 3381, 2885, 1741, 1685, 1338, 1163, 806 cm^{-1}; ^{1}H NMR (300 MHz, DMSO) δ 3.37–3.48 (m, 2H), 3.67–3.71 (m, 1H), 4.80 (s, 1H), 5.05 (bs, 1H), 5.37–5.49 (AB quartet, *J* = 12 Hz, 2H), 8.96 (bs, 1H); ^{13}C NMR (100 MHz, DMSO) δ 62.1, 68.8, 71.2, 74.9, 119.8, 128.2, 129.1, 133.3, 134.9, 149.3, 170.5; MS (M^+ + H): 301.01.

2-*O*-(4-bromobenzyl)-L-AA (2d)

White solid; m. p. 117-118°C; $[\alpha]_D^{25}$ = +21.60 (c 0.5, MeOH); IR: 3381, 2954, 1749, 1681, 1334, 1163, 800 cm^{-1}; ^{1}H NMR (400 MHz, DMSO) δ 3.40 (m, 1H), 3.79 (d, *J* = 5.7 Hz, 1H), 4.75 (m, 1H), 4.80 (s, 1H), 5.78 (AB quartet, *J* = 15 Hz, 2H), 7.45–7.51 (d, *J* = 7.6Hz, 2H), 7.67–7.76 (d, *J*

Table 2: Characterization data for synthesized compounds

Entry	Compound	R	% yield[a]	Observed M.P. °C	Reported[9] M.P. °C
1	**2a**	*i*-Pr	48	100–103	100–102
2	**2b**	Bn	44	Viscous liq.	Viscous liq.
3	**2c**	4-Cl-Bn	54	110–112	110–111
4	**2d**	4-Br-Bn	50	117-118	117-118
5	**2e**	3-NO_2-Bn	42	Viscous liq.	Viscous liq.
6	**2f**	4-NO_2-Bn	45	118–121	118–120
7	**3a**	Me	57	86–87	86–88
8	**3b**	Ethyl	51	91–93	92–93
9	**3c**	Bn	52	110–112	110–112
10	**3d**	4-Cl-Bn	44	122–123	122–124
11	**3e**	4-Br-Bn	40	137–138	136–138
12	**3f**	3-NO_2-Bn	43	Viscous liq.	Viscous liq.
13	**3g**	4-NO_2-Bn	47	152–153	152

= 7.6Hz, 2H), 8.76 (bs, 1H) ^{13}C NMR (100 MHz, DMSO) δ 61.9, 68.7, 70.5, 74.7, 120.0, 123.5, 124.9, 128.0, 133.5, 148.70, 170.1; MS (M^+ + H): 347.00.

2-*O*-(3-nitrobenzyl)-L-AA (2e)

Viscous liquid; IR: 3332, 3155, 2949, 1739, 1681, 1537, 1340, 1161, 731 cm^{-1}; ^{1}H NMR (400 MHz, DMSO) δ 3.47 (m, 2H), 3.75 (dd, *J* = 6.2 Hz, 1H), 4.86 (s, 2H), 5.05 (d, *J* = 6.2 Hz, 1H), 5.98 (AB quartet, *J* = 12.6 Hz, 2H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 8.21 (d, *J* = 7.6 and 1.5 Hz, 1H), 8.31 (s, 1H), 9.02 (bs, 1H); ^{13}C NMR (100 MHz, DMSO) δ 61.7, 68.5, 70.5, 74.6, 119.9, 122.1, 122.9, 129.7, 134.0, 138.8, 147.8, 149.5, 170.2; MS (M^+ + Na): 333.89.

2-*O*-(4-nitrobenzyl)-L-AA (2f)

Yellow solid; m. p.: 117–121°C; Lit.[9] 118–120°C; IR: 3385, 3238, 2960, 1743, 1685, 1543, 1336, 1163, 732 cm^{-1}; ^{1}H NMR (400 MHz, DMSO) δ 3.50 (m, 2H), 3.78 (m, 1H), 4.20–4.35 (bs, 3H), 4.73 (s, 1H), 5.6 (m, 2H), 7.72 (m, 2H), 8.20–8.27 (m, 2H), 9.04 (bs, 1H); ^{13}C NMR (100 MHz, DMSO) δ 61.7, 68.5, 70.5, 74.6, 119.9, 122.1, 122.9, 129.8, 133.9, 138.8, 147.7, 149.4, 170.2; MS (M^+ + Na): 333.99.

5,6-*O*-isopropylidene-2-*O*-methyl-L-AA (3a)

White solid; m. p.: 86–87°C; $[\alpha]_D^{25}$ = +41.96 (c 0.5, MeOH); IR: 3528, 3470, 3417, 2957, 1755, 1684, 1386, 1142, 832 cm^{-1};^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23 (s, 3H), 1.36 (s, 3H), 3.82 (s, 3H), 4.02 (dd, *J* = 6.7 and 8.6 Hz, 1H), 4.15 (dd, *J* = 6.7 and 8.6 Hz, 1H), 4.30 (dt, *J* = 3.4 and 6.7 Hz, 1H), 4.50 (d, *J* = 3.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.4, 25.7, 59.4, 65.1, 73.7, 74.5, 110.3, 123.1, 156.8, 169.0.

5,6-*O*-isopropylidene-2-*O*-ethyl-L-AA (3b)

White solid; m. p.: 91–93°C; Lit.[9] 92–93°C; $[\alpha]_D^{25}$ = + 15.52 (c 0.5, MeOH); IR: 3348, 2928, 1775, 1602, 1411, 1390, 707 cm^{-1};^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35–1.40 (m, 9H), 4.03 (dd, *J* = 6.7 and 8.5 Hz, 1H), 4.15 (dd, *J* = 6.7 and 8.5 Hz, 1H), 4.24–4.28 (m, 1H), 4.51–4.58 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3, 25.5, 25.8, 65.2, 68.1, 74.2, 75.6, 110.7, 118.8, 148.8, 171.3.

5,6-*O*-isopropylidene-2-*O*-benzyl-L-AA (3c)

White solid m. p.: 110–112°C. $[\alpha]_D^{25}$: +41.96 (c 0.5, MeOH) IR (neat) υ (cm^{-1}): 3326, 2977, 1757, 1697, 1371, 1162, 745. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.34 (s, 3H), 1.37 (s, 3H), 3.99–4.12 (m, 2H), 4.24 (dt, *J* = 3.8 and 6.7 Hz, 1H), 4.56 (d, *J* = 3.8 Hz, 1H), 5.51 (AB quartet, *J* = 12 Hz, 2H), 7.42 (m, 5H) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 25.5, 25.8, 65.3, 73.5, 74.2, 75.7, 110.2, 119.6, 128.1, 128.6, 135.6, 148.6, 171.2.

5,6-*O*-isopropylidene-2-*O*-(4-chlorobenzyl)-L-AA (3d)

White solid; m. p.: 122–123°C; Lit.[9] 122–124°C; $[\alpha]_D^{25}$ = + 12.56 (c 0.5, MeOH); IR: 3289, 2988, 1757, 1697, 1757, 1697, 1372, 1117, 810 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 3H), 1.37 (s, 3H), 3.99–4.14 (m, 2H), 4.27 (m, 1H), 4.58 (d, *J* = 2.9 Hz, 1H), 5.48 (s, 2H), 6.51 (s, 1H), 7.35 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.5, 25.8, 65.2, 72.5, 73.9, 75.6, 110.3, 119.7, 128.8, 129.5, 134.1, 134.6, 148.4, 171.2.

5,6-*O*-isopropylidene-2-*O*-(4-bromobenzyl)-L-AA (3e)

White solid; m. p.: 137–138°C; Lit.[9] 136–138°C; $[\alpha]_D^{25}$ = +82.84 (c 0.5, MeOH); IR: 3981, 2987, 1753, 1678, 1334, 1038, 806 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (s, 3H), 1.30 (s, 3H), 3.93 (dd, *J* = 6.4 and 8.4 Hz, 1H), 4.08 (dd, *J* = 6.4 and 8.4 Hz, 1H), 4.22 (dt, *J* = 3.3 and 6.4 Hz, 1H), 4.64 (m, 1H), 5.44 (s, 2H), 7.32 (m, *J* = 8.2 Hz, 2H), 7.51(m, 2H), 9.05 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.2, 25.6, 64.7, 71.2, 73.5, 74.4, 109.1, 120.1, 121.6, 129.4, 130.8, 135.5, 148.3, 169.7; MS (M^+ + H): 385.00.

5,6-*O*-isopropylidene-2-*O*-(3-nitrobenzyl)-L-AA (3f)

Viscous liquid; IR: 3502, 2987, 1745, 1687, 1529, 1346, 1115, 729 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.34 (s, 3H), 4.03 (m, *J* = 6.8 and 8.6 Hz, 1H), 4.15 (dd, *J* = 6.8 and 8.6 Hz, 1H), 4.31–4.35 (m, 1H), 4.61 (d, *J* = 3 Hz 1H), 5.56–5.63 (AB quartet, *J* = 12.6 Hz, 2H), 7.56 (m, 1H), 7.73 (d, *J* = 7.6 Hz 1H), 8.20 (m, 1H), 8.25 (d, *J* = 1.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.4, 25.8, 65.3, 71.8, 73.6, 75.5, 110.5, 120.1, 122.6, 123.5, 124.7, 129.7, 133.7, 137.9, 148.0, 171.0.

5,6-*O*-isopropylidene-2-*O*-(4-nitrobenzyl)-L-AA (3g)

Yellow Solid; m. p. 152–153°C; Lit.[9] 152°C; $[\alpha]_D^{25}$ = +59.96 (c 0.5, MeOH); IR: 3266, 2996, 1758, 1701, 1523, 1339, 1164 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 3H), 1.37 (s, 3H), 4.06 (dd, *J* = 6.7 and 8.5 Hz, 1H), 4.14 (dd, *J* = 6.7 and 8.5 Hz, 1H), 4.33 (dt, *J* = 3.3 and 6.7 Hz, 1H), 4.64 (d, *J* = 3.3 Hz, 1H), 5.60 (AB quartet, *J* = 13 Hz, 2H), 6.37 (bs, 1H), 7.58 (d, *J* = 8.6 Hz, 2H), 8.25 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.5, 25.8, 65.2, 71.8, 73.7, 75.4, 110.4, 119.8, 123.8, 128.1, 142.9, 147.8, 147.9, 170.8. MS (M^+ + Na): 373.9.

CYTOTOXICITY ASSAY

MCF-7 breast cancer cells were grown in Dulbecco's modified eagle's medium (DMEM) supplemented with 10% fetal bovine serum and 1% antibiotic solution (penicillin and streptomycin) at 37°C in humidified chamber under 5% CO_2. Cell viability was measured in 96-well plates by quantitative colorimetric assay using MTT.[10] Briefly, 105 cells per ml were seeded in 96-well plates for assay. The compounds were dissolved in DMSO and were diluted to the desired concentrations using plain DMEM. The compounds were treated to the cells at various concentrations ranging from 0 to 30 µM. The compound solutions were passed through 0.22 µM syringe filters for sterilization before treatment. After 24 h, media was removed, and 5 mg/ml MTT (final concentration) was added to the wells, and the cells were incubated at 37°C for another 3 h. The MTT solution was removed, and the colored formazan crystals in each well

were dissolved in 150 µL dimethyl sulfoxide. Absorbance at 595 nm was measured using a µQuant, Biotek Instruments microplate reader. The IC_{50} values of the compounds were calculated using ED_{50} V_{10} excel add-in tool. This assay was performed at Biometry and Nutrition Group, Agharkar Research Institute, Pune-411004, India, using the standard operating procedures.

CONCLUSION

We have demonstrated that 2-*O*-alkylation of L-AA is easily accessible through the silylation-alkylation-desilylation approach. Biological screening of the synthesized compounds showed that they exhibited moderate inhibition of breast cancer cell line (MCF-7). Further investigations concerning biology and application of these products in organic synthesis are in progress.

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