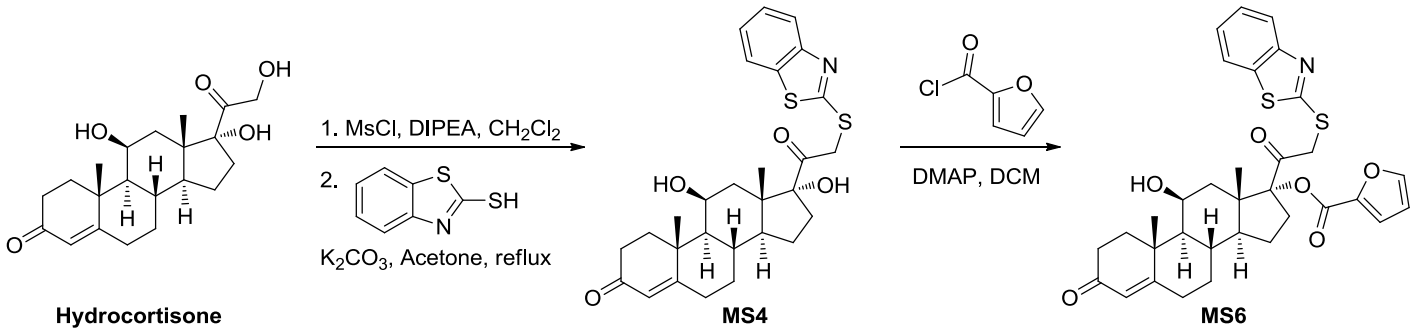
Supplementary Figure 1



General Methods: All reactions were performed under inert atmosphere using dry solvents unless otherwise noted. All solvents and chemicals were purchased through either Fisher Scientific or VWR and were reagent grade. NMRs were taken on either a Varian Mercury Vx 300 MHz or Varian VNMRS 500 MHz. High resolution mass spectrum were performed on JEOL AccuTOF mass spectrometer using DART ionization. IR were performed on a Thermo Nicolet IR-100 FTIR. Specific rotations were taken on a Perkin Elmer 241 polarimeter.

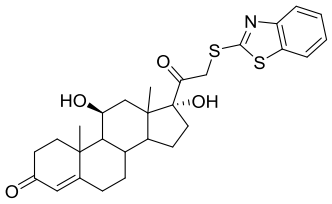
Synthesis of (11*S*,17*R*)-17-(2-(benzo[*d*]thiazol-2-ylthio)acetyl)-11,17-dihydroxy-10-methyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one (21-(benzo[*d*]thiazolyl)-21-thiohydrocoritsone, MS4): Hydrocortisone (1.000 g, 2.759 mmol) was stirred in 50 mL of dichloromethane and the mixture was cooled to 0 °C. At this point, diisopropylethylamine (DIPEA) (2.674 g, 20.961 mmol, 3.604 mL) followed directly by mesylchloride (MsCl) (0.474 g, 4.138 mmol, 0.320 mL). The reaction was slowly warmed to room temperature and monitored by TLC until completion. Once no change was observed on TLC, ~15 h, the reaction was concentrated *in vacuo*. The resulting oil was then redissolved in 50 mL dichloromethane, washed with 50 mL saturated bicarbonate. The water layer was then extracted with 20 mL dichloromethane. The organic layers were then combined and washed twice with 50 mL brine. The organic layer was then dried with $MgSO_4$, filtered, and the filtrate was concentrated to give a tan crystalline solid as the mesylate of **1**. This product was carried through crude to the next reaction.

The hydrocortisone mesylate (0.500 g, 1.135 mmol) was dissolved in 100 mL of reagent grade acetone. To this solution was added potassium carbonate (1.568 g, 11.350 mmol) followed directly by 2-mercaptobenzothiozole (0.380 g 2.270 mmol) and the resulting mixture was refluxed. The reaction was monitored by TLC for completion. Once no change was observed on TLC, ~ 1 h, the mixture was filtered through a short pad of silica and the filtrate was concentrated *in vacuo* to give an off-white crystalline solid. The crude product was then purified by column chromatography using 3:2 hexanes:ethyl acetate (Hex:EtOAc) to elute the product, MS4, as a white solid in 74% yield. R_f = 0.50, 10:1 CH_2Cl_2:MeOH; mp 137 °C; ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 8.1 Hz, 1H), 7.73 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.40 (ddd, *J* = 8.3, 7.2, 1.3 Hz, 1H), 7.34 – 7.27 (m, 1H), 5.69 (d, *J* = 1.7 Hz, 1H), 5.00 (d, *J* = 15.2 Hz, 1H), 4.49 (q, *J* = 3.2 Hz, 1H), 3.32 (d, *J* = 15.3 Hz, 1H), 2.83 (ddd, *J* = 14.3, 11.3, 2.5 Hz, 1H), 2.48 (dddd, *J* = 18.6, 13.6, 6.5, 3.4 Hz, 2H), 2.36 (ddt, *J* = 11.6, 8.6, 4.0 Hz, 2H), 2.30 – 2.14 (m, 2H), 2.05 (dddd, *J* = 18.2, 10.2, 8.5, 3.2 Hz, 2H), 1.99 – 1.81 (m, 2H), 1.68 – 1.53 (m, 2H), 1.45 (s, 4H), 1.30 – 1.13 (m, 3H), 1.10 (dd, *J* = 11.1, 3.3 Hz, 1H), 0.96 (s, 3H); ^{13}C NMR (126 MHz, Chloroform-*d*) δ 206.62, 199.46, 172.12, 167.39, 151.50, 134.90, 126.42, 124.86, 122.35, 121.32, 120.46, 91.08, 68.54, 55.99, 52.09, 46.77, 40.57, 39.18, 36.68, 35.07, 34.81, 33.81, 32.66, 32.10, 31.49, 23.85, 21.09, 17.74; IR: 3681, 2916, 2847, 1656, 1269, 755 cm^{-1}; HRMS-DART (*m/z*): $[M+H]^+$ calcd for $C_{28}H_{34}NO_4S_2^+$, 512.19238; found, 512.19378; $[\alpha]_D^{24}$ + 128.9 (*c* 0.51, CH_2Cl_2).

Synthesis of (11*S*,17*R*)-17-(2-(benzo[*d*]thiazol-2-ylthio)acetyl)-11-hydroxy-10-methyl-3-oxo-2,3,6,7,8,9,10,11,12,13, 14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl furan-2-carboxylate (21-(benzo[*d*]thiazolyl)-17-(2-furanoyl)-21-thiohydrocoritsone ,MS6): MS4 (0.118 g, 0.231 mmol) was dissolved in 5 mL dichloromethane and cooled to 0 °C. To this solution was added DMAP (0.036 g, 0.300 mmol) followed by furonyl chloride (0.036 g, 0.027 mL, 0.277 mmol). The reaction was slowly warmed to room temperature and monitored by TLC for completion. Once no change was observed on TLC, ~ 28 h, the reaction was diluted with ~5 mL CH_2Cl_2 and washed with brine (3 X 15 mL), dried with $MgSO_4$, and filtered. The filtrate was then concentrated *in vacuo* and the crude product was purified via column chromatography using 99:1 dichloromethane:methanol (CH_2Cl_2:MeOH) to elute the product as a white solid in 31% yield. R_f = 0.56, 10:1 CH_2Cl_2:MeOH; mp 188 °C;^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.80 (ddd, *J* = 8.1, 1.2, 0.6 Hz, 1H), 7.74 (ddd, *J* = 8.0, 1.3, 0.6 Hz, 1H), 7.62 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.39 (ddd, *J* = 8.2, 7.3, 1.2 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.24 (dd, *J* = 3.5, 0.8 Hz, 1H), 6.55 (dd, *J* = 3.5, 1.7 Hz, 1H), 5.73 – 5.69 (m, 1H), 4.64 (d, *J* = 17.1 Hz, 1H), 4.59 (q, *J* = 3.2 Hz, 1H), 4.37 (d, *J* = 17.1 Hz, 1H), 3.08 (ddd, *J* = 16.1, 11.2, 2.3 Hz, 1H), 2.57 – 2.47 (m, 2H), 2.44 – 2.32 (m, 2H), 2.30 – 2.21 (m, 2H), 2.17 – 2.09 (m, 2H), 2.08 – 1.90 (m, 4H), 1.88 – 1.78 (m, 2H), 1.53 – 1.46 (m, 4H), 1.22 – 1.11 (m, 2H), 1.09 (s, 3H); ^{13}C NMR (75 MHz, Chloroform-*d*) δ 199.53, 198.59, 171.80, 166.17, 158.14, 152.07, 147.20, 143.95, 135.26, 126.22, 124.59, 122.49, 121.21, 121.04, 119.50, 112.23, 96.45, 68.24, 55.97, 52.91, 47.32, 41.69, 40.27, 39.22, 35.00, 33.86, 32.61, 31.96, 31.47, 31.16, 23.90, 21.00, 16.71; IR: 3478, 2915, 2850, 2358, 754 cm^{-1}; HRMS-DART (*m/z*): $[M+H]^+$ calcd for $C_{33}H_{36}NO_6S_2^+$, 606.19786; found, 606.19888; $[\alpha]_D^{24}$ + 100.7 (*c* 0.61, CH_2Cl_2).

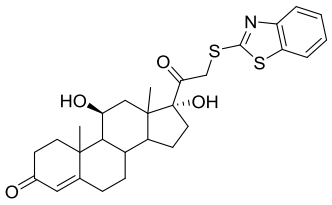
Note that the mercaptosteroids shown were originally designated as “4” and “6” in reference 26. Therefore, the MS4 and MS6 designations were used in the current study to maintain consistency with the existing literature.

A



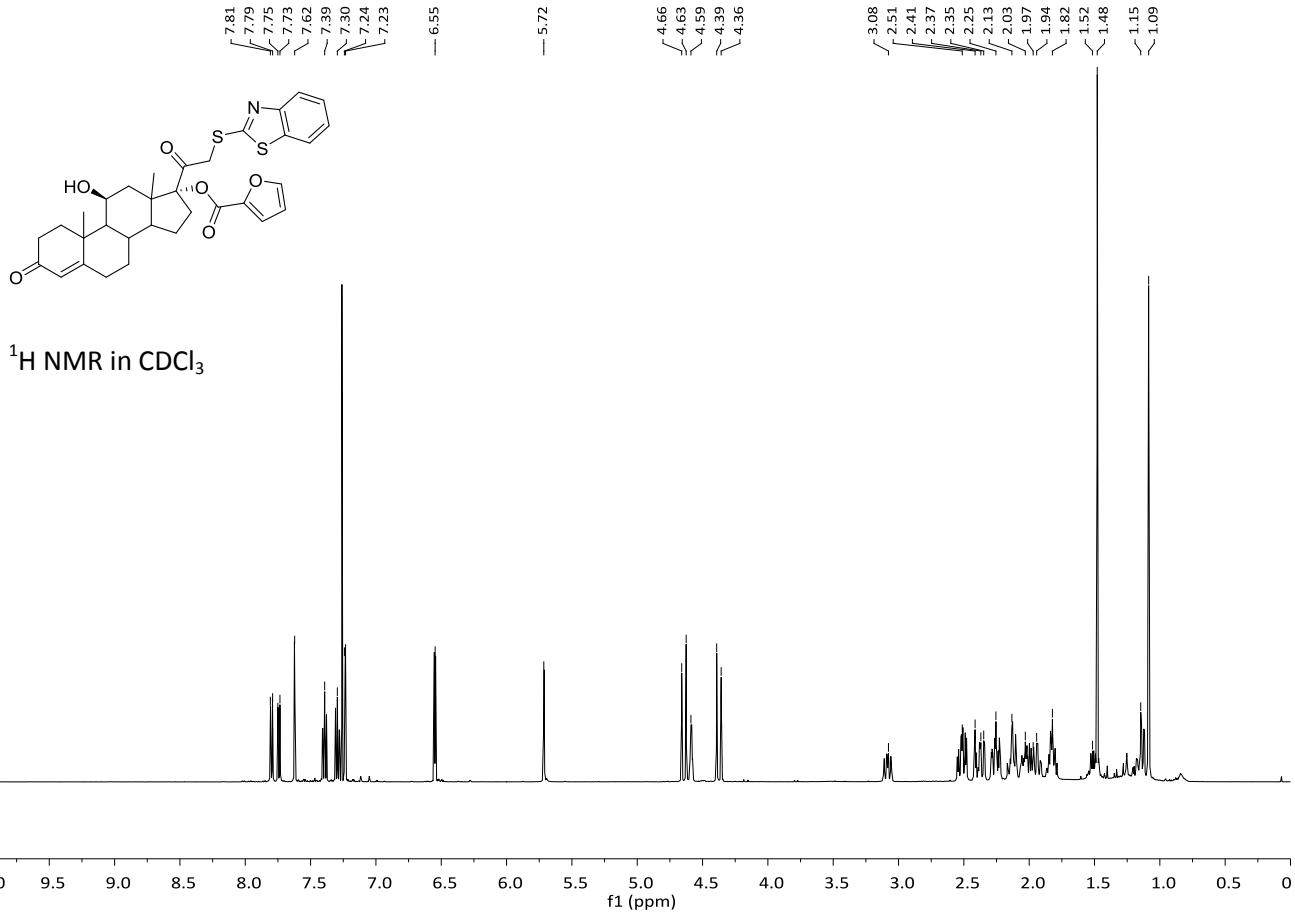
^{1}H NMR in $CDCl_3$

B

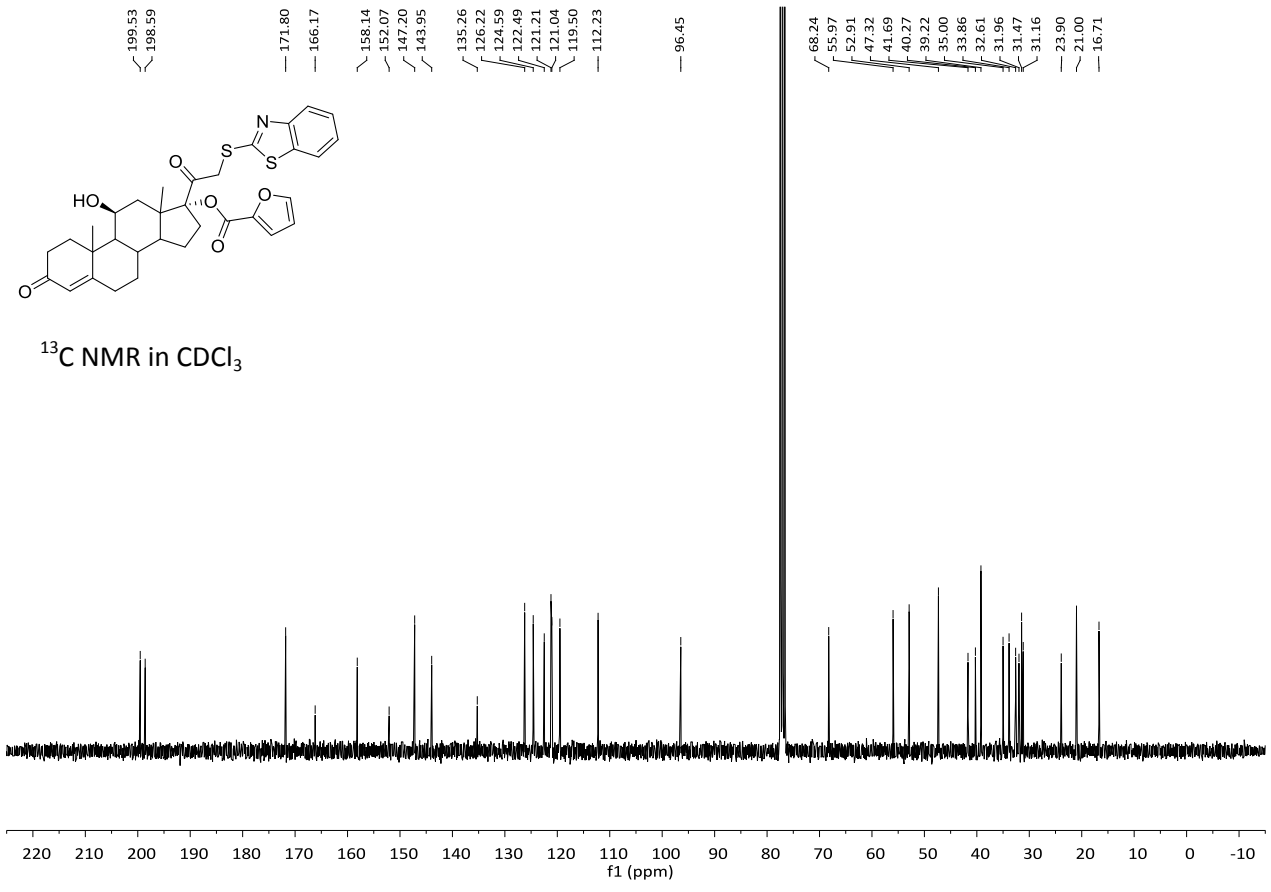


^{13}C NMR in $CDCl_3$

C


7.81
7.79
7.75
7.73
7.62
7.39
7.30
7.24
7.23
6.55
5.72
4.66
4.63
4.59
4.39
4.36
3.08
2.51
2.41
2.37
2.35
2.25
2.13
2.03
1.97
1.94
1.82
1.52
1.48
1.15
1.09
HO
O
N
S
S
O
O
O
O
^{1}H NMR in CDCl$_3$
f1 (ppm)

D


199.53
198.59
171.80
166.17
158.14
152.07
147.20
143.95
135.26
126.22
124.59
122.49
121.21
121.04
119.50
112.23
96.45
68.24
55.97
52.91
47.32
41.69
40.27
39.22
35.00
33.86
32.61
31.96
31.47
31.16
23.90
21.00
16.71
HO
O
N
S
S
O
O
O
O
^{13}C NMR in CDCl$_3$
f1 (ppm)