Supplementary Materials

Improved Synthesis and Determinatin of Biologically Active Diastereomer of YK11

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Experimental section

Luciferase reporter assay

Cells of the human embryonic kidney cell line HEK293 were cultured in Dulbecco's modified Eagle's medium (DMEM; WAKO) containing 10% fetal bovine serum (FBS) and penicillin-streptomycin in a humidified atmosphere containing 5 % CO_2 at 37 ℃. The cells maintained in phenol red-free DMEM containing 5% charcoal-stripped FBS (csFBS) were seeded in 48-well plates and transfected with AR expression plasmids, the ARE-luciferase reporter plasmids[1], and a Renilla pGL4.74 (hRluc/TK; Promega) as an internal standard using the reverse-transfection method with the PEI Max Reagent (Polysciences Inc.). After incubation overnight, the cells were treated with one of the AR ligands for 24 h prior to measuring the luciferase activity using the Dual-Luciferase Reporter Assay System (Promega).

Crystallographic parameters for structures of **YK-11** (**2a**).

X-ray data were collected on a Rigaku XtaLAB P200 diffractometer with multi-layer mirror monochromated Cu*K*α (λ = 1.54187 Å) and a hybrid photon counting detector (PILATUS 200K). The crystal structure was solved by direct methods (SHELXT Version 2014/5)[2] and refined by full-matrix least-squares SHELXL-2014/7.[3] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were generated theoretically added. The absolute configuration of the molecule was reasonable in terms of the Flack parameter[4] **YK-11** (**2a**) contains two crystallographically independent molecules in the asymmetric unit. Highly disordered solvent, which located in channels along [010], was unable to be modeled. As the identification of disordered solvent molecules riding on the center of symmetry was failed in the refinement of void space, PLATON/SQUEEZE program[5] was applied. PLATON/SQUEEZE shows the total potential solvent accessible void volume is 270 Å^3 and residual electrons count 76 in the unit cell. CCDC-1974030 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table S1 Crystallographic data and refinement parameters for **YK-11** (**2a**)

Compound	**YK11** (**2a**)
Empirical formula	$C_{25}H_{34}O_6$
Formula weight	430.54
Crystal system	monoclinic
Space group	$P2_1$
a / Å	15.7937(3)
b / Å	7.49440(10)
c / Å	20.8812(2)
α / deg	90.0000
β / deg	97.4360(13)
γ / deg	90.0000
V / Å^3	2450.80(6)
Z	4
Temperature / K	93
Goodness-of-fit on F^2 [a]	1.056
R_1 [$I > 2\sigma(I)$] on F [b]	0.0408
wR_2 (all data) on F^2 [c]	0.1136
Reflection collected (all data)	29206
Independent reflections [$I > 2\sigma(I)$]	8505
R_{int}	0.0310
Flack parameter	0.03(6)
T_{max}	0.849
T_{min}	0.954
$2\theta_{max}$	68.249
D_{calcd} ./ gcm^{-3}	1.167
μ /mm^{-1}	0.670
CCDC code	1974030

[a] Goodness of fit = $[\Sigma w(F_o^2\text{-}F_c^2)^2/(N_o\text{-}N_v)]^{1/2}$ (N_o = number of observations, N_v = number of variables). [b] $R_1 = \Sigma||F_o| - |F_c|| / \Sigma|F_o|$ [c] $wR_2 = [\Sigma(w(F_o^2\text{-}F_c^2)^2/ \Sigma w(F_o^2)^2)^{1/2}$

(a) (b)

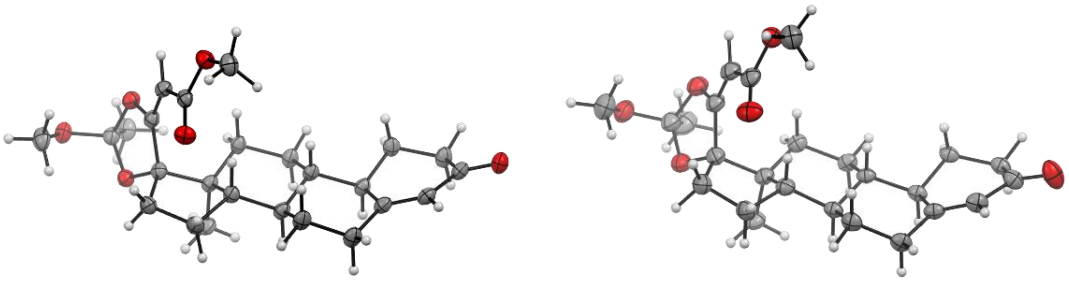


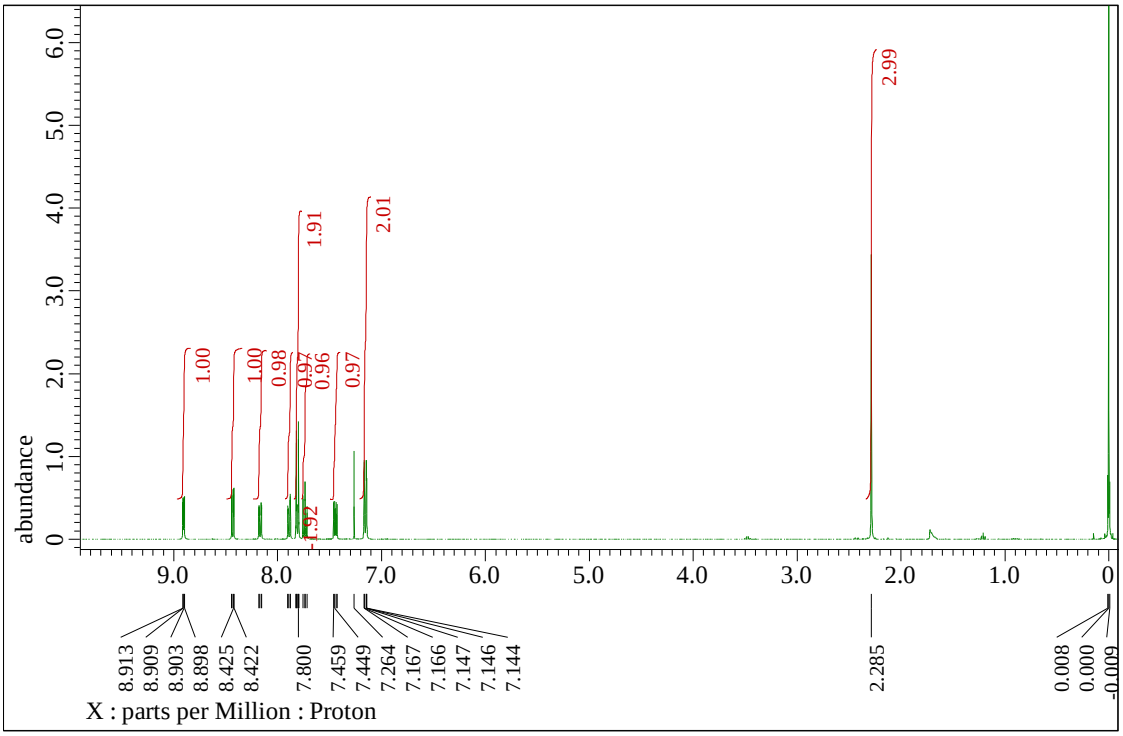
Figure S1 X-ray structure of **YK-11** (**2a**). **YK-11** (**2a**) contains two crystallographically independent molecules (a and b) in the asymmetric unit. Colors of atoms: C, gray spheres; O, red spheres; H, light gray spheres.

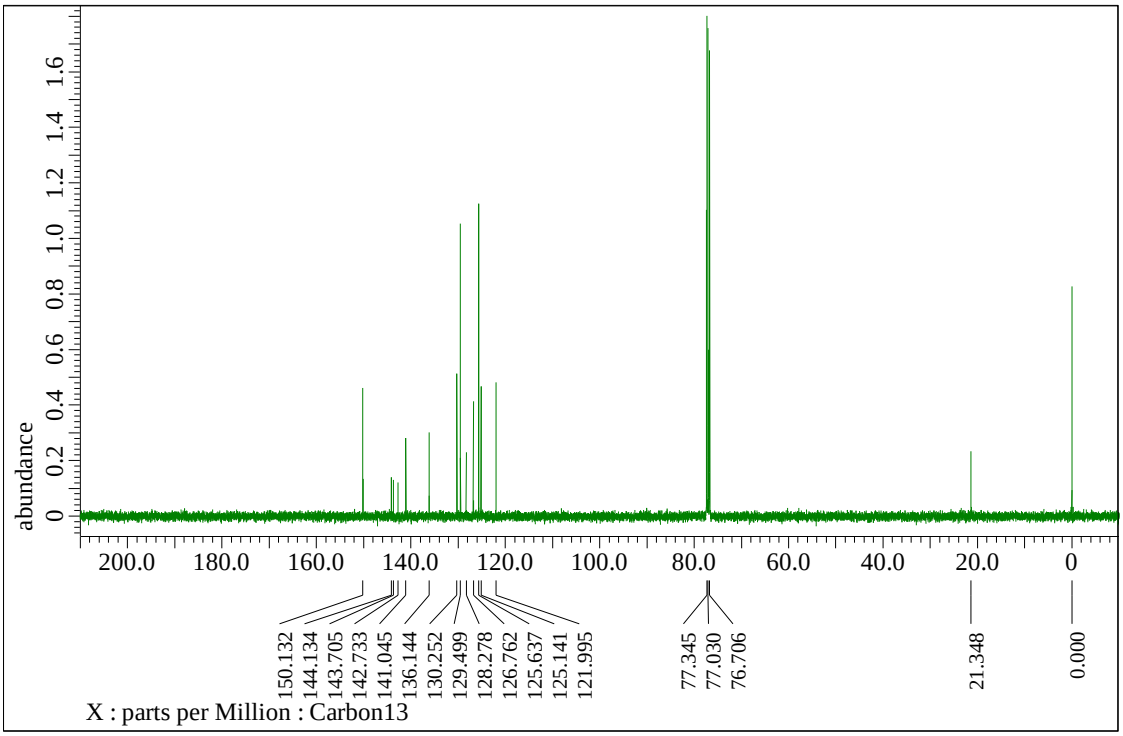
References

(1) Y. Kanno, R. Hikosaka, S-Y. Zhang, Y. Inoue, T. Nakahama, K. Kato, A. Yamaguchi, N. Tominaga, S. Kohra, K. Arizono, Y. Inoue, *Biol. Pharm. Bull.* **2011**, *34*, 318-323.
(2) G. M. Sheldrick, *Acta Crystallogr.* **2014**, *A70*, C1437.
(3) G. M. Sheldrick, *Acta Crystallogr.* **2015**, *C71*, 3-8.
(4) a) H. D. Flack, G. Bernardinelli, *Acta Crystallogr.* **1999**, *A55*, 908-915. b) H.D. Flack, G. Bernardinelli, *J. Appl. Crystallogr.* **2000**, *33*, 1143-1148.
(5) A. L. Spek, *Acta Crystallogr.* **2015**, *C71*, 9-18.

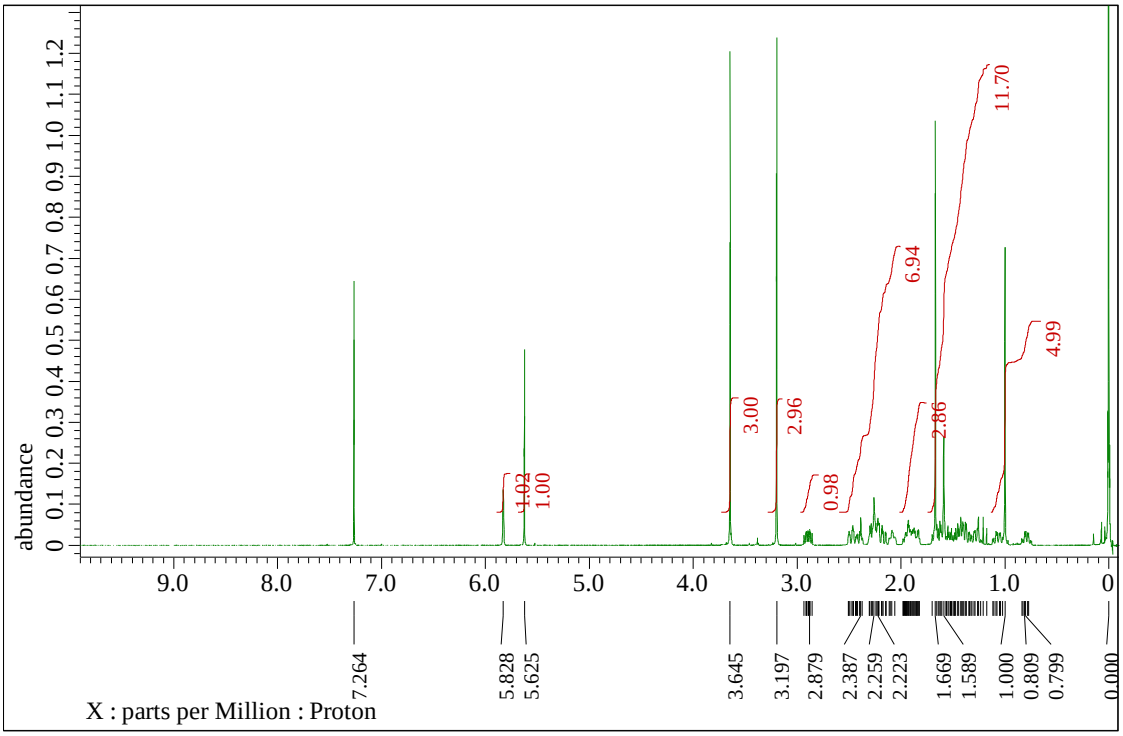
^{1}H NMR and ^{13}C NMR spectra

L3





YK11 (2a)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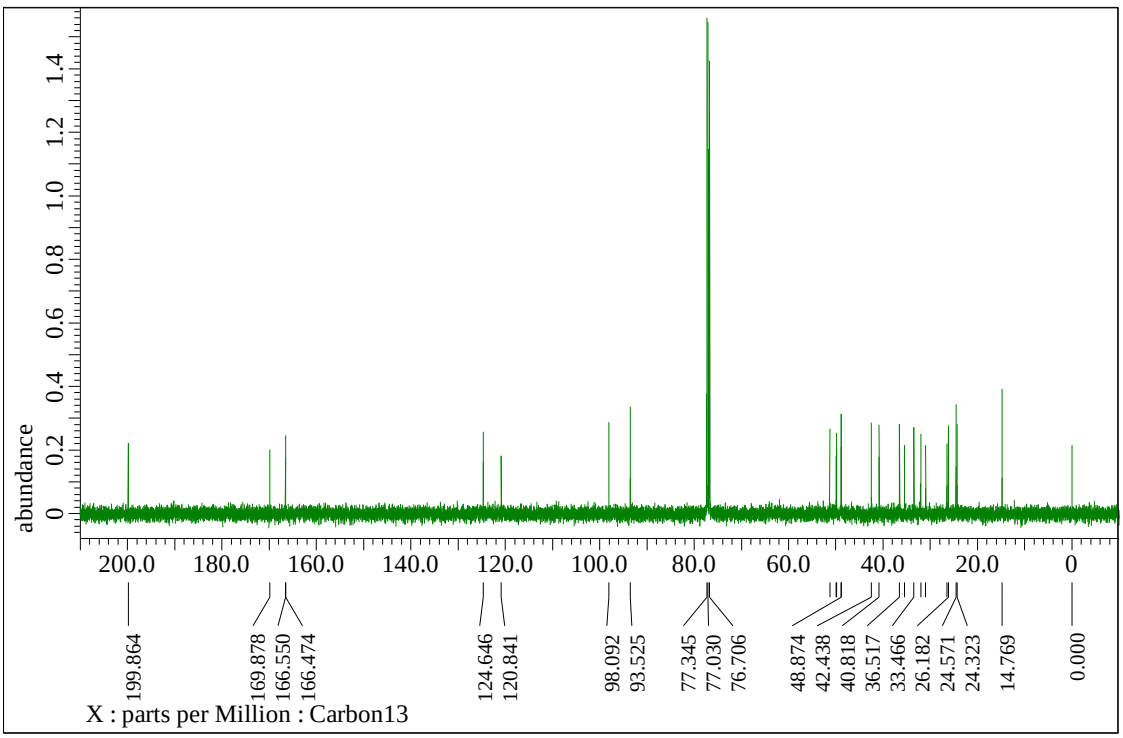
1.02
1.00
3.00
2.96
0.98
6.94
2.86
11.70
4.99
7.264
5.828
5.625
3.645
3.197
2.879
2.387
2.259
2.223
1.669
1.589
1.000
0.809
0.799
0.000
X : parts per Million : Proton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169.878
166.550
166.474
124.646
120.841
98.092
93.525
77.345
77.030
76.706
48.874
42.438
40.818
36.517
33.466
26.182
24.571
24.323
14.769
0.000
X : parts per Million : Carbon13