# Product Data Sheet

Product Name: PROTAC AR Degrader-12
Cat. No.: GC81303

## Chemical Properties

| | | | |
|---|---|---|---|
| Cas. No. | | | |
| Formula | $C_{57}H_{76}N_8O_{10}S$ | M.Wt | 1065.33 |
| Solubility | DMSO: 100 mg/mL (93.87 mM; Need ultrasonic) | Storage | Store at -20°C |
| General tips | For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months. | | |
| Shipping Condition | Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request. | | |

***Caution: Product has not been fully validated for medical applications. For research use only.***
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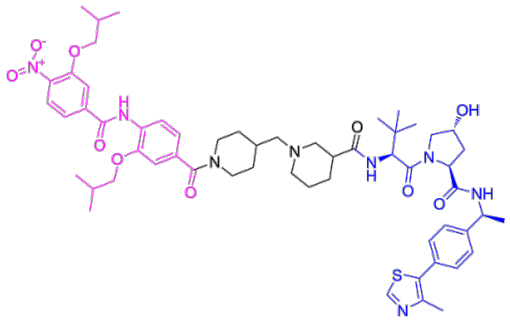
Structure



## Background

PROTAC AR Degrader-12 is a highly efficient PROTAC targeting AR coactivator binding site (AR-CBS). PROTAC AR Degrader-12 induces AR degradation in a ubiquitin proteasome system (UPS) pathway-dependent manner. PROTAC AR Degrader-12 inhibits tumor cell growth by affecting DNA replication and cell division PROTAC AR Degrader-12 could not only effectively degrade AR, but also potently inhibit the proliferation of MCF-7 and multiple mutant or resistant BC cells. PROTAC AR Degrader-12 effectively blocked estrogen receptor α ( ERα ) signaling through a dual mechanism involving ERα protein downregulation and suppression of its transcriptional activity. PROTAC AR Degrader-12 significantly inhibits the mRNA expression of FOXA1, GREB1, SRC, and PELP1. PROTAC AR Degrader-12 can be used for the study of breast cancer [1]. (Pink: AR ligand; Blue: VHL ligand; Black: linker).

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In Vivo, PROTAC AR Degrader-12 (Compound 18o) (5-10 μM/kg, i.p., once every other day) significantly inhibits tumor growth in MCF-7 cells and LCC2 cells xenograft mice, promotes AR protein degradation and ERα signaling inhibition, without weight loss or other toxicities[1].

In Vitro, PROTAC AR Degrader-12 (Compound 18o) shows good inhibitory activity against MCF-7 ($IC_{50}$ = 0.13 μM) and LCC2 cells($IC_{50}$ = 0.54 μM) and exhibits broad-spectrum efficacy against clinically relevant mutant variants, demonstrating potent submicromolar inhibition of MCF-7D538G($IC_{50}$ = 0.66 μM), MCF-7Y537S ($IC_{50}$ = 0.44 μM), and MCF-7EGFR($IC_{50}$ =0.52 μM)[1]. PROTAC AR Degrader-12 (0.01-2 μM, 24 h) effectively and in a dose-dependent manner degrades AR protein in MCF-7 cells ($DC_{50}$ = 0.72 μM)[1]. PROTAC AR Degrader-12 (1 μM, 0-24 h) shows a time-dependent effect on AR degradation in MCF-7 cells[1]. PROTAC AR Degrader-12 (0.01-2 μM, 24 h) causes a concentration-dependent downregulation of ERα protein in MCF-7 cells[1]. PROTAC AR Degrader-12 (0.01-2 μM, 12-24 h) significantly downregulates ERα protein in MCF-7D538G, MCF-7Y537S, MCF-7EGFR, LCC2, and T47D cells, and fails to downregulate ERβ protein in PC9 cells[1]. PROTAC AR Degrader-12 (1 μM, 24 h) induces a decrease in ERα through an indirect mechanism, rather than by directly targeting the degradation of CBS in MCF-7 cells[1]. PROTAC AR Degrader-12 (0-5 μM, 0-24 h) reduces AR protein in MCF-7 cells due to posttranscriptional degradation, while the reduction in ERα was a result of transcriptional repression[1]. PROTAC AR Degrader-12 exhibits potent antiproliferative activity in AR-overexpressing but ERα-deficient prostate cancer cells LNCaP ($IC_{50}$ = 0.46 μM), while its antiproliferative activity is significantly reduced in AR-negative MDA-MB-231 cells ($IC_{50}$ > 30 μM)[1]. PROTAC AR Degrader-12 was very effective in stabilizing the AR protein at high temperature, while it only displays a weak protective effect on ERα protein, suggesting that compound PROTAC AR Degrader-12 engages AR but does not bind to Erα in LCC2 cells[1]. PROTAC AR Degrader-12 (1 μM, 24 h) significantly inhibits the mRNA expression of FOXA1, GREB1, SRC, and PELP1 in MCF-7 cells[1]. PROTAC AR Degrader-12 (1-10 μM, 48 h) induces S-phase cell cycle arrest in MCF-7 and LCC2 cells[1].

References:

[1]. Wu Y, et al. Kill Two Birds with One Stone: An Efficient and Potent AR CBS-Targeted Degrader Reverses Breast Cancer Resistance via Concurrent AR Degradation and ERα Transcriptional

Suppression. J Med Chem. 2025 Nov 27;68(22):24136-24167.