## Q1: Propose reasonable reaction mechanisms of the following transformations.

Q2: Propose another synthetic plan to obtain the target compound (anti-cancer agent).


Compound $\mathbf{A}\left(\mathrm{C}_{14} \mathrm{H}_{16} \mathrm{O}_{3}\right)$. $\mathrm{NaH}(60 \%$ dispersion in mineral oil, $280 \mathrm{mg}, 7.00 \mathrm{mmol}$ ) was washed three times with anhydrous hexane and suspended in anhydrous THF ( 17.0 mL ). To this stirred suspension was added dropwise methyl acetoacetate ( $581 \mathrm{mg}, 5.00 \mathrm{mmol}$ ) with stirring at $0{ }^{\circ} \mathrm{C}$. The solution was stirred at $0^{\circ} \mathrm{C}$ for 30 min , and then $n-\mathrm{BuLi}(1.60 \mathrm{M}$ in hexane, $4.70 \mathrm{~mL}, 7.50 \mathrm{mmol}$ ) was added dropwise at $0{ }^{\circ} \mathrm{C}$. The resulting mixture was stirred at $0{ }^{\circ} \mathrm{C}$ for 30 min and cinnamyl chloride ( $839 \mathrm{mg}, 5.50 \mathrm{mmol}$ ) was added dropwise at $0^{\circ} \mathrm{C}$. The reaction mixture was warmed up to room temperature and stirred for 1 h . The reaction was quenched by addition of saturated aqueous $\mathrm{NH}_{4} \mathrm{Cl}$ solution at $0{ }^{\circ} \mathrm{C}$, and then the organic solvent was removed under reduced pressure. The residue was extracted three times with EtOAc. The combined organic layers were washed with saturated aqueous NaCl solution, dried over $\mathrm{MgSO}_{4}$, and filtered through Celite. The filtrate was concentrated to afford an oil. The crude product was purified by flash column chromatography with hexane-EtOAc ( $5: 1 \mathrm{v} / \mathrm{v}$ ) as an eluent to afford $\mathbf{A}(712 \mathrm{mg}, 62 \%)$ as a colorless oil.
${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 7.36-7.24(\mathrm{~m}, 4 \mathrm{H}), 7.21-7.17(\mathrm{~m}, 1 \mathrm{H}), 6.40(\mathrm{~d}, J=16.0 \mathrm{~Hz}, 1 \mathrm{H}), 6.16$ (dd, $J=6.8$, and $16.0 \mathrm{~Hz}, 1 \mathrm{H}), 3.72(\mathrm{~s}, 3 \mathrm{H}), 3.46(\mathrm{~s}, 2 \mathrm{H}), 2.71(\mathrm{t}, J=7.2 \mathrm{~Hz}, 2 \mathrm{H})$, and $2.49(2 \mathrm{H}, \mathrm{dt}, J$ $=6.8,7.2 \mathrm{~Hz}) .{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 201.9,167.6,137.4,131.2,128.6,128.3,127.3,126.1$, 52.5, 49.2, 42.6, and 26.9; IR (neat) 1748, 1715.

Compound $\mathbf{B}\left(\mathrm{C}_{14} \mathrm{H}_{12} \mathrm{O}_{3}\right) . \mathrm{Pd}(\mathrm{OAc})_{2}(4.50 \mathrm{mg}, 0.02 \mathrm{mmol})$ and $\mathrm{Cu}(\mathrm{OAc})_{2}(7.30 \mathrm{mg}, 0.04 \mathrm{mmol})$ were placed in a screw-top test tube, and a solution of $\mathbf{A}(46.5 \mathrm{mg}, 0.20 \mathrm{mmol})$ in DMSO $(0.02 \mathrm{~mL})$ was added at room temperature. The reaction mixture was stirred at $50^{\circ} \mathrm{C}$ for 24 h under one atmosphere of oxygen. After cooling to room temperature, the palladium residue was removed by filtering through Celite. The organic solvent was removed under reduced pressure, and then the reaction was quenched by addition of saturated aqueous $\mathrm{NaHCO}_{3}$ solution at room temperature. The solution was extracted three times with hexane-EtOAc ( $4: 1 \mathrm{v} / \mathrm{v}$ ). The combined organic layers were washed with saturated aqueous NaCl solution, dried over $\mathrm{MgSO}_{4}$, and filtered through Celite. The filtrate was concentrated to afford $\mathbf{B}(27.3 \mathrm{mg}, 60 \%)$ as an oil.
${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 10.6(\mathrm{~s}, 1 \mathrm{H}), 7.43-7.32(\mathrm{~m}, 4 \mathrm{H}), 7.27-7.22(\mathrm{~m}, 2 \mathrm{H}), 7.02-6.99(\mathrm{~m}, 1 \mathrm{H})$, 6.81-6.80 (m, 1H), and 3.48 (s, 3H); ${ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 171.4,161.3,144.9,142.7,133.7$, $128.1,127.6,126.8,122.6,116.6,112.1$, and 51.7.
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1) LDA, prenylbromide, THF, $-78^{\circ} \mathrm{C}$
2) prenylMgCl, THF, rt, $52 \%$ ( 2 steps)
3) $\mathrm{KH}, 18-C r o w n-6$, THF, rt; $\mathrm{MgBr}_{2}$, Mel, $50^{\circ} \mathrm{C}, 65 \%$
4) LiTMP, diketene

THF/Et ${ }_{2} \mathrm{O},-40^{\circ} \mathrm{C}, 44 \%$
5) $\mathrm{Pd}(\mathrm{OAc})_{2}$ (15 mol\%)
$\mathrm{Cu}(\mathrm{OAc})_{2}$ (1.1 eq.)
DMSO-TMSOH, rt, 95\%
A
$\mathrm{C}_{21} \mathrm{H}_{32} \mathrm{O}_{3}$
6) $\mathrm{Phl}(\mathrm{OAc})_{2}, \mathrm{KOH}$
-10 to $0^{\circ} \mathrm{C}, \mathrm{MeOH}, 75 \%$



