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Supplementary Material

Alkyne-Tagged Apigenin, a Chemical Tool to Navigate Potential Targets of Flavonoid Anti-Dengue Leads

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Overview:

Table S1. List of top10 proteins related to apigenin and their subcellular distribution

Figure S1. A structure overlay of Estradiol and apigenins B-C The 3D structure of dimeric NS1 of DENV2 with the top binding poses from 50 docking runs.

Figures S2–S7 ^{1}H and ^{13}C-NMR spectra

Figure S8 Pharmacokinetics, drug-likeness and medicinal chemistry by SwissADME

Table S1. List of top10 proteins related to apigenin and their subcellular distribution.

Targeted Proteins		Cellular Distribution	Prediction of Specific Actions	Experimental /Biochemical Data	Evidence Suggesting a Function Link (Combined Score)
ESR1	estrogen receptor 1	vesicles	activation, binding, expression	Yes	0.961
UGT1A1	UDP glucuronosyltransferase 1 family	cytosol	inhibition	None	0.949
MAOA	monoamine oxidase A	nucleoplasm, mitochondria	activation	None	0.947
TP53	tumor protein p53	nucleoplasm	Not available	None	0.944
CDK1	cyclin-dependent kinase 1	Not available	expression	None	0.938
CASP3	caspase 3, apoptosis-related cysteine peptidase	endoplasmic reticulum	binding	Yes	0.877
PTGS2	prostaglandin-endoperoxide synthase 2	nucleoplasm and microtubule	expression	None	0.876
AKT1	v-Akt murine thymoma viral oncogene homolog 1	mitochondria	binding, inhibition	Yes	0.876
PARP1	poly(ADP-ribose) polymerase 1	nucleoplasm	expression	None	0.868
CYP1B1	cytochrome P450	mitochondria, cytosol	binding	Yes	0.848

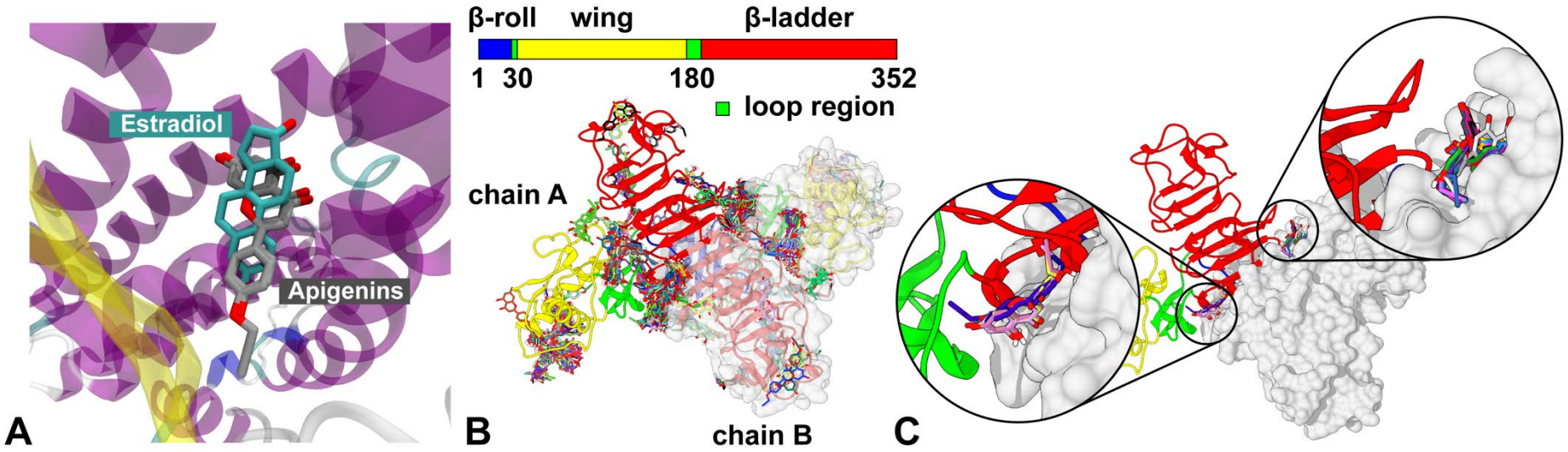
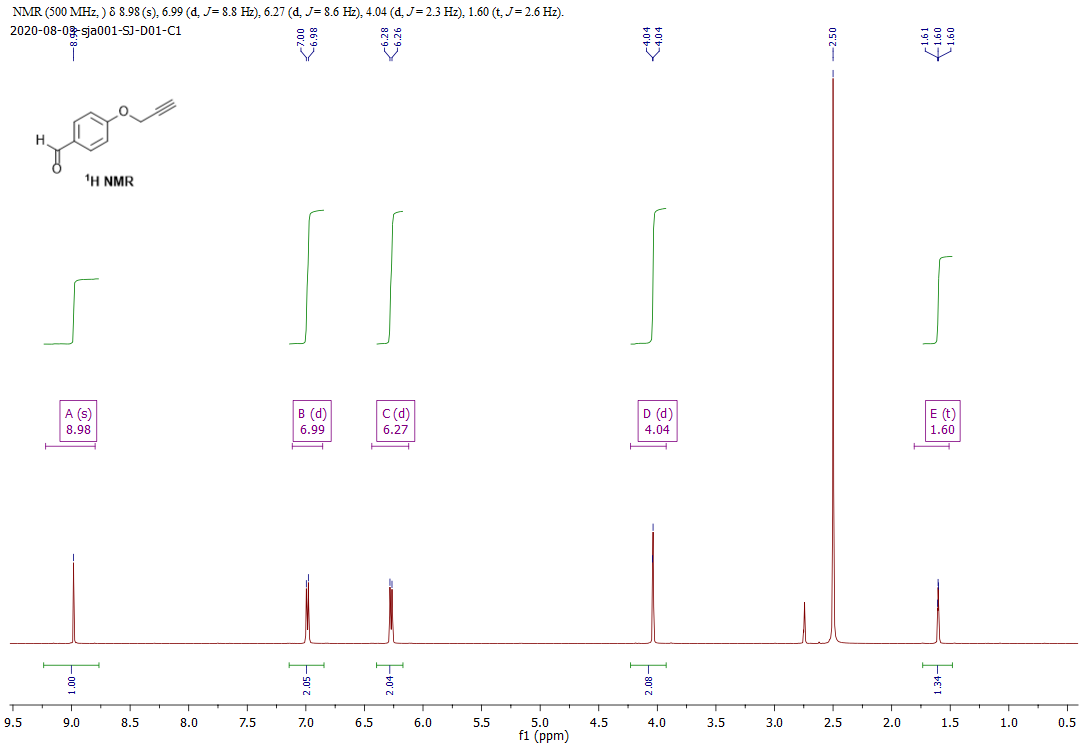
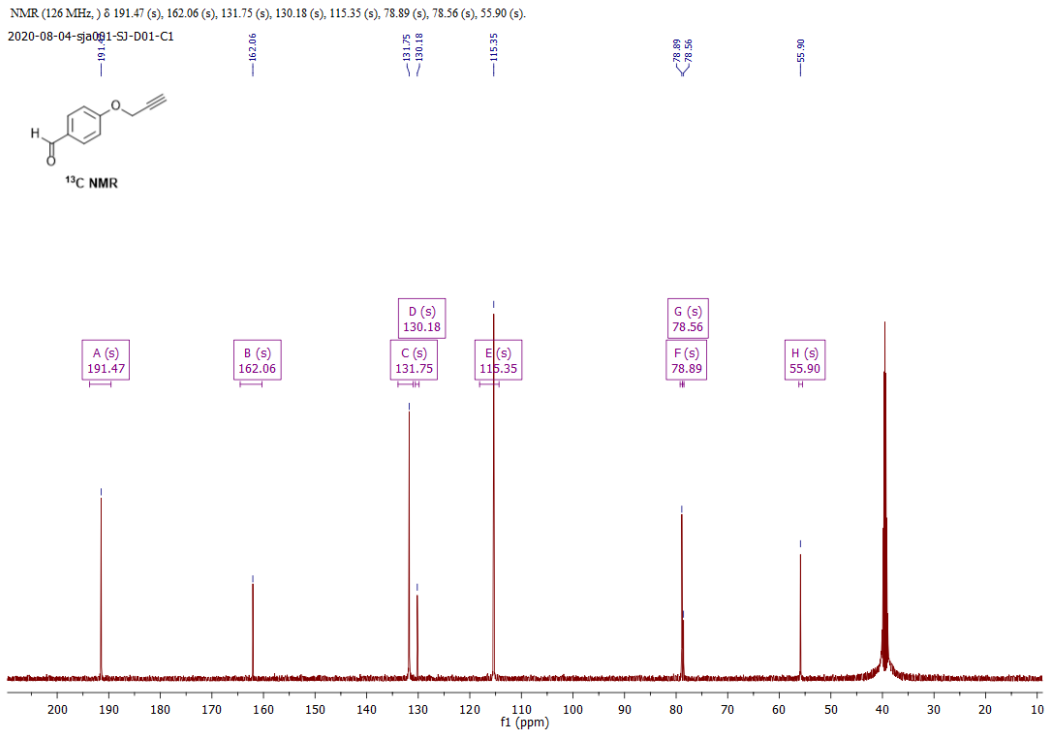


Figure S1. (A) structure overlay of Estradiol and apigenins (**B**,**C**) The 3D structure of dimeric NS1 of DENV2 with the top binding poses from 50 docking runs.



A



B

Figure S2. ^{1}H (**A**) and ^{13}C-NMR (**B**)of 4-(prop-2-yn-1-yloxy)benzaldehyde (**I**).

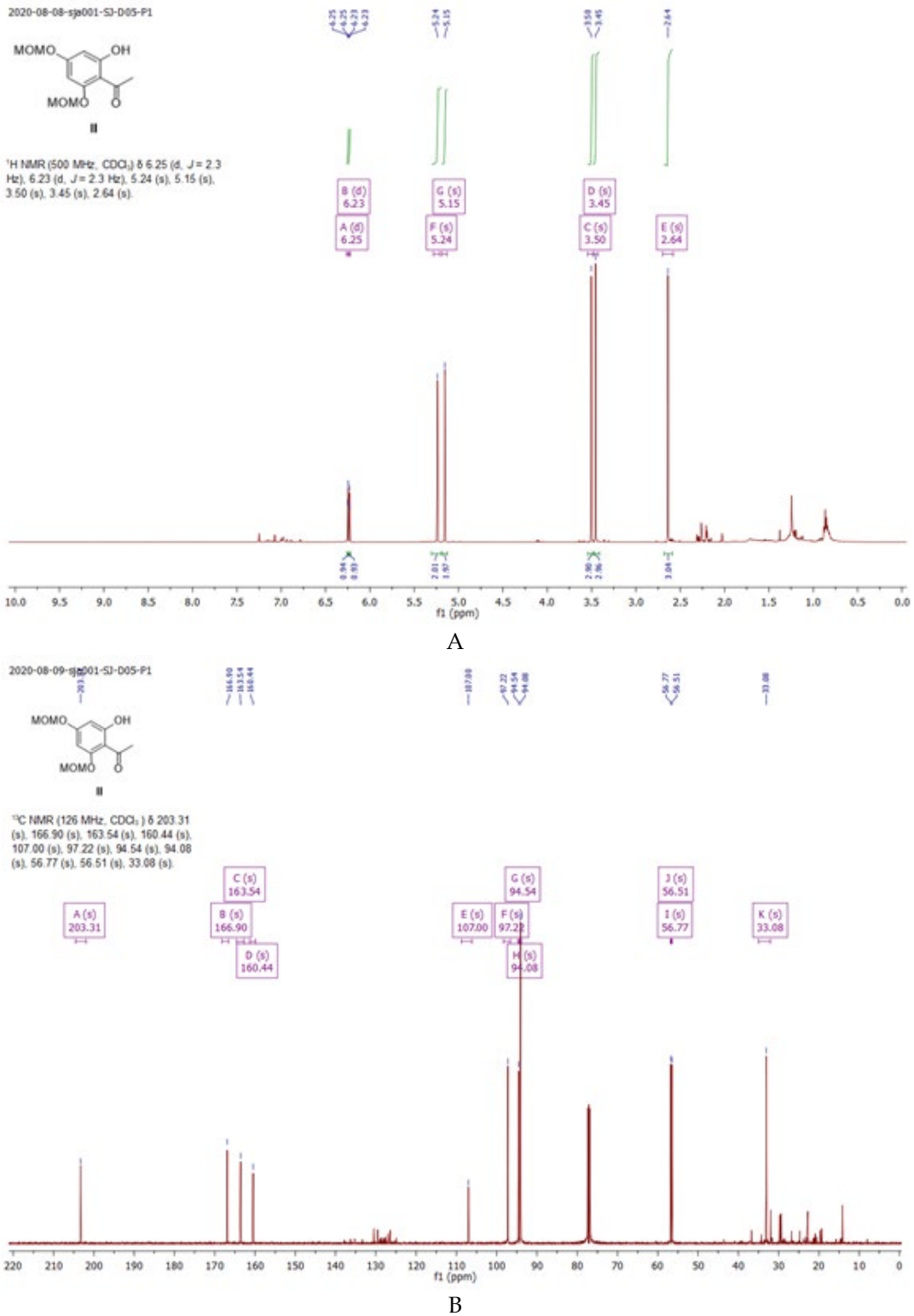
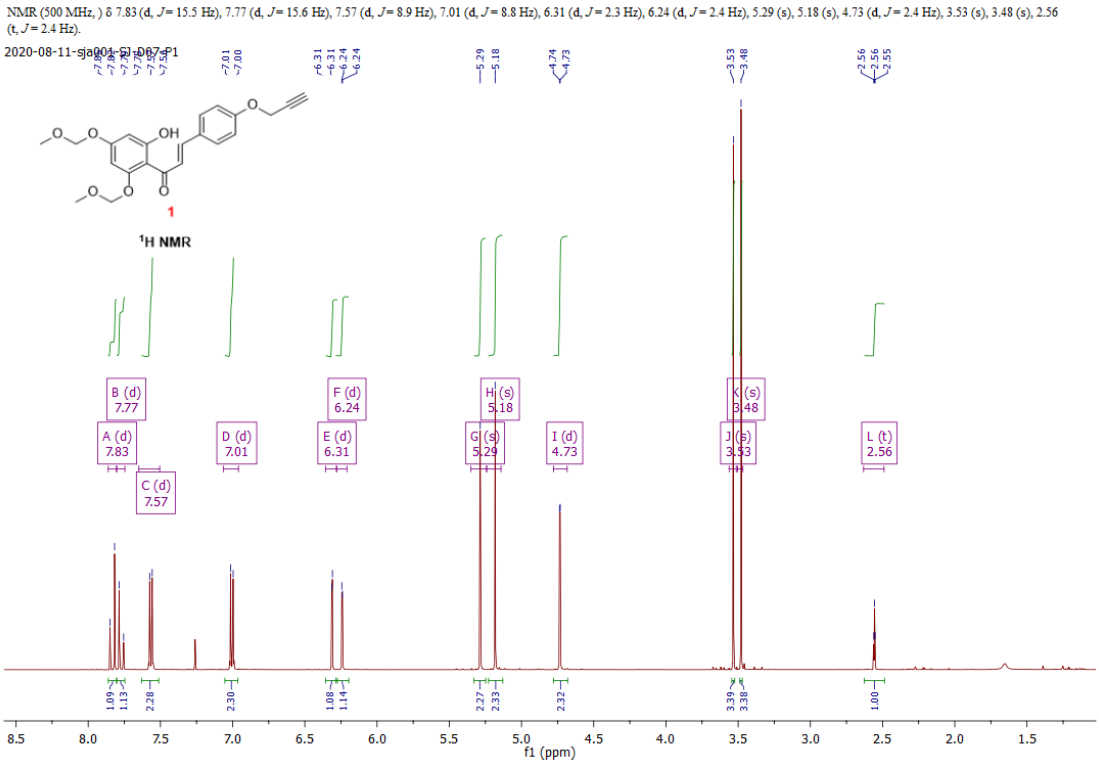
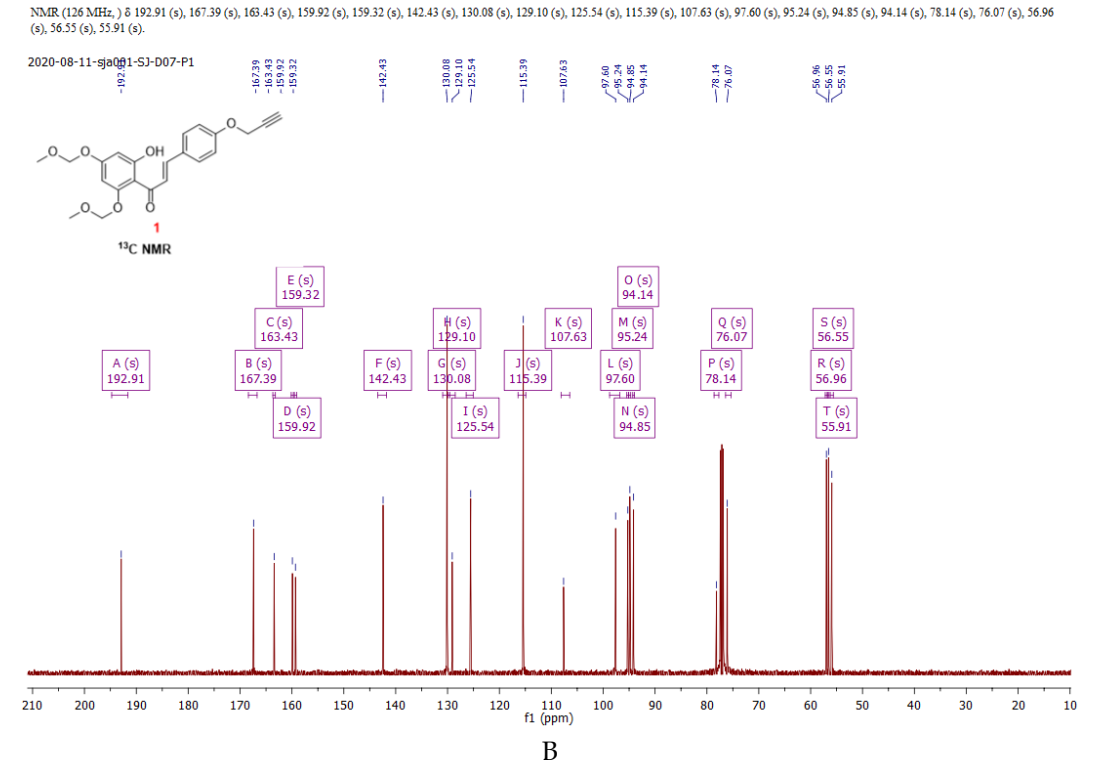


Figure S3. ¹H (**A**) and ¹³C-NMR (**B**) of 1-(2-hydroxy-4,6-bis(methoxymethoxy)phenyl)ethan-1-one (**II**).



A



B

Figure S4. ^{1}H (**A**) and ^{13}C-NMR (**B**) of (*E*)-1-(2-hydroxy-4,6-bis(methoxymethoxy)phenyl)-3-(4-(prop-2-yn-1-yloxy)phenyl)prop-2-en-1-one (**1**).

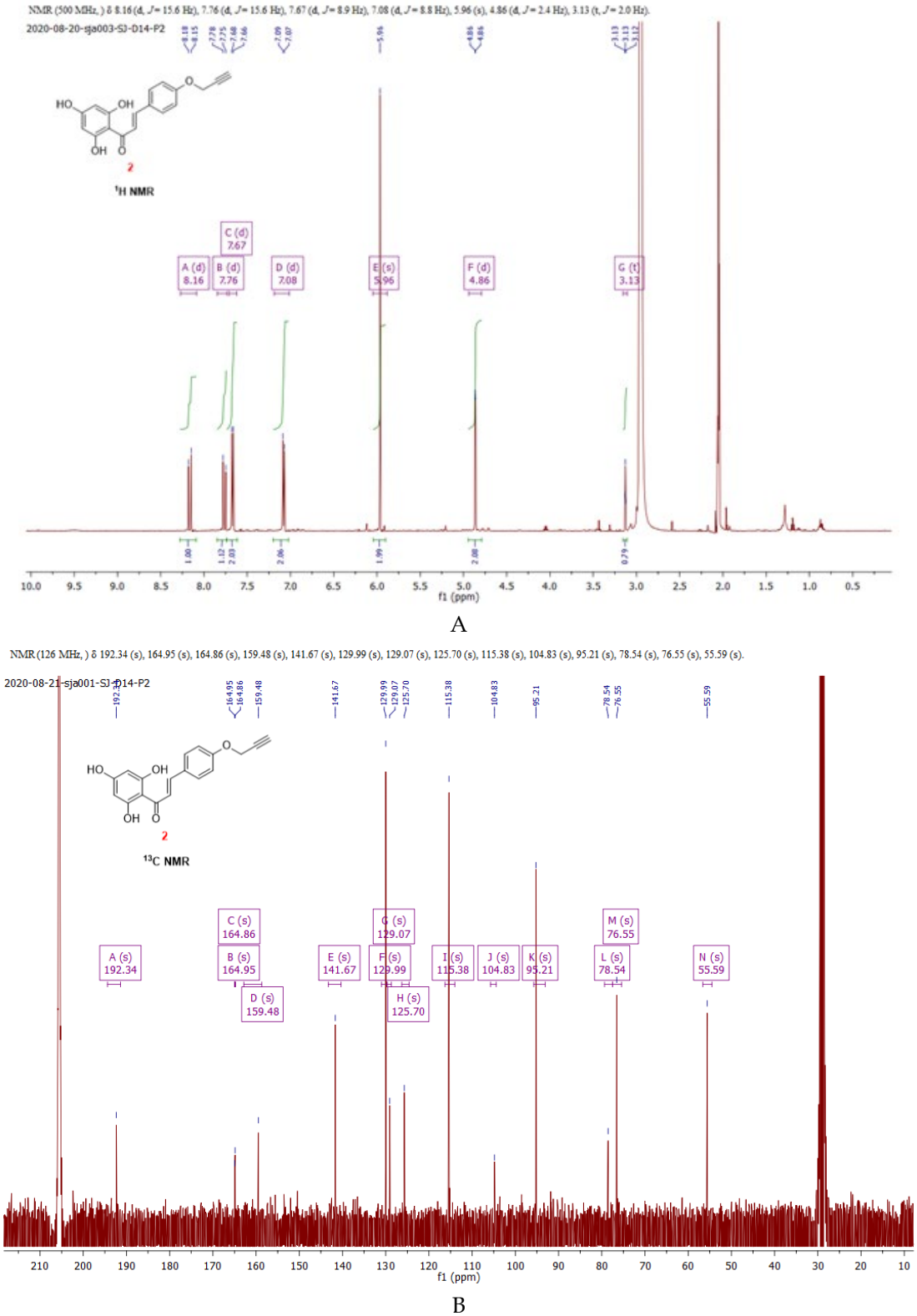


Figure S5. ^{1}H (**A**) and ^{13}C-NMR (**B**) of 5,7-bis(methoxymethoxy)-2-(4-(prop-2-yn-1-yloxy)phenyl)-4*H*-chromen-4-one (**2**).

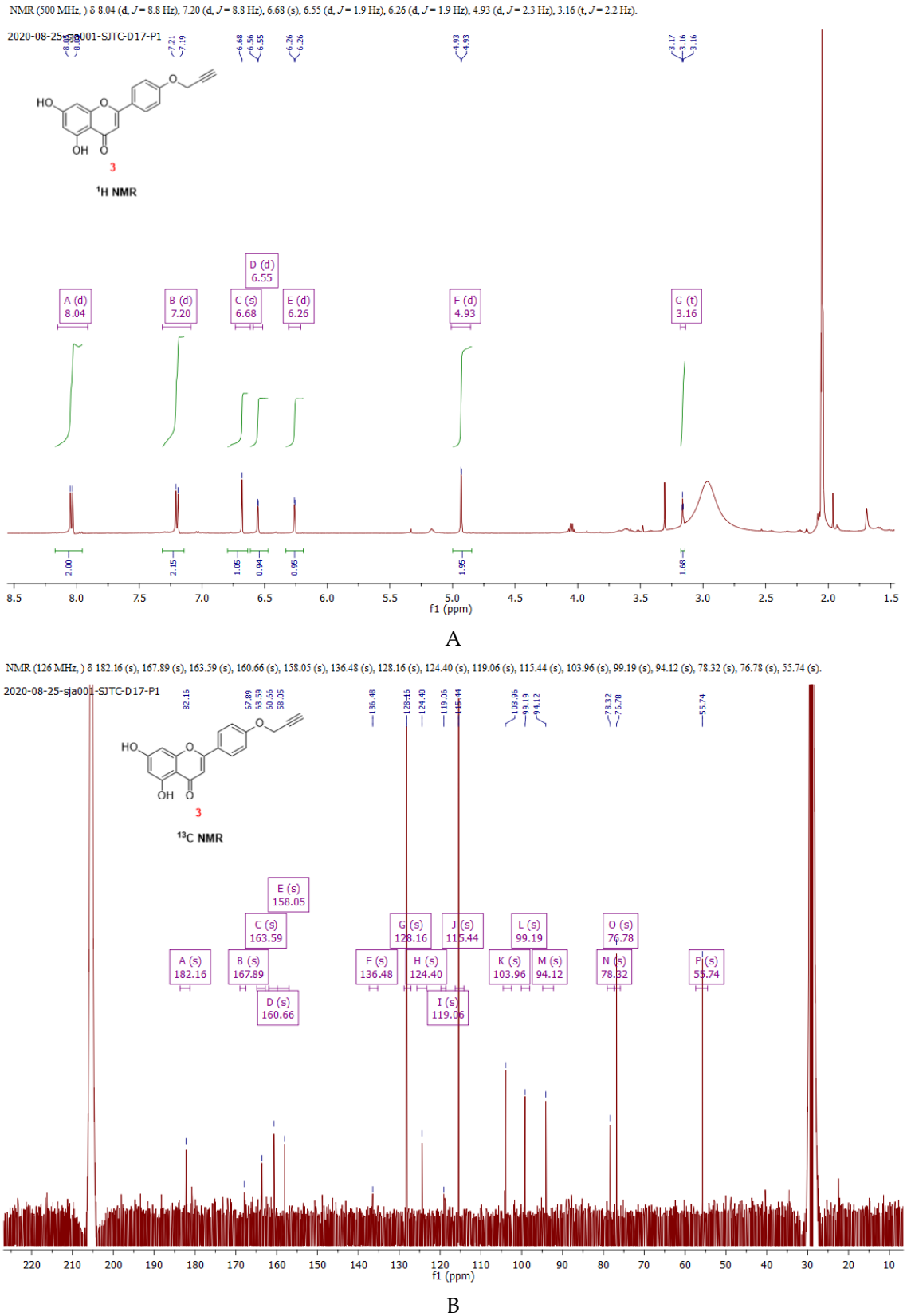


Figure S6. ^{1}H (**A**) and ^{13}C-NMR (**B**) of 5,7-dihydroxy-2-(4-(prop-2-yn-1-yloxy)phenyl)-4*H*-chromen-4-one (**3**).

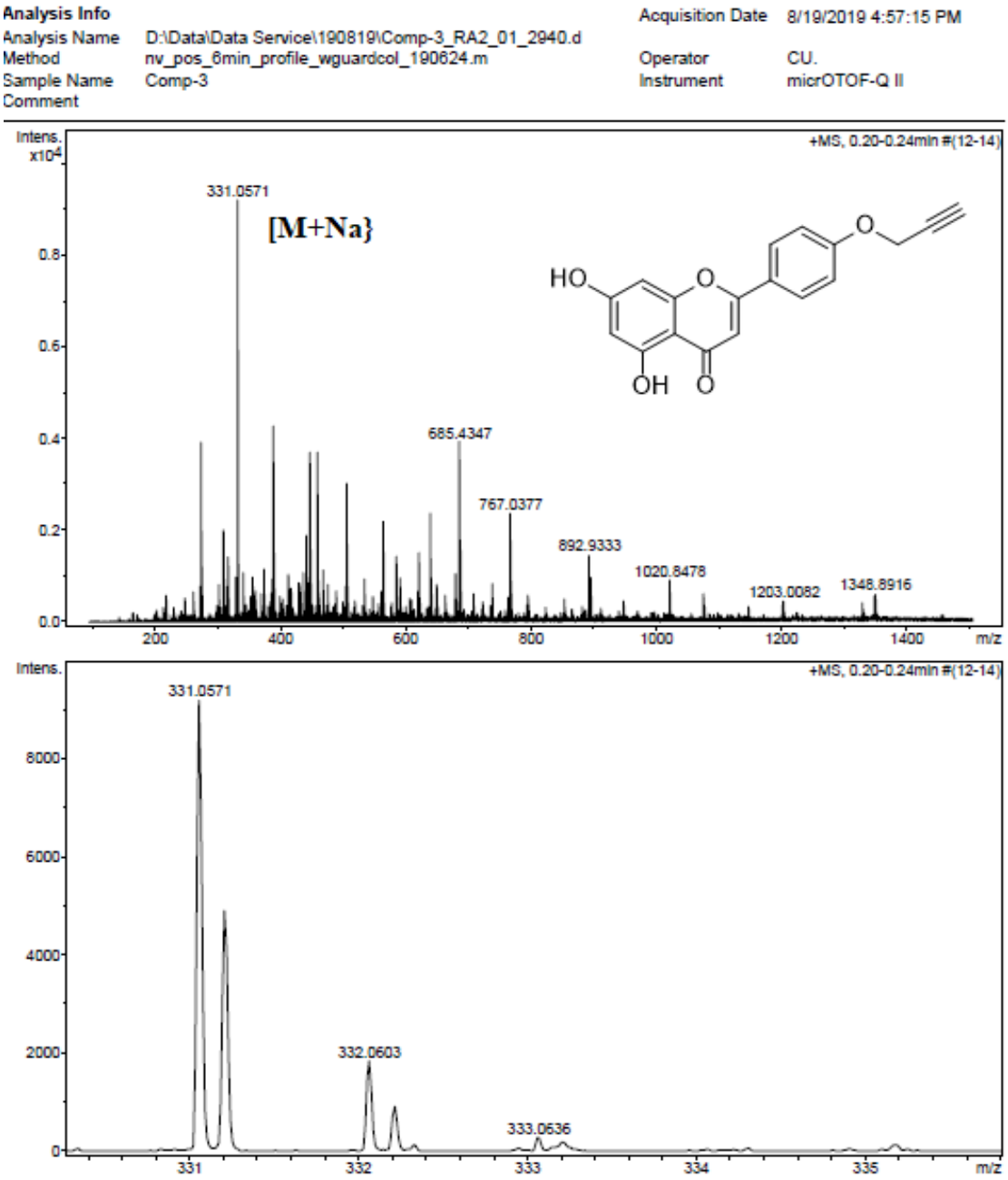
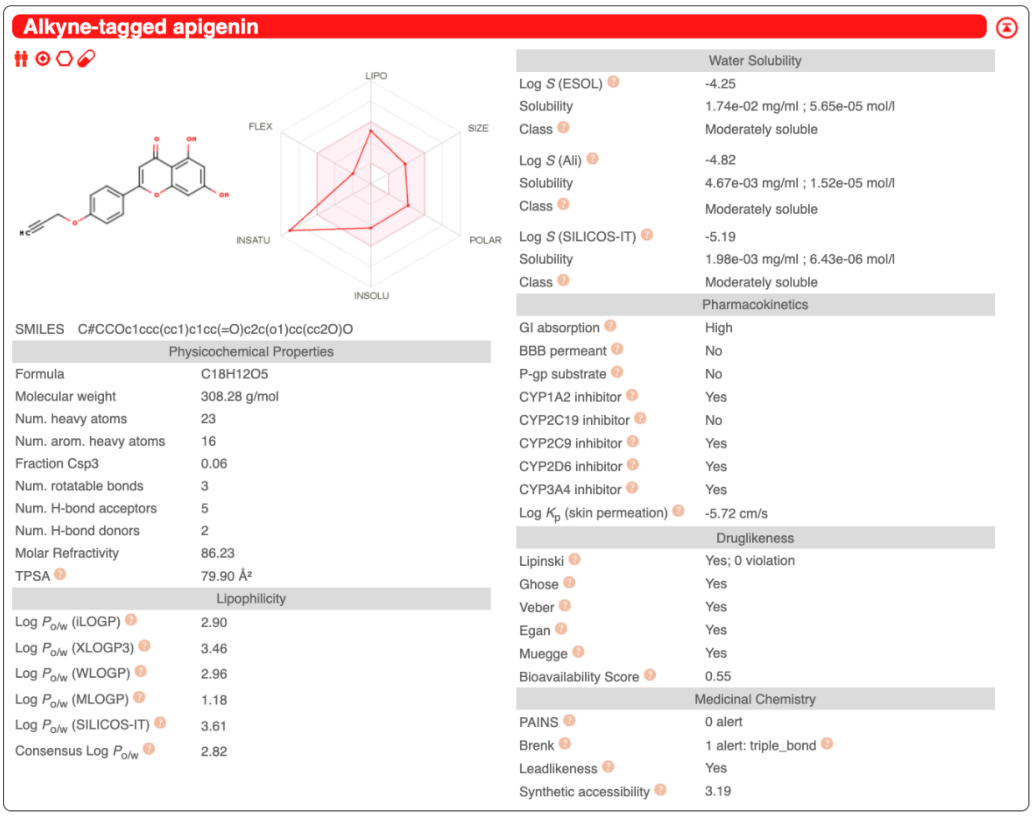
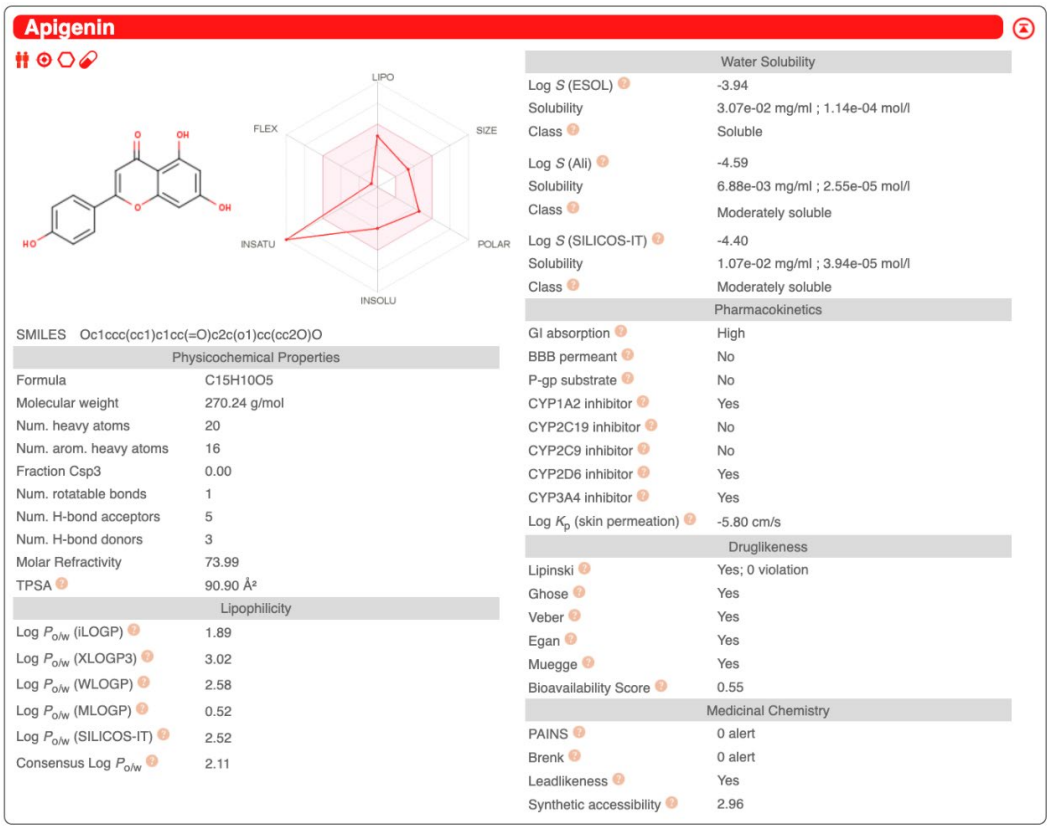


Figure S7. HRMS spectra of 5,7-dihydroxy-2-(4-(prop-2-yn-1-yloxy)phenyl)-4H-chromen-4-one (**3**).



A



B

Figure S8. Pharmacokinetics, drug-likeness and medicinal chemistry by SwissADME for alkyne-tagged apigenine (**A**) and Apigenin (**B**).