Supplementary Information for

Identification of psychoactive metabolites from *Cannabis sativa*, its smoke and other phytocannabinoids using machine learning and multivariate methods

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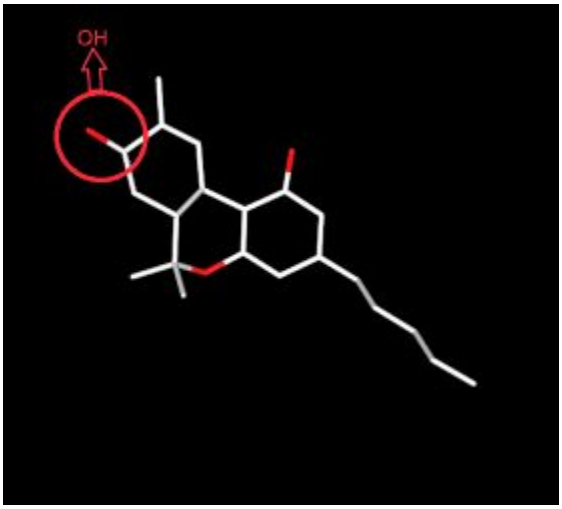
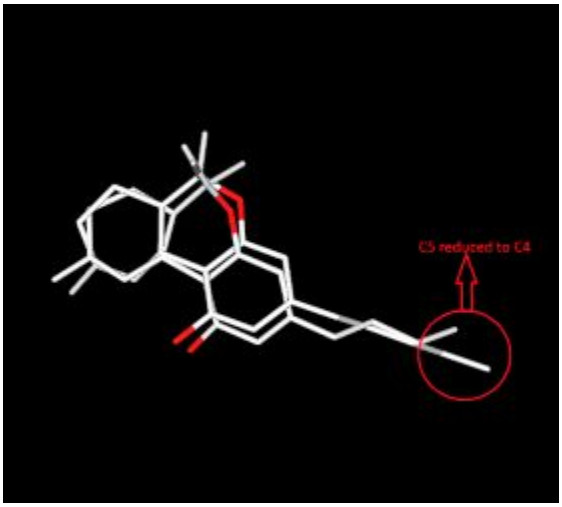
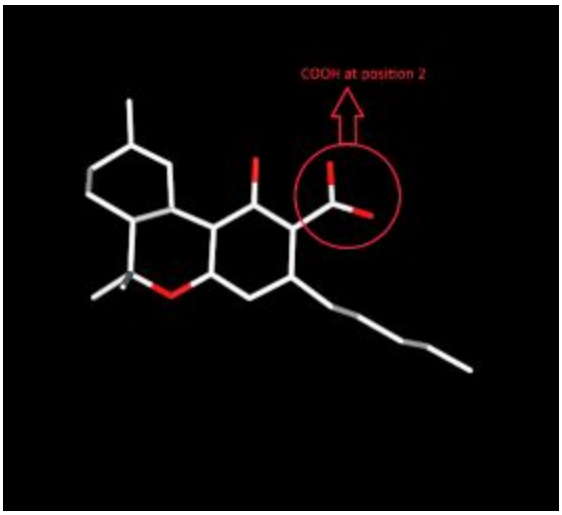


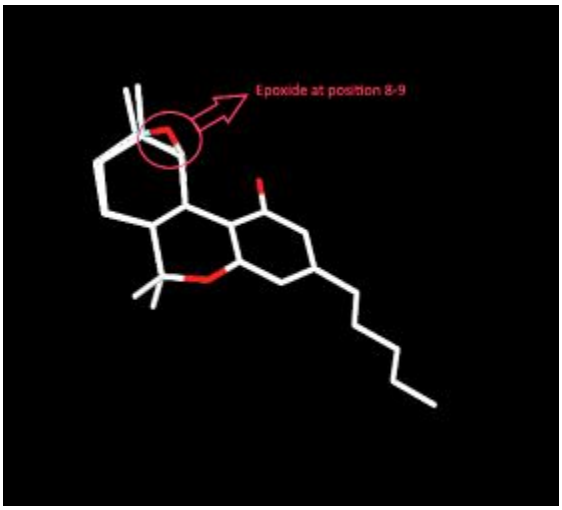
Supplement 4-1 : 8-Hydroxy-Tetrahydrocannabinol-THC scaffold. Addition of OH group at position 8 is circled.



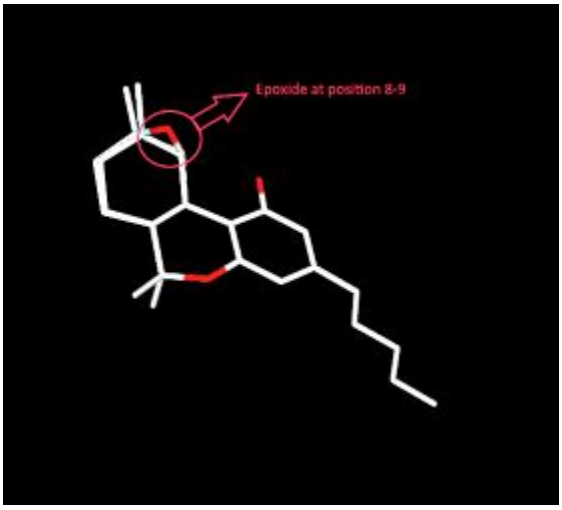
Supplement 4-2 : Delta-9-tetrahydrocannabinol-C4-THC scaffold. Pentyl group at position 3 in phenol is reduced to butyl reducing the receptor affinity.



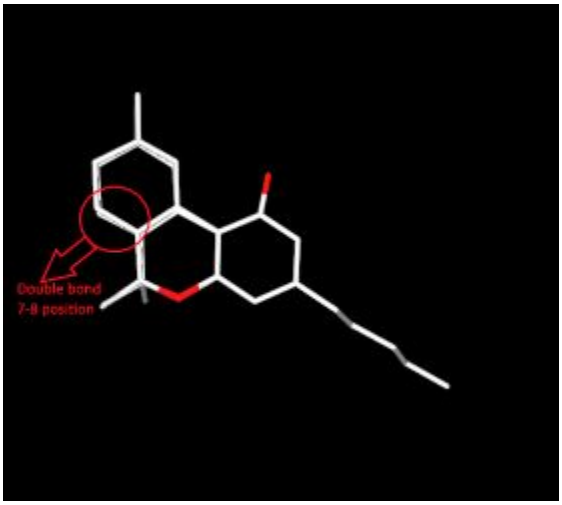
Supplement 4-3 : Tetrahydrocannabinolic acid-THC scaffold. Carboxylic moiety is added to position 2 in the phenolic group.



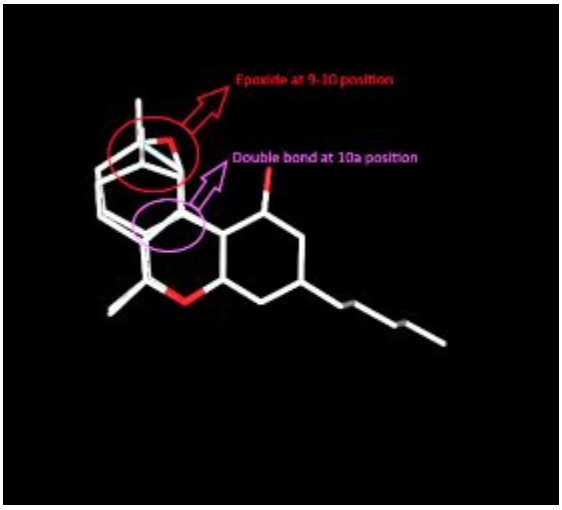
Supplement 4-4 : 9β ,10β -Epoxyhexahydrocannabinol -THC scaffold. Epoxide moiety at position 8-9.



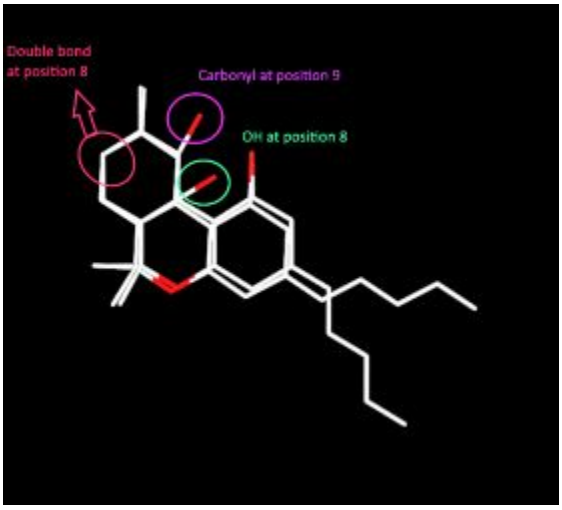
Supplement 4-5 : 9α ,10α -Epoxyhexahydrocannabinol -THC scaffold. Epoxide moiety at position 8-9.



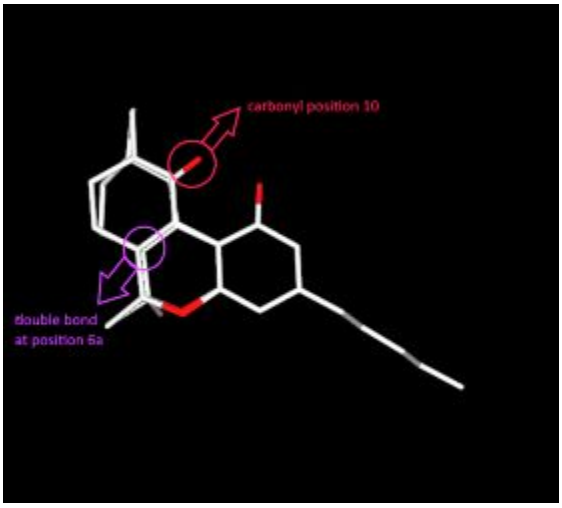
Supplement 4-6 : 7,8-Dihydrocannabinol-THC scaffold. Addition double bond at 7-8 position.



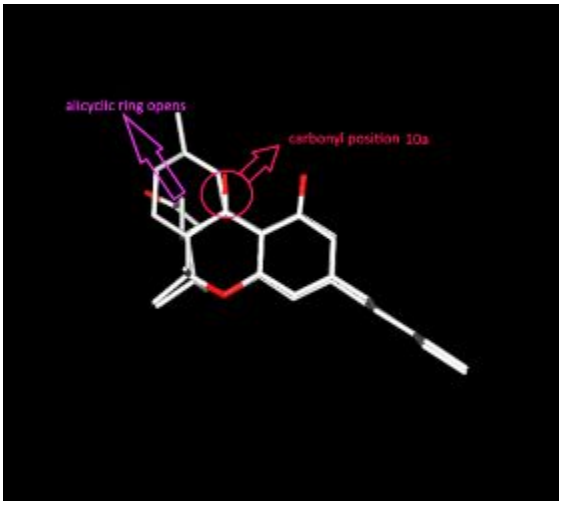
Supplement 4-7 : 9,10-Anhydrocannabitriol-THC scaffold. Epoxide ring at 9-10 position and double bond at 10a position.



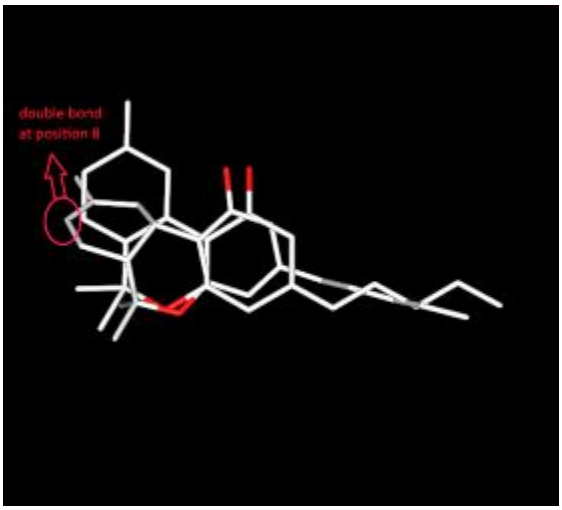
Supplement 4-8 : 10-Hydroxy-9-oxo-Delta-8-tetrahydrocannabinol-THC scaffold. Double bond at position 8, carbonyl at Position 9, OH group at position 10.



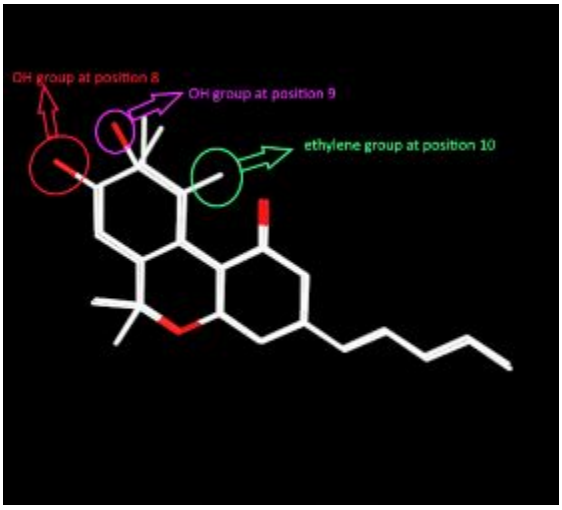
Supplement 4-9 : 10-Oxo-delta-6a-tetrahydrocannabinol (OTHC)-THC scaffold. Carbonyl group at position 10, double bond at position 6a.



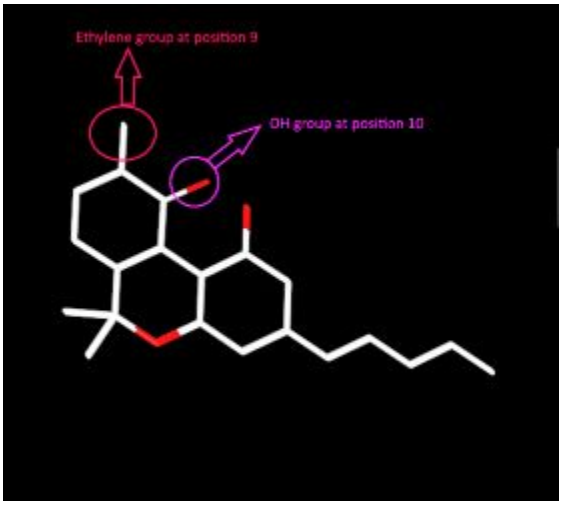
Supplement 4-10 : Cannabichromanone (CBCF)-THC scaffold. Alicyclic ring opens, carbonyl group at position 10a



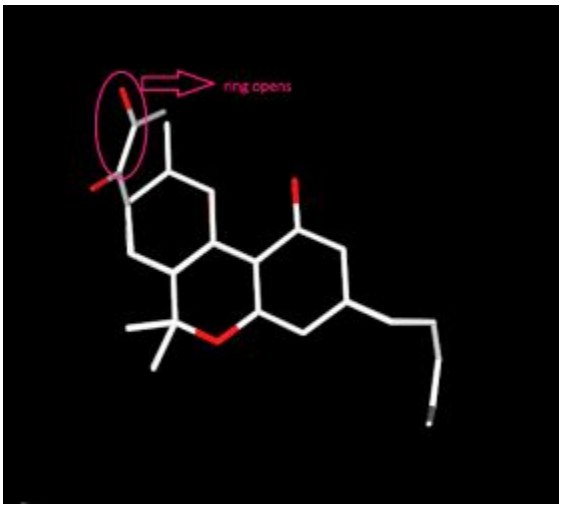
Supplement 4-11 : Delta-8-tetrahydrocannabinol-THC scaffold. Double bond at position 8 instead of 9 in alicyclic ring



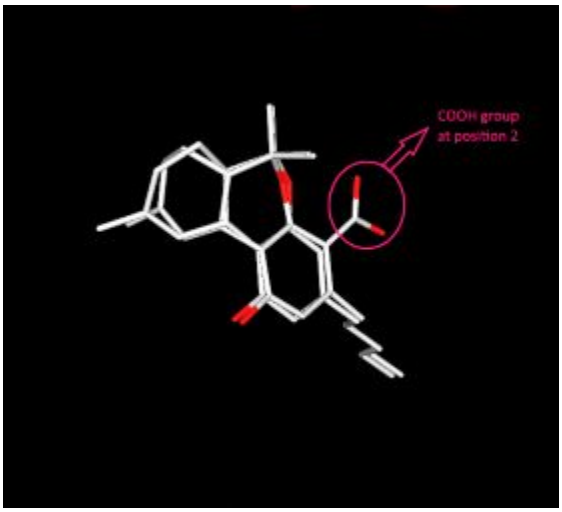
Supplement 4-12 : Isocannabitrol-THC scaffold. OH groups at positions 8, 9 in alicyclic ring. Ethylene group at position 10.



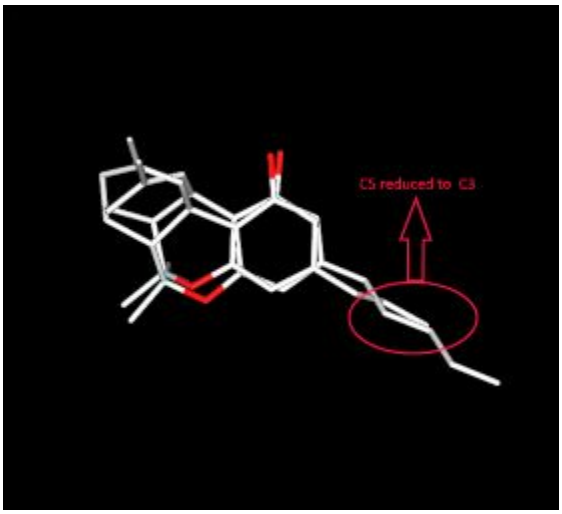
Supplement 4-13 : 10α -Hydroxy-Delta- 9,11 -hexahydrocannabinol -THC scaffold. Ethylene group at position 9, OH group at position 10.



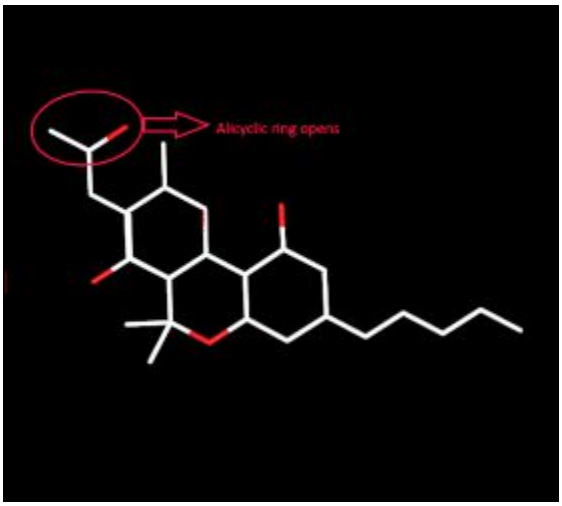
Supplement 4-14 : Compound 3-THC scaffold. Alicyclic ring opens.



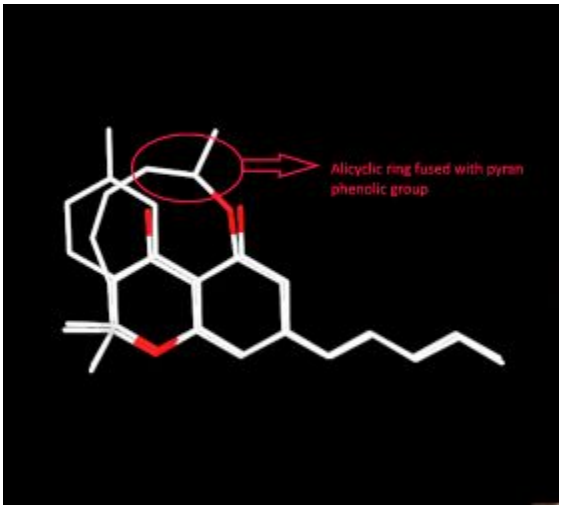
Supplement 4-15 : Delta-9-THCA-B—THC scaffold. COOH group at position 2.



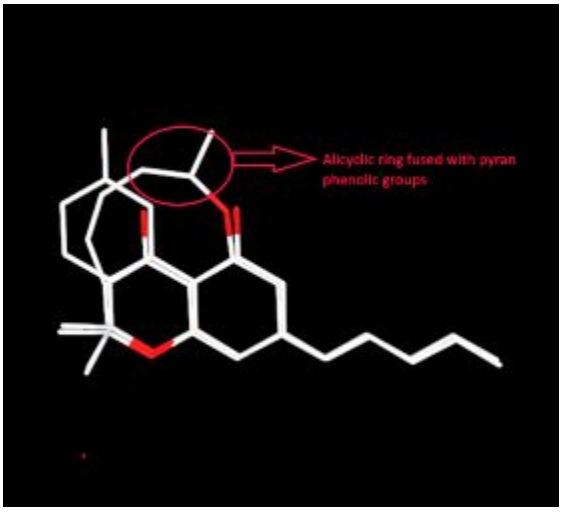
Supplement 4-16 : Delta-9-cis-tetrahydrocannabivarin-THC scaffold. Propyl group at position of phenolic group instead of Pentyl group in THC.



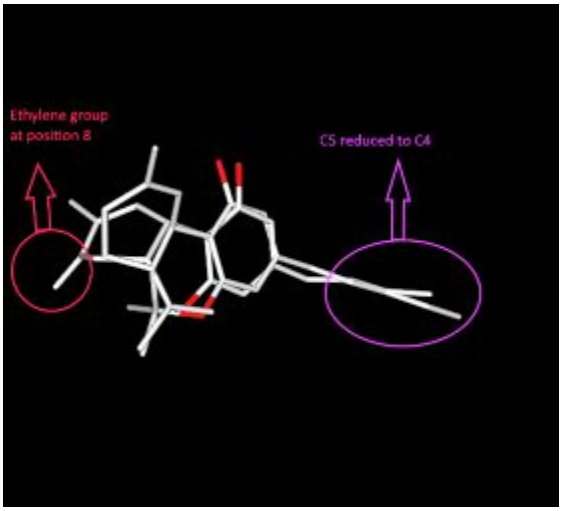
Supplement 4-17 : Compound 2-THC scaffold. Alicyclic ring opens.



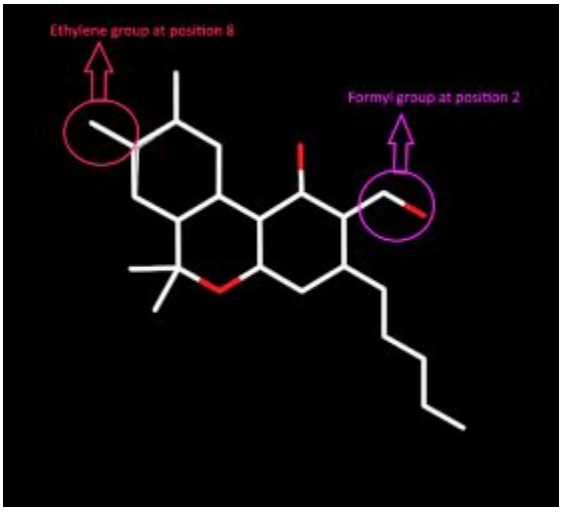
Supplement 4-18 : Cannabichromaonone D-THC scaffold. Alicyclic ring fused with pyran and phenolic groups.



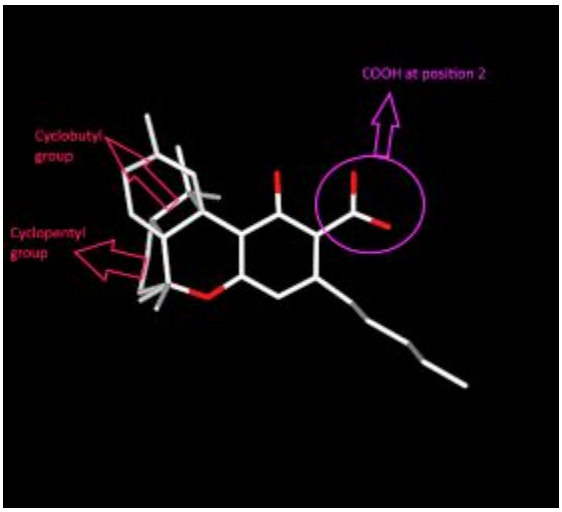
Supplement 4-19 : Compound 4-THC scaffold. Alicyclic ring fused with pyran and phenolic groups.



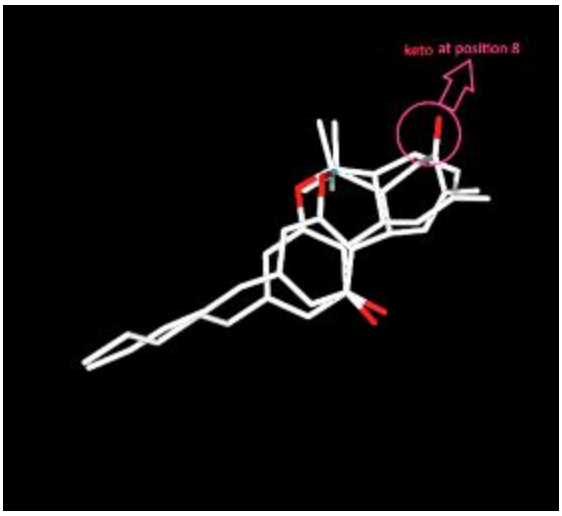
Supplement 4-20 : Delta-nor-9-Tetrahydrocannabinol-THC scaffold. Ethylene at position 8, butyl instead of pentyl Group at position 3 in the phenolic moiety.



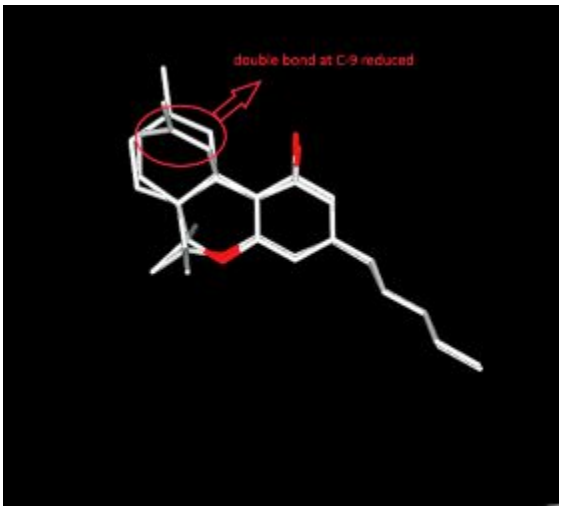
Supplement 4-21 : 2-Formyl-Delta-9-Tetrahydrocannabinol-THC scaffold. Ethylene group at position 8, Formyl group at position 2.



Supplement 4-22 : Cannabicylolic acid-THC scaffold. Fused cyclopentyl and cyclobutyl groups at pyran ring, COOH group at position 2.

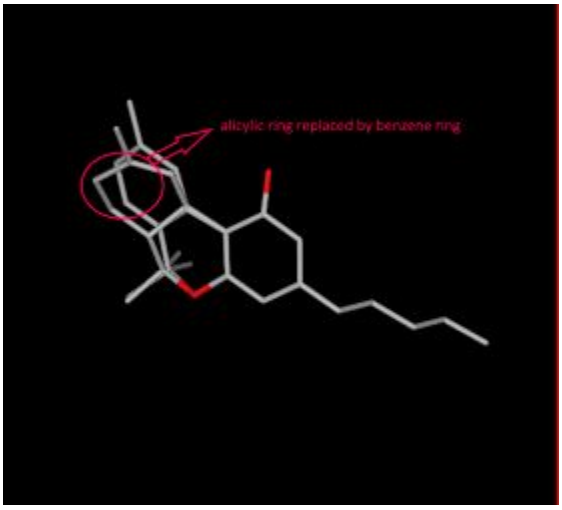


Supplement 4-23 : 8-oxo-Delta-9-Tetrahydrocannabinol-THC scaffold. keto group at position 8

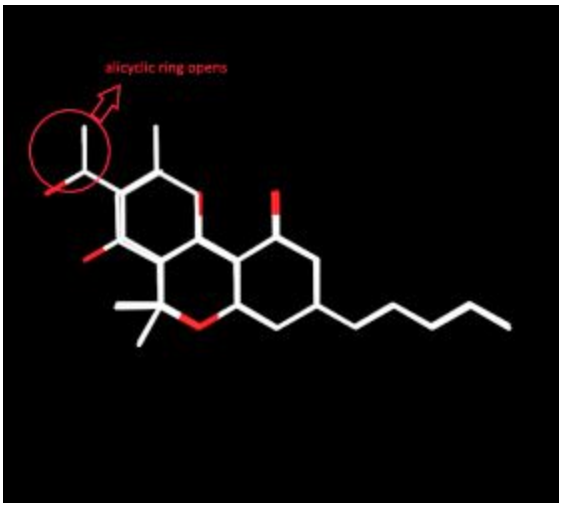


Supplement 4-24 : Hexahydrocannabinol-THC scaffold. Double bond at C-9 is reduced.

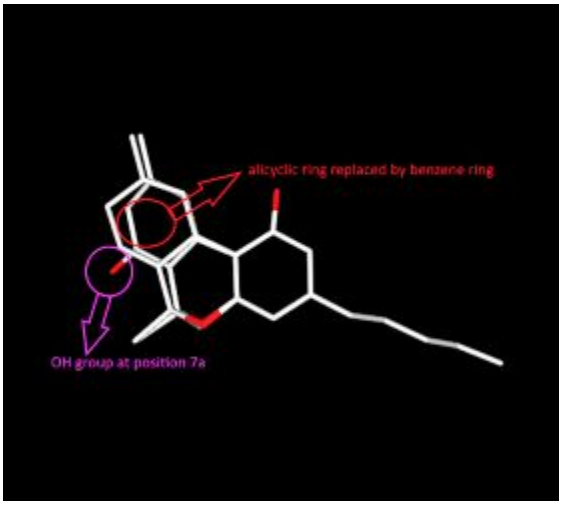
Supplement 4-25 : Bis-nor-cannabitrol-THC scaffold. Double bond at C-9 reduced, OH added at position 9, Vinyl alcohol added at position 10.



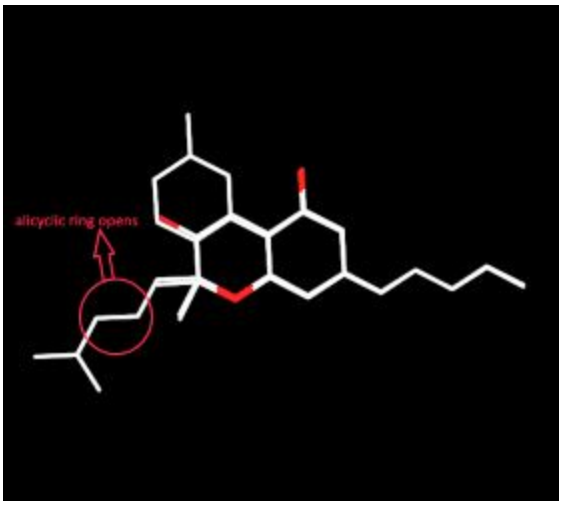
Supplement 4-26 : Cannabinol-THC scaffold. Alicyclic ring replaced by aromatic benzene ring.



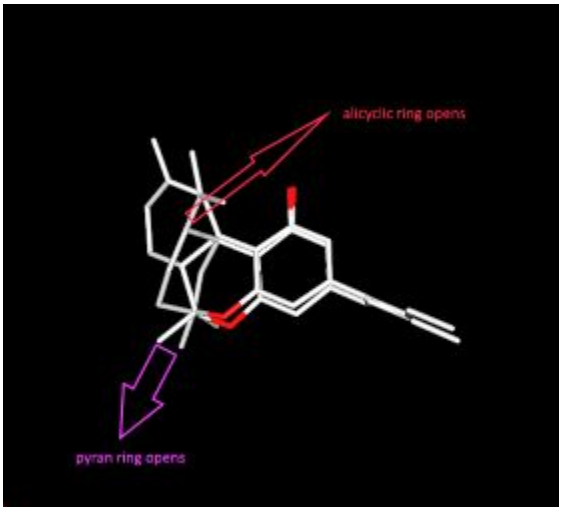
Supplement 4-27 : 6a-R-Cannabichromanone B-THC scaffold. Alicyclic ring opens.



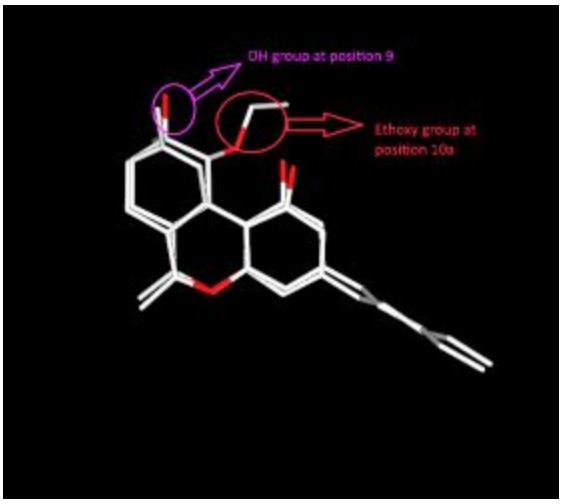
Supplement 4-28 : 7-hydroxy cannabinol-THC scaffold. Alicyclic ring replaced by aromatic bemzene ring, OH group at Position 7a.



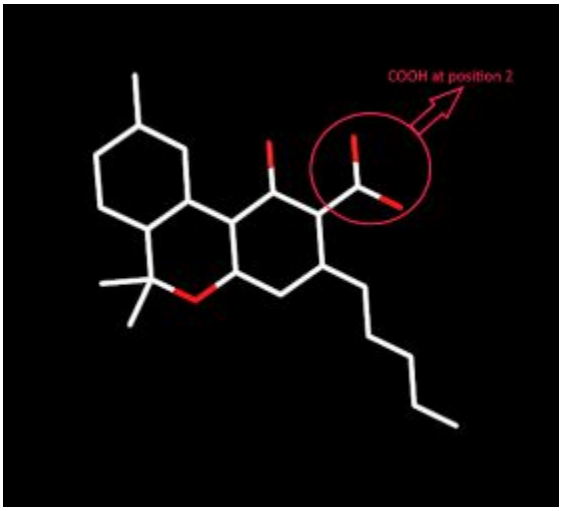
Supplement 4-29 : 7-Hydroxy Cannabichromane-THC scaffold. Alicyclic ring opens .



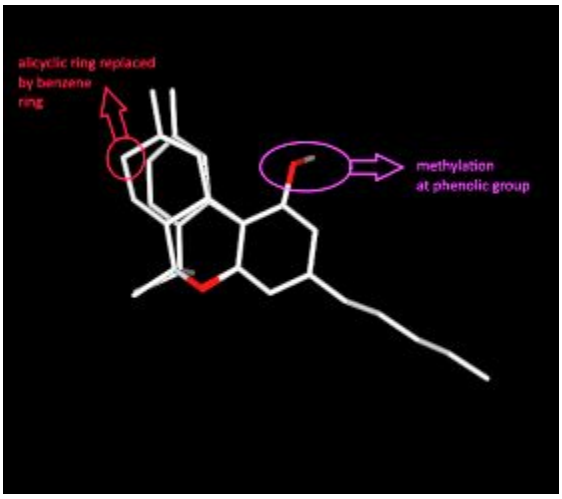
Supplement 4-30 : Delta-7-trans-Isotetrahydrocannabinol-THC scaffold. Alicyclic and pyran rings open. Cyclic rings Fused with phenolic group.



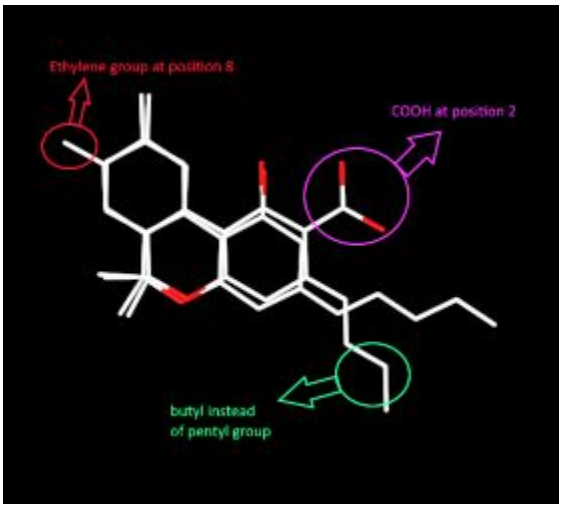
Supplement 4-31 : 10-Ethoxy-9-hydroxy-delta-6a-tetrahydrocannabinol-THC scaffold. Ethoxy group at position 10a Hydroxy group at position 9.



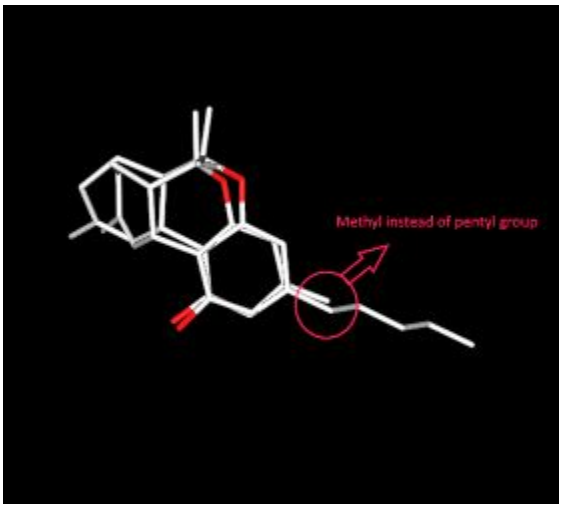
Supplement 4-32 : Delta-9-tetrahydrocannabinolic acid A (THCA-A)-THC scaffold. COOH group at position 2.



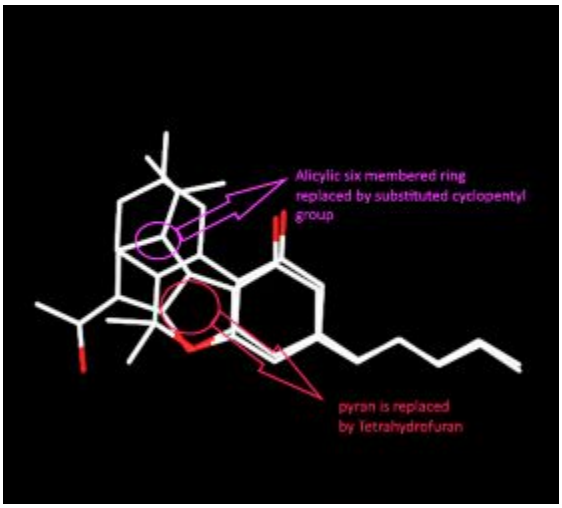
Supplement 4-33 : Cannabinol methylether (CBNM)-THC scaffold. Alicyclic ring replaced by aromatic benzene ring, Methylation of phenolic OH group.



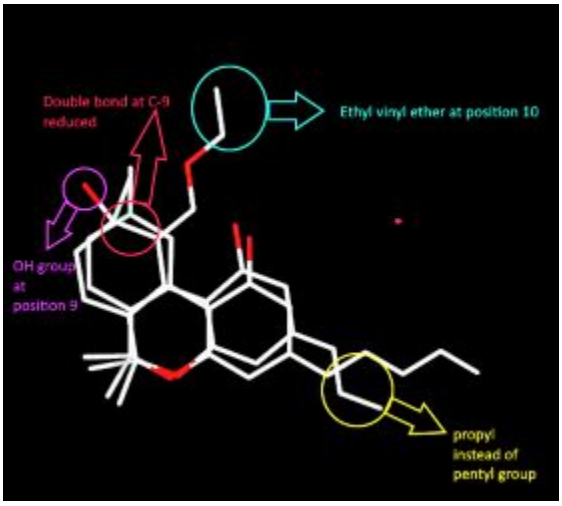
Supplement 4-34 : Delta-9-nor-tetrahydrocannbinolic acid-THC scaffold. Ethylene at position 8, COOH group at Position 2, butyl group instead of pentyl at C-3 position of phenolic group.



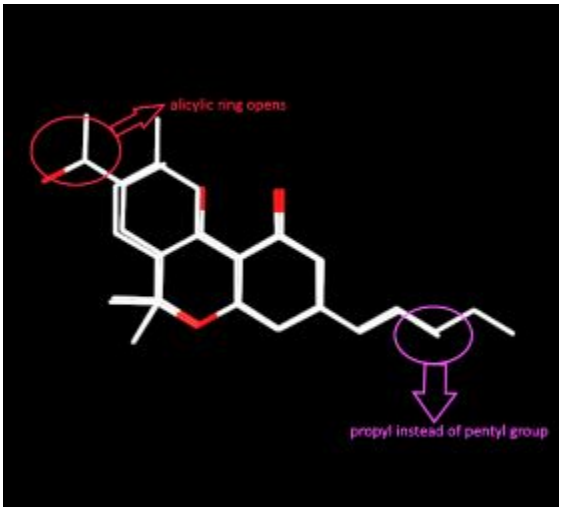
Supplement 4-35 : Delta-9-tetrahydrocannabiorcol (THC-C1)-THC scaffold. Methyl instead of pentyl group at Position 3 of phenolic group.



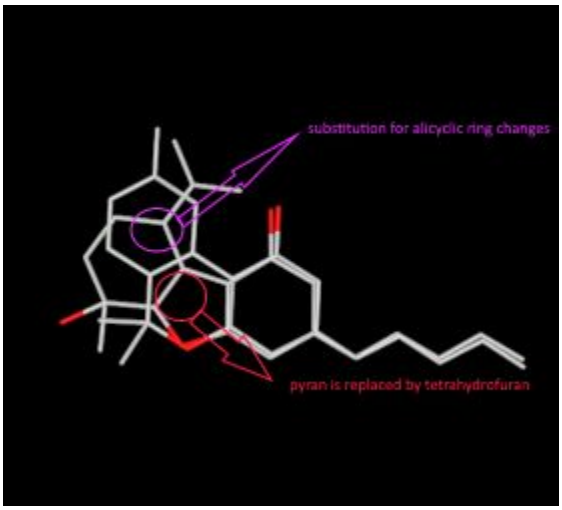
Supplement 4-36 : Anhydrocannabimovone-THC scaffold. Pyran is replaced by Tetrahydrofuran, six membered Alicylic ring is replaced by substituted cyclopentyl group.



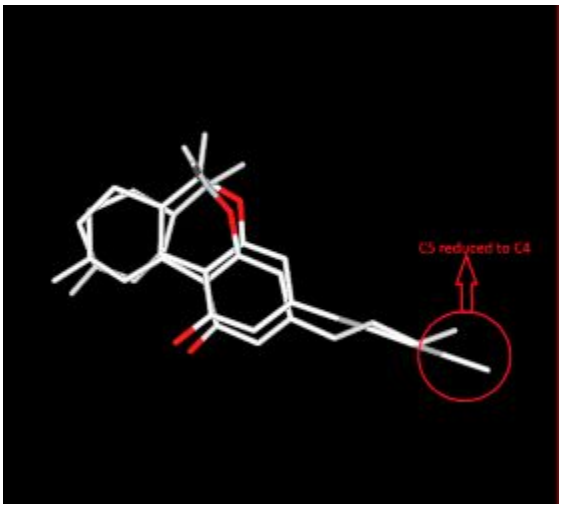
Supplement 4-37 : 10-O-Ethyl bis-nor cannabitriol-THC scaffold. Double bond at position 9 reduced, OH group at position 9, Ethyl vinyl ether at position 10, propyl group instead of pentyl group at C-3 of phenolic group.



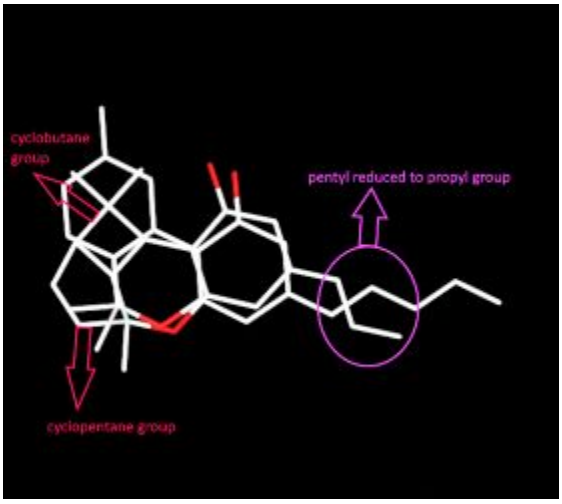
Supplement 4-38 : Bis-nor-cannabichromanone-THC scaffold. Alicyclic ring opens, propyl instead of pentyl group At C-3 position of phenolic group.



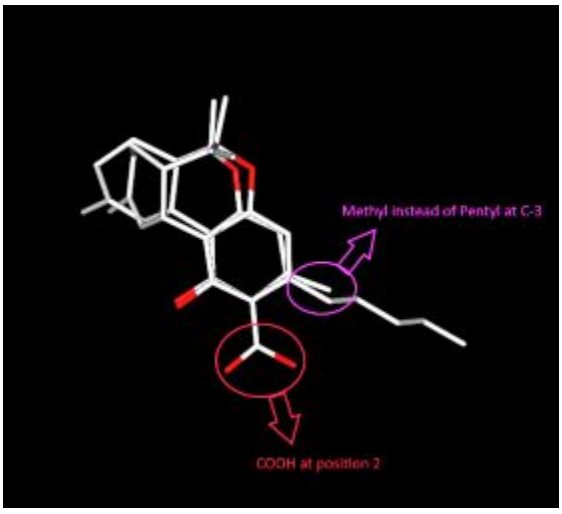
Supplement 4-39 : Cannabielsoin (CBE)-THC scaffold. Pyran ring is replaced by tetrahydrofuran group, substitution At C-9, C-6 changes for alicyclic ring.



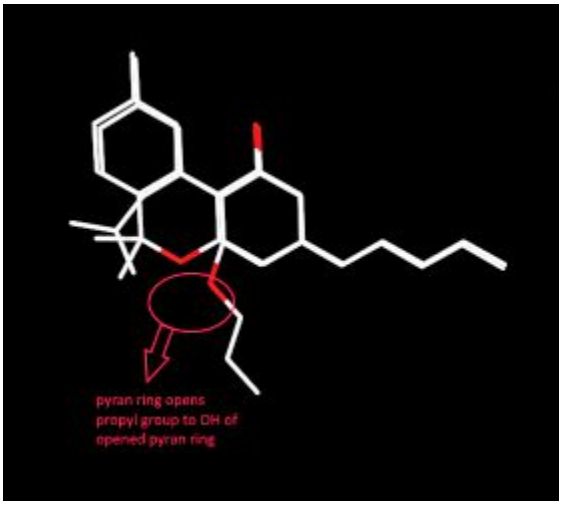
Supplement 4-40 : Delta-9-tetrahydrocannabinolic acid-C4 (THCA-C4)-THC scaffold. Pentyl at C-3 of phenolic moiety reduced to butyl group.



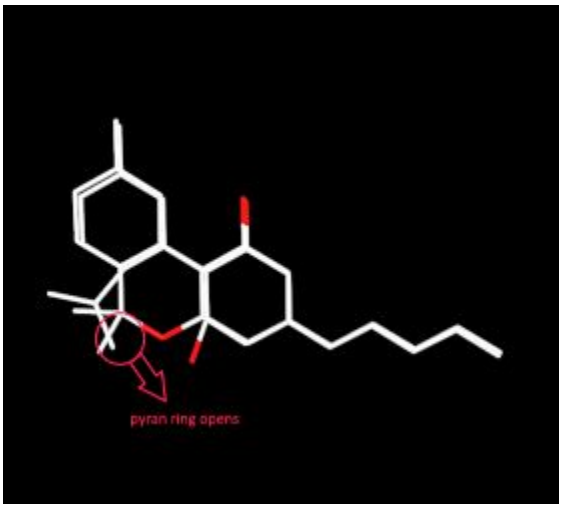
Supplement 4-41 : Cannabicyclovarin (CBLV)-THC scaffold. Alicyclic ring replaced by fused cyclobutyl and cyclopentyl groups. Pentyl at C-3 of phenolic moiety is reduced to propyl group.



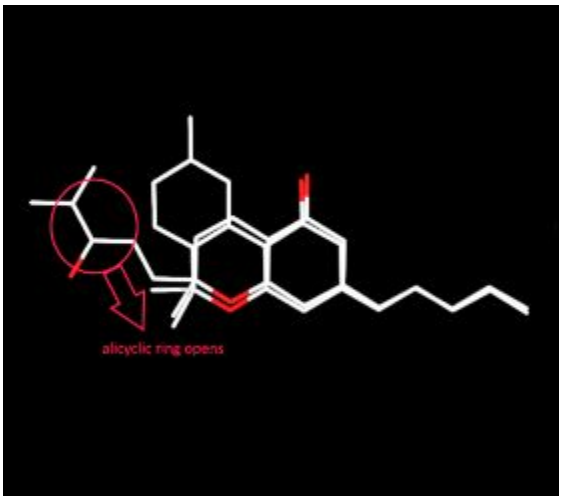
Supplement 4-42 : Delta-9-tetrahydrocannabiorcolic acid (THCA-C1)-THC scaffold. Carboxylic group at position 2, pentyl at C-3 reduced to methyl group.



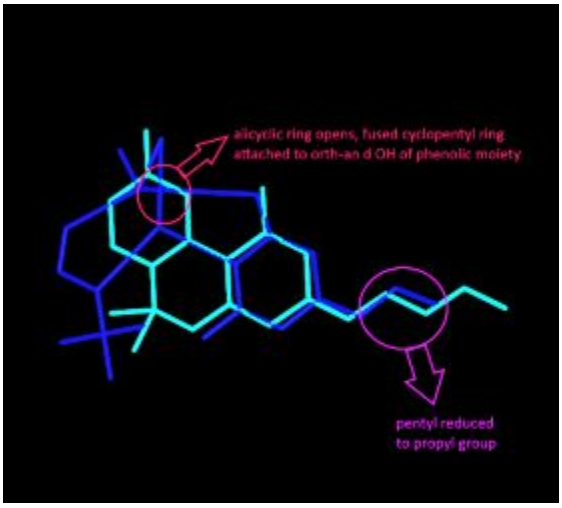
Supplement 4-43 : O-Propyl-cannabidiol-THC scaffold. Pyran ring opens, propyl group attached to OH of opened Pyran group.



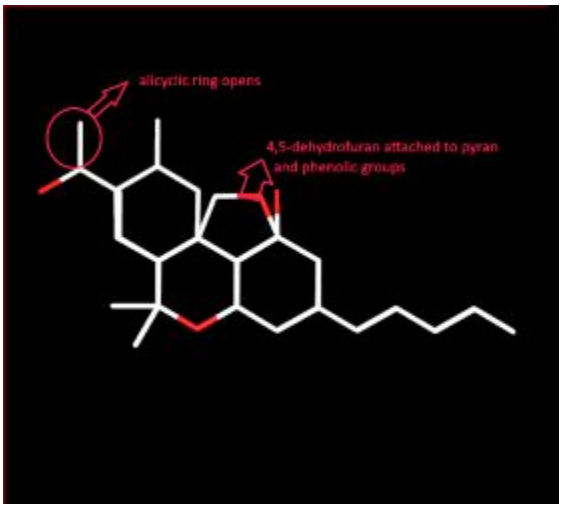
Supplement 4-44 : Cannabidiol-THC scaffold. Pyran ring opens.



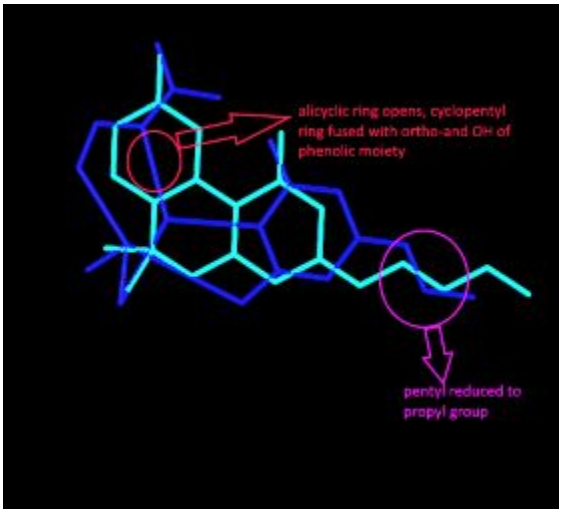
Supplement 4-45 : 3-Hydroxy-Delta-4,5-Cannabichromene-THC scaffold. Alicyclic ring opens.



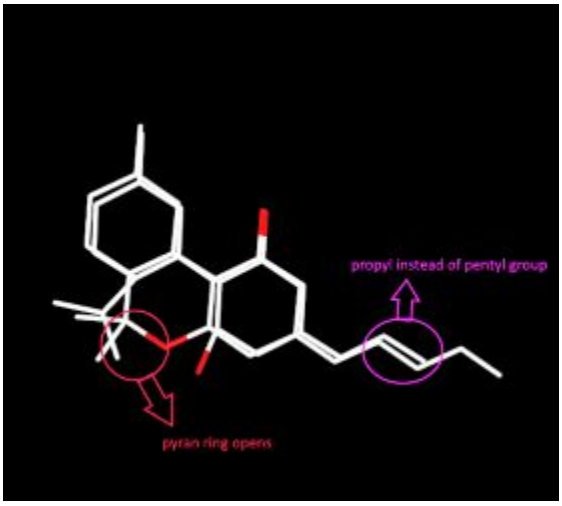
Supplement 4-46 : 3,4,5,6-tetrahydro-7-hydroxy-a,a-2-trimethyl-9-n-propyl-2,6-methano-2H-1-Benzoxocin-5-methanol-THC Scaffold. Alicyclic ring opens, cyclopentyl ring fused with ortho and OH group of phenolic moiety.



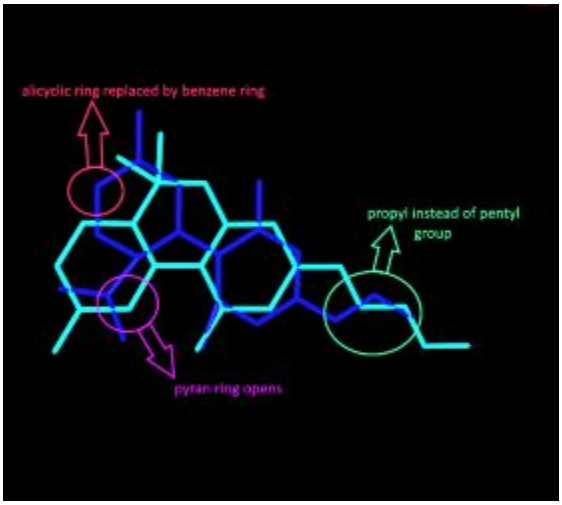
Supplement 4-47 : Cannabicoumaronone-THC scaffold. Alicyclic ring opens, 4,5-Dehydrofuran fused with pyran and Phenolic groups.



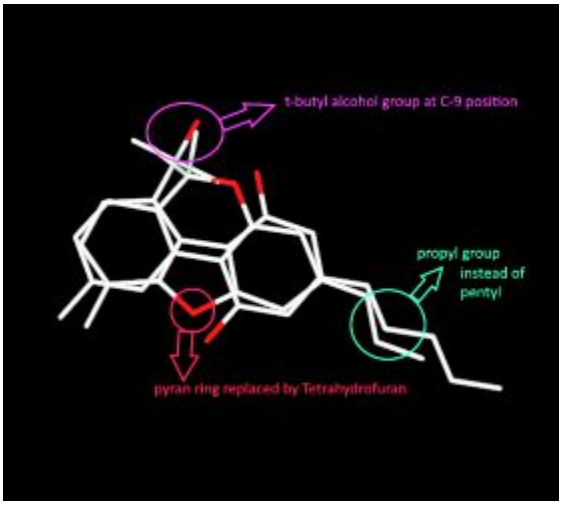
Supplement 4-48 : Delta-7-cis-Isotetrahydrocannabivarin-THC scaffold. Alicyclic ring opens, cyclopentyl group Fused with orth-and OH of phenolic moiety. Pentyl group reduced to propyl group.



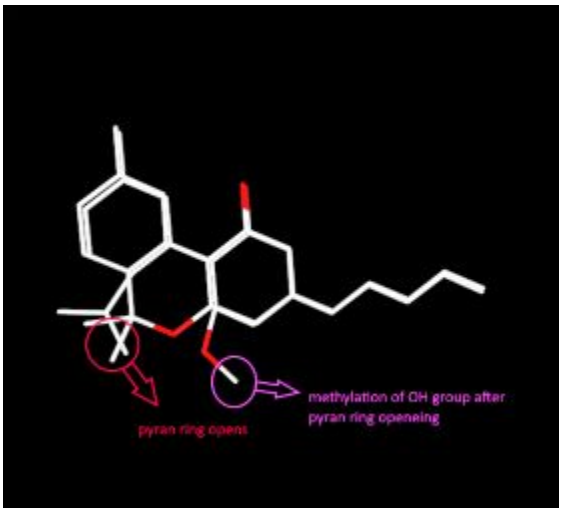
Supplement 4-49 : Cannabidivarin (CBDV)-THC scaffold. Benzopyran ring opens, propyl group at C-3 position of phenolic group.



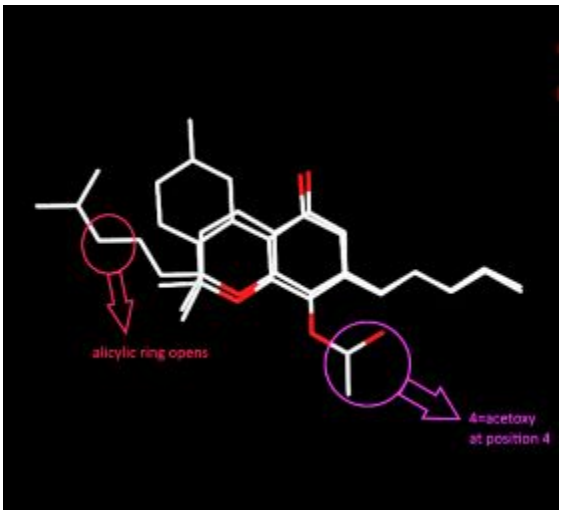
Supplement 4-50 : Cannabinodivarin (CBVD)-THC scaffold. Alicyclic ring replaced by aromatic benzene ring, pyran Ring opens, propyl at C-3 of phenolic moiety instead of pentyl group.



Supplement 4-51 : Cannabiglendol-THC scaffold. Benzopyran replaced by Tetrahydrofuran group, t-butyl alcohol at C-9 position, propyl at C-3 of phenolic group.



Supplement 4-52 : Cannabidiol methyl ether-THC scaffold. Pyran ring opens, methylation of OH group after opening of Of pyran ring.



Supplement 4-53 : 4-Acetoxy Cannabichromene-THC scaffold. Alicyclic ring opens, 4-acetoxy group at position 4 of Phenolic moiety.

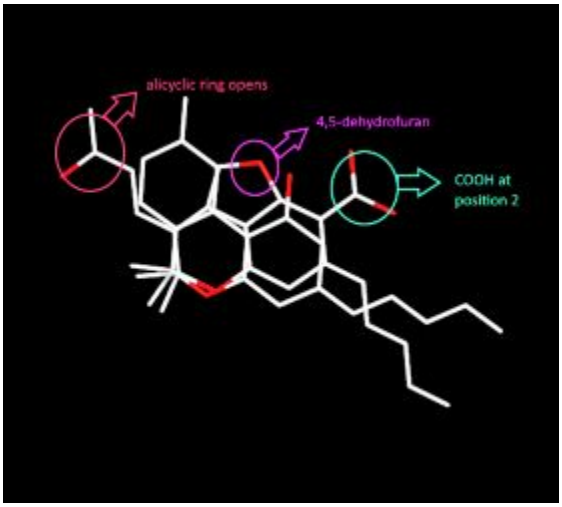


Figure 5-54 : 7-R-cannabicoumarononic acid-THC scaffold. Alicyclic ring opens, 4-5-dehydrofuran fused with pyran and phenolic rings, COOH at position 2 of phenolic group.