Supporting Information

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Nano $TiO_2.SiO_2$ catalyzed, microwave assisted synthesis of new *α*-aminophosphonates as potential anti-diabetic agents: *In silico* ADMET and molecular docking study

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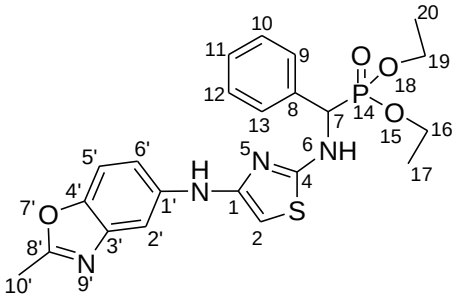
2.2.1. Preparation of Nano TiO_2/SiO_2[1]

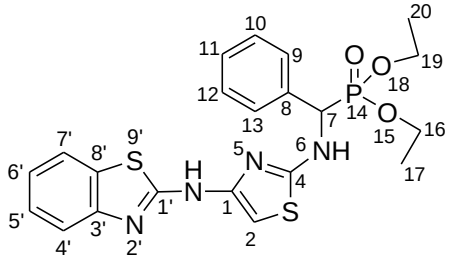
To a mixture of SiO_2 60 (for column chromatography, mesh 70-230, 0.06-0.2 mm, 2 g) in 50 mL $CHCl_3$, nano TiO_2 (Anatase phase, 10-25 nm, 2 g) was added. The mixture was stirred at room temperature for 90 min. The solvent was evaporated at room temperature overnight to obtain a white solid of 50% (W/W) nano TiO_2/SiO_2. IR (KBr) (ν_{max} cm^{-1}): 1092 (Si-O str.), 967 (Si-O-Ti str.), 703 (Ti-O-Ti str.)

*Spectral data of compounds (**7b-j**)*



Compound **7b**

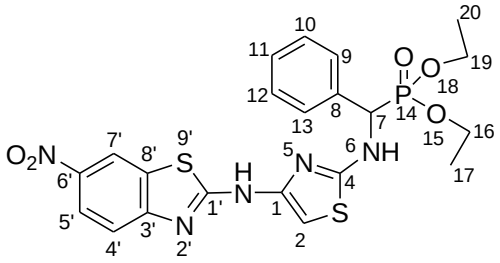
*Diethyl (4-(2-methylbenzo[d]oxazol-5-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7b**):* Solid. M.P. 171-173 °C. Yield: 90%. δ_H (DMSO-d_6): 9.42 (s, 1H, -NH), 7.24 (t, *J*=7.6 Hz,2H, Ar-H), 7.15 (t, *J*=7.6 Hz, 1H, Ar-H), 7.07 (d, *J*=7.2 Hz,2H, Ar-H), 7.03 (d, *J*=6.8 Hz,1H, Ar-H), 6.54 (d, *J*=7.2 Hz,2H, Ar-H), 5.84 (s, 1H, Thiazole-H), 5.53 (s, 1H, -NH), 4.17 (q, *J*=7.2 Hz,4H, O-$\underline{CH_2}CH_3$), 3.87 (s, 1H, methine-H), 2.25 (s, 3H, -CH_3), 1.25 (t, *J*= 6.8 Hz, 6H, O-$CH_2\underline{CH_3}$); δ_C (DMSO-d_6): 145.5 (C-1), 112.2 (C-2), 166.5 (C-4), 58.2 (C-7), 135.5 (C-8), 128.4 (C-9 and C-13), 129.4 (C-10, C-12), 127.5 (C-11), 61.3 (C-16 and C-19), 14.2 (C-17 and C-20), 141.2 (C-1'), 102.4 (C-2'), 110.1 (C-3'), 138.8 (C-4'), 143.7 (C-5'), 108.9 (C-6'), 162.7 (C-8'), 14.2 (C-10'); δ_P (DMSO-d_6): 19.5 ppm; IR (KBr) (ν_{max} cm^{-1}): 3294, 3166 (NH), 1216 (P=O), 1005 (P-O-C_{alip}); LCMS (*m/z*, %): 473 ($M+H^+$,100); For $C_{22}H_{25}N_4O_4PS$; calcd: C, 55.92; H, 5.33; N, 11.86%; found: C, 55.87; H, 5.47; N, 11.96%.



Compound **7c**

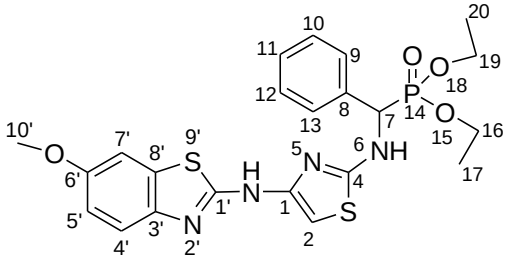
*Diethyl (4-(benzo[d]thiazol-2-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7c**):* Solid. M.P. 155-157 °C. Yield: 94%. δ_H (DMSO-d_6): 9.42 (s, 1H, -NH), 8.18 (d, *J*=8.0 Hz,1H, Ar-H), 8.06 (d, *J*=7.6 Hz,1H, Ar-H), 7.48 (t, *J*=7.2 Hz,2H, Ar-H), 7.24 (t, *J*=7.6 Hz,2H, Ar-H), 7.07 (d, *J*=7.2 Hz,2H, Ar-H), 7.15 (t, *J*=7.6 Hz,1H, Ar-H), 5.84 (s, 1H, Thiazole-H), 5.53 (s, 1H, -NH), 4.17 (q, *J*=7.2 Hz,4H, O-$\underline{CH_2}CH_3$), 3.87 (s, 1H, methine-H), 1.25 (t, *J*= 6.8 Hz, 6H, O-$CH_2\underline{CH_3}$); δ_C (DMSO-d_6): 145.5 (C-1), 112.2 (C-2), 166.5 (C-4), 58.2 (C-7), 135.5 (C-8), 128.4 (C-9 and C-13), 129.4 (C-10, C-12), 127.5 (C-

11), 61.3 (C-16 and C-19), 14.2 (C-17 and C-20), 171.7 (C-1'), 142.4 (C-8'), 122.1 (C-3'), 120.5 (C-4' and C-7'), 124.7 (C-5'), 125.9 (C-6'); δ_P (DMSO-d_6): 19.8 ppm; IR (KBr) (ν_{max} cm^{-1}): 3315, 3173 (NH), 1213 (P=O), 1008 (P-O-C_{alip}); LCMS (*m/z*, %): 475 ($M+H^+$,100); For $C_{21}H_{23}N_4O_3PS_2$; calcd: C, 53.15; H, 4.89; N, 11.81%; found: C, 53.26; H, 4.80; N, 11.91%.



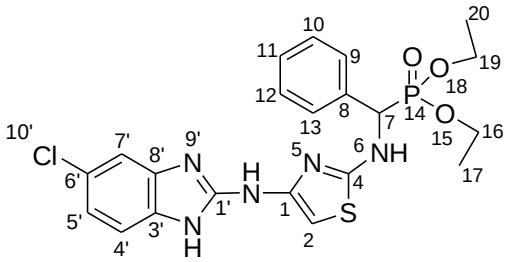
Compound **7d**

*Diethyl (4-(6-nitrobenzo[d]thiazol-2-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7d**):* Solid. M.P. 211-213 °C. Yield: 93%. δ_H (DMSO-d_6): 9.42 (s, 1H, -NH), 8.86 (s, 1H, Ar-H), 8.37 (d, *J*=8.0 Hz,1H, Ar-H), 8.33 (d, *J*=7.6 Hz,1H, Ar-H), 7.24 (t, *J*=7.6 Hz,2H, Ar-H), 7.07 (d, *J*=7.2 Hz,2H, Ar-H), 7.15 (t, *J*=7.6 Hz,1H, Ar-H), 5.84 (s, 1H, Thiazole-H), 5.53 (s, 1H, -NH), 4.17 (q, *J*=7.2 Hz,4H, O-$\underline{CH_2}CH_3$), 3.87 (s, 1H, methine-H), 1.25 (t, *J*= 6.8 Hz, 6H, O-$CH_2\underline{CH_3}$); δ_C (DMSO-d_6): 145.5 (C-1), 112.2 (C-2), 166.5 (C-4), 58.2 (C-7), 135.5 (C-8), 128.4 (C-9 and C-13), 129.4 (C-10, C-12), 127.5 (C-11), 61.3 (C-16 and C-19), 14.2 (C-17 and C-20), 172.8 (C-1'), 153.6 (C-3'), 124.2 (C-4'), 120.7 (C-5'), 145.1 (C-6'), 116.3 (C-7'), 121.6 (C-8'); δ_P (DMSO-d_6): 22.4 ppm; IR (KBr) (ν_{max} cm^{-1}): 3342, 3192 (NH), 1224 (P=O), 1013 (P-O-C_{alip}); LCMS (*m/z*, %): 520 ($M+H^+$,100); For $C_{21}H_{22}N_5O_5PS_2$; calcd: C, 48.55; H, 4.27; N, 13.48%; found: C, 48.67; H, 4.18; N, 13.57%.



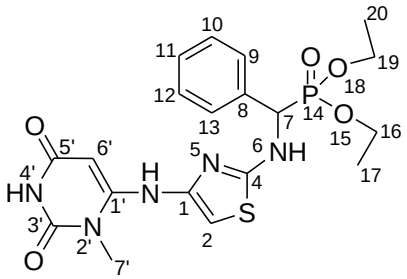
Compound **7e**

*Diethyl (4-(6-methoxybenzo[d]thiazol-2-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7e**):* Solid. M.P. 233-235 °C. Yield: 92%. δ_H (DMSO-d_6): 9.42 (s, 1H, -NH), 8.04 (d, *J*=7.6 Hz,1H, Ar-H), 7.55 (s, 1H, Ar-H), 7.24 (t, *J*=7.6 Hz,2H, Ar-H), 7.07 (d, *J*=7.2 Hz,2H, Ar-H), 7.15 (t, *J*=7.6 Hz,1H, Ar-H), 7.01 (d, *J*=8.0 Hz,1H, Ar-H), 5.84 (s, 1H, Thiazole-H), 5.53 (s, 1H, -NH), 4.17 (q, *J*=7.6 Hz,4H, O-$\underline{CH_2}CH_3$), 3.87 (s, 1H, methine-H), 3.65 (s, 3H, -CH_3), 1.25 (t, *J*= 6.8 Hz, 6H, O-$CH_2\underline{CH_3}$); δ_C (DMSO-d_6): 145.5 (C-1), 112.2 (C-2), 166.5 (C-4), 58.2 (C-7), 135.5 (C-8), 128.4 (C-9 and C-13), 129.4 (C-10, C-12), 127.5 (C-11), 61.3 (C-16 and C-19), 14.2 (C-17 and C-20), 173.2 (C-1'), 143.2 (C-3'), 124.6 (C-4'), 114.5 (C-5'), 155.3 (C-6'), 106.4 (C-7'), 121.7 (C-8'), 56.4 (C-10'); δ_P (DMSO-d_6): 20.5 ppm; IR (KBr) (ν_{max} cm^{-1}): 3268, 3146 (NH), 1207 (P=O), 1004 (P-O-C_{alip}); LCMS (*m/z*, %): 505 ($M+H^+$,100); For $C_{22}H_{25}N_4O_4PS_2$; Calcd: C, 52.37; H, 4.99; N, 11.10%; found: C, 52.46; H, 4.88; N, 11.22%.



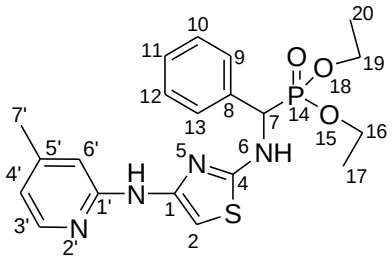
Compound **7f**

*Diethyl (4-(6-chlorobenzo[d]thiazol-2-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7f**)*. Solid. M.P. 196-198 °C. Yield: 95%. δ_H (DMSO-d_6): 9.42 (s, 1H, -NH), 8.14 (d, *J*=7.6 Hz,1H, Ar-H), 8.11 (s, *J*=8.0 Hz,1H, Ar-H), 7.45 (d, *J*=7.6 Hz,1H, Ar-H), 7.24 (t, *J*=7.6 Hz,2H, Ar-H), 7.07 (d, *J*=7.2 Hz,2H, Ar-H), 7.15 (t, *J*=7.6 Hz,1H, Ar-H), 5.84 (s, 1H, Thiazole-H), 5.53 (s, 1H, -NH), 4.17 (q, *J*=7.2 Hz,4H, O-$\underline{CH_2}CH_3$), 3.87 (s, 1H, methine-H), 1.25 (t, *J*= 6.8 Hz, 6H, O-$CH_2\underline{CH_3}$); δ_C (DMSO-d_6): 145.5 (C-1), 112.2 (C-2), 166.5 (C-4), 58.2 (C-7), 135.5 (C-8), 128.4 (C-9 and C-13), 129.4 (C-10, C-12), 127.5 (C-11), 61.3 (C-16 and C-19), 14.2 (C-17 and C-20), 173.7 (C-1'), 125.1 (C-3'), 122.8 (C-4'), 128.5 (C-5'), 124.5 (C-6'), 122.1 (C-7'),146.3 (C-8'); δ_P (DMSO-d_6): 22.1 ppm; IR (KBr) (ν_{max} cm^{-1}): 3349, 3288 (NH), 1228 (P=O), 1016 (P-O-C_{alip}); LCMS (*m/z*, %): 509 ($M+H^+$,100); For $C_{21}H_{22}ClN_4O_3PS_2$; calcd: C, 49.55; H, 4.36; N, 11.01%; found: C, 49.62; H, 4.25; N, 11.13%.



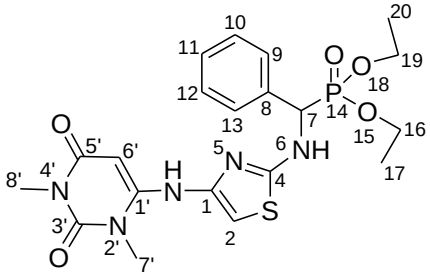
Compound **7g**

*Diethyl (4-(1,2,3,6-tetrahydro-3-methyl-2,6-dioxopyrimidin-4-ylamino)thiazol-2-ylamino) (phenyl)-methylphosphonate (**7g**):* Solid, M.P. 178-180 °C. Yield: 95%. δ_H (DMSO-d_6): 9.87 (s, 1H, -NH), 9.42 (s, 1H, -NH), 7.24 (t, *J*=7.6 Hz,2H, Ar-H), 7.15 (t, *J*=7.6 Hz,1H, Ar-H), 7.07 (d, *J*=7.2 Hz,2H, Ar-H), 5.84 (s, 1H, Thiazole-H), 5.53 (s, 1H, -NH), 5.14 (s, 1H, ethylene-H), 4.17 (q, *J*=7.2 Hz,4H, O-$\underline{CH_2}CH_3$), 3.87 (s, 1H, methine-H), 2.66 (s, 3H, N-CH_3), 1.25 (t, *J*= 6.8 Hz, 6H, O-$CH_2\underline{CH_3}$); δ_C (DMSO-d_6): 145.5 (C-1), 112.2 (C-2), 166.5 (C-4), 58.2 (C-7), 135.5 (C-8), 128.4 (C-9 and C-13), 129.4 (C-10, C-12), 127.5 (C-11), 61.3 (C-16 and C-19), 14.2 (C-17 and C-20), 163.6 (C-1'), 151.2 (C-3'), 164.3 (C-5'), 74.7 (C-6'), 31.4 (C-7'); δ_P (DMSO-d_6): 17.6 ppm; IR (KBr) (ν_{max} cm^{-1}): 3315, 3277, 3163 (NH), 1218 (P=O), 1019 (P-O-C_{alip}); LCMS (*m/z*, %): 466 ($M+H^+$,100); For $C_{19}H_{24}N_5O_5PS$; calcd: C, 49.03; H, 5.20; N, 15.05%; found: C, 49.15; H, 5.09; N, 15.14%.



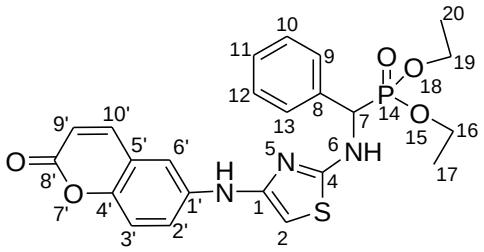
Compound **7h**

*Diethyl (4-(4-methylpyridin-2-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7h**):* Solid. M.P. 214-216 °C. Yield: 93%. δ_H (DMSO-d_6): 9.42 (s, 1H, -NH), 8.06 (d, *J*=8.0 Hz,1H, Py-H), 7.24 (t, *J*=7.6 Hz,2H, Ar-H), 7.07 (d, *J*=7.2 Hz,2H, Ar-H), 7.15 (t, *J*=7.6 Hz,1H, Ar-H), 6.54 (s, 1H, Py-H), 6.44 (d, *J*=7.6 Hz,1H, Py-H), 5.84 (s, 1H, Thiazole-H), 5.53 (s, 1H, -NH), 4.17 (q, *J*=7.2 Hz,4H, O-$\underline{CH_2}CH_3$), 3.87 (s, 1H, methine-H), 2.25 (s, 3H, -CH_3), 1.25 (t, *J*= 6.8 Hz, 6H, O-$CH_2\underline{CH_3}$); δ_C (DMSO-d_6): 145.5 (C-1), 112.2 (C-2), 166.5 (C-4), 58.2 (C-7), 135.5 (C-8), 128.4 (C-9 and C-13), 129.4 (C-10, C-12), 127.5 (C-11), 61.3 (C-16 and C-19), 14.2 (C-17 and C-20), 154.5 (C-1'), 147.7 (C-3'), 116.9 (C-4'), 148.9 (C-5'), 113.4 (C-6'), 25.4 (C-7'); δ_P (DMSO-d_6): 16.5 ppm; IR (KBr) (ν_{max} cm^{-1}): 3316, 3135 (NH), 1215 (P=O), 1006 (P-O-C_{alip}); LCMS (*m/z*, %): 433 ($M+H^+$,100); For $C_{20}H_{25}BrN_4O_3PS$; calcd: C, 55.54; H, 5.83; N, 12.95%; found: C, 55.66; H, 5.71; N, 12.87%.



Compound **7i**

*Diethyl (4-(1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopyrimidin-4-ylamino)thiazol-2-ylamino)(phenyl)-methylphosphonate (**7i**):* Solid. M.P. 181-183 °C. Yield: 96%. δ_H (DMSO-d_6): 9.42 (s, 1H, -NH), 7.24 (t, *J*=7.6 Hz,2H, Ar-H), 7.07 (d, *J*=7.2 Hz,2H, Ar-H), 7.15 (t, *J*=7.6 Hz,1H, Ar-H), 5.84 (s, 1H, Thiazole-H), 5.53 (s, 1H, -NH), 5.24 (s, 1H, ethylene-H), 4.17 (q, *J*=7.2 Hz,4H, O-$\underline{CH_2}CH_3$), 3.87 (s, 1H, methine-H), 2.59 (s, 6H, N-CH_3), 1.25 (t, *J*= 6.8 Hz, 6H, O-$CH_2\underline{CH_3}$); δ_C (DMSO-d_6): 145.5 (C-1), 112.2 (C-2), 166.5 (C-4), 58.2 (C-7), 135.5 (C-8), 128.4 (C-9 and C-13), 129.4 (C-10, C-12), 127.5 (C-11), 61.3 (C-16 and C-19), 14.2 (C-17 and C-20), 163.7 (C-1'), 150.4 (C-3'), 162.9 (C-5'), 74.8 (C-6'), 31.5 (C-7'), 29.1 (C-8'); δ_P (DMSO-d_6): 18.2 ppm; IR (KBr) (ν_{max} cm^{-1}): 3283, 3197 (NH), 1214 (P=O), 1012 (P-O-C_{alip}); LCMS (*m/z*, %): 480 ($M+H^+$,100); For $C_{20}H_{26}N_5O_5PS$; calcd: C, 50.10; H, 5.47; N, 14.61%; found: C, 50.23; H, 5.34; N, 14.72%.



Compound **7j**

*Diethyl (4-(2-oxo-2H-chromen-6-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7j**):* Solid. M.P. 232-234 °C. Yield: 90%. δ_H (DMSO-d_6): 9.41 (s, 1H, -NH), 7.42 (d, *J*=7.6 Hz,1H, ethylene-H), 7.24 (t, *J*=7.6 Hz,2H, Ar-H), 7.07 (d, *J*=7.2 Hz,2H, Ar-H), 7.15 (t, *J*=7.6 Hz,1H, Ar-H), 6.85 (d, *J*=7.2 Hz,1H, Ar-H), 6.61 (d, *J*=7.6 Hz,1H, Ar-H), 6.45 (s, 1H, Ar-H), 6.14 (d, *J*=6.0 Hz,1H, ethylene-H), 5.84 (s, 1H, Thiazole-H), 5.53 (s, 1H, -NH), 4.17 (q, *J*=7.2 Hz,4H, O-$\underline{CH_2}CH_3$), 3.87 (s, 1H, methine-H), 1.25 (t, *J*= 6.8 Hz, 6H, O-$CH_2\underline{CH_3}$); δ_C (DMSO-d_6): 145.5 (C-1), 112.2 (C-2), 166.5 (C-4), 58.2 (C-7), 135.5 (C-8), 128.4 (C-9 and C-13), 129.4 (C-10, C-12), 127.5 (C-11), 61.3 (C-16 and C-19), 14.2 (C-17 and C-20), 138.3 (C-1'), 114.8 (C-2'), 121.6 (C-3'), 141.3 (C-4'), 124.2 (C-5'), 110.6 (C-6'), 161.4 (C-8'), 112.7 (C-9'), 142.9 (C-10'); δ_P (DMSO-d_6): 23.6 ppm; IR (KBr) (ν_{max} cm^{-1}): 3320, 3217 (NH), 1211 (P=O), 1011 (P-O-C_{alip}); LCMS (*m/z*, %): 486 ($M+H^+$,100); For $C_{23}H_{24}N_3O_5PS$; calcd: C, 56.90; H, 4.98; N, 8.66%; found: C, 56.99; H, 4.90; N, 8.57%.

α-Amylase Inhibitory Activity[2,3]

The In vitro α-amylase inhibition assay of all extracts was performed with slight modification of a previously reported method which is based on the spectrophotometric assay using acarbose as the reference compound. Stock solutions of the newly prepared compounds and positive control sample of acarbose were prepared in distilled water. A total of 500 µL of different concentrations of each sample (25, 50, 100, 150 and 200µg/mL) were added to a 500 µL α-amylase solution (0.5 mg/mL in 0.02M sodium phosphate buffer, pH 6.9) and incubated for 10 min at. Then 500 µL of 1% (w/v) starch solution was added and then the colouring reagent, 0.5 mL of DNS reagent (12.0 g of sodium potassium tartrate tetrahydrate in 8 mL of 2M NaOH and 96 mM 3,5-dinitrosalicylic acid solution was added and the reaction mixture was heated in a boiling water bath for 5 minutes and cooled to room temperature. It was diluted with 10 mL distilled water and the absorbance was measured at 540 nm using a UV-VIS spectrophotometer. The absorbance of blank was prepared by replacing enzyme solution with 500µl buffer. A positive control, representing 100% enzyme activity was prepared using acarbose in a similar procedure, without plant extract as mentioned above.

Repeat the experiments thrice using the same protocol.

% inhibition = [(AC-AS) / AC] x 100, Where AC is the absorbance of the control and AS is the absorbance of the sample

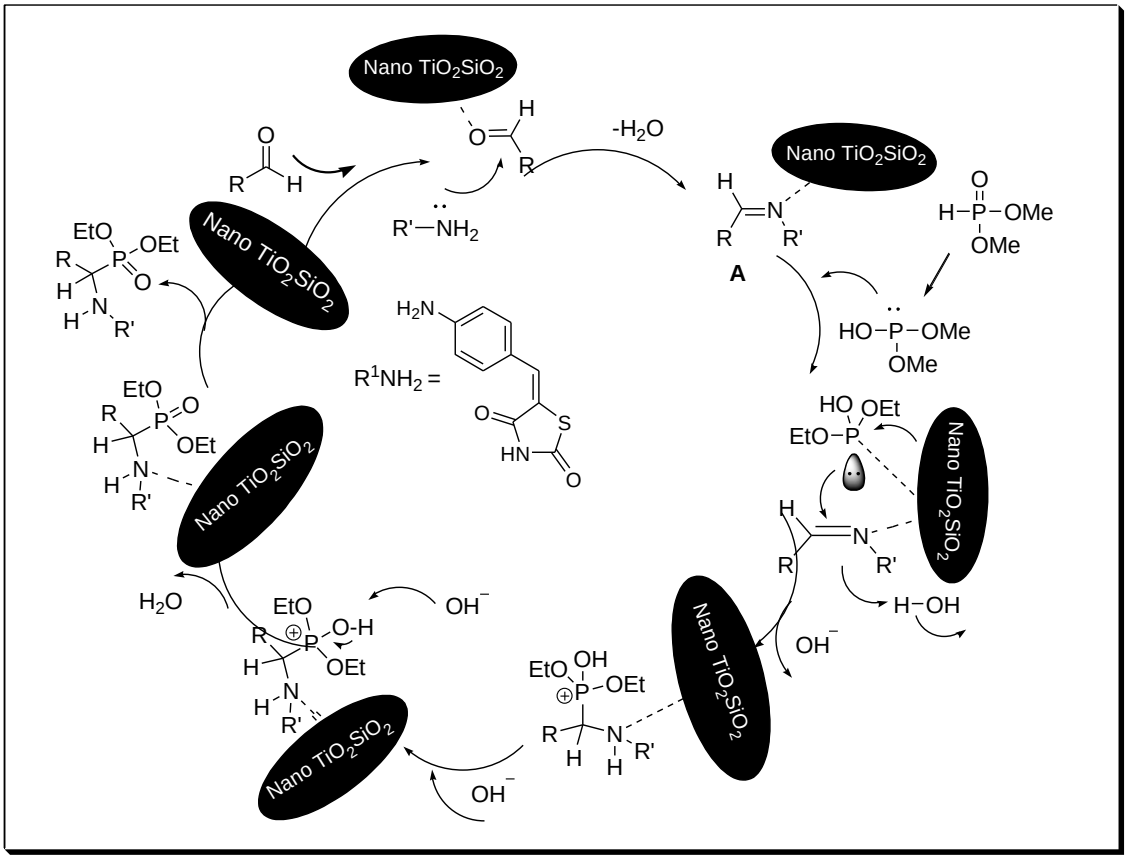


Figure S1 : Mechanism for the nano TiO_2.SiO_2 catalyzed synthesis of α-Aps (**7a**-**j**)

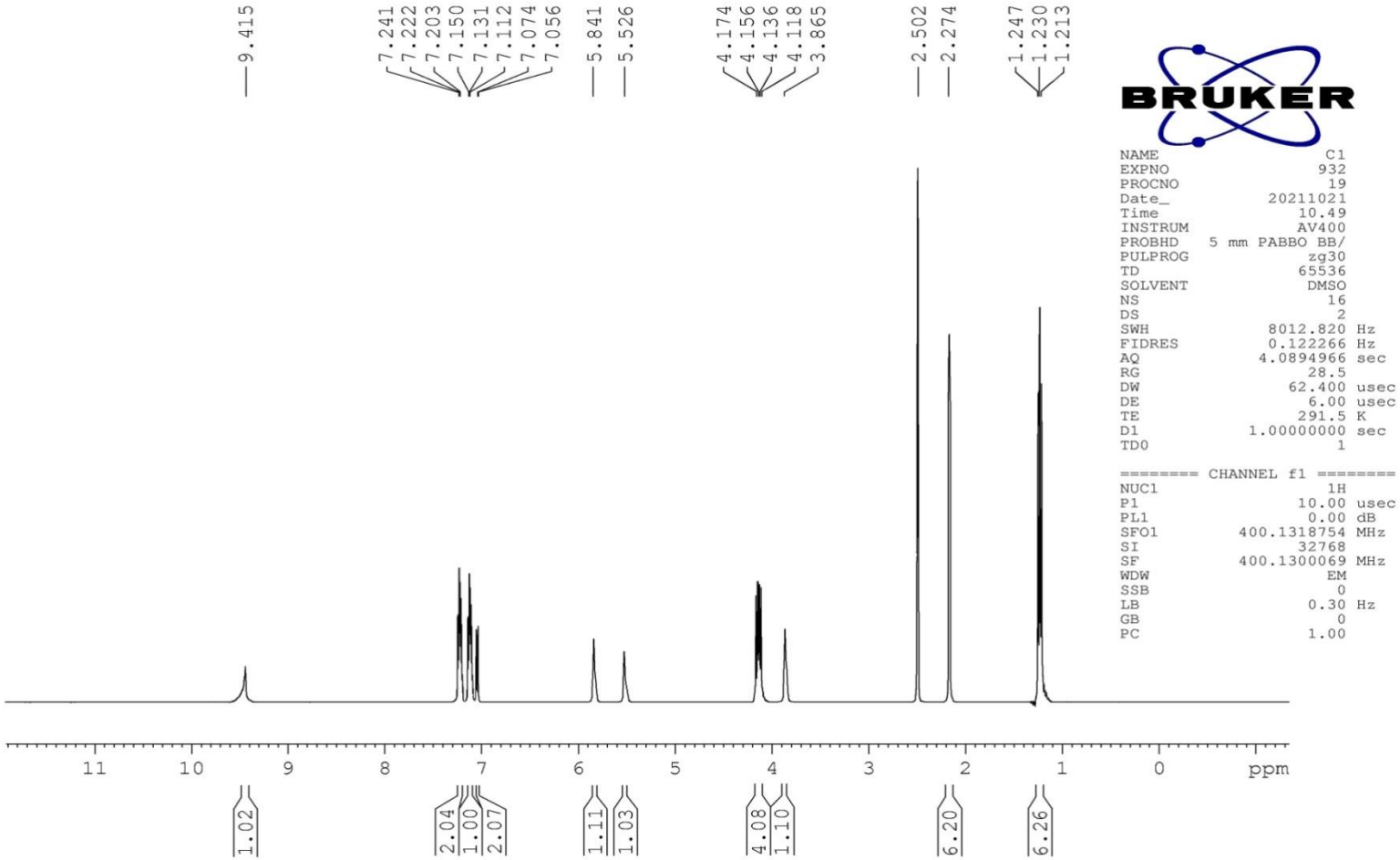


Figure S2: [1]H Spectrum of compound **7a**

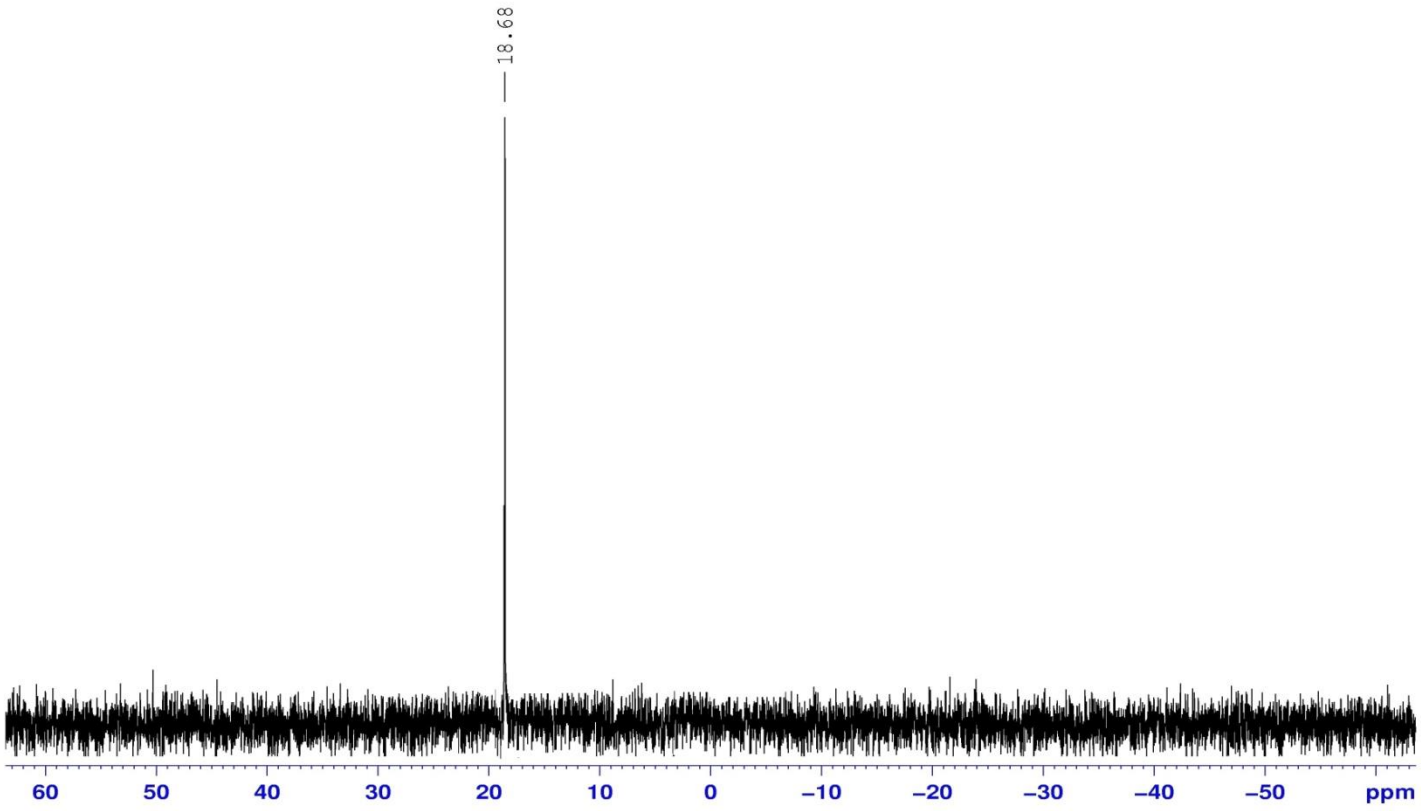


Figure S3: ^{31}P Spectrum of compound **7a**

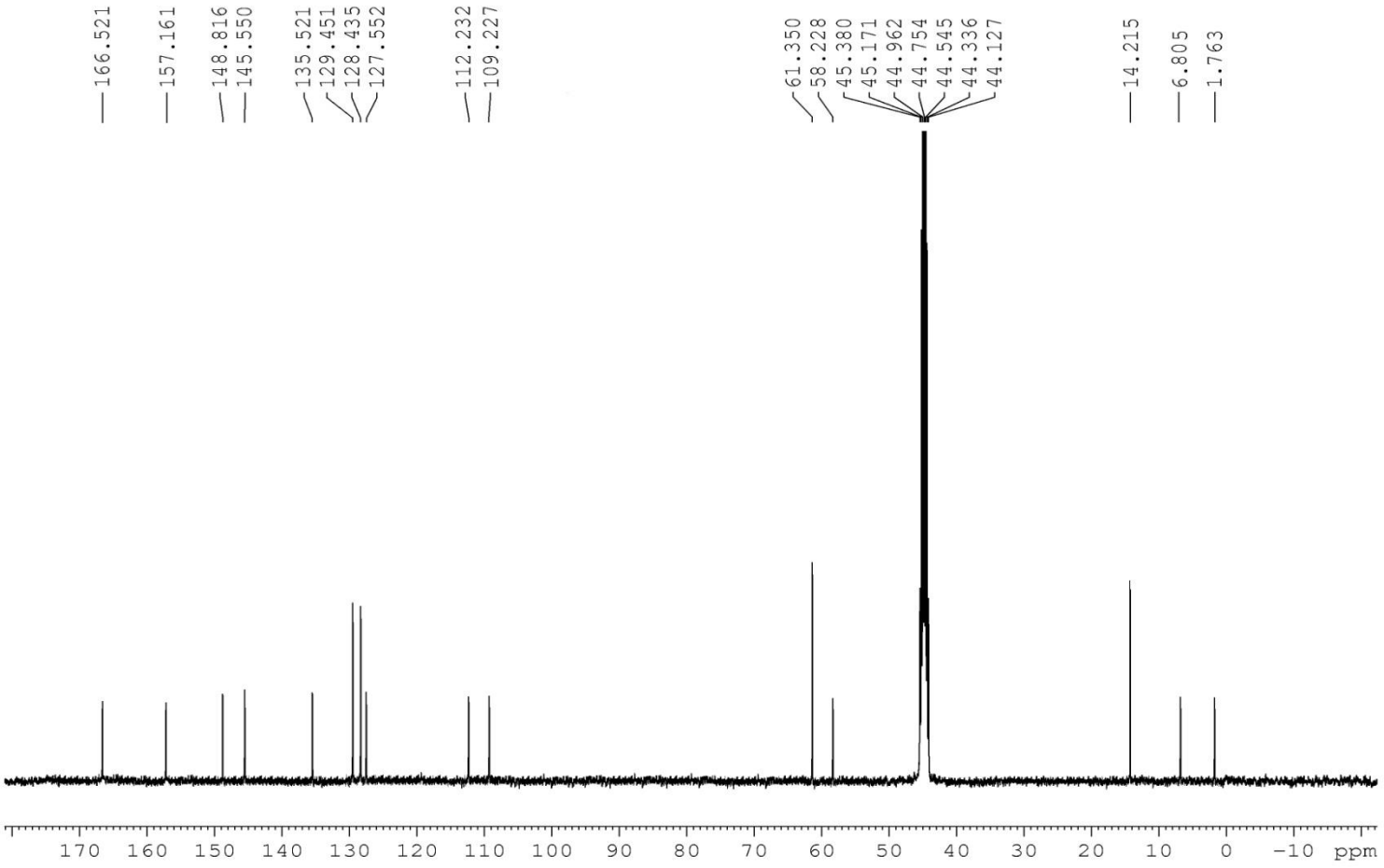


Figure S4: ^{13}C NMR Spectrum of compound **7a**

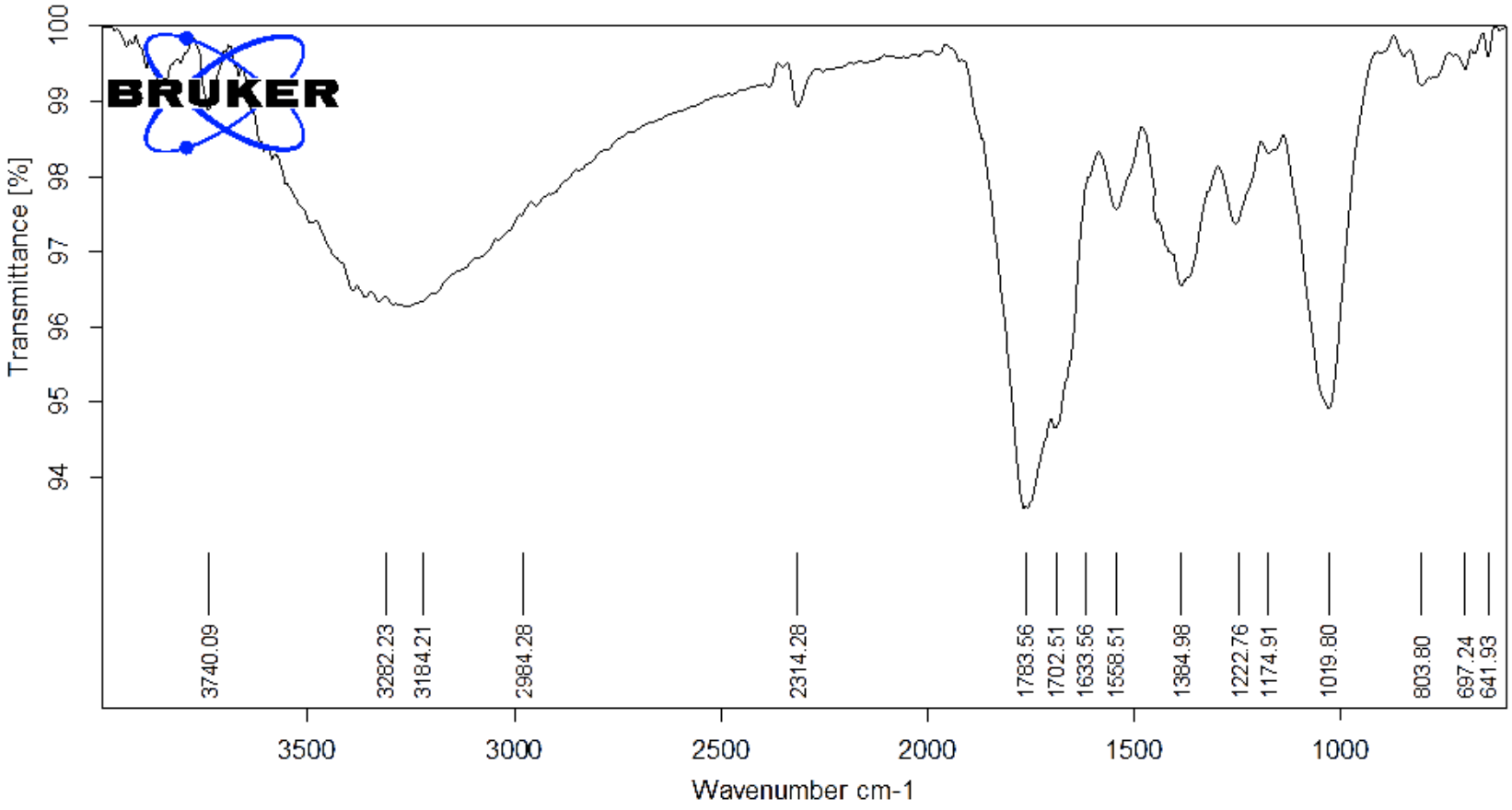
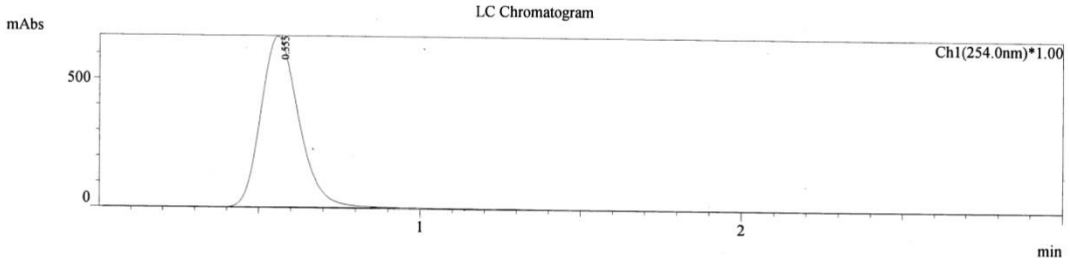
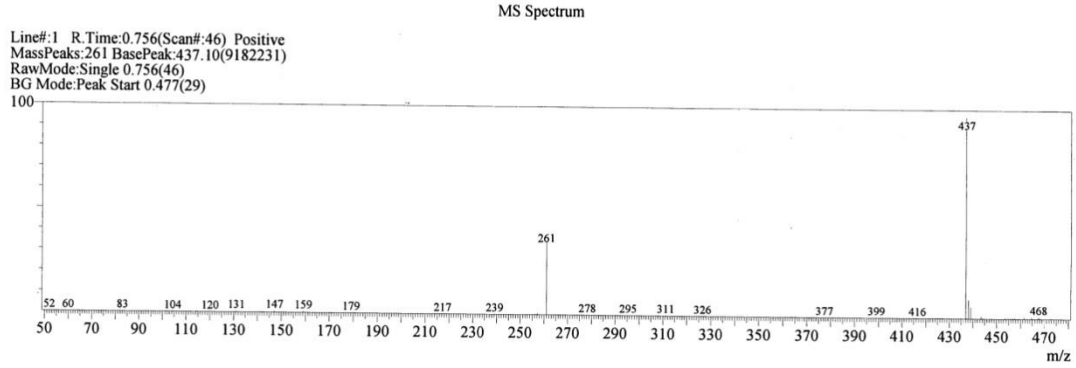


Figure S5: IR Spectrum of compound **7a**

LCMS-2010A DATA REPORT
SHIMADZU

User	: Admin
Sample	: S-7a
Inj. Volume	: 5.000
Data Name	: C:\LCMSsolution\User\Data\S-7a -ESI-POS1.qld
Method Name	: C:\LCMSsolution\User\Method\esi.qlm





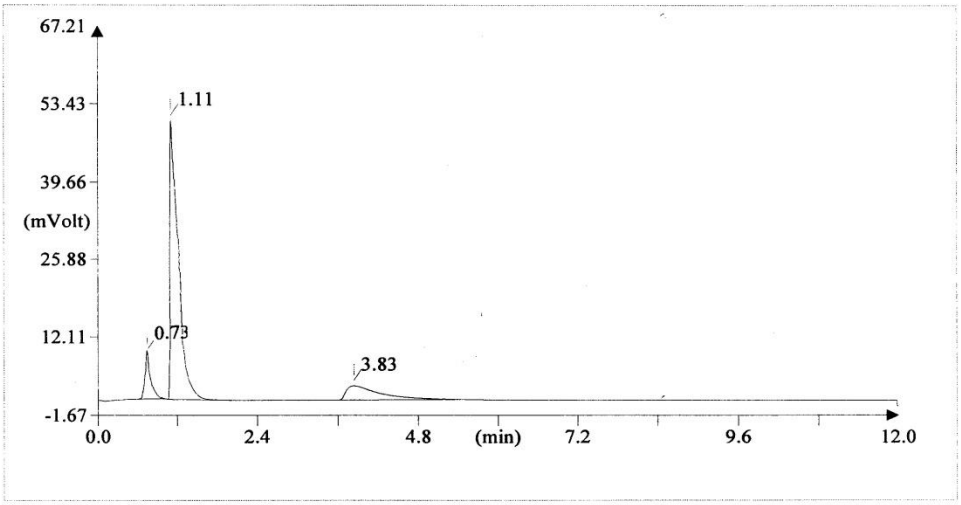
MS Peak Table

Peak#	R.Time	I.Time	F.Time	Area	Height	A/H	Mark	%Total	Name	Base m/z	Base Int.
1	0.756	0.477	1.143	932355911	40778373	22.86		100.00		437.10	9182231
				932355911	40778373			100.00			

Figure S6: Mass Spectrum of compound **7a**

FLASH EA 1112 SERIES CHN REPORT
THERMO FINNIGAN

Method filename:	C:\Program Files\Thermo Finnigan\Eager 300 for EA1112\DATA\Sys_data_ex
Sample ID:	SAMPLE-7 (# 7)
Analysis type:	UnkNown
Chromatogram filename:	UNK-27102021-7.dat
Sample weight:	1.161



Element Name	Element %	Ret. Time
Nitrogen	12.95	0.73
Carbon	52.20	1.11
Hydrogen	5.89	3.83

Figure S7: CHN analysis of compound **7a**

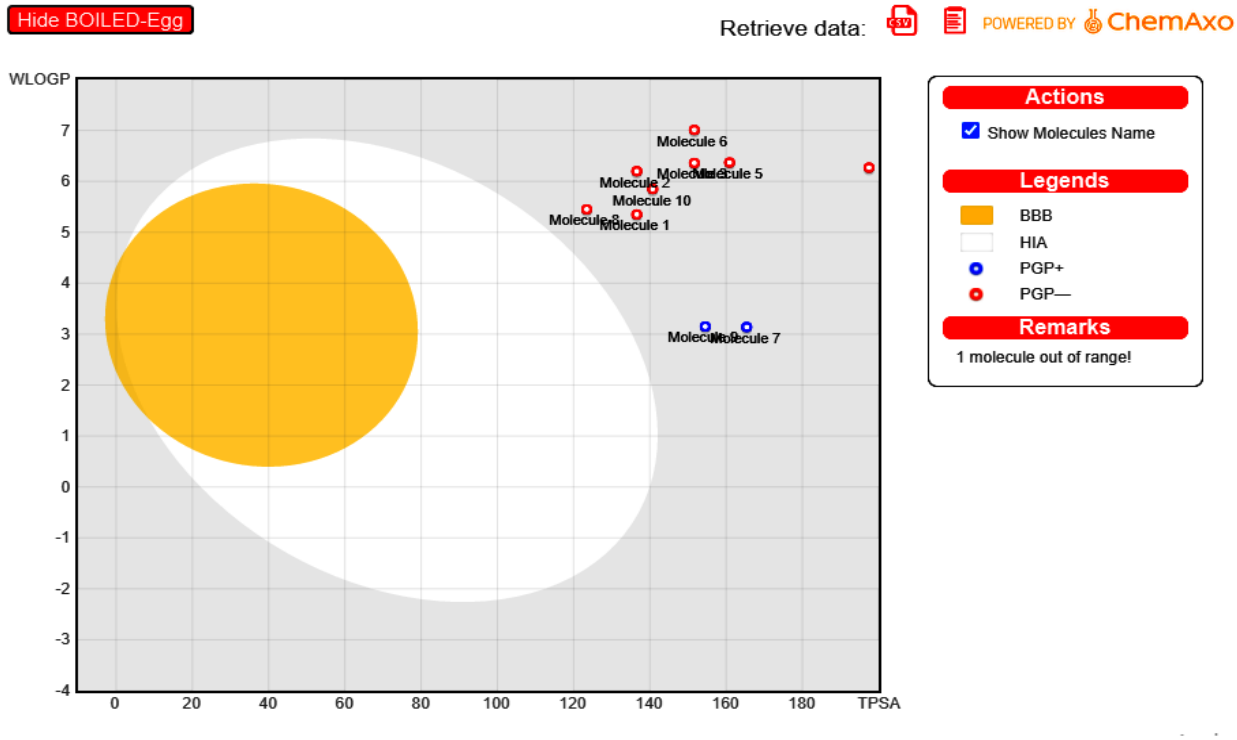


Figure S8: The BOILED-Eggdiagram of the tested molecules 1-10 (**7a-j**)

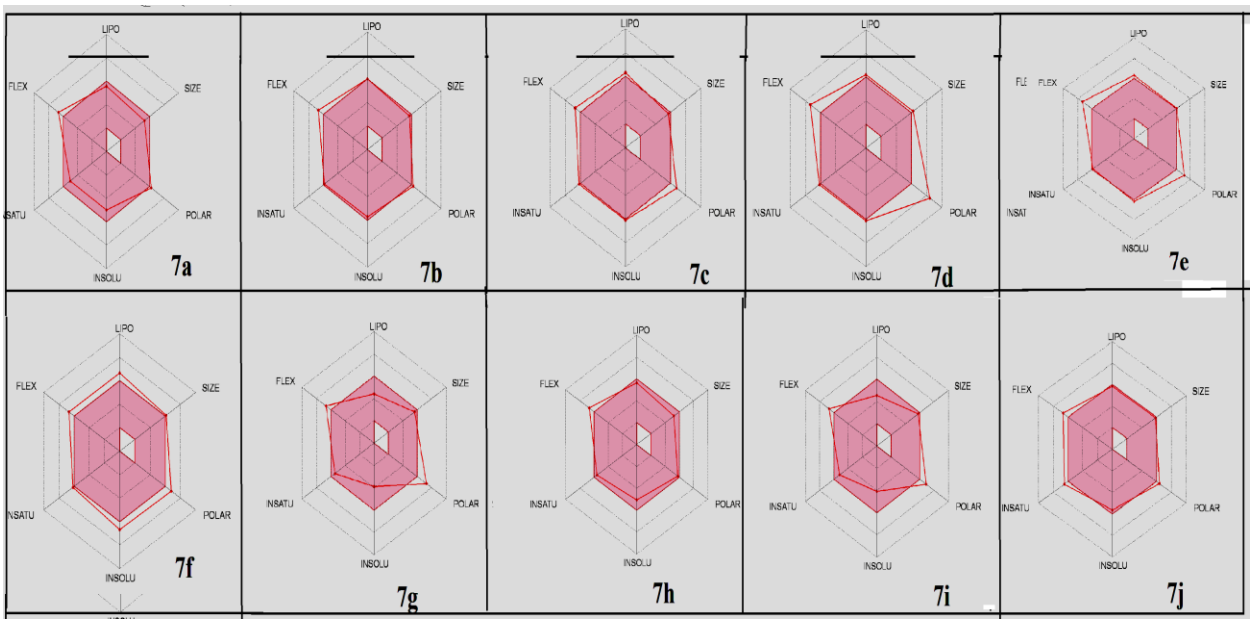


Figure S9: The bio radar map of the tested molecules (**7a-j**)

Table S1: Physicochemical properties of compounds (**7a-j**)

Compd.	[a]MW	Heavy atoms	Aromatic heavy atoms	[b]Fraction Csp3	Rotatable bonds	H-bond acceptors	H-bond donors	[c]MR	[d]TPSA	[e]iLOGP	[f]Silicos-IT class
7a	436.46	29	16	0.37	10	6	2	115.5	136.56	2.95	Poorly soluble
7b	472.5	32	20	0.27	10	6	2	128.04	136.56	3.31	Poorly soluble
7c	474.54	31	20	0.24	10	5	2	128.69	151.66	3.14	Poorly soluble
7d	519.53	34	20	0.24	11	7	2	137.51	197.48	3.08	Poorly soluble
7e	504.56	33	20	0.27	11	6	2	135.18	160.89	3.77	Poorly soluble
7f	508.98	32	20	0.24	10	5	2	133.7	151.66	3.69	Poorly soluble
7g	465.46	31	17	0.32	10	6	3	121.65	165.39	2.87	Poorly soluble
7h	432.48	29	17	0.3	10	5	2	118.27	123.42	2.49	Poorly soluble
7i	479.49	32	17	0.35	10	6	2	126.56	154.53	3.44	Moderately soluble
7j	485.49	33	21	0.22	10	6	2	131.55	140.74	3.42	Poorly soluble
Acarbose	645.6	44	0	0.92	9	19	14	136.69	321.17	0.63	Soluble

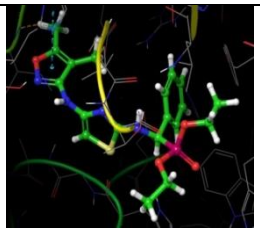
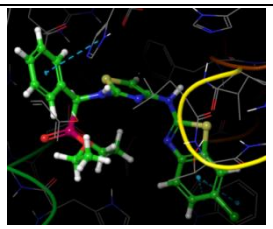
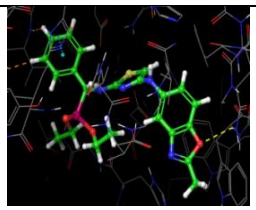
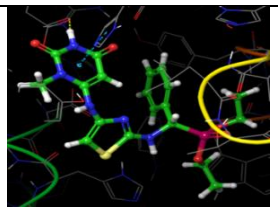
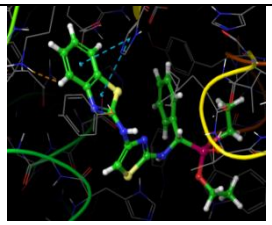
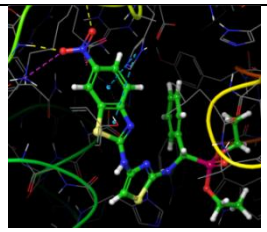
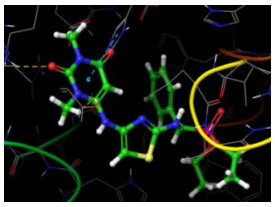
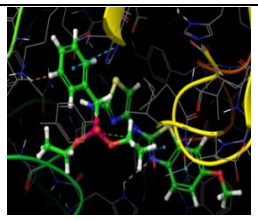
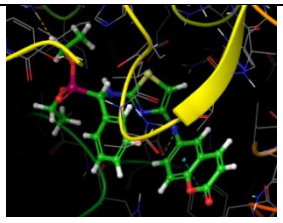
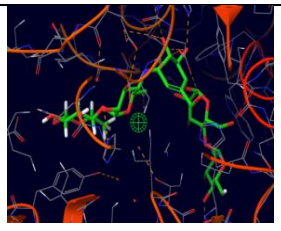
[a] Molecular weight; [b] The ratio of sp3 hybridized carbons over the total carbon count of the molecule; [c] Molar refractivity; [d] topological polar surface area (Å2); [e] lipophilicity; [f] water solubility (SILICOS-IT)

Table S2: Pharmacokinetic/ADME properties of compounds (**7a-j**)

Compd	[a]GI absorption	[b]BBB permeant	[c]Pgp substrate	[d]CYP1A2 inhibitor	[e]CYP2C19 inhibitor	[f]CYP2C9 inhibitor	[g]CYP2D6 inhibitor	[h]CYP3A4 inhibitor	[i]log Kp (cm/s)
7a	Low	No	No	Yes	Yes	Yes	No	Yes	-5.91
7b	Low	No	No	Yes	Yes	Yes	Yes	Yes	-5.64
7c	Low	No	No	No	Yes	Yes	Yes	Yes	-5.26
7d	Low	No	No	No	Yes	Yes	No	Yes	-5.66
7e	Low	No	No	Yes	Yes	Yes	Yes	Yes	-5.47
7f	Low	No	No	No	Yes	Yes	Yes	Yes	-5.02
7g	Low	No	Yes	No	No	No	No	Yes	-7.54
7h	Low	No	No	Yes	Yes	Yes	No	Yes	-5.83
7i	Low	No	Yes	No	No	Yes	No	Yes	-7.5
7j	Low	No	No	No	Yes	Yes	No	Yes	-5.9
Acarbose	Low	No	Yes	No	No	No	No	No	-16.29

[a]Gastro intestinal absorption; [b]blood brain barrier permeant; [c]p-glycoprotein substrate; [d]CYP1A2: Cytochrome P450 family 1 subfamily A member 2; [e]CYP2C19: Cytochrome P450 family 2 subfamily C member 19; [f]CYP2C9: Cytochrome P450 family 2 subfamily C member 9; [g]CYP2D6: Cytochrome P450 family 2 subfamily D member 6; [h]CYP3A4: Cytochrome P450 family 3 subfamily A member 4; [i]skin permeation in cm/s.

Table S3 : Bonding interactions of the title lead compounds (**7a-j**) and standard with *α*-amylase

Compd	Image	Binding energy (kcal /mol)	Compd	Image	Binding energy (kcal/mol)
7a		-7.7	**7f**		-7.9
7b		-8.2	**7g**		-8.2
7c		-7.9	**7h**		-7.9
7d		-7.8	**7i**		-8.1
7e		-8.4	**7j**		-8.2
			Std*		-8.2

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[2] Nickavar, B.; Amin, G. Enzyme assay guided isolation of an alpha-amylase inhibitor flavonoid from vaccinium arctostaphylos leaves. *Iran J. Pharm. Res.***2011**, *10*, 849-853..

[3] Patil, V. S.; Nandre, K. P.; Ghosh, S.; Rao, V. J.; Chopade, B. A.; Sridhar, B.; Bhosale, S. V.; Bhosale, S. V. Synthesis, crystal structure and anti-diabetic activity of substituted (E)-3-(benzo[d]thiazol-2-ylamino)phenylprop-2-en-1-one. *Eur. J. Med. Chem.***2013**, *59*, 304-309.