**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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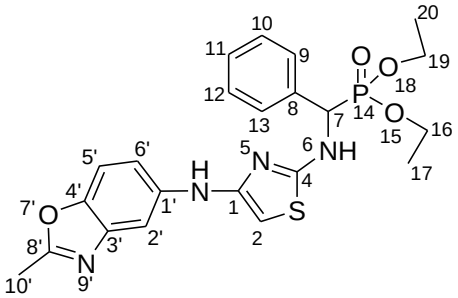
*2.2.1. Preparation of Nano $TiO_2/SiO_2$*[1]

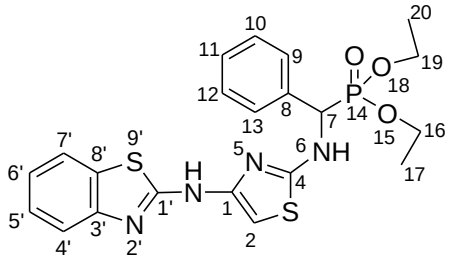
To a mixture of $SiO_2$ 60 (for column chromatography, mesh 70-230, 0.06-0.2 mm, 2 g) in 50 mL $CHCl_3$, nano $TiO_2$ (Anatase phase, 10-25 nm, 2 g) was added. The mixture was stirred at room temperature for 90 min. The solvent was evaporated at room temperature overnight to obtain a white solid of 50%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

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



Compound **7b**

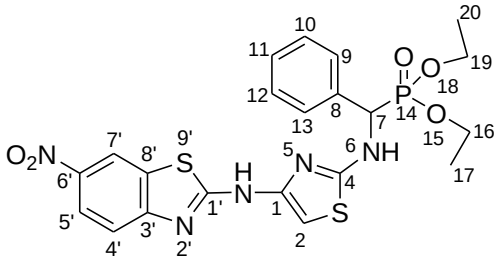
*Diethyl (4-(2-methylbenzo[d]oxazol-5-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7b**):* Solid. M.P. 171-173 °C. Yield: 90%. $\delta_H$ (DMSO-$d_6$): 9.42 (s, 1H, -NH), 7.24 (t, *J*=7.6 Hz,2H, Ar-H), 7.15 (t, *J*=7.6 Hz, 1H, Ar-H), 7.07 (d, *J*=7.2 Hz,2H, Ar-H), 7.03 (d, *J*=6.8 Hz,1H, Ar-H), 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-$CH_2\underline{CH_3}$); $\delta_C$ (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'); $\delta_P$ (DMSO-$d_6$): 19.5 ppm; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 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**

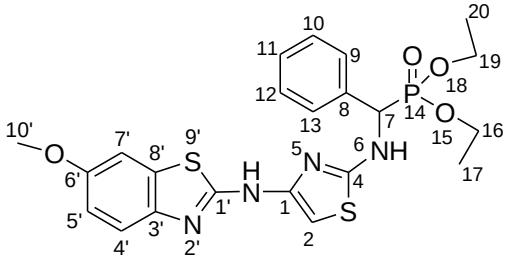
*Diethyl (4-(benzo[d]thiazol-2-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7c**):* Solid. M.P. 155-157 °C. Yield: 94%. $\delta_H$ (DMSO-$d_6$): 9.42 (s, 1H, -NH), 8.18 (d, *J*=8.0 Hz,1H, Ar-H), 8.06 (d, *J*=7.6 Hz,1H, Ar-H), 7.48 (t, *J*=7.2 Hz,2H, Ar-H), 7.24 (t, *J*=7.6 Hz,2H, Ar-H), 7.07 (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-$CH_2\underline{CH_3}$); $\delta_C$ (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'); $\delta_P$ (DMSO-$d_6$): 19.8 ppm; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 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%.



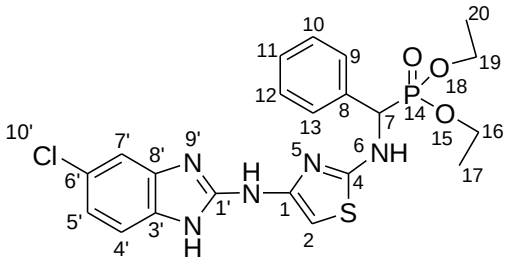
Compound **7d**

*Diethyl (4-(6-nitrobenzo[d]thiazol-2-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7d**):* Solid. M.P. 211-213 °C. Yield: 93%. $\delta_H$ (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-$CH_2\underline{CH_3}$); $\delta_C$ (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'); $\delta_P$ (DMSO-$d_6$): 22.4 ppm; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 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%.



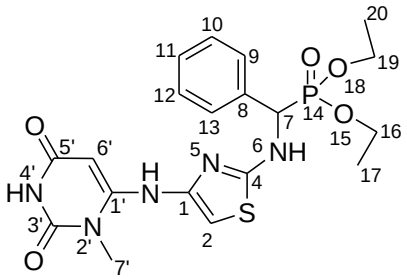
Compound **7e**

*Diethyl (4-(6-methoxybenzo[d]thiazol-2-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7e**):* Solid. M.P. 233-235 °C. Yield: 92%. $\delta_H$ (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-$CH_2\underline{CH_3}$); $\delta_C$ (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'); $\delta_P$ (DMSO-$d_6$): 20.5 ppm; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 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%.



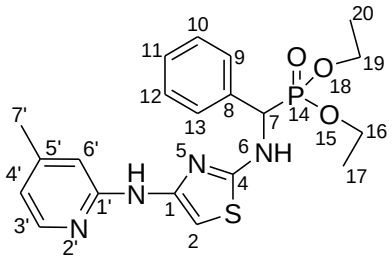
Compound **7f**

*Diethyl (4-(6-chlorobenzo[d]thiazol-2-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7f**)*. Solid. M.P. 196-198 °C. Yield: 95%. $\delta_H$ (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-$CH_2\underline{CH_3}$); $\delta_C$ (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'); $\delta_P$ (DMSO-$d_6$): 22.1 ppm; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 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%.



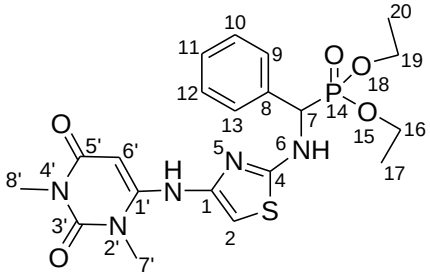
Compound **7g**

*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%. $\delta_H$ (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-$CH_2\underline{CH_3}$); $\delta_C$ (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'); $\delta_P$ (DMSO-$d_6$): 17.6 ppm; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 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%.



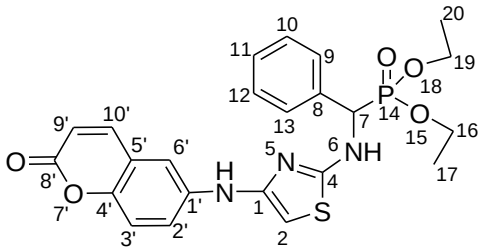
Compound **7h**

*Diethyl (4-(4-methylpyridin-2-ylamino)thiazol-2-ylamino)(phenyl)methylphosphonate (**7h**):* Solid. M.P. 214-216 °C. Yield: 93%. $\delta_H$ (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-$CH_2\underline{CH_3}$); $\delta_C$ (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'); $\delta_P$ (DMSO-$d_6$): 16.5 ppm; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 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%. $\delta_H$ (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-$CH_2\underline{CH_3}$); $\delta_C$ (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'); $\delta_P$ (DMSO-$d_6$): 18.2 ppm; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 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%. $\delta_H$ (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-$CH_2\underline{CH_3}$); $\delta_C$ (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'); $\delta_P$ (DMSO-$d_6$): 23.6 ppm; IR (KBr) ($\nu_{max}$ $cm^{-1}$): 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

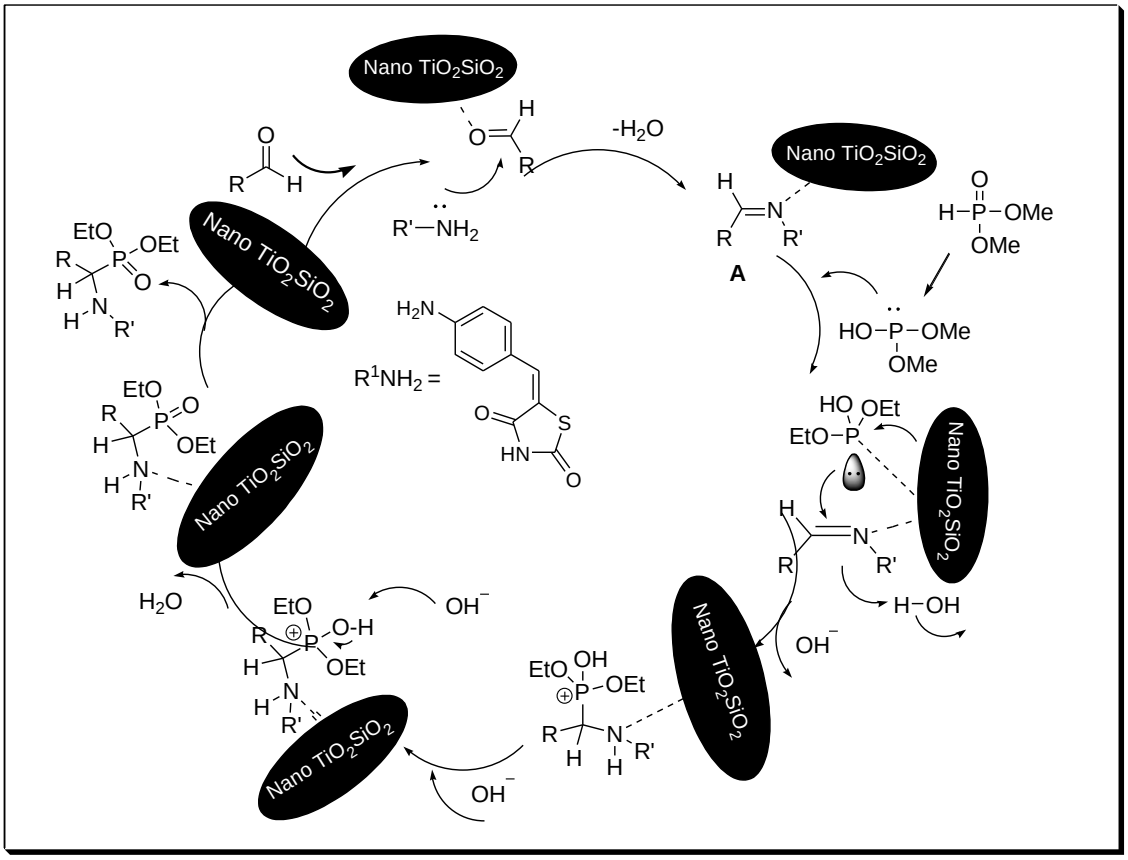



**Figure S1 :**Mechanism for the nano $TiO_2$.$SiO_2$ catalyzed synthesis of $\alpha$-Aps (**7a**-**j**)

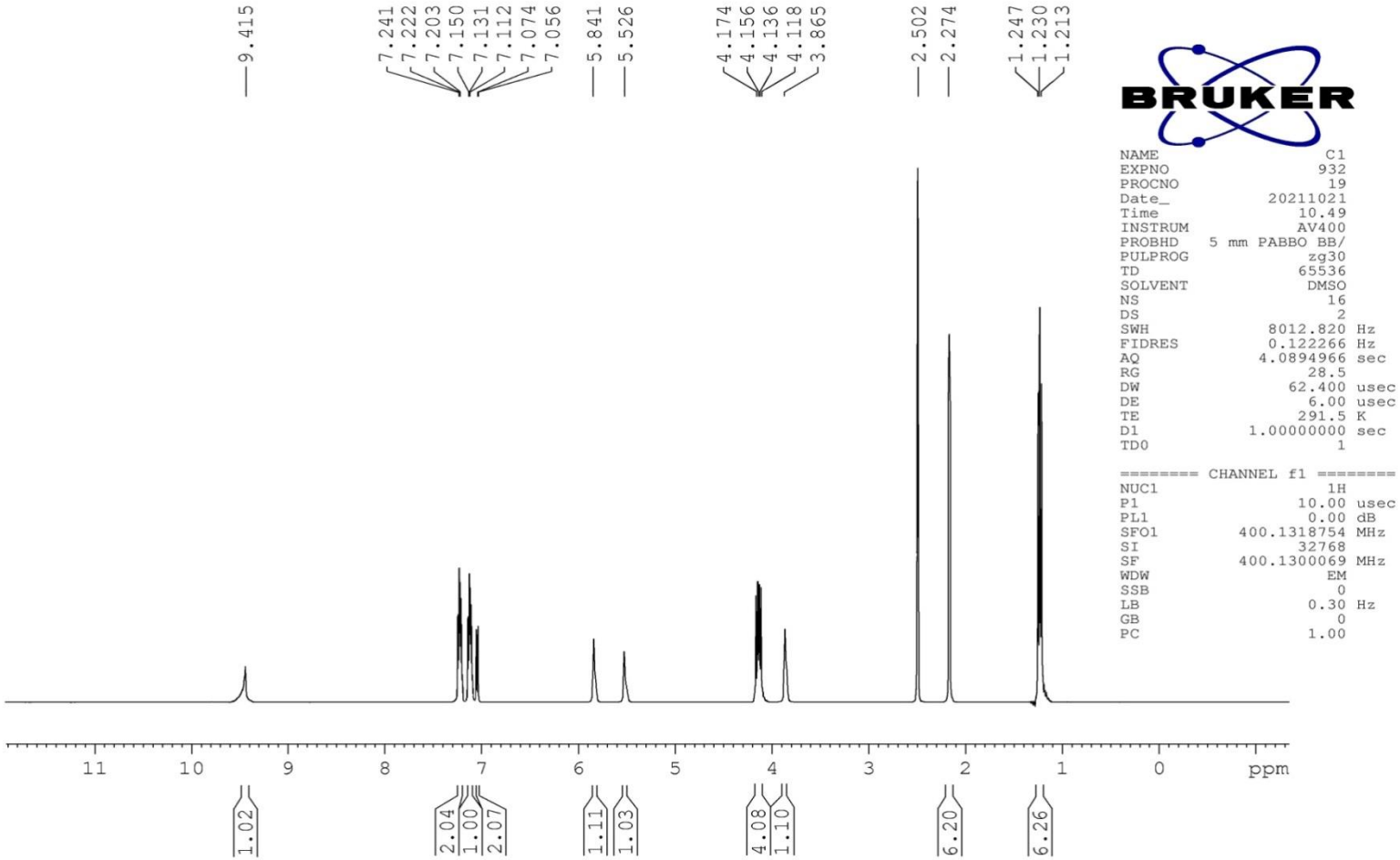



**Figure S2:** [1]H Spectrum of compound **7a**

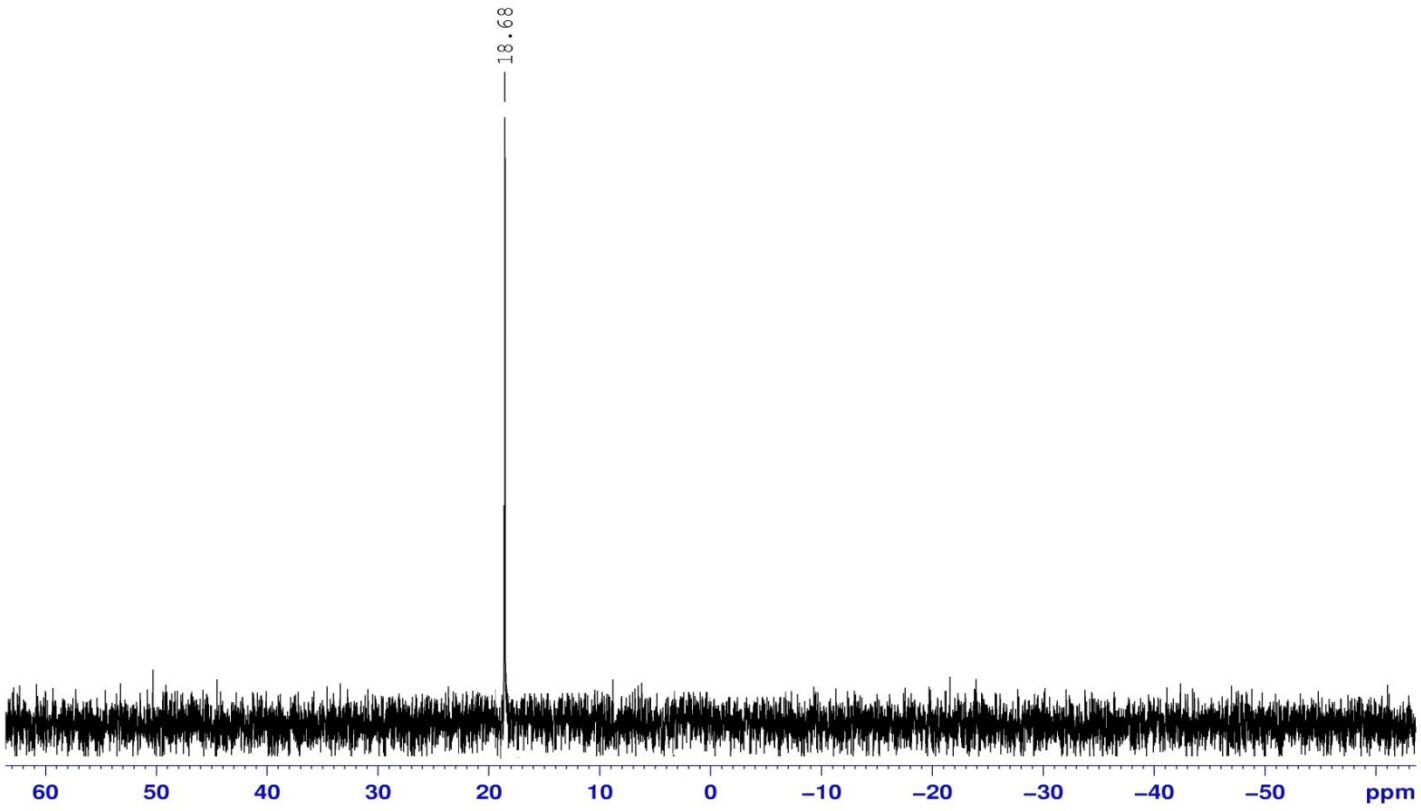



**Figure S3:** $^{31}$P Spectrum of compound **7a**

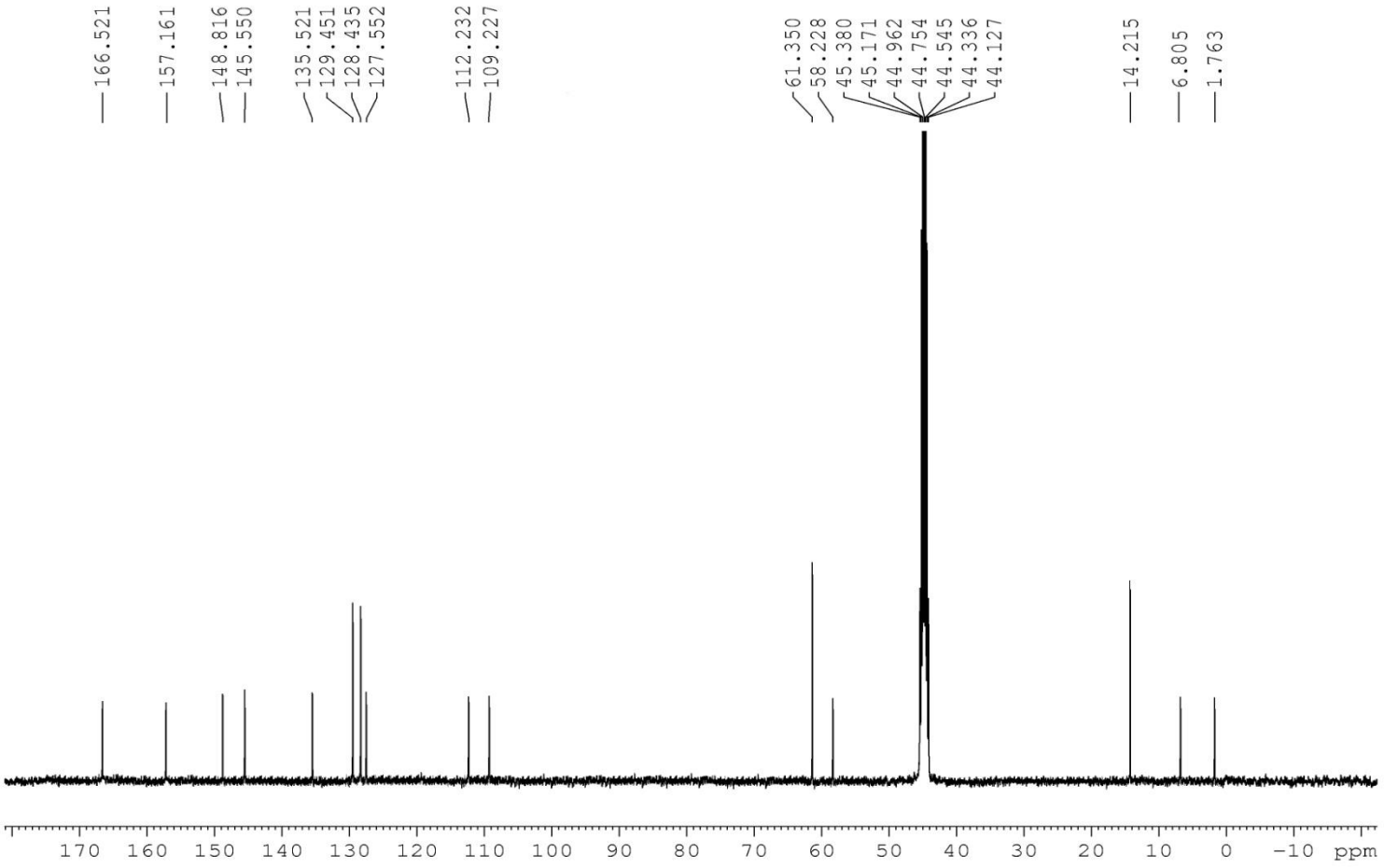



**Figure S4:** $^{13}$C NMR Spectrum of compound **7a**

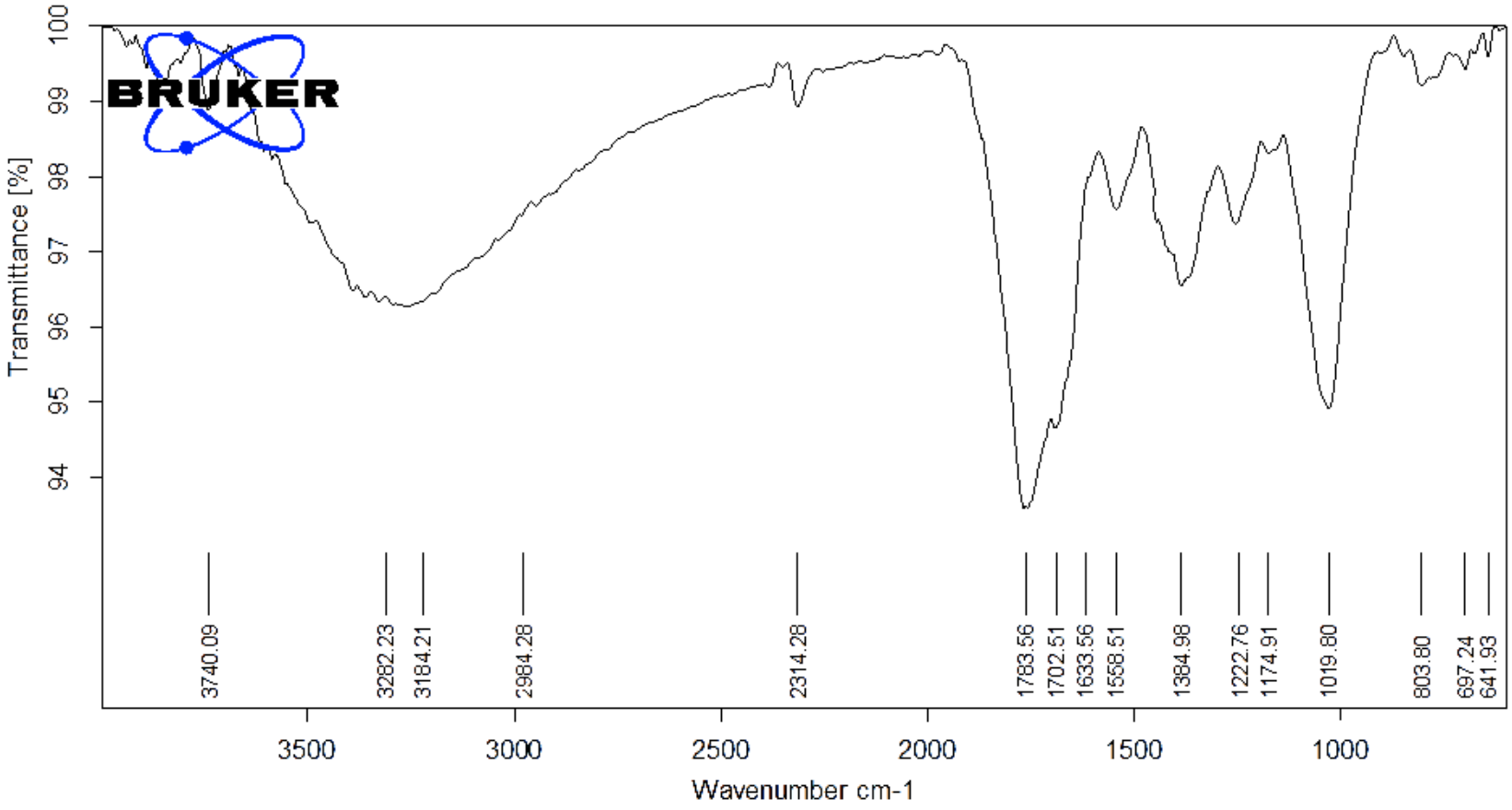
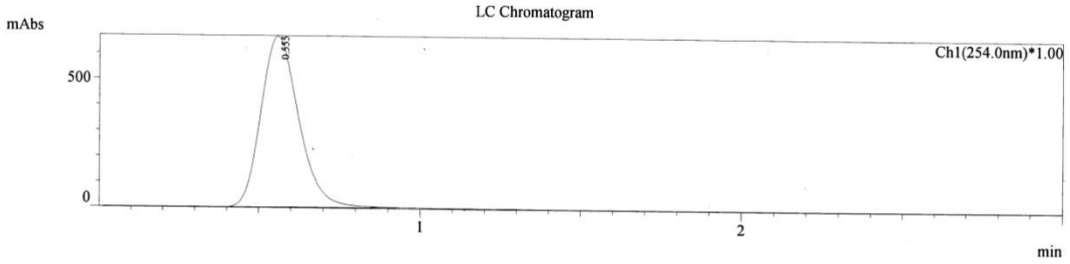
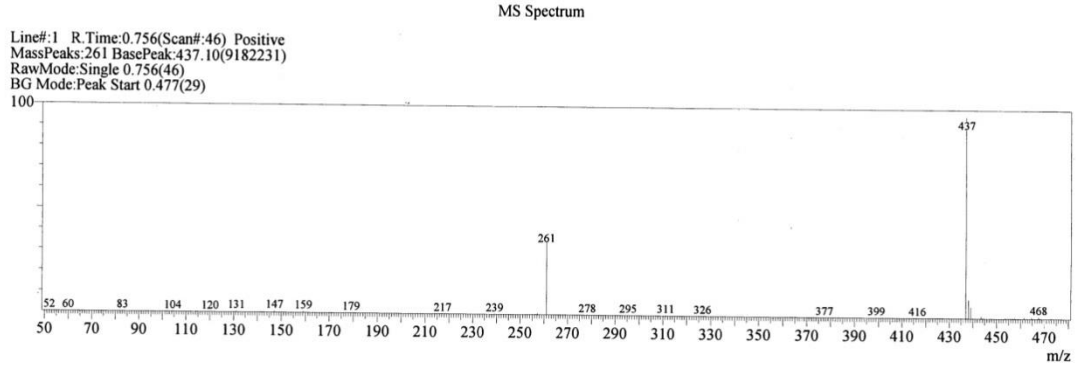



**Figure S5:** IR Spectrum of compound **7a**

**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 |



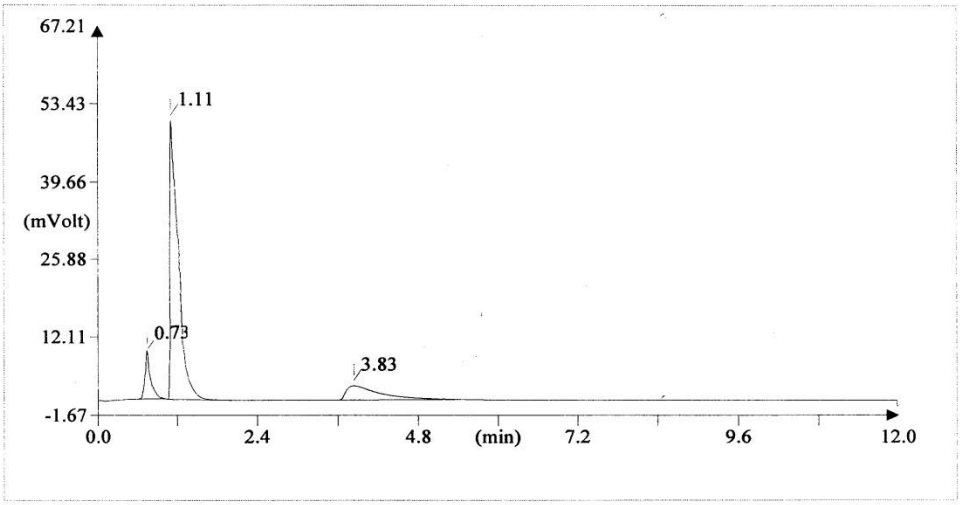

MS Peak Table

| 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**

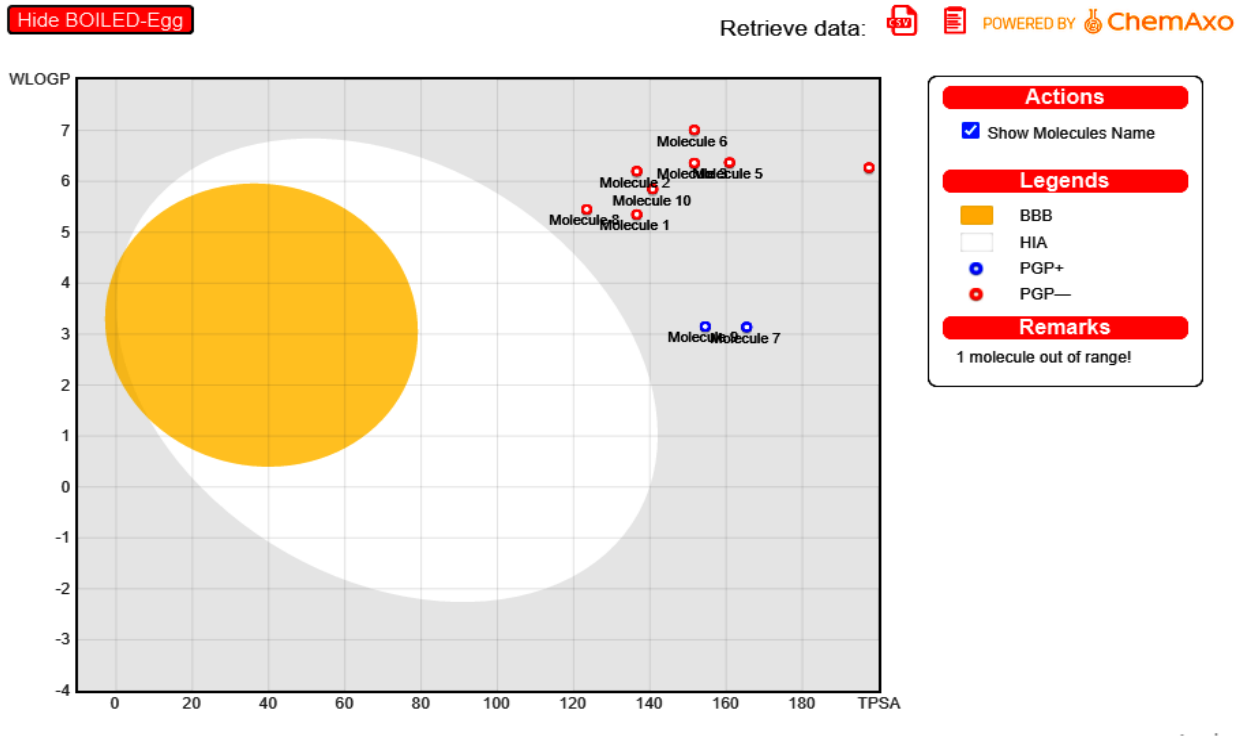



**Figure S8:** The BOILED-Eggdiagram of the tested molecules 1-10 (**7a-j**)

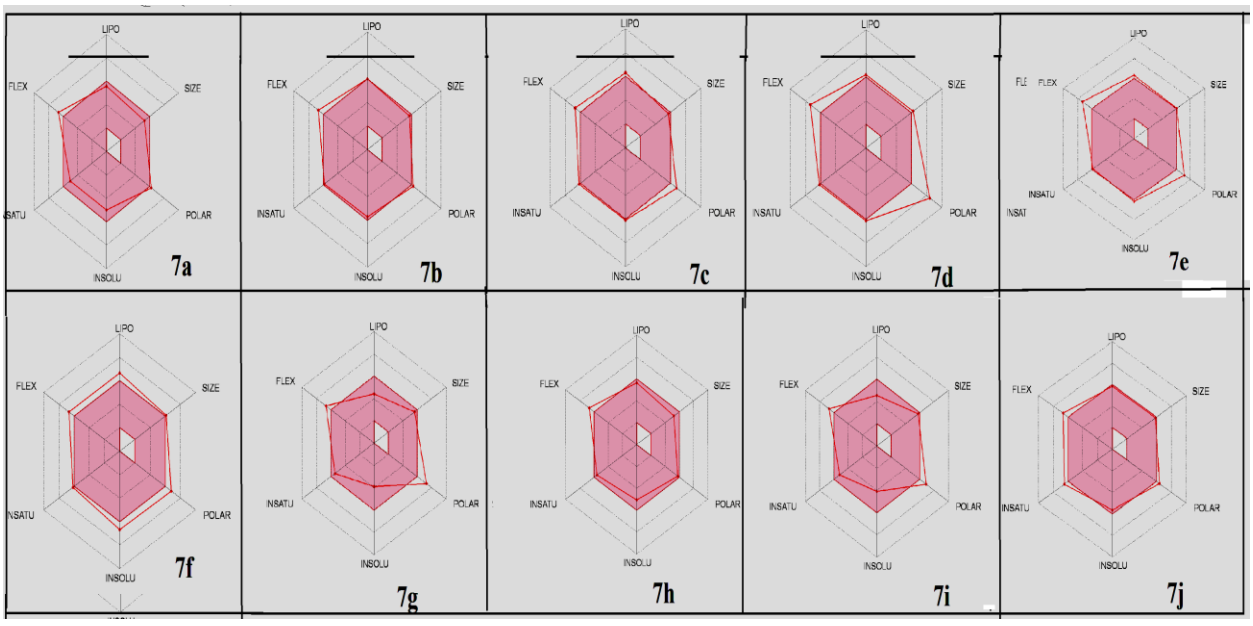



**Figure S9:** The bio radar map of the tested molecules (**7a-j**)

**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 |

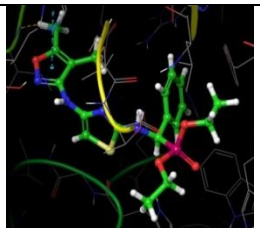
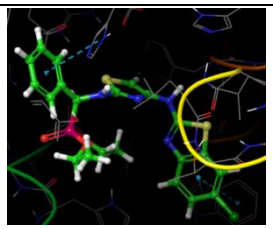
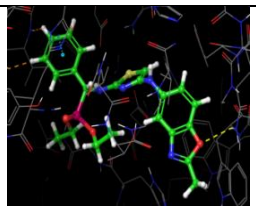
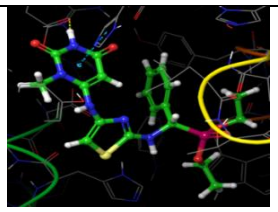
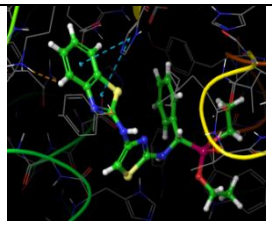
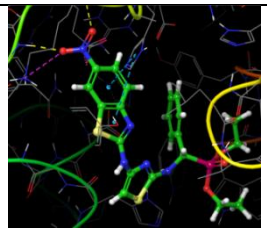
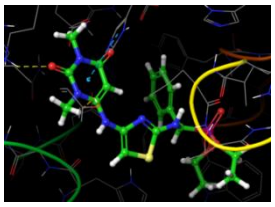
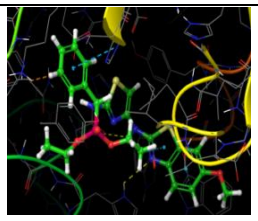
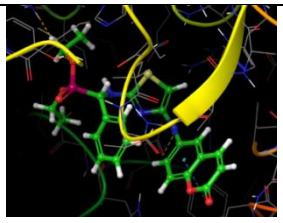
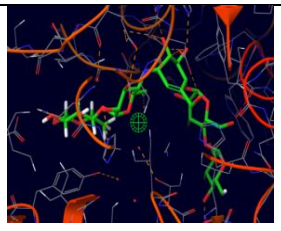
[a] Molecular weight; [b] The ratio of sp3 hybridized carbons over the total carbon count of the molecule; [c] Molar refractivity; [d] topological polar surface area (Å2); [e] lipophilicity; [f] water solubility (SILICOS-IT)

**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.