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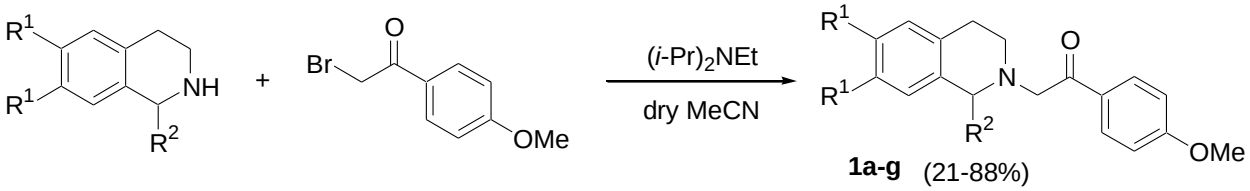
Reaction of benzyne with 1,2,3,4-tetrahydroisoquinolines as an access to 1*H*-3-benzazepines

Natalia I. Guranova, Alexey V. Varlamov, Roman A. Novikov, Alexander V. Aksenov, Tatiana N. Borisova, Elena A. Sorokina and Leonid G. Voskressensky

General information

Aryne precursor, 2-trimethylsilylphenyl trifluoromethanesulfonate (Sigma-Aldrich), was used as purchased. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AMX-400 (400 MHz for ^{1}H and 100.6 MHz for ^{13}C) and JEOL JNM ECA (600 MHz and 150.9 MHz, respectively) instruments. Proton chemical shifts are reported relative to the residual solvent peak ($CDCl_3$ at δ 7.26 ppm). Carbon chemical shifts are reported relative to $CDCl_3$ at δ 77.2 ppm. Mass spectra were recorded using LCMS-8040 Shimadzu (Japan) machine. ESI. IR spectra were recorded on FT spectrometer Infralum FT-801. For the elemental analyses, a Euro Vector EA-3000 apparatus was used. Melting points were measured on SMP 10 set in open capillaries. TLC on Sorbfil plates was used for the monitoring of reactions. Kieselgel from Macherey-Nagel GmbH&Co (0.04–0.06 mm/230–400 mesh), 60 Å, was used for column chromatography. All solvents were dried according to standard procedures.

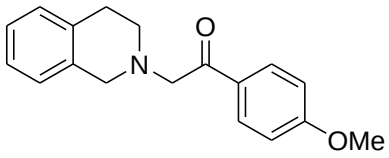
General procedure for the synthesis of tetrahydroisoquinolines 1a-g



1a-g (21-88%)

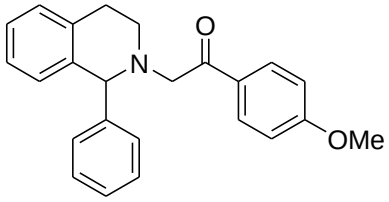
In 50 ml cone flask with dry acetonitrile (25 ml), *N*,*N*-diisopropylethylamine (1.2 equiv.) and then 1,2,3,4-tetrahydroisoquinoline (2.0g, 1 equiv.) were added. After the dissolution of the starting compound, 4-metoxyphenacyl bromide (1 equiv.) was added. Reaction proceeded at room temperature with TLC monitoring. In cases of **1c,d**, the products were precipitated from the reaction mixture. The precipitate was filtered off and washed 3 times with water (50 ml). In cases of isoquinolines **1a,b,e-g** the solvent was removed under vacuum and ethyl acetate (50 ml)

was added to the crude product. The precipitate of *N*-ethyl-*N*,*N*-diisopropylethylammonium bromide was filtered off and washed with ethyl acetate (30 ml). The solvent was removed under the vacuum. The powder residue was recrystallized from EtOAc-hexane.



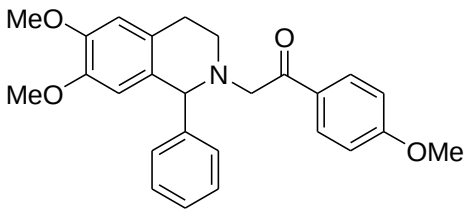
2-(3,4-Dihydroisoquinolin-2(1*H*)-yl)-1-(4-methoxyphenyl)-ethan-1-one (1a)

Yellow powder. Yield 59% (1.23 g). Mp 94-96°C (EtOAc-hexane). NMR ^{1}H (400 MHz, $CDC1_3$), δ, ppm (*J*, Hz): 2.92-2.96 (m, 4H, CH_2), 3.84 (s, 2H, CH_2), 3.87 (s, 3H, OCH_3), 3.96 (s, 2H, CH_2CO), 6.94 (d, *J*=8.8, 2H, Ar), 7.02 (d, *J* = 5.9, 1H, Ar), 7.13-7.15 (m, 3H, Ar), 8.09 (d, 2H, Ar). NMR ^{13}C (100 MHz), δ, ppm: 28.7, 50.9, 55.3, 55.8, 64.1, 113.6 (2C), 125.5, 126.1, 126.4, 128.6, 128.9, 130.6 (2C), 133.8, 134.1, 163.5, 195.1. IR spectra, ν (KBr), cm^{-1}: 1677 (C=O). ESI MS 282 $[M+H]^+$. Analysis [Found, %: C, 76.96; H, 6.94; N, 4.88. $C_{18}H_{19}NO_2$. Calc., %: C, 76.84; H, 6.81; N, 4.98].



1-(4-Methoxyphenyl)-2-(1-phenyl-3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one (1b)

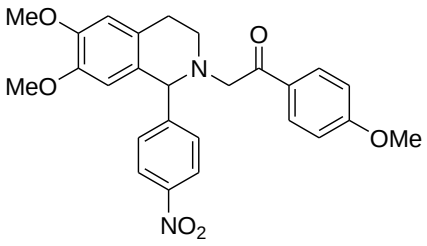
White powder. Yield 21% (0.355 g). Mp 125-128°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDC1_3$), δ, ppm (*J*, Hz): 2.76-2.95 (m, 2H, CH_2), 3.07-3.19 (m, 2H, CH_2), 3.58 (d, *J* = 15.8, 1H, CH_2CO), 3.83 (s, 3H, OCH_3), 3.97 (d, *J* = 15.8, 1H, CH_2CO), 4.84 (br. s., 1H, CH), 6.69 (d, *J* = 7.7, 1H, Ar), 6.84 (d, *J* = 8.8, 2H, Ar), 7.00 (t, *J* = 8.1, 1H, Ar), 7.06-7.16 (m, 2H, Ar), 7.25-7.35 (m, 5H, Ar), 7.87 (d, *J* = 8.8, 2H, Ar). NMR ^{13}C (150 MHz), δ, ppm: 29.1, 48.6, 55.5, 61.3, 68.4, 113.6 (2C), 125.8, 126.2, 127.7, 128.5 (2C), 128.5, 128.9, 129.2, 130.1 (2C), 130.9 (2C), 134.6, 138.0, 143.3, 163.6, 196.7. IR spectra, ν (KBr), cm^{-1}: 1679 (C=O). ESI MS 358 $[M+H]^+$. Analysis [Found, %: C, 80.77; H, 6.65; N, 3.80; $C_{24}H_{23}NO_2$. Calc., %: C, 80.64; H, 6.49; N, 3.92].



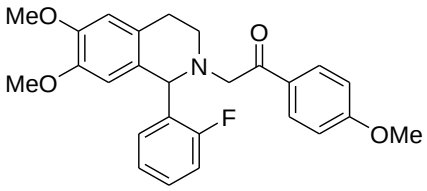
2-(6,7-Dimethoxy-1-phenyl-3,4-dihydroisoquinolin-2(1*H*)-yl-1-(4-methoxyphenyl)ethan-1-one (1c)

White powder. Yield 67% (3.1 g). Mp 121-123°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDC1_3$), δ, ppm (*J*, Hz): 2.72 (d.t, *J* = 15.8, *J* = 4.1, 1H, CH_2), 2.76-2.85 (m, 1H, CH_2), 2.90-2.99 (m, 1H, CH_2), 3.04-3.12 (m, 1H, CH_2), 3.53-3.58 (m, 4H, CH_2CO, OCH_3), 3.80 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.92 (d, *J* = 15.8, 1H, CH_2CO), 4.71 (s, 1H, CH), 6.13 (s, 1H, Ar), 6.57 (s, 1H, Ar), 6.81 (d, *J* = 8.9, 2H, Ar), 7.21-7.25 (m, 1H, Ar), 7.28 (d, *J* = 4.1, 4H, Ar), 7.84 (d, *J* = 8.9, 2H, Ar). NMR ^{13}C (150 MHz), δ, ppm: 48.2, 55.5 (2C), 55.9 (2C), 61.1, 67.6, 110.9, 111.8, 113.6 (2C), 126.8, 127.7, 128.4 (2C), 129.2, 129.9 (2C), 130.9 (2C), 132.2, 143.3, 147.2, 147.6, 163.6,

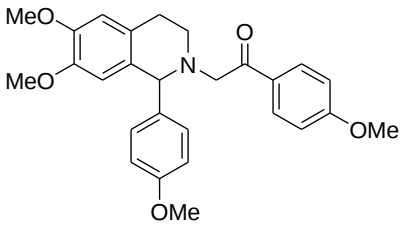
196.7. IR spectra, ν (KBr), cm^{-1}: 1681 (C=O). ESI MS 418 $[M+H]^+$. Analysis [Found, %: C, 74.93; H, 6.67; N, 3.21; $C_{26}H_{27}NO_4$. Calc., %: C, 74.80; H, 6.52; N, 3.35].



2-[6,7-Dimethoxy-1-(4-nitrophenyl)-3,4-dihydroisoquinolin-2(1*H*)-yl]-1-(4-methoxyphenyl)ethan-1-one (1d) Yellowish powder. Yield 88% (3.3 g). Mp 127-130°C (EtOAc-hexane). NMR ^1H (600 MHz, $CDC1_3$), δ, ppm (*J*, Hz): 2.75-2.81 (m, 1H, CH_2), 2.86-2.94 (m, 2H, CH_2), 3.01-3.08 (m, 1H, CH_2), 3.57 (s, 3H, OCH_3), 3.74 (d, *J* = 16.5, 1H, CH_2CO), 3.79 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.91 (d, *J* = 16.5, 1H, CH_2CO), 4.93 (s, 1H, CH), 6.09 (s, 1H, Ar), 6.60 (s, 1H, Ar), 6.82 (d, *J* = 8.9, 2H, Ar), 7.46 (d, *J* = 8.9, 2H, Ar), 7.81 (d, *J* = 8.9, 2H, Ar), 8.08 (d, *J*=8.2, 2H, Ar). NMR ^{13}C (150 MHz), δ, ppm: 27.3, 47.5, 55.6 (2C), 55.9 (2C), 60.2, 65.7, 111.3, 111.5, 113.8, 123.6, 126.9, 127.3, 128.9, 130.5 (2C), 130.6 (2C), 132.2, 147.4, 147.5, 148.1, 151.6, 163.8, 195.9. IR spectra, ν (KBr), cm^{-1}: 1682 (C=O), 1518, 1355 (NO_2). ESI MS 463 $[M+H]^+$. Analysis [Found, %: C, 67.68; H, 5.81; N, 5.93; $C_{26}H_{26}N_2O_6$. Calc., %: C, 67.52; H, 5.67; N, 6.06].

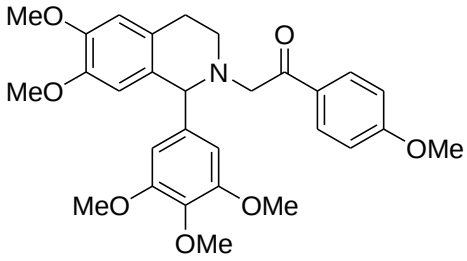


2-[1-(2-Fluorophenyl)-6,7-dimethoxy-3,4-dihydroisoquinolin-2(1*H*)-yl]-1-(4-methoxyphenyl)ethan-1-one (1e) Almost white powder. Yield 62% (1.42 g). Mp 126-129°C (EtOAc-hexane). NMR ^1H (400 MHz, $CDC1_3$), δ, ppm (*J*, Hz): 2.77-2.81 (m, 1H, CH_2), 2.87-3.05 (m, 2H, CH_2), 3.08-3.19 (m, 1H, CH_2), 3.63 (s, 3H, OCH_3), 3.68 (d, *J* = 16.1, 1H, CH_2CO), 3.86 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.98 (d, *J* = 15.6, 1H, CH_2CO), 4.83 (br.s., 1H, CH), 6.15 (s, 1H, Ar), 6.62 (s, 1H, Ar), 6.87 (d, *J*=8.8, 2H, Ar), 7.01 (t, *J*=8.6, 2H, Ar), 7.24-7.34 (m, 2H, Ar), 7.88 (d, *J* = 8.8, 2H, Ar). NMR ^{13}C (150 MHz), δ, ppm: 27.9, 47.9, 55.5, 55.9 (2C), 60.8, 66.5, 111.0, 111.7, 113.6 (2C), 115.1, 115.3, 126.8, 129.2, 130.7 (2C), 131.3, 131.4, 139.3, 147.3, 147.7, 161.4, 163.0, 163.6, 196.5. IR spectra, ν (KBr), cm^{-1}: 1680 (C=O). ESI MS 436 $[M+H]^+$. Analysis [Found, %: C, 71.88; H, 6.15; N, 3.08; $C_{26}H_{26}FNO_4$. Calc., %: C, 71.71; H, 6.02; N, 3.22].



2-[6,7-Dimethoxy-1-(4-methoxyphenyl)-3,4-dihydroisoquinolin-2(1*H*)-yl]-1-(4-methoxyphenyl)ethan-1-one (1f) Almost white powder. Yield 43% (0.635 g). Mp 117-119°C. NMR ^1H (600 MHz, $CDC1_3$), δ, ppm (*J*, Hz): 2.72 (d.t, *J* =

15.8, J = 4.2, 1H, CH_2), 2.77-2.85 (m, 1H, CH_2), 2.91-3.00 (m, 1H, CH_2), 3.06 - 3.13 (m, 1H, CH_2), 3.56 (d, J = 15.8, 1H, CH_2CO), 3.59 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.94 (d, J = 15.8, 1H, CH_2CO), 4.69 (s, 1H, CH), 6.16 (s, 1H, Ar), 6.58 (s, 1H, Ar), 6.83 (d.d, J = 8.8, J = 2.2, 4H, Ar), 7.20 (d, J = 8.8, 2H, Ar), 7.87 (d, J = 8.8, 2H, Ar). NMR ^{13}C (150 MHz), δ, ppm: 28.3, 48.3, 55.3, 55.5 (2C), 55.9, 61.2, 67.1, 110.9, 111.8, 113.5 (2C), 113.7 (2C), 126.8, 129.3, 130.0, 130.9 (2C), 131.0 (2C), 135.4, 147.2, 147.6, 159.0, 163.5, 196.9. IR spectra, ν (KBr), cm^{-1}: 1682 (C=O). ESI MS 448 $[M+H]^+$. Analysis [Found, %: C, 72.58; H, 6.67; N, 2.98; $C_{27}H_{29}NO_5$. Calc., %: C, 72.46; H, 6.53; N, 3.13].



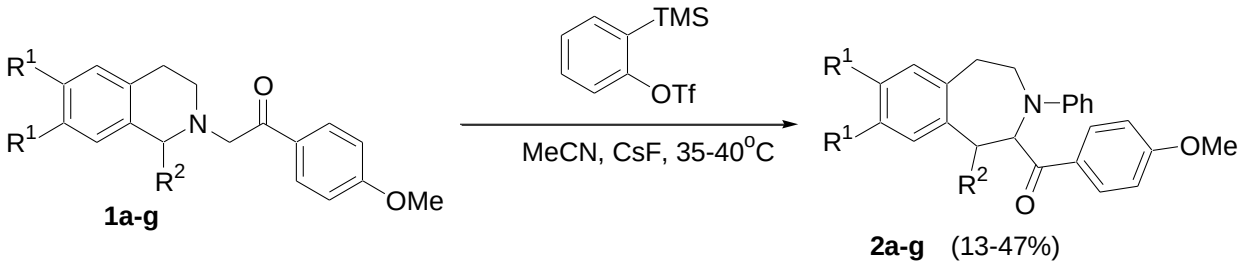
2-[6,7-Dimethoxy-1-(3,4,5-trimethoxyphenyl)-3,4-dihydroisoquinolin-2(1*H*)-yl]-1-(4-methoxyphenyl)-ethan-1-one (1g)

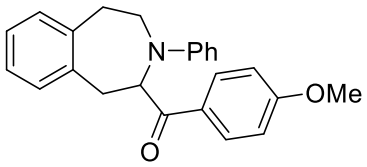
Beige powder. Yield 53% (0.378 g). Mp 112-114°C (EtOAc-hexane). NMR ^1H (600 MHz, $CDC1_3$), δ, ppm (J, Hz): 2.72 (d.t, J = 16.1, J = 4.1, 1H, CH_2), 2.83-2.88 (m, 1H, CH_2), 2.96-3.00 (m, J = 9.9, 1H, CH_2), 3.09-3.17 (m, 1H, CH_2), 3.59-3.62 (m, 4H, OCH_3, CH_2CO), 3.72 (s, 6H, OCH_3), 3.80 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.93 (d, J = 16.1, 1H, CH_2CO), 4.66 (br. s, 1H, CH), 6.21 (s, 1H, Ar), 6.49 (s, 2H, Ar), 6.57 (s, 1H, Ar), 6.82 (d, J = 8.8, 2H, Ar), 7.87 (d, J = 8.8, 2H, Ar). NMR ^{13}C (150 MHz), δ, ppm: 28.1, 48.7, 55.5, 55.9, 56.0, 56.2 (2C), 60.9, 67.9, 106.9, 110.9, 111.7, 113.5 (4C), 126.7, 129.2, 130.8 (4C), 132.0, 137.4, 147.2, 147.7, 153.1 (2C), 163.6. IR spectra, ν (KBr), cm^{-1}: 1679 (C=O). ESI MS 508 $[M+H]^+$. Analysis [Found, %: C, 68.76; H, 6.69; N, 2.61; $C_{29}H_{33}NO_7$. Calc., %: C, 68.62; H, 6.55; N, 2.76].

Reactions of tetrahydroisoquinolines 1 with benzyne

(7,8-Dimethoxy-1,3-diphenyl-2,3,4,5-tetrahydro-1*H*-benz[*d*]azepin-2-yl)(4-methoxy-phenyl)methanone (2c). To a suspension of CsF (0.105g, 3eq.) in dry acetonitrile (5 ml) dihydroisoquinoline **1c** (0.100g, 0.23 mmol, 1 equiv.) was added. After dissolution of the starting material, 2-trimethylsilylphenyl trifluoromethanesulfonate (0.27 mmol, 1.2 equiv.) was added. The mixture was stirred at 35°C with TLC monitoring (Sorbfil, EtOAc-hexane, 1:3). The solvent was removed under reduced pressure. To the oily residue, chloroform (5 ml) was added, and the precipitate of CsOTf was filtered off and washed several times with $CHCl_3$. The solvent was removed, the crude oily material was purified on SiO_2 (glass column, H=100 mm, d=15 mm),

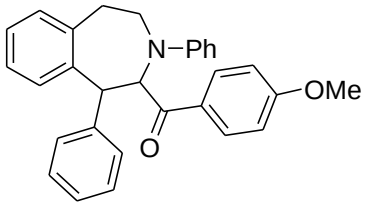
eluent EtOAc-hexane, 1:5. Tetrahydro-1*H*-benz[*d*]azepines **2a,b,d-g** were synthesized by the same protocol.





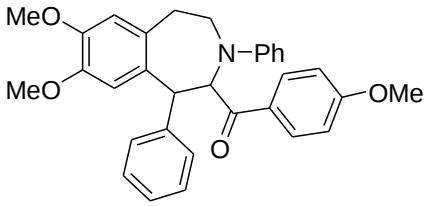
(4-Methoxyphenyl)(3-phenyl-2,3,4,5-tetrahydro-1*H*-benz-[*d*]azepin-2-yl)methanone (2a)

White powder. Yield 26% (0.050 g). Mp 105-107°C (EtOAc-hexane). NMR ^{1}H (400 MHz, CDC1$_3$), δ, ppm (*J*, Hz): 3.16 (t, *J* = 5.4, 2H, CH_2), 3.84 (s, 3H, OCH_3), 4.03 (t, *J* = 5.4, 2H, CH_2), 4.99 (s, 2H, CH_2), 6.02 (s, 1H, CH), 6.84 - 6.93 (m, 3H, Ar), 6.97 (d, *J* = 8.8, 2H, Ar), 7.13 - 7.41 (m, 6H, Ar), 7.49 (d, *J* = 8.8, 2H, Ar). NMR ^{13}C (100 MHz, CDC1$_3$), δ, ppm: 32.8, 50.0, 55.3, 71.7, 113.5, 113.7 (2C), 114.4, 118.7, 126.1 (2C), 126.6, 128.5, 129.3 (2C), 130.2, 130.4, 135.5, 140.8, 142.4, 146.4, 159.0, 160.9, 195.1. IR spectra, ν (KBr), cm^{-1}: 1604 (C=O). ESI MS 358 $[M+H]^+$. Analysis [Found, %: C, 80.77; H, 6.63; N, 3.81; $C_{24}H_{23}NO_2$. Calc., %: C, 80.64; H, 6.49; N, 3.92].



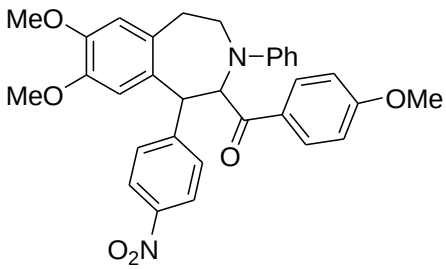
(1,3-Diphenyl-2,3,4,5-tetrahydro-1*H*-benz[*d*]azepin-2-yl)(4-methoxyphenyl)methanone (2b)

Yellowish powder. Yield 43% (0.052 g). Mp 65-66°C (EtOAc-hexane). NMR ^{1}H (600 MHz, CDC1$_3$), δ, ppm (*J*, Hz): 3.05-3.10 (m, 1H, CH_2), 3.36-3.40 (m, 1H, CH_2), 3.59-3.68 (m, 1H, CH_2), 3.72-3.80 (m, 4H, CH_2, OCH_3), 5.48 (d, *J* = 8.8, 1H, CH), 5.69 (d, *J* = 8.8, 1H, CH), 6.62 (t, *J* = 7.2, 1H, Ar), 6.68 (d, *J* = 8.1, 2H, Ar), 6.77 (d, *J* = 8.8, 2H, Ar), 6.87-6.91 (m, 1H, Ar), 7.00-7.07 (m, 5H, Ar), 7.22-7.26 (m, 1H, Ar), 7.34 (t, *J* = 7.5, 2H, Ar), 7.41 (d, *J* = 7.7, 2H, Ar), 7.76 (d, *J* = 8.8, 2H, Ar). NMR ^{13}C (150 MHz, CDC1$_3$), δ, ppm: 34.1, 48.9, 55.5, 65.4, 113.7 (2C), 115.7 (2C), 118.4, 126.6, 127.8, 126.9, 128.5, 128.8 (2C), 129.0 (3C), 129.4, 129.5 (2C), 129.7, 130.7 (2C), 138.3, 140.4, 140.8, 150.1, 163.5, 195.1. IR spectra, ν (KBr), cm^{-1}: 1672 (C=O). ESI MS 434 $[M+H]^+$. Analysis [Found, %: C, 83.25; H, 6.42; N, 3.12; $C_{30}H_{27}NO_2$. Calc., %: C, 83.11; H, 6.28; N, 3.23].



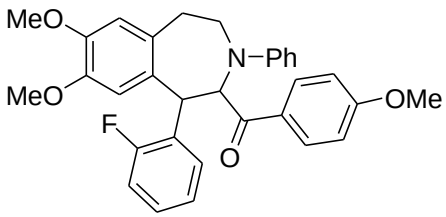
(7,8-Dimethoxy-1,3-diphenyl-2,3,4,5-tetrahydro-1*H*-benz[*d*]azepin-2-yl)(4-methoxyphenyl)methanone (2c)

White powder. Yield 47% (0.107 g). Mp 107-110°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDC1_3$), δ, ppm (*J*, Hz): 1.19-1.34 (m, 1H, CH_2), 3.02-3.07 (m, 1H, CH_2), 3.62 (s, 3H, OCH_3), 3.63-3.68 (m, 1H, CH_2), 3.71-3.76 (m, 1H, CH_2), 3.77 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 5.33 (d, *J* = 8.3, 1H, CH), 5.60 (d, *J* = 8.3, 1H, CH), 6.42 (s, 1H, Ar), 6.57 (s, 1H, Ar), 6.62 (t, *J* = 7.0, 1H, Ar), 6.70 (d, *J* = 7.4, 2H, Ar), 6.76 (d, *J*=9.1, 2H, Ar), 7.04 (t, *J*=7.8, 2H, Ar), 7.17-7.21 (m, 1H, Ar), 7.26-7.30 (m, 2H, Ar), 7.31-7.34 (m, 2H, Ar), 7.74 (d, *J*=9.1, 2H, Ar). NMR ^{13}C (100 MHz, $CDC1_3$), δ, ppm: 33.9, 45.3, 49.2, 55.4, 55.8, 55.9, 56.0, 65.6, 113.4, 113.5 (2C), 113.6, 115.4 (2C), 118.2, 126.7, 128.6, 128.9 (2C), 129.0, 129.5, 129.7, 130.1, 130.5 (2C), 130.6, 130.8, 132.2, 141.2, 149.9, 163.3, 195.8. IR spectra, ν (KBr), cm^{-1}: 1683 (C=O). ESI MS 494 $[M+H]^+$. Analysis [Found, %: C, 78.01; H, 6.45; N, 2.88; $C_{32}H_{31}NO_4$. Calc., %: C, 77.87; H, 6.33; N, 2.74].



[7,8-Dimethoxy-1-(4-nitrophenyl)-3-phenyl-2,3,4,5-tetrahydro-1*H*-benz[*d*]azepin-2-yl](4-methoxyphenyl)-methanone (2d)

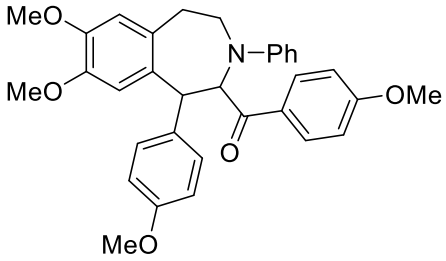
Yellow powder. Yield 38% (0.060 g). Mp 89-92°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDC1_3$), δ, ppm (*J*, Hz): 1.21-1.33 (m, 1H, CH_2), 3.08 (t, *J* = 6.2, 2H, CH_2), 3.56-3.64 (m, 1H, CH_2), 3.66 (s, 3H, OCH_3), 3.79 (s, 6H, OCH_3), 5.42 (d, *J* = 8.3, 1H, CH), 5.53 (d, *J* = 8.3, 1H, CH), 6.39 (s, 1H, Ar), 6.57-6.65 (m, 4H, Ar), 6.79 (d, *J* = 9.1, 2H, Ar), 7.03 (t, *J* = 7.8, 2H, Ar), 7.44 (d, *J*=9.1, 2H, Ar), 7.75 (d, *J*=9.1, 2H, Ar), 8.11 (d, *J*=9.1, 2H, Ar). NMR ^{13}C (150 MHz, $CDC1_3$), δ, ppm: 34.2, 50.3, 55.5, 56.0, 56.1, 66.1, 113.6 (2C), 113.8 (2C), 114.4, 115.5 (2C), 118.7, 123.8 (2C), 128.5, 128.9 (2C), 129.1 (2C), 129.8 (2C), 130.6 (2C), 131.4, 132.4, 146.7, 147.7, 147.9, 149.3, 195.3. IR spectra, ν (KBr), cm^{-1}: 1674 (C=O), 1598, 1345 (NO_2). ESI MS 539 $[M+H]^+$. Analysis [Found, %: C, 71.51; H, 5.75; N, 5.08; $C_{32}H_{30}N_2O_6$. Calc., %: C, 71.36; H, 5.61; N, 5.20].



[1-(2-Fluorophenyl)-7,8-dimethoxy-3-phenyl-2,3,4,5-tetrahydro-1*H*-benz[*d*]azepin-2-yl](4-methoxyphenyl)-methanone (2e)

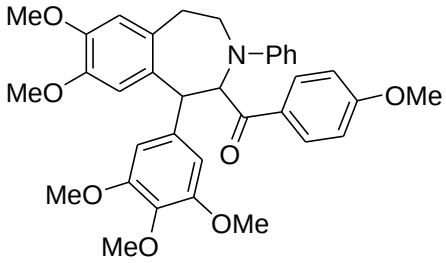
Yellow oil. Yield 13% (0.016 g). R_f 0.71 (EtOAc-hexane, 1:5). NMR ^{1}H (400 MHz, $CDC1_3$), δ, ppm (*J*, Hz): 2.99-3.12 (m, 1H, CH_2), 3.14-3.26 (m, 1H, CH_2), 3.60-3.65 (m, 1H, CH_2), 3.67 (s, 3H, OCH_3), 3.70-3.78 (m, 1H, CH_2), 3.80 (s, 6H, OCH_3), 5.34 (d, *J*=8.3, 1H, CH), 5.55 (d, *J* = 8.3, 1H, CH), 6.43

(s, 1H, Ar), 6.59 (s, 1H, Ar), 6.61 - 6.69 (m, 3H, Ar), 6.80 (d, *J* = 8.8, 3H, Ar), 6.96-7.10 (m, 2H, Ar), 7.28-7.33 (m, 3H, Ar), 7.77 (d, *J* = 8.3, 2H, Ar). NMR ^{13}C (100 MHz, CDC1$_3$), δ, ppm: 22.5, 33.8, 48.5, 65.3, 55.8, 55.9, 65.7, 113.1, 113.5 (2C), 115.2, 115.3 (2C), 115.4, 118.2, 120.4, 124.4, 128.8 (2C), 130.3, 130.4 (2C), 130.9, 131.9, 132.5, 147.2, 147.3, 149.5, 159.9, 162.5, 163.3, 195.7. IR spectra, ν (film), cm^{-1}: 1673 (C=O). ESI MS 512 [M+H]$^+$. Analysis [Found, %: C, 75.51; H, 6.25; N, 2.48; $C_{32}H_{30}FNO_4$. Calc., %: C, 75.13; H, 5.91; N, 2.74].



[7,8-Dimethoxy-1-(4-methoxyphenyl)-3-phenyl-2,3,4,5-tetrahydro-1*H*-benz[*d*]azepin-2-yl](4-methoxyphenyl)-methanone (2f)

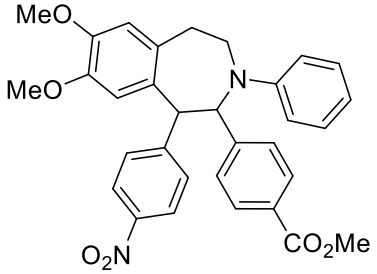
Yellow oil. Yield 30% (0.035 g). R_f 0,45 (EtOAc-hexane, 1:3). NMR ^{1}H (600 MHz, CDC1$_3$), δ, ppm (*J*, Hz): 2.99-3.04 (m, 1H, CH_2), 3.17-3.25 (m, 1H, CH_2), 3.58-3.65 (m, 4H, CH_2, OCH_3), 3.68-3.74 (m, 1H, CH_2), 3.76 (s, 6H, OCH_3), 3.77 (s, 3H, OCH_3), 5.28 (d, *J* = 8.4, 1H, CH), 5.55 (d, *J* = 8.4, 1H, CH), 6.44 (s, 1H, Ar), 6.55 (s, 1H, Ar), 6.60 (t, *J*=7.2, 1H, Ar), 6.65 (d, *J*=8.1, 2H, Ar), 6.76 (d, *J* = 8.8, 2H, Ar), 6.84 (d, *J* = 8.8, 2H, Ar), 7.02 (t, *J*=7.7, 2H, Ar), 7.25 (d, *J*=8.8, 2H, Ar), 7.74 (d, *J* = 8.8, 2H, Ar). NMR ^{13}C (150 MHz, CDC1$_3$), δ, ppm: 33.9, 48.3, 55.3, 55.5, 56.0, 56.1, 65.7, 113.3, 113.6, 113.7 (2C), 114.1 (2C), 115.5 (2C), 118.3, 128.9 (2C), 129.6, 130.1 (2C), 130.5, 130.6 (2C), 132.6, 133.2, 147.3, 147.4, 150.0, 158.4, 163.4, 195.9. ESI MS 524 [M+H]$^+$. Analysis [Found, %: C, 76.05; H, 6.65; N, 2.32; $C_{33}H_{33}NO_5$. Calc., %: C, 75.69; H, 6.35; N, 2.67].



[7,8-Dimethoxy-1-(3,4,5-trimethoxyphenyl)-3-phenyl-2,3,4,5-tetrahydro-1*H*-benz[*d*]azepin-2-yl]-(4-methoxyphenyl)methanone (2g)

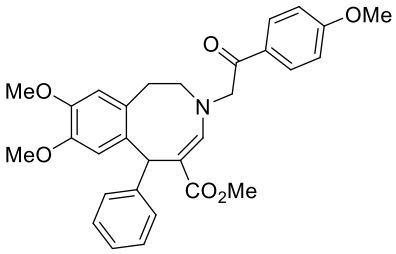
Yellow oil. Yield 44% (0.052 g). R_f 0,5 (EtOAc-hexane, 1:3). NMR ^{1}H (600 MHz, CDC1$_3$), δ, ppm (*J*, Hz): 3.02-3.17 (m, 2H, CH_2), 3.55-3.64 (m, 1H, CH_2), 3.66 (s, 3H, OCH_3), 3.70 (s, 6H, OCH_3), 3.71-3.76 (m, 1H, CH_2), 3.78 (s, 9H, OCH_3), 5.22 (d, *J*=7.7, 1H, CH), 5.54 (d, *J*=7.7, 1H, CH), 6.48 (s, 3H, Ar), 6.57 (s, 1H, Ar), 6.60 (t, *J*=7.3, 1H, Ar), 6.63 (d, *J*=8.4, 2H, Ar), 6.79 (d, *J*=8.8, 2H, Ar), 7.03 (t, *J*=7.7, 2H, Ar), 7.77 (d, *J*=8.8, 2H, Ar). NMR ^{13}C (150 MHz, CDC1$_3$), δ, ppm: 14.3, 34.0, 50.0, 55.5, 55.9, 56.1, 56.2 (2C), 60.5, 60.9, 65.8, 106.4, 113.5, 113.6, 113.8 (2C), 115.3 (2C), 118.3, 126.8, 129.0 (2C), 129.5, 130.6 (2C), 132.1, 136.8, 137.2, 147.4, 147.5, 149.8, 153.2 (2C), 163.5, 196.5. IR spectra, ν (film), cm^{-1}: 1680 (C=O). ESI MS 584 [M+H]$^+$. Analysis [Found, %: C, 72.38; H, 6.71; N, 2.15; $C_{35}H_{37}NO_7$. Calc., %: C, 72.02; H, 6.39; N, 2.40].

Methyl 4-[7,8-dimethoxy-1-(4-nitrophenyl)-3-phenyl-2,3,4,5-tetrahydro-1*H*-benz[*d*]azepin-2-yl]benzoate (4). 2-[6,7-Dimethoxy-1-(4-nitrophenyl)-3,4-dihydroisoquinolin-2(1*H*)-yl]-1-(4-methoxycarbonylphenyl)ethan-1-one **(3)** (0.200 g, 0.0004 mol) was dissolved in acetonitrile (10 ml, HPLC grade), then tetrabutylammonium difluorotriphenyl silicate (0.647 g, 1.2 mmol) was added followed by addition of 2-trimethylsilylphenyl trifluoromethanesulfonate (0.143 g, 0.5 mmol, 0.116 ml). The mixture was stirred at room temperature with the TLC monitoring. The solvent was removed under reduced pressure. The oily residue was purified by column chromatography (glass column, H=100 mm, d=15 mm, eluent: DCM : hexane, 1:15).



Methyl 4-[7,8-dimethoxy-1-(4-nitrophenyl)-3-phenyl-2,3,4,5-tetrahydro-1*H*-benz[*d*]azepin-2-yl]benzoate (4) Yellow oil. Yield 12 % (0.026 g). R_f 0.75 (EtOAc-hexane, 1:3). NMR ^{1}H (400 MHz, $CDC1_3$), δ, ppm (*J*, Hz): 2.91-2.93 (m, 2H, CH_2), 3.47 (t, *J* = 5.3, 2H, CH_2), 3.69 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 5.01 (d, *J* = 5.9, 1H, CH), 5.74 (d, *J*=5.9, 1H, CH), 6.44 (s, 1H, Ar), 6.51 (s, 1H, Ar), 6.54 - 6.67 (m, 3H, Ar), 6.99-7.08 (m, 2H, Ar), 7.22 (d, *J* = 8.5, 2H, Ar), 7.32-7.39 (m, 2H, Ar), 7.84 (d, *J* = 8.5, 2H, Ar), 7.94 (d, *J*=8.7, 2H, Ar). IR spectra, ν (film), cm^{-1}: 1675 (CO_2Me), 1541, 1322 (NO_2). ESI MS 539 $[M+H]^+$. Analysis [Found, %: C, 71.71; H, 5.94; N, 4.89. $C_{32}H_{30}N_2O_6$. Calc., %: C, 71.36; H, 5.61; N, 5.20].

Reaction of tetrahydroisoquinoline 1c with methyl propiolate. Tetrahydroisoquinoline **1c** (0.200 g, 0.48 mmol) was dissolved in methanol (10 ml), and methyl propiolate (0.068 ml, 0.81 mmol) was added. The mixture was stirred at 50°C with the TLC monitoring. The obtained precipitate of product **5** was filtered off and dried in air.



Methyl 8,9-dimethoxy-3-[2-(4-methoxyphenyl)-2-oxo-ethyl]-6-phenyl-1,2,3,6-tetrahydrobenz[*d*]azocine-5-carboxylate (5). White powder. Yield 35% (0.085 g). Mp 179-181°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDC1_3$), δ, ppm (*J*, Hz): 2.64 (d.d, *J* = 15.41, *J* = 5.14, 1H, CH_2), 2.69 - 2.82 (m, 2H, CH_2), 3.60 - 3.69 (m, 1H, CH_2), 3.74 (s, 3H, OCH_3) 3.80 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 4.32 (d, *J*=16.9, 1H, CH_2CO), 4.51 (d, *J*=16.9, 1H, CH_2CO), 5.90 (s, 1H, CH), 6.45 (s, 1H, Ar), 6.76 (s, 1H, Ar,) 6.84 (d, *J*=8.8, 2H, Ar), 7.12 (d, *J*=8.1, 3H, Ar), 7.21 - 7.28 (m, 2H, Ar), 7.66 (s, 1H, *N*-CH), 7.76 (d, *J*=8.8, 2H, Ar). NMR ^{13}C (100 MHz, $CDC1_3$), δ, ppm: 36.2, 49.3, 50.8, 51.6, 55.6, 55.8, 56.0, 62.5, 100.0, 100.8, 114.0 (2C), 114.9, 116.7, 125.5, 126.3 (2C), 127.8, 128.5 (2C), 129.1, 130.4 (2C), 131.6, 146.9, 147.5, 153.7, 164.1, 170.9, 193.1. IR spectra, ν (KBr), cm^{-1}: 1690 (CO_2Me), 1661(C=O). ESI MS 502 $[M+H]^+$. Analysis [Found, %: C, 71.96; H, 6.36; N, 2.73; $C_{30}H_{31}NO_6$. Calc., %: C, 71.84; H, 6.23; N, 2.60].