Electronic supplementary materials *Mendeleev Commun.*, 2018, **28**, 128–130

DBU as a scaffold for the synthesis of [1,3]oxazolo[2',3':2,3]pyrimido-[1,2-*a*]azepines: annulation with aromatic cyanopropargylic alcohols

Olesya A. Shemyakina, Ol'ga G. Volostnykh, Anton V. Stepanov, Anastasiya G. Mal'kina, Igor A. Ushakov, Konstantin A. Apartsin, Victoriya V. Kireeva and Boris A. Trofimov

General remarks

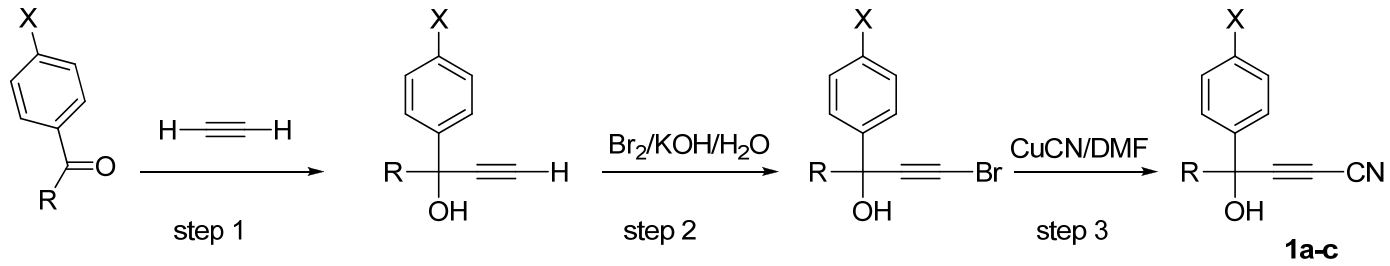
^{1}H, ^{13}C and ^{15}N NMR spectra of the synthesized compounds were recorded on a Bruker DPX-400 and Bruker AV-400 spectrometers (400.1, 100.6 and 40.6 MHz, respectively) in $CDCl_3$ at room temperature and referred to DMSO (^{1}H, ^{13}C) or nitromethane (^{15}N). NMR signals were assigned using 2D NMR techniques (NOESY, HSQC, HMBC ^{1}H-^{13}C and HMBC ^{1}H-^{15}N).

IR spectra were measured on a Bruker Vertex-70 in KBr pellets or film. Mass spectra of compounds **2a-c** were recorded on a GCMS-QP5050A spectrometer made by Shimadzu Company. Chromatographic column parameters were as follows: SPB^{TM}-5, length 60 m, internal diameter 0.25 mm, thickness of stationary phase film 0.25 μm; injector temperature 250 °C, gas carrier – helium, flow rate 0.7 ml min^{-1}; detector temperature 250 °C; mass analyzer: quadrupole, electron ionization, electron energy: 70 eV, ion source temperature 200 °C; mass range 34-650 Da. Elemental analyses were performed on a FLASH 2000. Melting points were taken on a Kofler micro hot stage.

Column chromatography was performed on silica gel 60 (70-230 mesh, particle size 0.063-0.200 nm, Merck). DBU is a commercial reagent (“Merck”). Commercially available starting materials were used without further purification.

Synthesis of aromatic cyanopropargylic alcohols 1a-c

Aromatic cyanopropargylic alcohols **1a,b** were prepared for the first time according to a published method (S. R. Landor, B. Demetriou, R. Grzeskowiak and D. Pavey, *J. Organometal. Chem*., 1975, **93**, 129). Aromatic cyanopropargylic alcohol **1c** was prepared according to a published method (A. G. Mal'kina, L. V. Sokolyanskaya, R. N. Kudyakova, L. M. Sinegovskaya, A. I. Albanov, O. A. Shemyakina and B. A. Trofimov, *Russ. J. Org. Chem.*, 2005, **41**, 61).

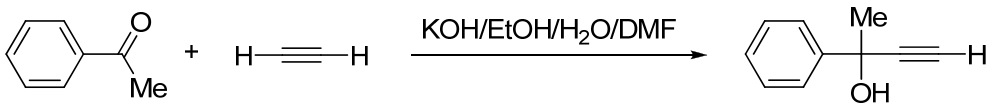


R = Me, X = H (**1a**)
R = Me, X = Cl (**1b**)
R = Ph, X = H (**1c**)

4-Hydroxy-4-phenylpent-2-ynenitrile (1a)

Step 1.

E. Yu. Shmidt, I. A. Bidusenko, N. I.Protsuk, A. I. Mikhaleva and B. A. Trofimov, *Russ. J. Org. Chem.*, 2013, **49**(1), 8.

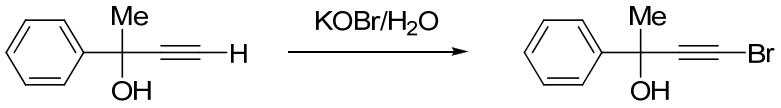


A mixture of KOH·0.5H_2O (10.00 g, 154.0 mmol) in EtOH (5 ml) and DMSO (50 ml) was stirred at 120 °C until it turned homogeneous. The mixture was then cooled to 15°C and saturated with acetylene by passing it over a period of 30 min. Then, a solution of acetophenone (10.33 g, 86.0 mmol) in DMSO (10 ml) was added dropwise over a period of 1 h on continuous bubbling acetylene, and the mixture was stirred for 2 h under a stream of acetylene. The reaction mixture was diluted

with cold (7-10 ºC) aqueous solution (100 ml) of NH_4Cl (16.47 g, 308.0 mmol) and extracted with Et_2O (7×20 ml). The ether extracts were washed with H_2O (3×20 ml) and dried over $MgSO_4$ for ~12 h. The solvent was removed and the residue was passed through a column of Al_2O_3 (basic), eluent: hexane, to afford 11.10 g (88%) of 2-phenylbut-3-yne-2-ol as colourless crystals, mp 43-47 ºC.

Step 2.

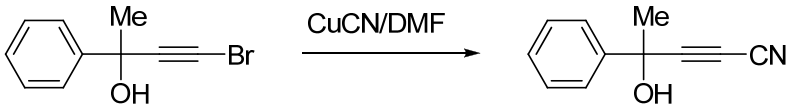
I. V. Nazarov and G. A. Shvekhgeimer*, Zh. Obshch. Khim.*, 1959, **29**, 457.



To a cooled (6-8 °C) solution of 2-phenylbut-3-yn-2-ol (2.47 g, 17.0 mmol) in Et_2O (10 ml) an aqueous solution of KOBr prepared from Br_2 (1.2 ml, 3.7 g, 23.0 mmol) and KOH (9.0 g, 161.0 mmol) in water (33 ml) was slowly (1 h) added with vigorous stirring. The reaction mixture was stirred at room temperature for 20 h. The ether layer was separated, and the aqueous one was extracted with Et_2O. The ether extracts were combined, washed with H_2O (3×40 ml) and dried over $MgSO_4$. After removal of the solvent, the residue was passed through a column of SiO_2 (eluent: hexane-Et_2O, 1: 1) to give 3.44 g (90%) of 4-bromo-2-phenylbut-3-yn-2-ol.

Step 3.

S. R. Landor, B. Demetriou, R. Grzeskowiak and D. Pavey, *J. Organometal. Chem*., 1975, **93**, 129.



To a suspension of CuCN (5.00 g, 55.8 mmol) in dry DMF (10 ml) under argon a solution of 4-bromo-2-phenylbut-3-yn-2-ol (3.00 g, 13.0 mmol) in dry DMF (10 ml) was added. The reaction mixture was stirred for 4 h at 60-65 ºC, then it was diluted with cold water (250 ml) and vigorously stirred until the formation of a solid mass. The solid residue was filtered; the aqueous solution was extracted with Et_2O (5×100 ml). The solid residue was stirred with Et_2O (3×50 ml) and filtered. The ether extracts were washed with H_2O, dried over $MgSO_4$. After removal of the solvent the resulting crude product was dried *in vacuo* to afford 2.00 g (90%) of 4-hydroxy-4-phenylpent-2-ynenitrile (**1a**).

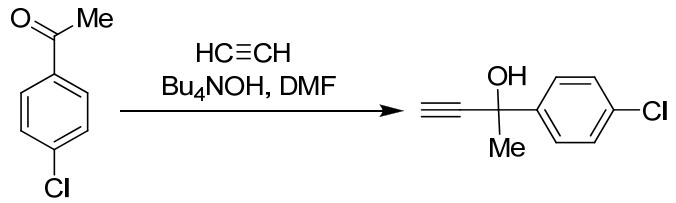
^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.76 (s, 3H, Me), 2.64 (s, 1H, OH), 7.26-7.29 (m, 1H, Ph), 7.32-7.36 (m, 2H, Ph), 7.63-7.65 (m, 2H, Ph).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ 33.2 (Me), 69.9 (C≡*C*CN), 73.1 (*C*≡CCN), 87.4 (COH), 109.6 (CN), 124.9 (C_o), 127.8 (C_p), 128.4 (C_m), 145.1 (C_i).

4-(4-Chlorophenyl)- 4-hydroxypent-2-ynenitrile (1b)

Step 1.

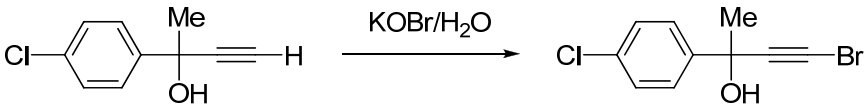
E. Yu. Schmidt, N. A. Cherimichkina, I. A. Bidusenko, N. I. Protzuk and B. A. Trofimov, *Eur. J. Org. Chem.*, 2014, 4663.



A 40% aqueous solution of Bu_4NOH (13.86 g of a solution containing 21.0 mmol of pure Bu_4NOH) and DMSO (85 ml, a H_2O content in the mixture ~10%) was cooled to 5 °C, and acetylene was bubbled (30 min) through the cooled (2-5 °C) solution. Then, a solution of 4-chloroacetophenone (3.00 g, 19.4 mmol) in DMSO (10 ml) was added dropwise over 15 min with continuous bubbling of acetylene. The reaction mixture was stirred at 5 °C for 5 h and diluted with cold water (300 ml, 3-5 °C), extracted with Et_2O (3×50 ml), the ether extracts were washed with H_2O (3×50 ml), dried over $MgSO_4$. After removal of the Et_2O the residue was separated by column chromatography (SiO_2, eluent: hexane) to give 1.12 g (32%) of 2-(4-chlorophenyl)but-3-yn-2-ol with a purity of > 95%.

Step 2.

I. V. Nazarov and G. A. Shvekhgeimer, *Zh. Obshch. Khim.*, 1959, **29**, 457.

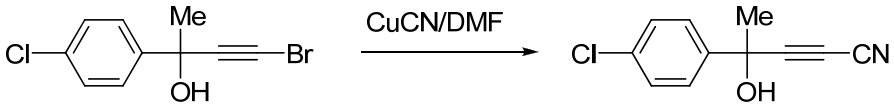


To a cooled (6-8 ºC) solution of 2-(4-chlorophenyl)but-3-yn-2-ol (2.47 g, 17.0 mmol) in Et_2O (10 ml), an aqueous solution of KOBr prepared from Br_2 (1.5 ml, 4.65 g, 29.0 mmol) and KOH (11.0 g, 196.0 mmol) in H_2O (40 ml) was slowly (1 h) added with vigorous stirring. The reaction mixture was stirred at room temperature for 20 h. The ether layer was separated, and the aqueous one was

extracted with Et_2O. The ether extracts were combined, washed with H_2O (3×40 ml), and dried over $MgSO_4$. After removal of the solvent, the residue was passed through a column of SiO_2 (eluent: hexane-Et_2O, 1:1) to give 3.50 g (80%) of 4-bromo-2-(4-chlorophenyl)but-3-yn-2-ol.

Step 3.

S. R. Landor, B. Demetriou, R. Grzeskowiak and D. Pavey, *J. Organometal. Chem*., 1975, **93**, 129.



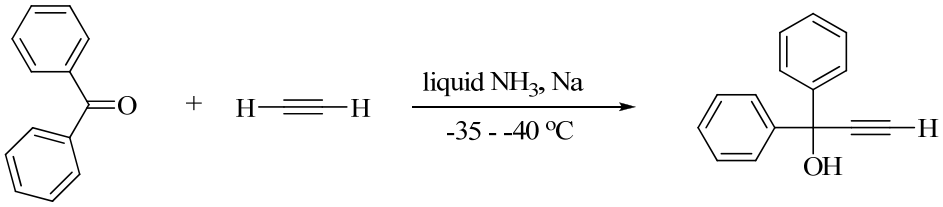
To a suspension of CuCN (4.80 g, 53.6 mmol) in dry DMF (10 ml) under argon a solution of 4-bromo-2-(4-chlorophenyl)but-3-yn-2-ol (3.50 g, 13.6 mmol) in dry DMF (10 ml) was added. The reaction mixture was stirred for 4 h at 60-65 ºC, diluted with cold water (250 ml) and vigorously stirred until the formation of a solid mass. The solid residue was filtered; the aqueous solution was extracted with Et_2O (5×100 ml). The solid residue was stirred with Et_2O (3×50 ml) and filtered. The ether extracts were washed with H_2O, dried over $MgSO_4$. After removal of the solvent the residue was dried *in vacuo* to afford 1.90 g (68%) of 4-(4-chlorophenyl)- 4-hydroxy-pent-2-ynenitrile (**1b**).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ 1.80 (s, 3H, Me), 2.55 (s, 1H, OH), 7.34-7.36 (m, 2H, Ph), 7.45-7.47 (m, 2H, Ph).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ 34.0 (Me), 58.5 (C≡*C*CN), 69.4 (*C*≡CCN), 87.3 (COH), 104.5 (CN), 126.0 (C_o), 128.8 (C_m), 134.4 (C_p), 140.8 (C_i).

4-Hydroxy-4,4-diphenylbut-2-ynenitrile (1c)

Step 1.

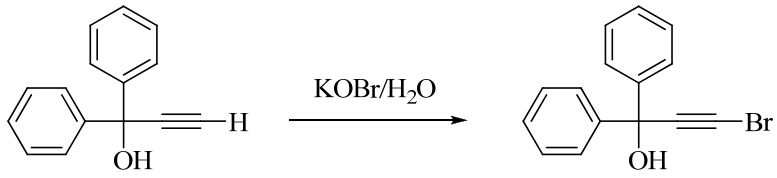


A liquid ammonia (1000 ml) was cooled to -35÷-40 ºC and metallic Na (11.50 g, 500.0 mmol) was added for 2 h (previously there were added 2-3 crystals of $FeCl_3$). Acetylene was bubbled through the reaction mixture for 1 h. A solution of benzophenone (45.55 g, 250.0 mmol) in Et_2O (50 ml) was slowly added, with bubbling of acetylene. The reaction mixture was further stirred for 3 h and left

overnight. With stirring, Et_2O (100 ml) and small portions of NH_4Cl (26.00 g) were added. After removal of traces of ammonia, the mixture was slowly decomposed with cold water (250 ml), extracted with Et_2O (5×100 ml). The ether extracts were combined, washed with H_2O (3×50 ml) and dried over $MgSO_4$. The solvent was removed and the residue was dried in vacuo to give 51.00 g (98%) of 1,1-diphenylprop-2-yn-1-ol, mp 44-45 ° C.

Step 2.

I. V. Nazarov and G. A. Shvekhgeimer*, Zh. Obshch. Khim.*, 1959, **29**, 457 (in Russian).

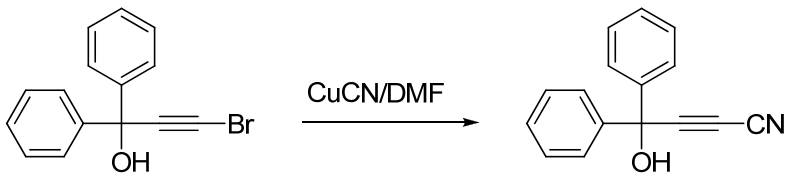


To a cooled (6-8 °C) solution of 1,1-diphenylprop-2-yn-1-ol (2.70 g, 13.0 mmol) in Et_2O (10 ml), an aqueous solution of KOBr prepared from Br_2 (0.72 ml, 2.23 g, 14.0 mmol) and KOH (5.30 g, 94.6. mmol) in H_2O (20 ml) was slowly (1 h) added with vigorous stirring. The reaction mixture was stirred at room temperature for 20 h. The ether layer was separated, and the aqueous one was extracted with Et_2O, the ether extracts were combined, washed with H_2O (3×40 ml) and dried over $MgSO_4$. After removal of the solvent, the residue was passed through a column of SiO_2 (eluent: hexane-Et_2O, 1:1) to give 2.70 g (72%) of 3-bromo-1,1-diphenylprop-2-yn-1-ol.

Step 3.

S. R. Landor, B. Demetriou, R. Grzeskowiak and D. Pavey, *J. Organomet. Chem*., 1975, **93**, 129.

A. G. Mal'kina, L. V. Sokolyanskaya, R. N. Kudyakova, L. M. Sinegovskaya, A. I. Albanov, O. A. Shemyakina and B. A. Trofimov, *Russ. J. Org. Chem.*, 2005, **41**, 61 (*Zh. Org. Khim*., 2005, **41**, 64).



To a suspension of CuCN (5.00 g, 55.8 mmol) in dry DMF (10 ml) under argon a solution of 3-bromo-1,1-diphenylbut-2-yn-1-ol (2.73 g, 9.5 mmol) in dry DMF (10 ml) was added. The reaction mixture was stirred for 6 h at 75-80 ºC, diluted with cold water (250 ml) and vigorously stirred until the formation of a solid mass. The solid residue was filtered; the aqueous solution was extracted with Et_2O (5×100 ml). The solid was stirred with Et_2O (3×50 ml) and filtered. The ether extracts were

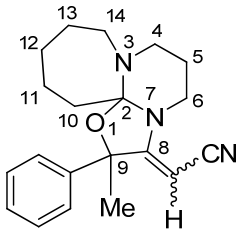
washed with H_2O and dried over $MgSO_4$. After removal of the solvent the residue was dried *in vacuo* to afford 1.90 g (68%) of 4-hydroxy-4,4-diphenylbut-2-ynenitrile (**1c**).

^{1}H NMR (400.1 MHz, $CDCl_3$): δ 3.66 (s, 1H, OH), 7.28-7.33 (m, 6H, Ph), 7.42-7.45 (m, 4H, Ph).
^{13}C NMR (100.6 MHz, $CDCl_3$): δ 60.8 (C≡*C*CN), 74.8 (*C*≡CCN), 86.4 (COH), 104.8 (CN), 126.0 (C_o), 128.7 (C_m), 128.8 (C_p), 142.0 (C_i).

General procedure for the synthesis of compounds 2a-c.

To a solution of DBU (0.152 g, 1 mmol) in CH_2Cl_2 (4 ml) aromatic cyanopropargylic alcohol **1a-c** (1 mmol) in CH_2Cl_2 (4 ml) was added dropwise over 10 min. The reaction mixture was stirred at 20-25 ºC for 20 min. The solvent was evaporated *in vacuo* and the crude product was purified by column chromatography (SiO_2, eluent: hexane–Et_2O, 1:1) to give tricyclic products **2a-c**.

2-[2-Methyl-2-phenylhexahydro-5H,9H-[1,3]oxazolo[2',3':2,3]pyrimido-[1,2-a]azepin-3(2H)-yliden]acetonitrile (2a)



Yield 0.239 g, 74%. Light yellow oil. Diastereomer ratio, 1:2.

^{1}H NMR (400.1 MHz, $CDCl_3$) *Z*-isomer: δ 1.37 (m, 1H, CH_2-13), 1.52 (m, 1H, CH_2-11), 1.54 (m, 1H, CH_2-12), 1.64 (m, 1H, CH_2-14), 1.71 (m, 1H, CH_2-12), 1.76 (m, 2H, CH_2-5, CH_2-13), 1.75, 1.81 (s, 3H, Me), 1.83 (m, 1H, CH_2-11), 2.00 (m, 1H, CH_2-5), 2.13 (m, 1H, CH_2-14), 2.78 (m, 1H, CH_2-10), 2.90 (m, 1H, CH_2-4), 2.92 (m, 1H, CH_2-4), 3.20 (m, 1H, CH_2-10), 3.21 (m, 1H, CH_2-6), 3.46, 3.70 (s, 1H, =CH), 4.59, 4.60 (m, 1H, CH_2-6), 7.25 (m, 1H, Ph, H_p), 7.30 (m, 2H, Ph, H_m), 7.44, 7.58 (m, 2H, Ph, H_o).

E-isomer: δ 1.40 (m, 2H, CH_2-13, CH_2-11), 1.56 (m, 1H, CH_2-5), 1.59 (m, 1H, CH_2-12), 1.75 (m, 1H, CH_2-13), 1.79 (m, 1H, CH_2-12), 1.80 (m, 1H, CH_2-14), 1.83 (m, 1H, CH_2-5), 1.85 (m, 1H, CH_2-11), 2.00, 2.12 (s, 3H, Me), 2.36 (m, 1H, CH_2-14), 2.47 (m, 1H, CH_2-10), 2.80 (m, 1H, CH_2-4), 2.98 (m, 1H, CH_2-4), 3.10 (m, 1H, CH_2-10), 3.34 (m, 1H, CH_2-6), 3.39, 3.42 (m, 1H, CH_2-6), 3.76, 3.89 (s, 1H, =CH), 7.25 (m, 1H, Ph, H_p), 7.30 (m, 2H, Ph, H_m), 7.52, 7.73 (m, 2H, Ph, H_o).

^{13}C NMR (100.6 MHz, $CDCl_3$) *Z*-isomer: δ 20.7, 21.2 (CH_2-12), 23.1, 24.3 (CH_2-5), 24.5, 26.3 (CH_2-11), 26.7, 27.2 (CH_2-13), 27.8, 28.7 (Me), 35.0, 36.9 (CH_2-14), 39.9, 41.2 (CH_2-6), 45.4, 45.9 (CH_2-4), 47.1, 48.6 (CH_2-10), 53.9, 55.4 (=CH), 86.5, 87.7 (C-9), 107.7, 108.7 (C-2), 119.6, 119.9 (CN), 125.3, 126.4 (C_o, Ph), 128.2, 128.3 (C_m, Ph), 127.9, 128.0 (C_p, Ph), 143.2, 143.5 (C_i, Ph), 163.7, 164.0 (C-8). *E*-isomer: δ 20.4, 20.8 (CH_2-12), 22.0, 23.8 (CH_2-5), 23.9, 25.3 (CH_2-11), 24.6,

25.9 (Me), 26.0, 26.7 (CH_2-13), 35.1, 36.5 (CH_2-14), 40.7, 41.3 (CH_2-6), 45.9, 46.1 (CH_2-4), 46.5, 47.5 (CH_2-10), 54.9, 57.0 (=CH), 86.8, 87.6 (C-9), 106.1, 106.9 (C-2), 119.7 (CN), 124.9, 126.4 (C_o, Ph), 127.6, 127.9 (C_p, Ph), 128.1, 128.2 (C_m, Ph), 141.6, 142.0 (C_i, Ph), 165.5, 166.7 (C-8).

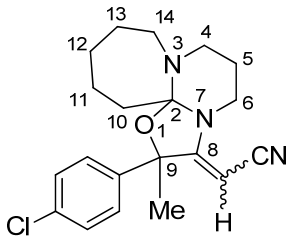
^{15}N NMR (40.6 MHz, $CDCl_3$) *Z*-isomer: δ -123.4 (CN), -259.7 (N-7), -317.3 (N-3).
E-isomer: δ -123.4 (CN), -261.6 (N-7), -317.3 (N-3).

IR: 3059, 2930, 2862, 2752, 2722, 2691, 2194, 1613, 1441, 1400, 1360, 1311, 1255, 1229, 1153, 1124, 1089, 1039, 963, 869, 821, 762, 700, 651 cm^{-1}.

MS (EI) *m/z*: 324 (29) $[M+H]^+$, 323 (100) $[M]^+$, 295 (20) 294 (78), 283 (14), 280 (25), 268 (10), 267 (28), 253 (16), 252 (12), 210 (11), 197 (13), 183 (12), 167 (11), 155 (10), 154 (14), 140 (15), 139 (16), 128 (12), 127 (14), 115 (17), 98 (18), 97 (12), 96 (14), 77 (15), 70 (16), 69 (16), 68 (11) 56 (19), 55 (23), 44 (11), 43 (17), 42 (33), 41 (43).

Found (%): C, 74.51; H, 7.84; N, 12.72. Calc. for $C_{20}H_{25}N_3O$ (%): C, 74.27; H, 7.79; N, 12.99.

2-[2-(4-Chlorophenyl)-2-methylhexahydro-5H,9H-[1,3]oxazolo[2',3':2,3]pyrimido-[1,2-a]azepin-3(2H)-yliden]acetonitrile (2b)



Yield 0.216 g, 60%. Yellow oil. Diastereomer ratio, 1:2. Upon standing, a single diastereomer crystallized from the mixture. Colorless crystals, mp 134-137 °C.

^{1}H NMR (400.1 MHz, $CDCl_3$) *Z*-isomer: δ 1.37 (m, 1H, CH_2-13), 1.51 (m, 1H, CH_2-11), 1.54 (m, 1H, CH_2-12), 1.65 (m, 1H, CH_2-14), 1.69 (m, 1H, CH_2-12), 1.75 (m, 2H, CH_2-5, CH_2-13), 1.72, 1.78 (s, 3H, Me), 1.83 (m, 1H, CH_2-11), 2.00 (m, 1H, CH_2-5), 2.13 (m, 1H, CH_2-14), 2.78 (m, 1H, CH_2-10), 2.90 (m, 1H, CH_2-4), 2.92 (m, 1H, CH_2-4), 3.19 (m, 1H, CH_2-10), 3.20 (m, 1H, CH_2-6), 3.44,

3.70 (s, 1H, =CH), 4.59, 4.61 (m, 1H, CH_2-6), 7.28 (m, 2H, 4-ClPh, H_m), 7.38, 7.52 (m, 2H, 4-ClPh, H_o).
E-isomer: δ 1.38 (m, 2H, CH_2-13, CH_2-11), 1.58 (m, 1H, CH_2-5), 1.60 (m, 1H, CH_2-12), 1.75 (m, 1H, CH_2-13), 1.77 (m, 1H, CH_2-12), 1.79 (m, 1H, CH_2-14), 1.81 (m, 1H, CH_2-5), 1.83 (m, 1H, CH_2-11), 1.99, 2.09 (s, 3H, Me), 2.38 (m, 1H, CH_2-14), 2.44 (m, 1H, CH_2-10), 2.82 (m, 1H, CH_2-4), 2.96 (m, 1H, CH_2-4), 3.12 (m, 1H, CH_2-10), 3.31 (m, 1H, CH_2-6), 3.40, 3.43 (m, 1H, CH_2-6), 3.76, 3.88 (s, 1H, =CH), 7.28 (m, 2H, 4-ClPh, H_m), 7.45, 7.67 (m, 2H, 4-ClPh, H_o).

^{13}C NMR (100.6 MHz, $CDCl_3$) *Z*-isomer: δ 20.6, 21.2 (CH_2-12), 23.1, 24.3 (CH_2-5), 26.3, 26.7 (CH_2-11), 26.7, 27.2 (CH_2-13), 27.8, 28.7 (Me), 35.2, 36.7 (CH_2-14), 40.0, 41.4 (CH_2-6), 45.5, 45.9 (CH_2-4), 47.1, 48.7 (CH_2-10), 54.3, 55.7 (=CH), 86.1, 87.3 (C-9), 107.8, 108.9 (C-2), 119.3, 119.6 (CN), 126.9, 128.0 (C_o, 4-ClPh), 128.2, 128.5 (C_m, 4-ClPh), 133.7, 133.9 (C_p, 4-ClPh), 141.9, 142.2 (C_i, 4-ClPh), 163.3, 163.7 (C-8). *E*-isomer: δ 20.4, 20.7 (CH_2-12), 23.7, 23.8 (CH_2-5), 23.8, 25.1 (CH_2-11), 24.5, 26.0 (Me), 26.6, 26.7 (CH_2-13), 35.2, 36.4 (CH_2-14), 41.0, 41.4 (CH_2-6), 46.0, 46.2 (CH_2-4), 46.5, 47.5 (CH_2-10), 55.1, 57.2 (=CH), 86.3, 87.2 (C-9), 106.3, 106.9 (C-2), 119.5, 119.6 (CN), 127.9, 128.5 (C_m, 4-ClPh), 128.0, 129.5 (C_o, 4-ClPh), 133.6, 134.0 (C_p, 4-ClPh), 140.2, 140.7 (C_i, 4-ClPh), 165.2, 166.5 (C-8).

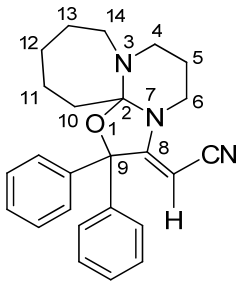
^{15}N NMR (40.6 MHz, $CDCl_3$) *Z*-isomer: δ -123.3 (CN), -258.5 (N-7), -317.2 (N-3).
E-isomer: δ -123.3 (CN), -261.4 (N-7), -317.1 (N-3).

IR: 3065, 2931, 2863, 2194, 1617, 1487, 1436, 1404, 1359, 1310, 1256, 1223, 1152, 1124, 1094, 1015, 964, 870, 828, 727, 508 cm^{-1}.

MS (EI) *m/z*: 359 (32) $[M+2H]^+$, 358 (30) $[M+H]^+$, 357 (100), 342 (11), 330 (32), 329 (27), 328 (88), 317 (14), 314 (19), 302 (10), 301 (23), 287 (11), 189 (10), 167 (12), 154 (22), 139 (22), 137 (11), 127 (15), 98 (20), 97 (15), 96 (16), 85 (14), 84 (10), 83 (21), 70 (19), 69 (17), 68 (13), 56 (21), 55 (26), 44 (14), 43 (18), 42 (35), 41 (47).

Found (%): C, 66.97; H, 6.89; Cl, 9.56; N, 11.43. Calc. for $C_{20}H_{24}ClN_3O$ (%): C, 67.12; H, 6.76; Cl, 9.91; N, 11.74.

2-[2,2-Diphenylhexahydro-5H,9H-[1,3]oxazolo[2',3':2,3]pyrimido-[1,2-a]azepin-3(2H)-yliden]acetonitrile (2c)



Yield 0.229 g, 59%. Colorless crystals, mp 215-216 ºC.

^{1}H NMR (400.1 MHz, $CDCl_3$) *Z*-isomer: δ 1.34-1.44 (m, 2H, CH_2-5), 1.48-1.55 (m, 2H, CH_2-12,), 1.63-1.69 (m, 2H, C-11), 1.77-1.83 (m, 2H, C-13) 1.93-2.00 (m, 2H, CH_2-10), 2.67-2.73 (m, 1H, CH_2-4), 2.83-2.89 (m, 1H, CH_2-4), 3.00-3.13 (m, 1H, CH_2-14), 3.16-3.24 (m, 1H, CH_2-6), 3.63 (s, 1H, =CH), 4.61-4.66 (m, 1H, CH_2-6), 7.26-7.31 (m, 8H, Ph), 7.39-7.42 (m, 2H, Ph).

^{13}C NMR (100.6 MHz, $CDCl_3$) *Z*-isomer: δ 21.6 (C-11), 23.4 (C-5), 27.5 (C-12), 27.8 (C-13), 36.0 (C-10), 39.4 (C-6), 45.3 (C-4), 49.2 (C-14), 58.7 (=CH), 90.5 (C-9), 109.7 (C-2), 119.5 (CN), 127.3, 127.6 (C_o, Ph), 127.9, 128.0 (C_m, Ph), 128.0, 128.1 (C_p, Ph), 142.6, 143.3 (C_i, Ph), 160.9 (C-8).

^{15}N NMR (40.6 MHz, $CDCl_3$) *Z*-isomer: δ -122.6 (CN), -259.2 (N-7), -319.3 (N-3).

IR: 3061, 2924, 2856, 2820, 2188, 1620, 1485, 1440, 1358, 1313, 1255, 1223, 1197, 1153, 1123, 1093, 1030, 987, 933, 874, 762, 703, 615, 524, 480 cm^{-1}.

MS (EI) *m/z*: 386 (41) $[M+H]^+$, 385 (100) $[M]^+$, 384 (15) $[M-H]^+$, 357 (22), 356 (70), 217 (31), 216 (35), 167 (13), 165 (15), 151 (15), 139 (19), 98 (16).

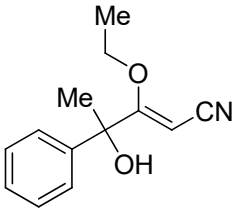
Found (%): C, 77.54; H, 7.21; N, 10.68. Calc. for $C_{25}H_{27}N_3O$ (%): C, 77.89; H, 7.06; N, 10.90.

Reaction of DBU and cyanopropargylic alcohol 1a in MeCN. a) To solution of DBU (0.076 g, 0.5 mmol) in MeCN (2 ml) cyanopropargylic alcohol **1a** (0.086 g, 0.5 mmol) in MeCN (2 ml) was added dropwise over 5 min. The reaction mixture was stirred at 20-25 ºC for 5 min. The solvent was evaporated *in vacuo* and the crude product was purified by column chromatography (SiO_2, eluent: hexane–Et_2O, 1:1) to give 0.050 g (31%) of product **2a.**

b) To cooled (-5÷0 ºC) solution of DBU (0.076 g, 0.5 mmol) in MeCN (2 ml) cyanopropargylic alcohol **1a** (0.086 g, 0.5 mmol) in MeCN (2 ml) was added dropwise over 10 min. The reaction mixture was stirred at -5÷0 ºC for 5 min. The solvent was evaporated *in vacuo* and the crude product was purified by column chromatography (SiO_2, eluent: hexane–Et_2O, 1:1) to give 0.057 g (35%) of product **2a**.

Reaction of DBU and cyanopropargylic alcohol 1a in EtOH. To solution of DBU (0.076 g, 0.5 mmol) in EtOH (2 ml) cyanopropargylic alcohol **1a** (0.086 g, 0.5 mmol) in EtOH (2 ml) was added dropwise over 10 min. The mixture was stirred at 20-25 ºC for 5 min. The solvent was evaporated *in vacuo* and the crude product was purified by column chromatography (SiO_2, eluent: MeCN) to give 0.032 g (29%) (*Z*)-3-ethoxy-4-hydroxy-4-phenylpent-2-enenitrile.

(Z)-3-Ethoxy-4-hydroxy-4-phenylpent-2-enenitrile



Yield 0.032 g, 29%. Yellow oil.

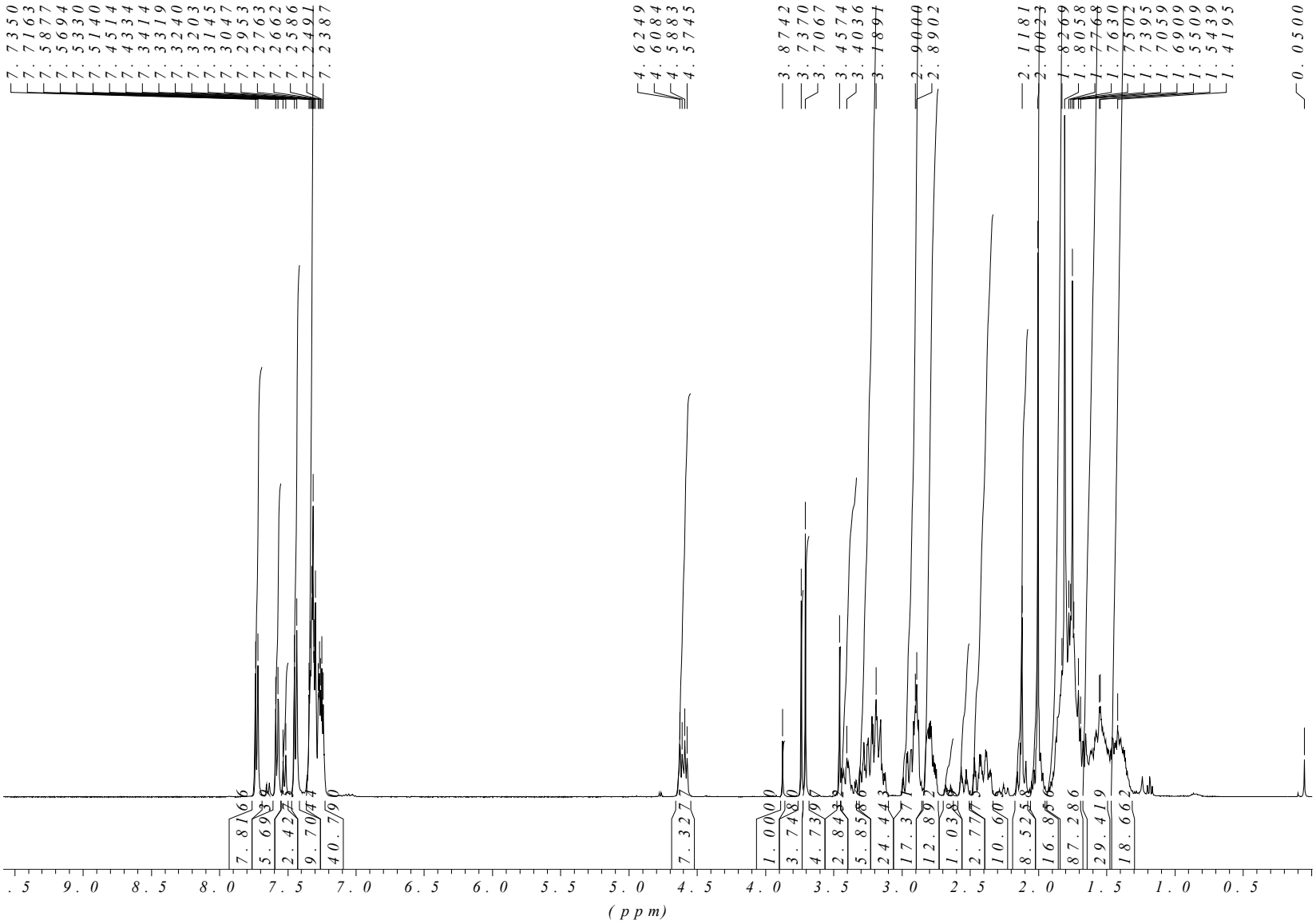
^{1}H NMR ($CDCl_3$) δ 1.23 t (3H, J = 7.0 Hz, C*H*$_3$CH$_2$), 1.71 s (3H, Me), 4.41 m (1H, CH$_3$C*H*$_2$), 4.54 m (1H, CH$_3$C*H*$_2$), 5.12 s (1H, =CH), 7.28 m (1H, H$_p$, Ph), 7.33 m (2H, H$_m$, Ph), 7.42 m (2H, H$_o$, Ph).

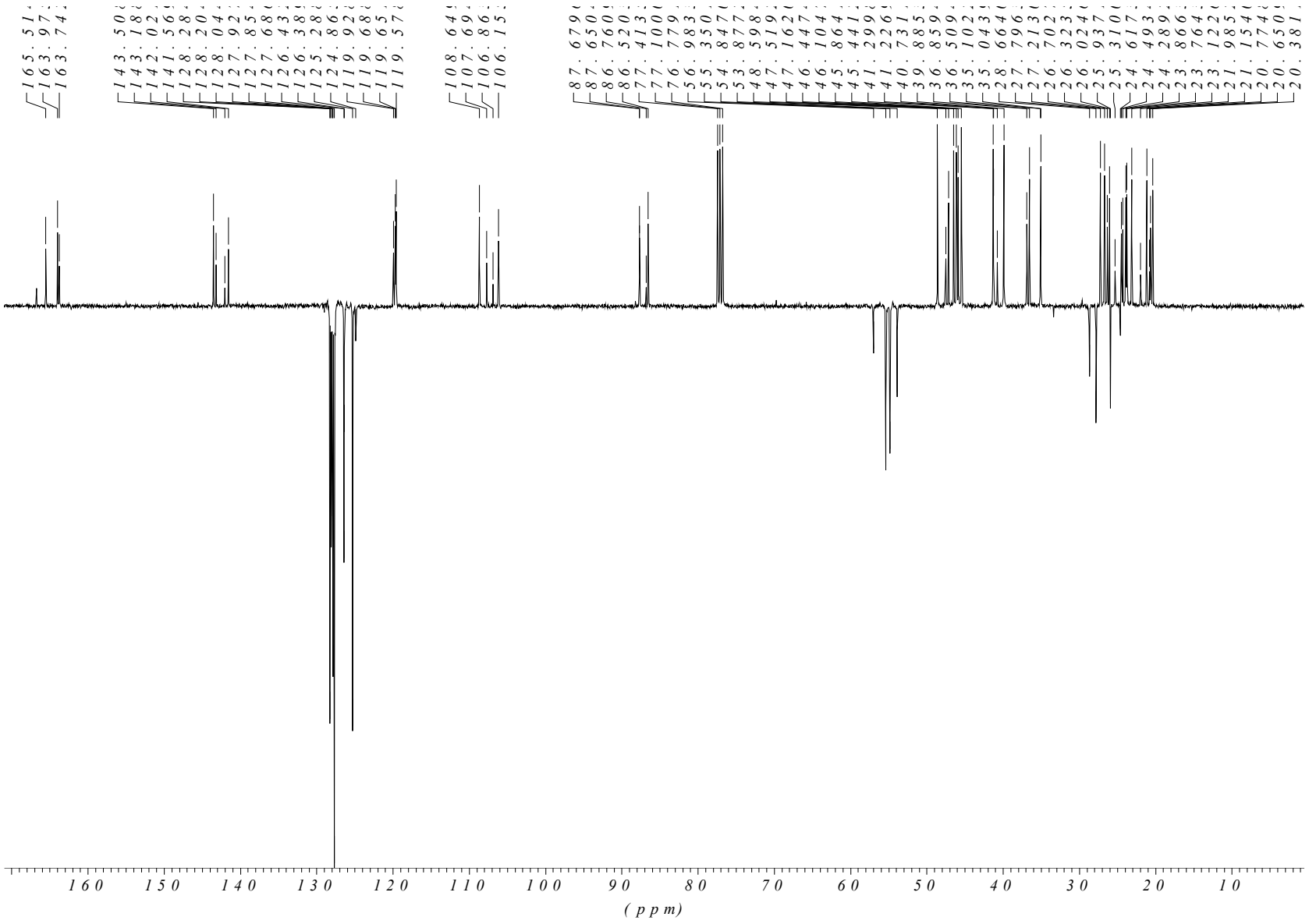
^{13}C NMR ($CDCl_3$): δ 14.8 (*C*H$_3$CH$_2$), 27.1 (Me), 68.1 (=CH), 68.2 (CH$_3$*C*H$_2$), 76.0 (COH), 117.8 (CN), 125.4 (C$_o$, Ph), 128.0 (C$_p$, Ph), 128.5 (C$_m$, Ph), 143.8 (C$_i$, Ph), 176.75 (*C*=CH).

IR: 3421, 3069, 2984, 2933, 2867, 2211, 1619, 1550, 1491, 1448, 1374, 1328, 1186, 1142, 1117, 1073, 1023, 941, 925, 846, 762, 701, 646, 556 cm^{-1}.

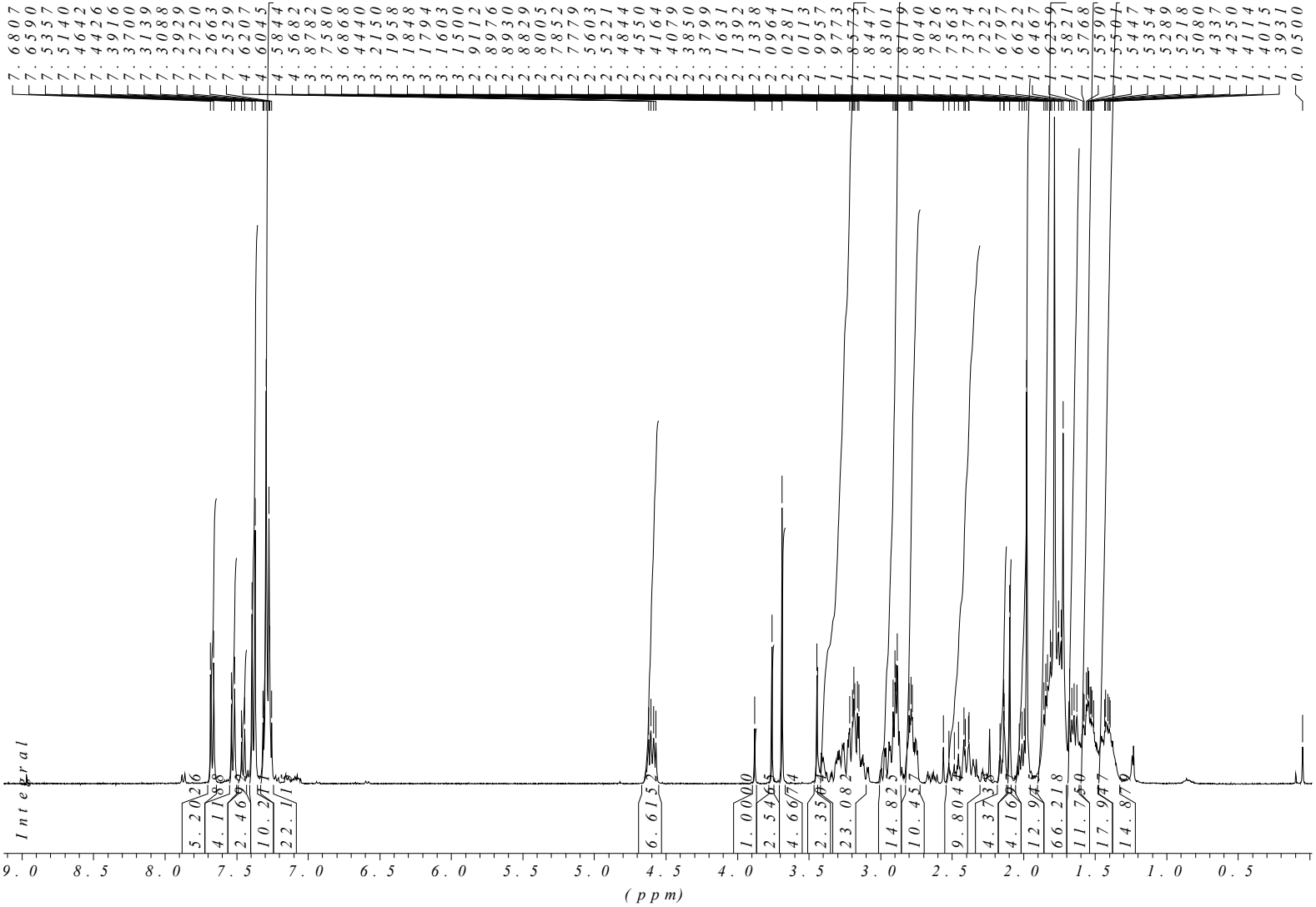
Found (%): C, 72.00; H, 6.77; N, 6.61. Calc. for $C_{13}H_{15}NO_2$ (%): C, 71.87; H, 6.96; N, 6.45.

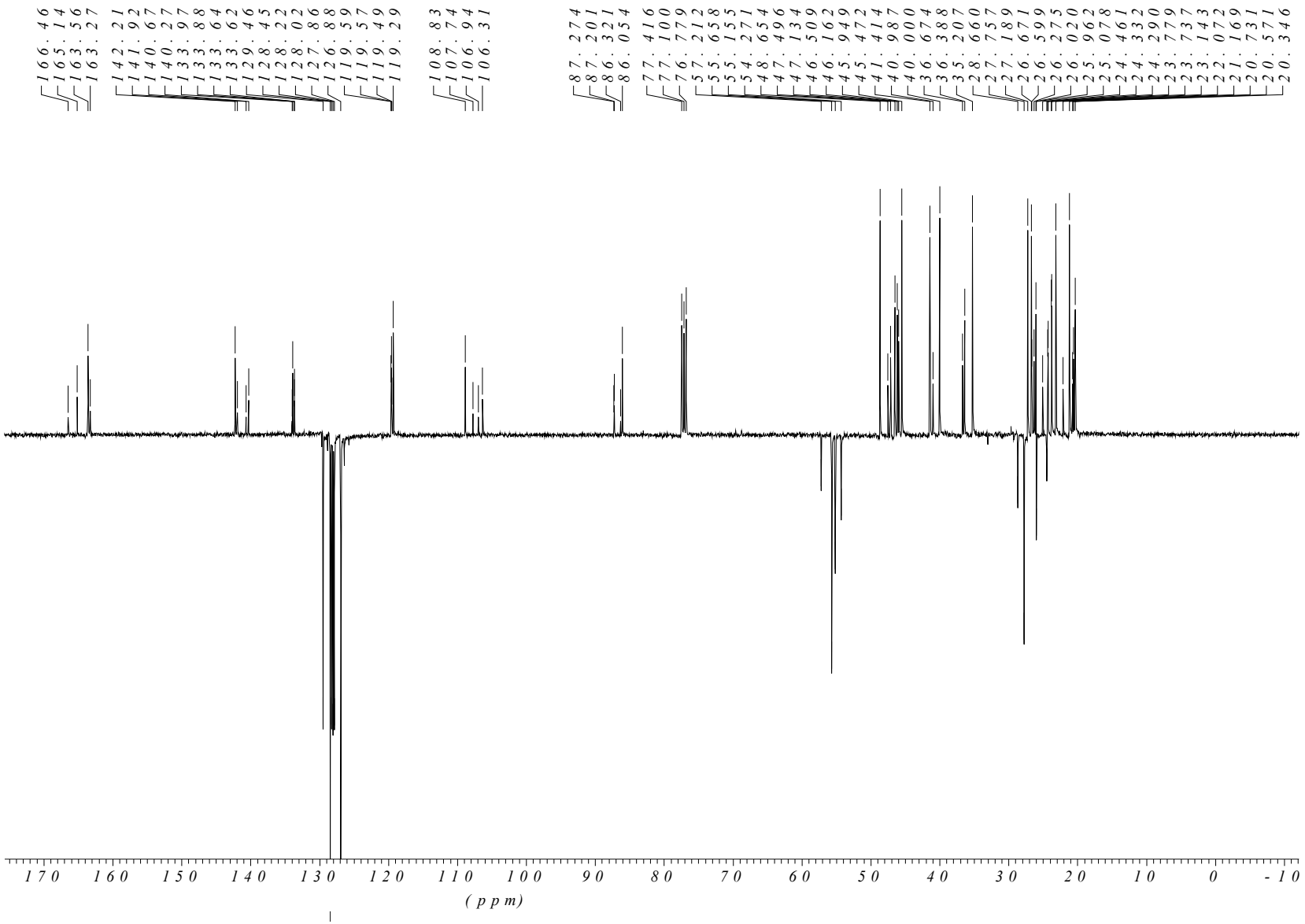
^{1}H and ^{13}C spectra of 2-[2-methyl-2-phenylhexahydro-5H,9H-[1,3]oxazolo[2',3':2,3]pyrimido-[1,2-a]azepin-3(2H)-yliden]acetonitrile (2a)



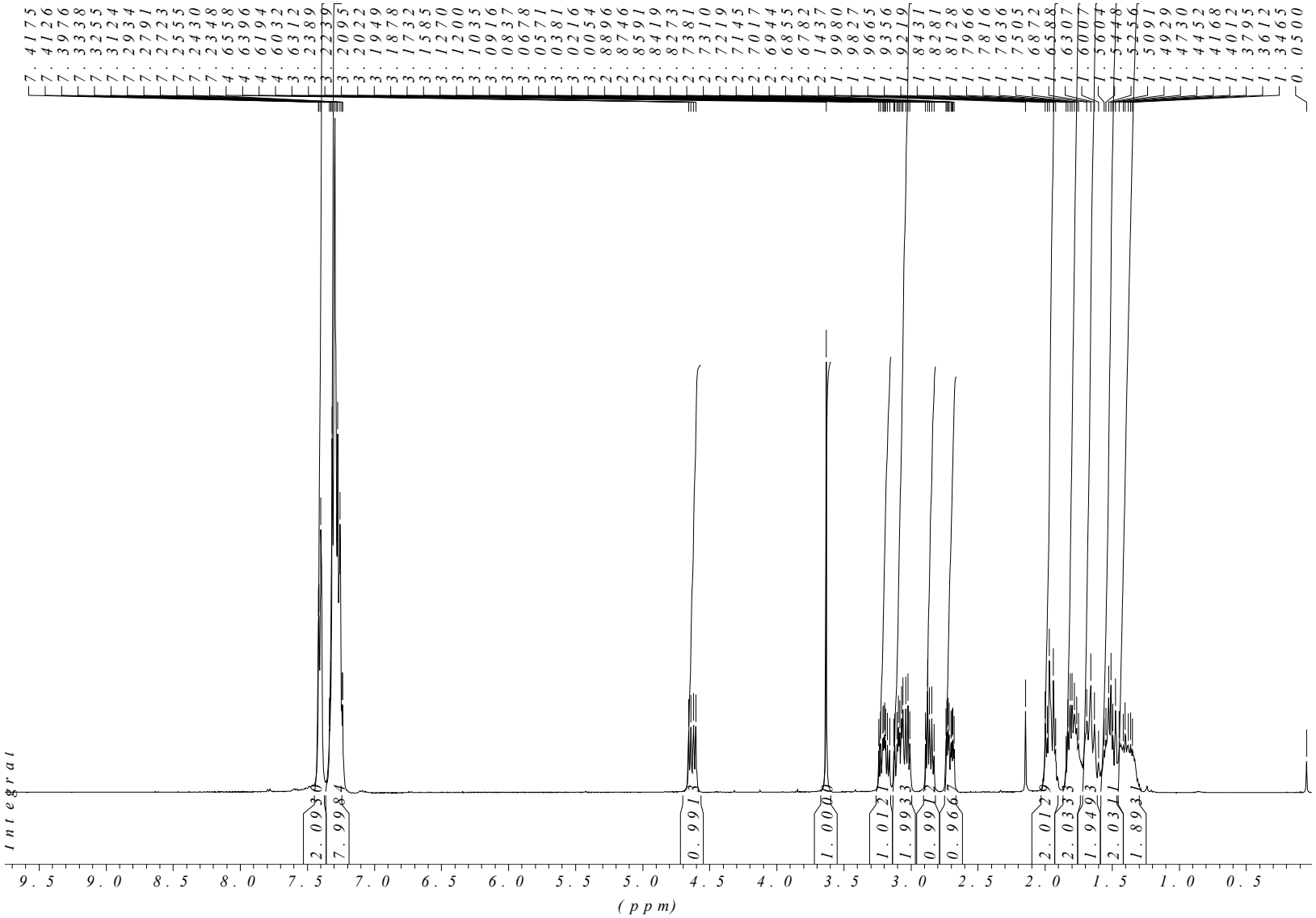

160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

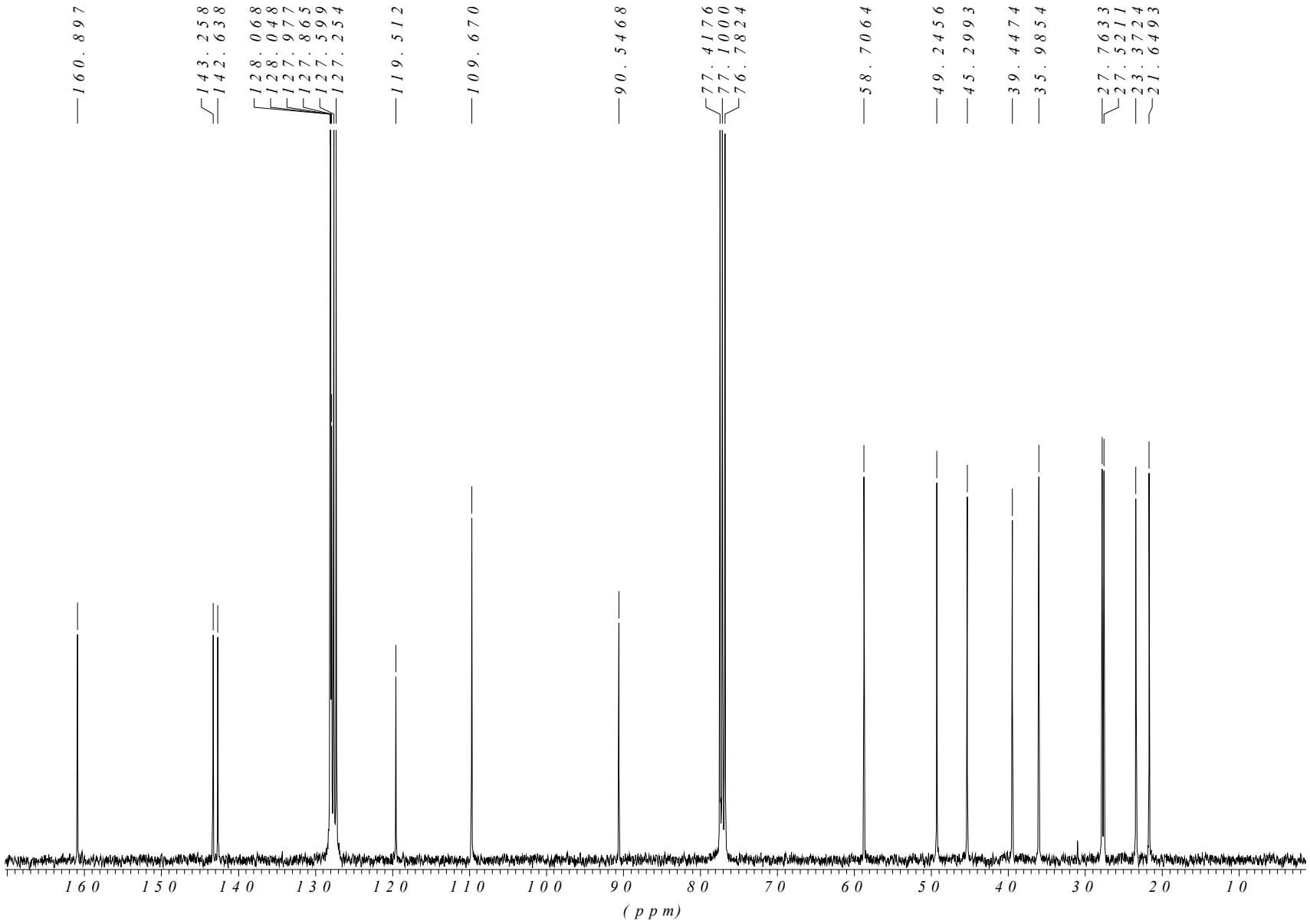
^{1}H and ^{13}C spectra of 2-[2-(4-chlorophenyl)-2-methylhexahydro-5H,9H-[1,3]oxazolo[2',3':2,3]pyrimido-[1,2-a]azepin-3(2H)-yliden]acetonitrile (2b)




166.46
165.14
163.56
163.27
142.21
141.92
140.67
140.27
133.97
133.88
133.64
133.62
129.46
128.45
128.22
128.02
127.86
126.88
119.59
119.57
119.49
119.29
108.83
107.74
106.94
106.31
87.274
87.201
86.321
86.054
77.416
77.100
76.779
76.212
57.658
55.155
54.271
48.654
47.496
47.134
46.509
46.162
45.949
45.472
41.414
41.987
40.000
40.674
36.388
35.207
28.660
27.757
27.189
26.671
26.599
26.275
26.020
25.962
25.078
24.461
24.332
24.290
23.779
23.737
23.143
22.072
21.169
20.731
20.571
20.346
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
(ppm)

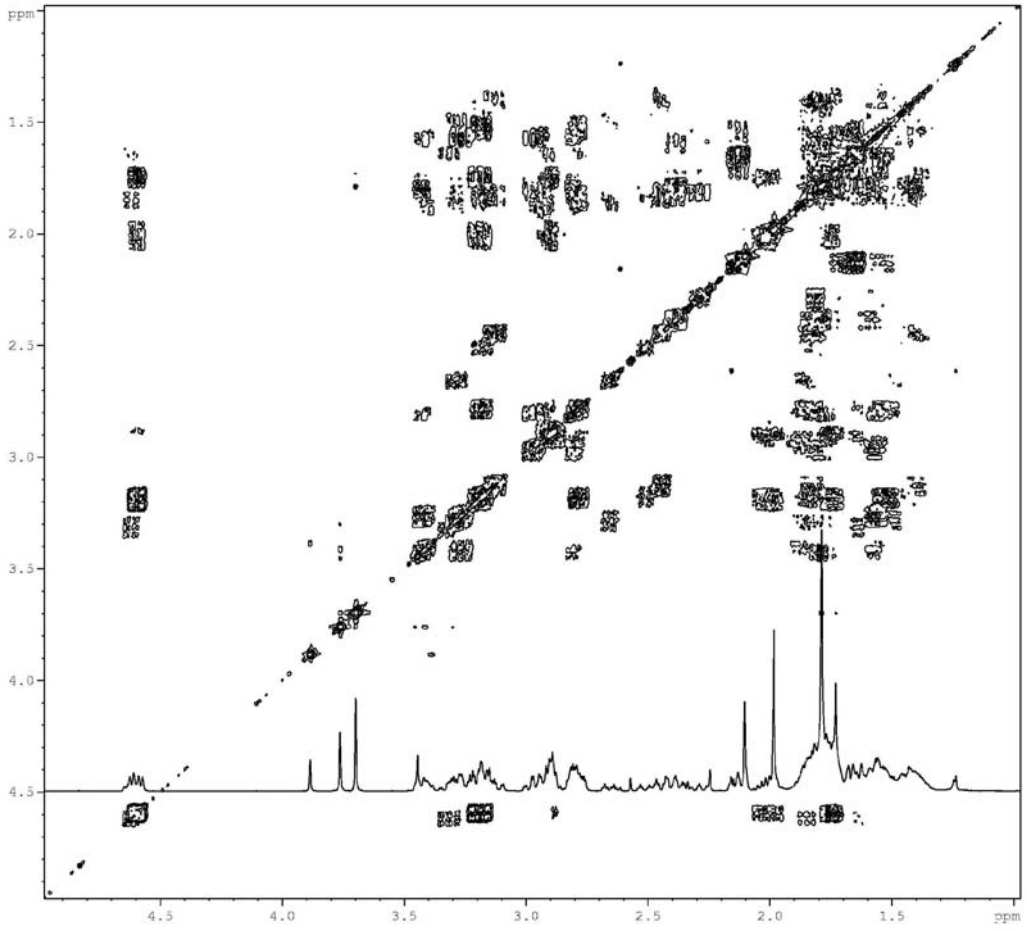
^{1}H and ^{13}C spectra of 2-[2,2-diphenylhexahydro-5H,9H-[1,3]oxazolo[2',3':2,3]pyrimido-[1,2-a]azepin-3(2H)-yliden]acetonitrile (2c)



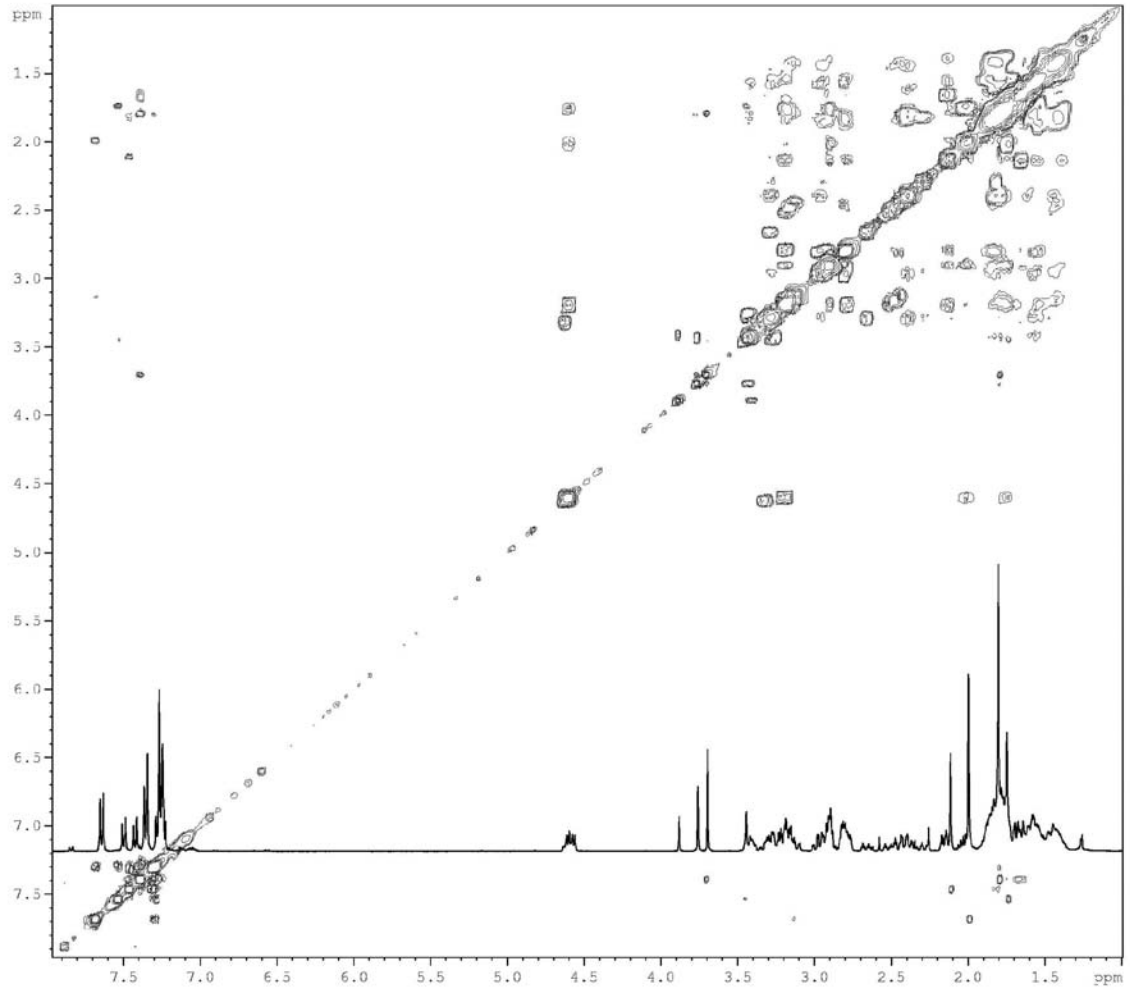

160.897
143.258
142.638
128.068
128.048
127.977
127.865
127.599
127.254
119.512
109.670
90.5468
77.4176
77.1000
76.7824
58.7064
49.2456
45.2993
39.4474
35.9854
27.7633
27.5211
23.3724
21.6493
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)

Selected 2D NMR spectra

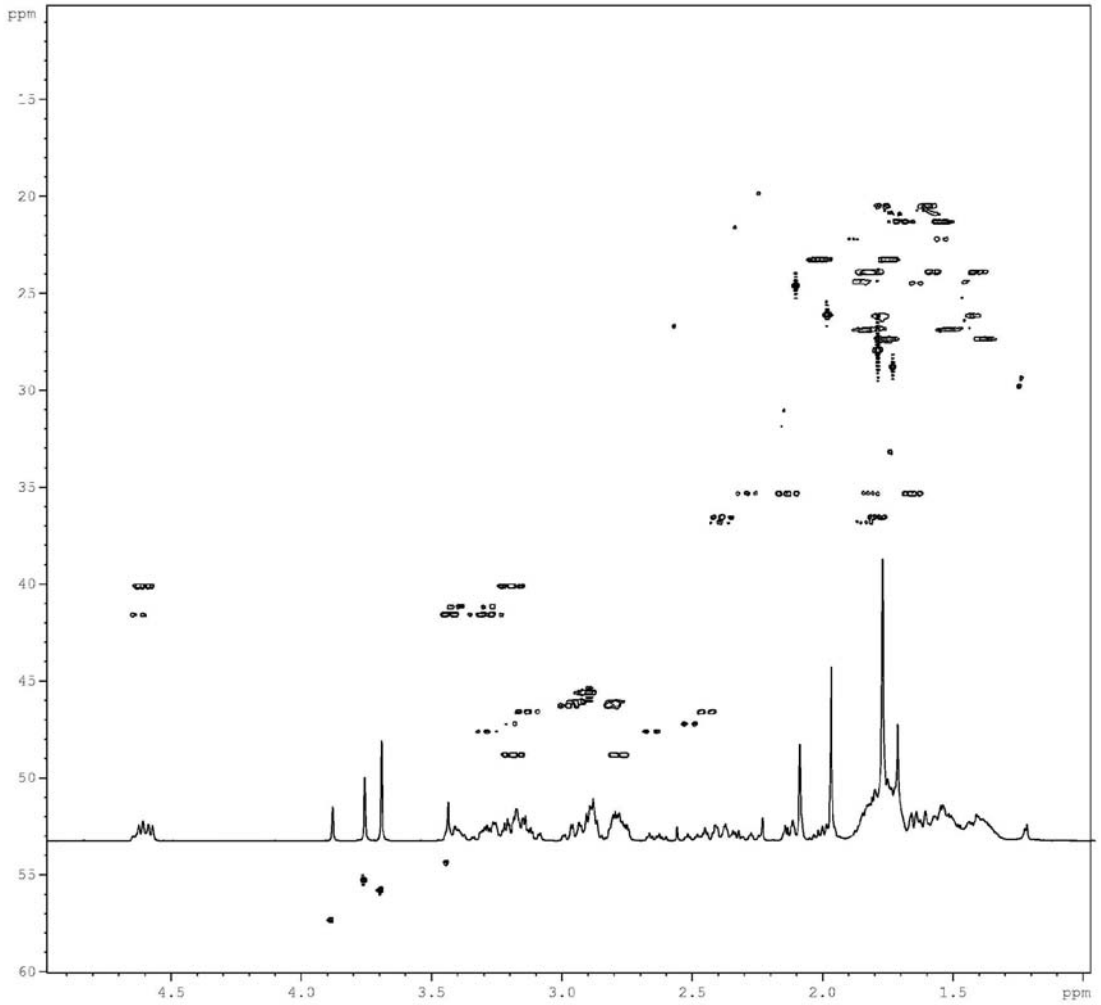
2D COSY spectrum of 2b (aliphatic region, $CDCl_3$)



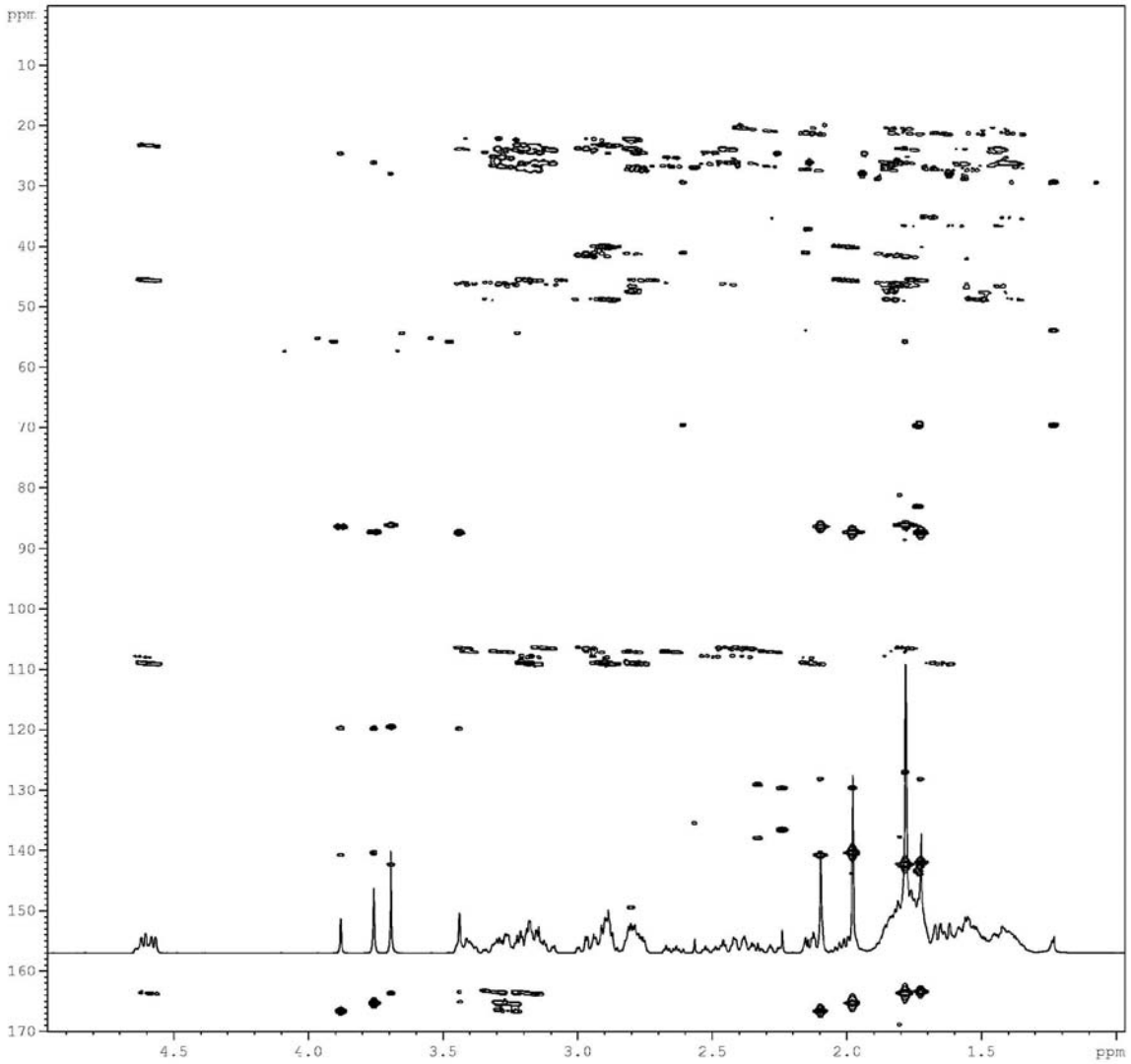
2D NOESY spectrum of 2b ($CDCl_3$)



2D ^{1}H-^{13}C HSQC spectrum of 2b (aliphatic region, $CDCl_3$)



2D ^{1}H-^{13}C HMBC spectrum of 2b ($CDCl_3$)



2D ^{1}H-^{15}N HMBC spectrum of 2b ($CDCl_3$)