SUPPORTING INFORMATION

Surfactant micelles as microreactors for the synthesis of quinoxalines in water: scope and limitations of surfactant catalysis

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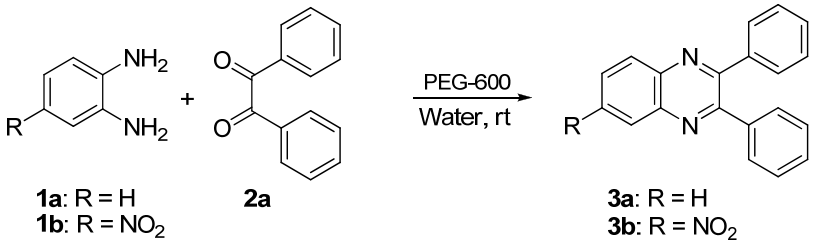
Comparison of the method developed under the present study with the literature report on PEG-600 mediated synthesis of quinoxaline in water (H. V. Chavan, L. K. Adsul and B. P. Bandgar, *J. Chem. Sci*. 2011, 123, 477).



1a: R = H
1b: R = NO_2

2a

3a: R = H
3b: R = NO_2

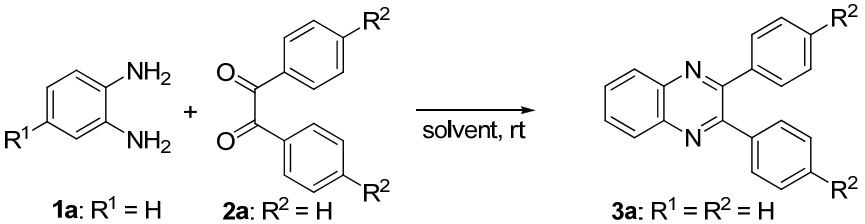
Table A: The use of PEG-600 in catalytic amount (20 mol%) and as co solvent during the synthesis of quinoxaline in water.

Entry	Amount (mol%)[b]	R	R^1	Time (h)	Yield (%)[c,d]
1	20	H	H	1	55[e]
2	2.5 mL	H	H	5 min	82 (98)
4	20	NO_2	H	5	38
5	20	NO_2	H	1	12
6	20	NO_2	H	5 min	nil
7	2.5 mL	NO_2	H	5	60
8	2.5 mL	NO_2	H	1	32
9	2.5 mL	NO_2	H	0.5	08[f]
10	2.5 mL	NO_2	H	5 min	nil

[a]The *o*-phenylelediamine (1 mmol) was treated with the 1,2-diketone (1 mmol, 1 equiv) in the presence of the PEG-600 in water (5 mL for reactions using 20 mol% of PEG-600 and 2.5 mL for reactions using 2.5 mL of PEG-600) at rt for different time intervals. [b]Amount of the PEG-600 used. [c]Isolated yield of the quinoxaline. [d]The data in the paranthesis is the yield of the quinoxaline reported in *J. Chem. Sci*., 2011, **123**, 477. [e]The quinoxaline was obtained in 98% yield in performing the reaction using Tween 40 (10 mol%) in water (5 mL) for 5 min at rt. [f]The quinoxaline was obtained in 80% yield in performing the reaction using Tween 40 (10 mol%) in water (5 mL) for 30 min at rt.

Superiority of the present work over a recent report on catalyst-free quinoxaline synthesis in water:

At the time of preparation of the revision of this manuscript a report appeared on quinoxaline synthesis in water in the absence of any catalyst (C. Delpivo, G. Micheletti and C. Boga, *Synthesis*, 2013, 45, 1546). However this is applicable for aliphatic 1,2-diketone. Poor yields (10-30%) are obtained for reactions using 1,2-diaryl ketones as observed in the present investigation (this data are in concurrence with the observation under the present study. Rev manuscript: table 1, entry 1). Thus the works described in the present manuscript is distinctly superior to this recent literature report (C. Delpivo, G. Micheletti and C. Boga, *Synthesis*, 2013, 45, 1546). Further, some of the reactions reported in this recent report performed in organic solvent were repeated following the literature report as well as under the conditions of the present manuscript and the results are summarized in Table A. These clearly demonstrate that the protocol (water as the reaction medium and 10 mol% of Tween 40) is the most effective methodology for the preparation of quinaxolines.



1a: R^1 = H
1c: R^1 = Cl
1d: R^1 = Me

2a: R^2 = H
2b: R^2 = OMe

3a: $R^1 = R^2$ = H
3d: R^1 = H; R^2 = OMe
3e: R^1 = Cl; R^2 = H
3f: R^1 = Me; R^2 = H

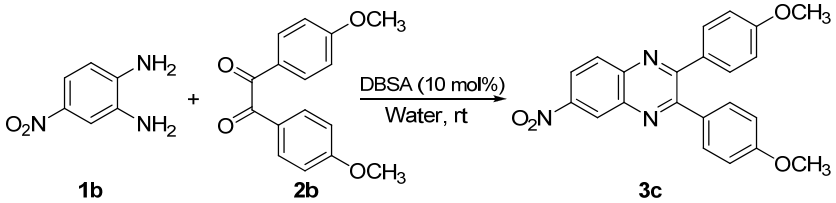
Table B:

Entry	solvent	R^1	R^2	Time (h)	Yield (%)[a,b]
1	EtOH	H	H	0.5	70 (90)[c]
2	EtOH	H	H	5 min	20
3	water	H	H	0.5	18
4	water	H	H	5 min	trace[d]
5	DCM	H	H	3	52 (70)[c]
6	DCM	H	H	5 min	trace
7	water	H	H	3	32
8	EtOH	H	4-OMe	2	41 (70)[c]
9	EtOH	H	4-OMe	20 min	trace
10	water	H	4-OMe	2	12
11	water	H	4-OMe	20 min	trace[e]
12	DCM	H	4-OMe	3	15 (40)[c]
13	DCM	H	4-OMe	20 min	trace
14	water	H	4-OMe	3	trace
15	EtOH	Cl	H	0.5	61 (95)[c]

16	EtOH	Cl	H	5 min	18
17	water	Cl	H	0.5	15
18	water	Cl	H	5 min	trace[f]
19	EtOH	Me	H	0.5	55 (89)[c]
20	EtOH	Me	H	5 min	15
21	water	Me	H	0.5	12
22	water	Me	H	5 min	trace[g]

[a]*o*-Phenyleledіamine (1 mmol) was treated with 1,2-diketone (1 mmol, 1 equiv) in various solvent at rt for different time intervals in absence of catalyst. [b]Isolated yield. [c]Yield reported in *Synthesis*, 2013, **45**, 1546. [d]The quinoxaline was formed in 98% yield in performing the reaction in water in the presence of 10 mol% of Tween 40 following the procedure developed under the present study. [e]The quinoxaline was formed in 90% yield in performing the reaction in water in the presence of 10 mol% of Tween 40 following the procedure developed under the present study. [f]The quinoxaline was formed in 96% yield in performing the reaction in water in the presence of 10 mol% of Tween 40 following the procedure developed under the present study. [g]The quinoxaline was formed in 95% yield in performing the reaction in water in the presence of 10 mol% of Tween 40 following the procedure developed under the present study.

Comparison of the method developed under the present study with the literature report on DBSA-catalysed reaction in water (E. Kolvari, M. A. Zolfigol and M. Peiravi, *Green Chem. Lett. Rev.*, 2011, 5, 155) for the synthesis of 2,3-bis(4-methoxyphenyl)-6-nitroquinoxaline 3c.



1b **2b** **3c**

Table C:

Entry	Condition	Time (h)	Yield (%)[a,b]
1	rt	6	nil (86)[c]
2	reflux (oil bath 110 °C)	6	48[d]

[a]**1b** (1 mmol) was treated with **2b** (0.27 g, 1 mmol, 1 equiv) in the presence of the DBSA (10 mol%) in water (5 mL) under different condition for 6 h. [b]Isolated yield of **3c**. [c]The figure in the parenthesis is the yield of **3c** reported in *Green Chem. Lett. Rev.*, 2011, **5**, 155. [d]The **3c** was obtained in 95% yield in performing the reaction following the procedure developed under the present study.

Spectral data

6-Methyl-2,3-diphenylquinoxaline (entry 2, table 6): White solid; mp = 118-119 °C; IR (neat) ν_{max} = 3400, 1621, 1445, 1345, 1058, 752, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.5 Hz, 1 H), 7.97 (s, 1H), 7.60 (dd, *J* = 1.7 Hz & *J* = 8.5 Hz, 1H), 7.49-7.53 (m, 4H), 7.27-7.39 (m, 6H), 2.63 (s, 1H); MS (APCI) m/z 297.38 $(M+H)^+$.[1]

6-Methoxy-2,3-diphenylquinoxaline (entry 3, table 6): White solid; mp = 160-161 °C; IR (neat) ν_{max} = 3400, 1617, 1448, 1350, 1204, 1024, 831, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 3.4 Hz, 2H), 7.54-7.48 (m, 5H), 7.43 (dd, *J* = 2.7 Hz & *J* = 9.1 Hz, 1H), 7.25-7.36 (m, 6H), 3.98 (s, 3H); MS (APCI) m/z 313.32 $(M+H)^+$.[2]

6-Fluoro-2,3-diphenylquinoxaline (entry 4, table 6): White solid; mp = 130-131 °C; IR (neat) ν_{max} = 3060, 1421, 1481, 1345, 1206, 757, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.16 (dd, *J* = 5.7 Hz & 9.2 Hz, 1H), 7.79 (dd, *J* = 2.7 Hz & 9.2 Hz, 1H), 7.48-7.54 (m, 5H), 7.23-7.37 (m, 6 H); MS (APCI) m/z 301.32 $(M+H)^+$.[2]

6-Chloro-2,3-diphenylquinoxaline (entry 5, table 6): White solid; mp = 124-125 °C; IR (neat) ν_{max} = 3435, 2924, 1596, 1467, 1342, 1068, 767, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 2.2 Hz, 1H), 7.54-7.48 (d, *J* = 8.9 Hz, 1H), 7.70 (dd, *J* = 2.8 Hz & *J* = 8.8 Hz, 1H), 7.50 (dd, *J* = 0.5 Hz & *J* = 6.8 Hz, 1H), 7.25-7.39 (m, 6H); MS (APCI) m/z 317.75 $(M+H)^+$.[2]

6-Bromo-2,3-diphenylquinoxaline (entry 6, table 6): White solid; mp = 120-122 °C; IR (neat) ν_{max} = 3435, 1594, 1470, 1343, 1058, 831.97, 766.93, 696.81 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 2.0 Hz, 1H), 8.02 (d, *J* = 8.9 Hz, 1H), 7.82 (dd, *J* = 2 Hz & *J* = 8.9 Hz, 1H), 7.49 (t, *J* = 6.6 Hz, 4 H), 7.32-7.41 (m, 6H); MS (APCI) m/z 362.24 $(M+H)^+$.[3]

6-Nitro-2,3-diphenylquinoxalineq (entry 7, table 6): White solid; mp = 190-191 °C; IR (neat) ν_{max} = 3411, 1766, 1523, 1340, 1054, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 9.08 (d, *J* = 2.4 Hz, 1H), 8.55 (dd, *J* = 2.5 Hz & 9.2 Hz, 1H), 7.31(d, *J* = 9.1 Hz, 1H), 7.55-7.59 (m, 4H), 7.36-7.46 (m, 6H); MS (APCI) m/z: 328.36 $(M+H)^+$. [3]

2,3-Diphenylquinoxaline-6-carbonitrile (entry 8, table 6): White solid; mp = 184-185 °C; IR (neat) ν_{max} = 3438, 2225, 1637, 1547, 1450, 1341, 1223, 1026, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.53 (d, *J* = 0.9 Hz, 1H), 8.24 (d, *J* = 8.6 Hz, 1H), 7.89 (dd, *J* = 1 Hz & *J* = 9.6 Hz, 1H), 7.51-7.55 (m, 4 H), 7.33-7.42 (m, 6H); MS (APCI) m/z 308.35 $(M+H)^+$.[2]

6,7-Dimethyl-2,3-diphenylquinoxaline (entry 9, table 6): White solid; mp = 176-178 °C; IR (KBr) ν_{max} = 3071, 2958, 2361, 1727, 1460, 1344, 1272, 1124, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.94 (s, 2 H), 7.50-7.52 (m, 2H), 7.27-7.36 (m, 2H), 2.53 (s, 6H); MS (APCI) m/z 311.11 $(M+H)^+$.[4]

6,7-Chloro-2,3-diphenylquinoxaline (entry 10, table 6): White solid; mp = 148-149 °C; IR (KBr) ν_{max} = 3057, 1604, 1439, 1338, 1190, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.24 (s, 2H), 7.48-7.51 (m, 2H), 7.32-7.39 (m, 2H); MS (APCI) m/z 352.23 $(M+H)^+$.[5]

2,3-Bis(4-methoxyphenyl)quinoxaline (entry 11, table 6): White solid; mp = 148-150 °C; IR (KBr) ν_{max} = 2838, 1665, 1597, 1512, 1252, 1160, 1024, 834, 762, 579 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.13 (q, *J* = 3.4 Hz, 2H), 7.53 (q, *J* = 3.4 Hz, 2H), 7.49-7.53 (m, 2H), 6.87-6.90 (m, 2H); MS (APCI) m/z 343.41 $(M+H)^+$.[1]

2,3-Di(furan-2-yl)quinoxaline (entry 13, table 6): White solid; mp = 130-131 °C; IR (neat) ν_{max} = 3104, 2932, 2362. 1580, 1493, 1394, 1333, 1021, 765 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.57 (m, 2H), 6.65 (d, *J* = 3.4 Hz, 2H), 7.63 (d, *J* = 0.4 Hz, 2H), 7.73-7.76 (m, 2H), 8.12-8.15 (m, 2H); MS (APCI) m/z 263.21 $(M+H)^+$.[1]

2,3-Diphenylpyrido[2,3-b]pyrazine (entry 14, table 6): White solid; mp = 135-136 °C; IR (KBr) ν_{max} = 3359, 1541, 1428, 1071, 835, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 9.18 (m, 1H), 8.52 (dd, *J* = 1.3 Hz & 1.3 Hz, 8.2 Hz, 1H), 7.70-7.74 (m, 1H), 7.63-7.65 (m, 2H), 7.55 (d, *J* = 1.6 Hz, 2H), 7.32-7.43 (m, 6H); MS (APCI) m/z 284.35 $(M+H)^+$.[2]

2,3-Diphenylpyrido[3,4-b]pyrazine (entry 15, table 6): White solid; mp = 173-175 °C; IR (KBr) ν_{max} = 3352, 1542, 1435, 1075, 1032, 830, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 9.60 (s, 1H), 8.82 (d, *J* = 5.7 Hz, 1H), 8.00 (d, *J* = 5.8 Hz, 1H), 7.52-7.55 (m, 4H), 7.39-7.43 (m, 6H); MS (APCI) m/z 284.28 $(M+H)^+$.[6]

6-Bromo-2,3-diphenylpyrido[2,3-b]pyrazine (entry 16, table 6): White solid; mp = 152-153 °C; IR (KBr) ν_{max} = 3395, 3060, 1390, 1335, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 9.15 (d, *J* = 2.4 Hz, 1H), 8.67 (d, *J* = 2.4 Hz, 1H), 7.53-7.63 (m, 2H), 7.53-7.55 (m, 2H), 7.31-7.43 (m, 6H); MS (APCI) m/z 362.21 $(M+H)^+$.[4]

2-Methyl-3-phenylquinoxaline (entry 17, table 6): White solid; mp = 54-55 °C; IR (KBr) ν_{max} = 3120, 1510, 1460, 1320, 1052, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 7.64 Hz, 2H), 8.06 (d, *J* = 7.92 Hz, 2H), 7.70-7.77 (m, 2H), .66 (d, *J* = 7.4 Hz, 2H), 7.48-7.56 (m, 2H), 2.78 (s, 3 H); MS (APCI) m/z 221.21 $(M+H)^+$.[7]

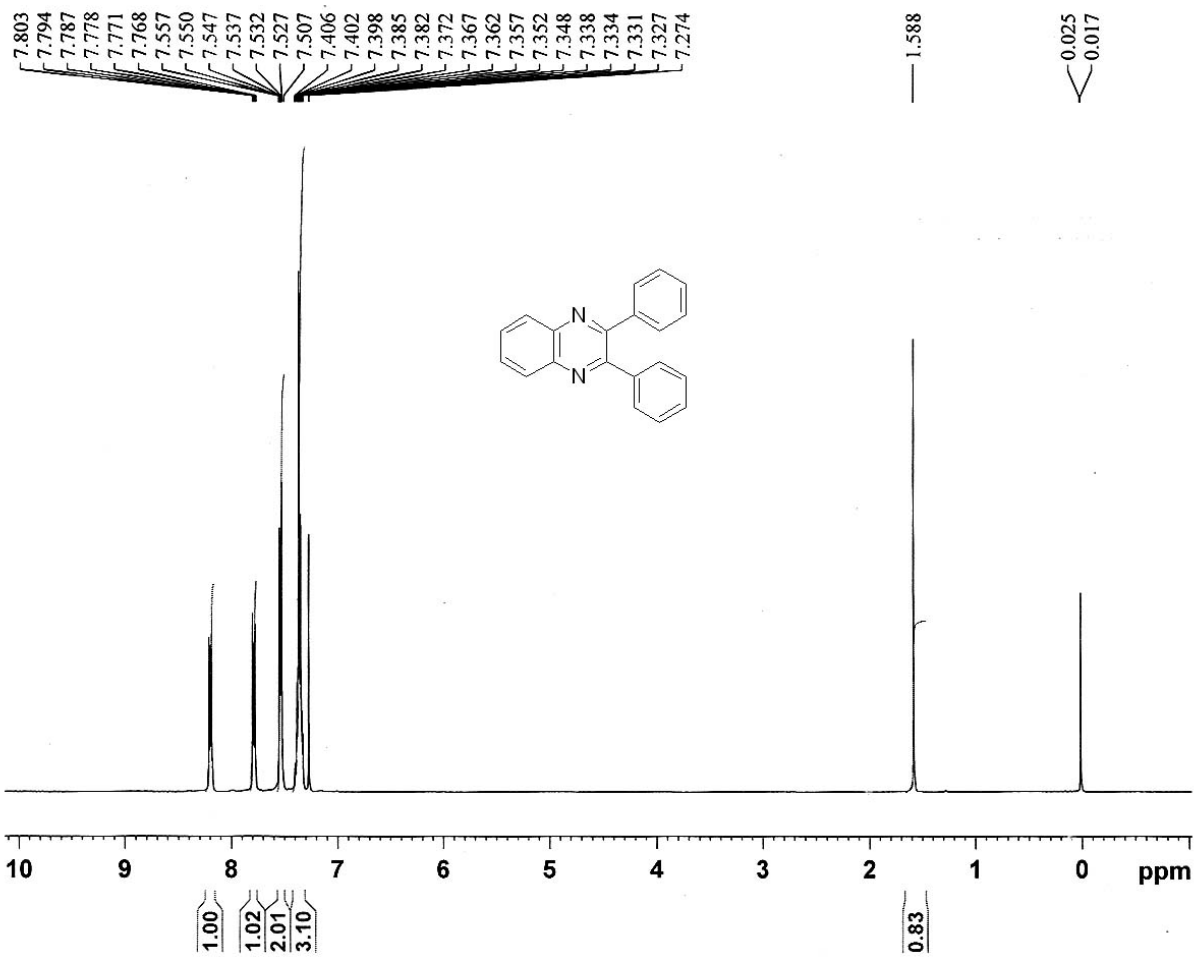
2,3-Diethylquinoxaline (entry 18, table 6): White solid; mp = 50-51 °C; IR (KBr) ν_{max} = 2970, 1710, 1455, 1290, 765 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.00 (dd, *J* = 6.24 Hz & 3.52 Hz , 2H), 7.65 (dd, *J* = 6.24 Hz & 3.44 Hz, 2H), 3.04 (q, 4H), 1.41 (t, *J* = 7.48 Hz, 6H); MS (APCI) m/z 187.45 $(M+H)^+$.[8]

2,3-Dimethylquinoxaline (entry 19, table 6): White solid; mp = 105-106 °C; IR (KBr) ν_{max} = 2970, 1710, 1455, 1290, 765 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.99-7.97 (m, 2H), 7.65-7.68 (m, 2H), 2.74 (s, 6H); MS (APCI) m/z 159.15 $(M+H)^+$.[3]

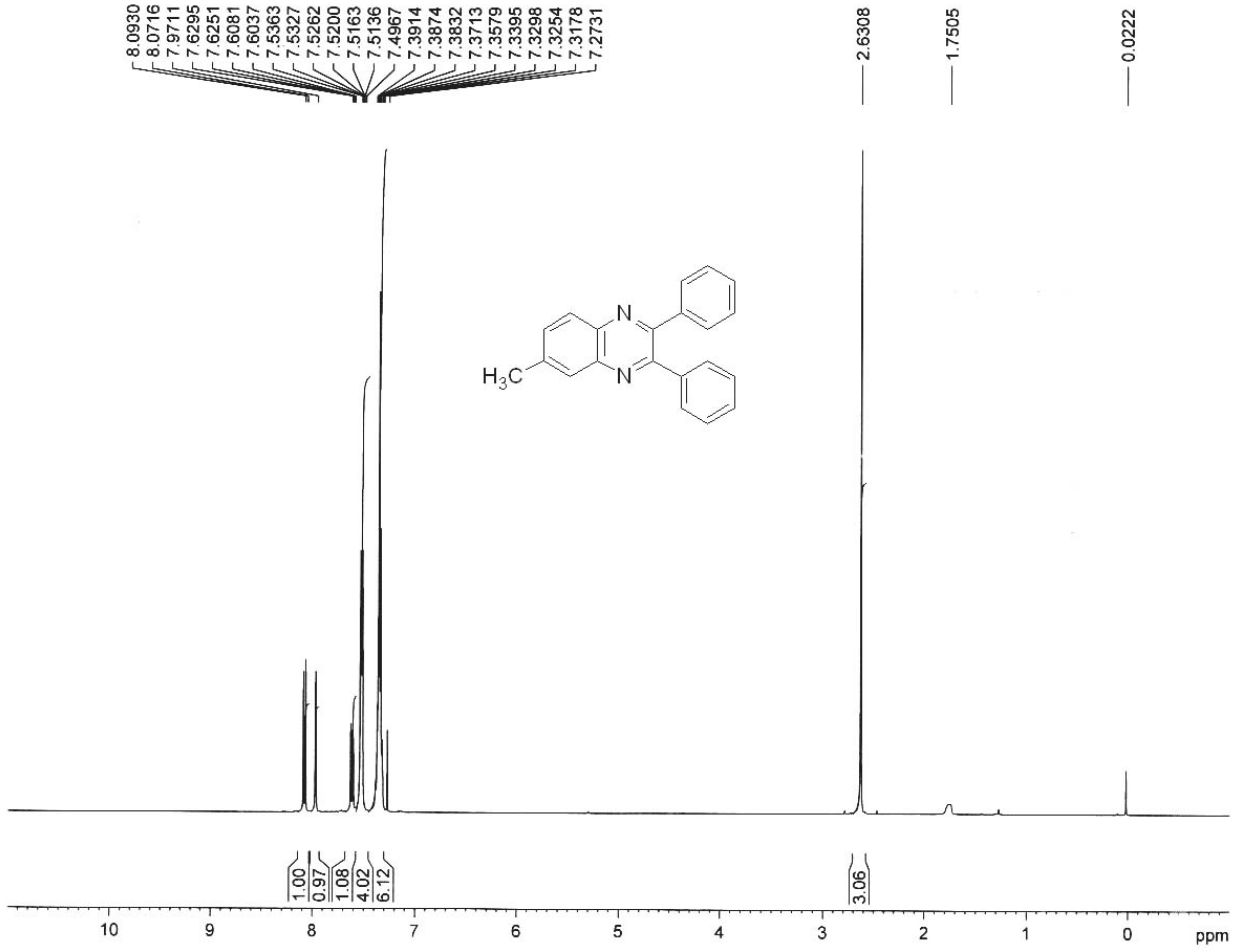
5,6-Diphenyl-2,3-dihydropyrazine (entry 21, table 6): White solid; mp = 165-166 °C; IR (KBr) ν_{max} = 2965, 1562, 1473, 982, 742, 712 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39 (d, *J* = 7.4 Hz, 4H), 7.31 (t, *J* = 7.31 Hz, 2H), 7.24 (t, *J* = 6.72 Hz, 4H); MS (APCI) m/z 235.32 $(M+H)^+$.[3]

Scanned NMR Spectra

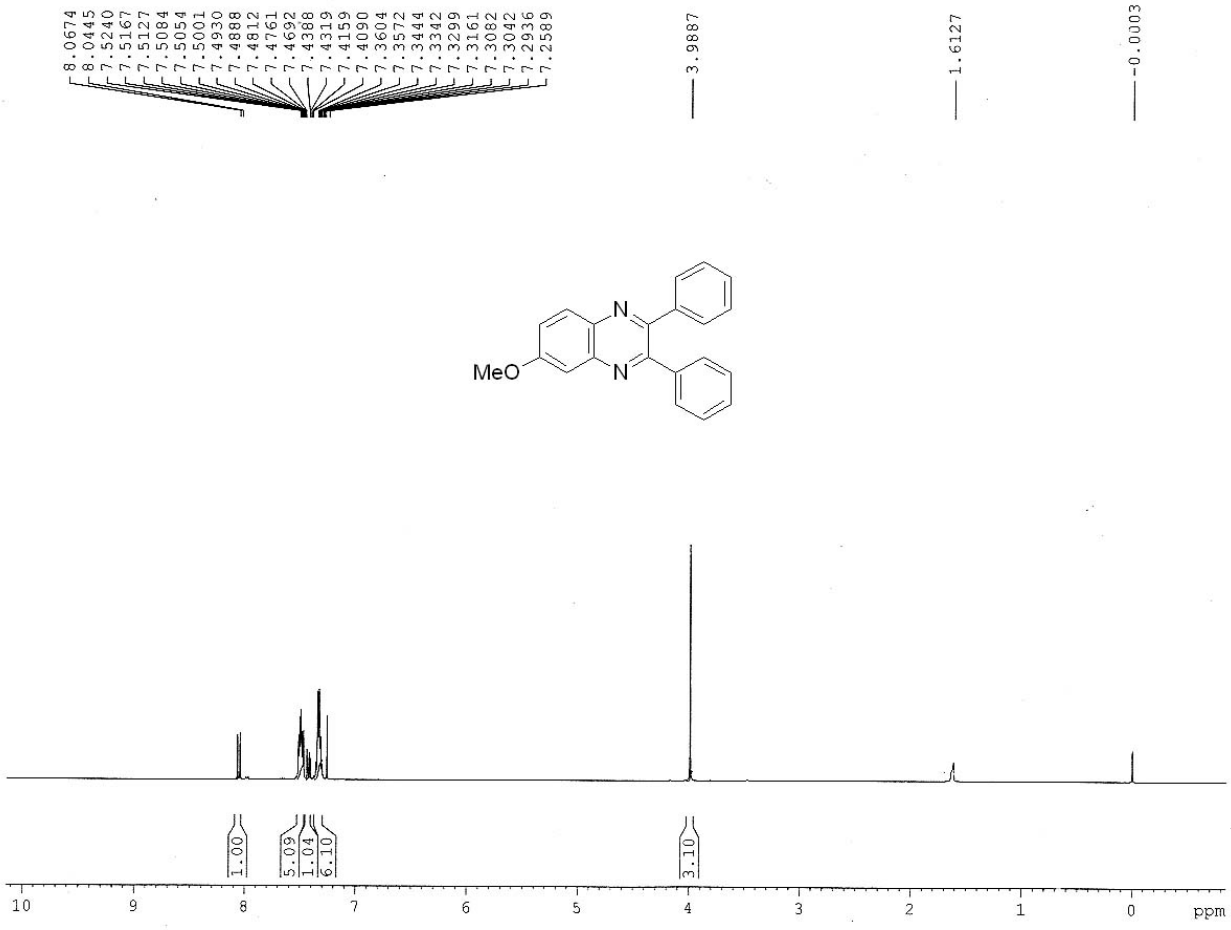
2,3-Diphenylquinoxaline (entry 1, table 6)



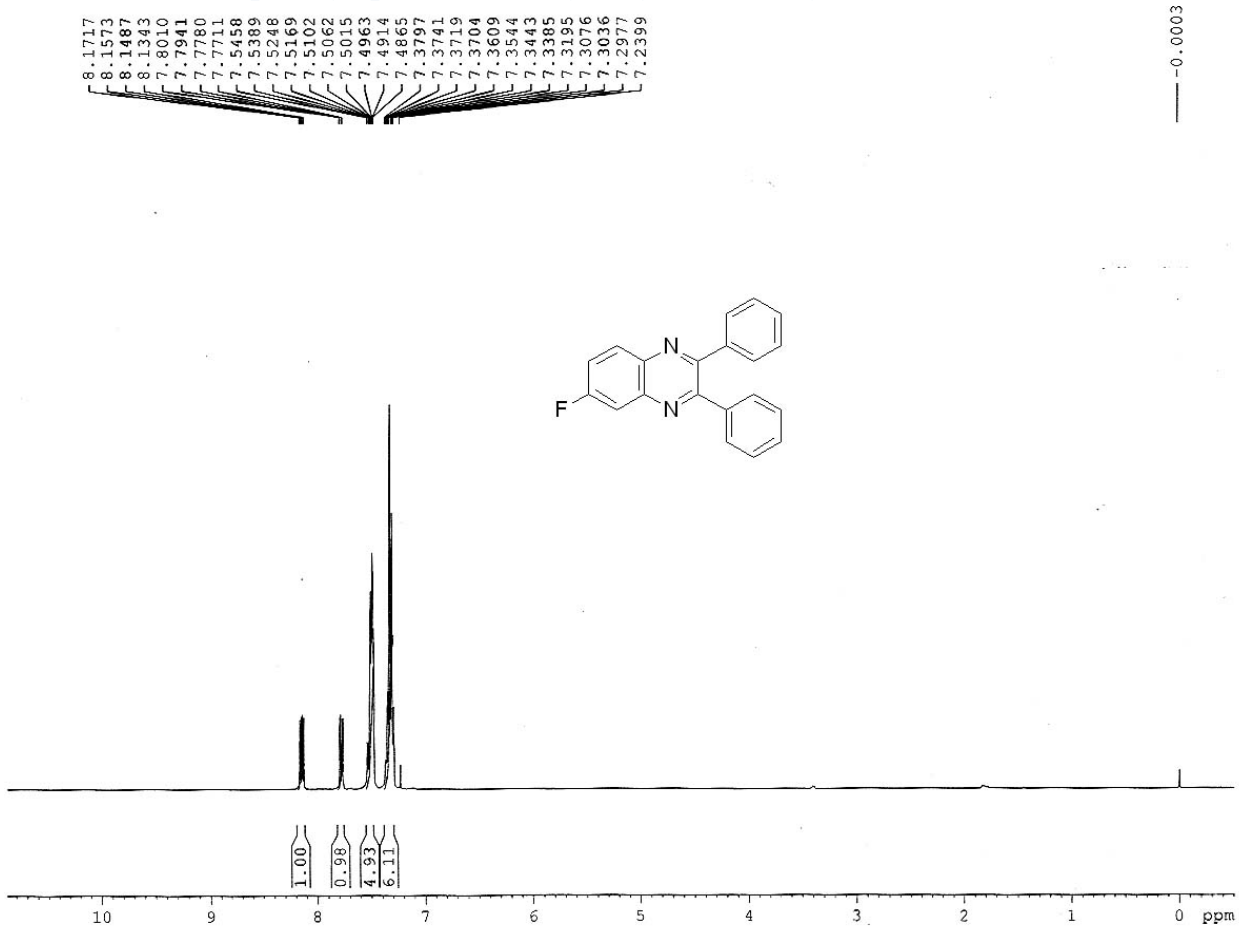
6-Methyl-2,3-diphenylquinoxaline (entry 2, table 6)



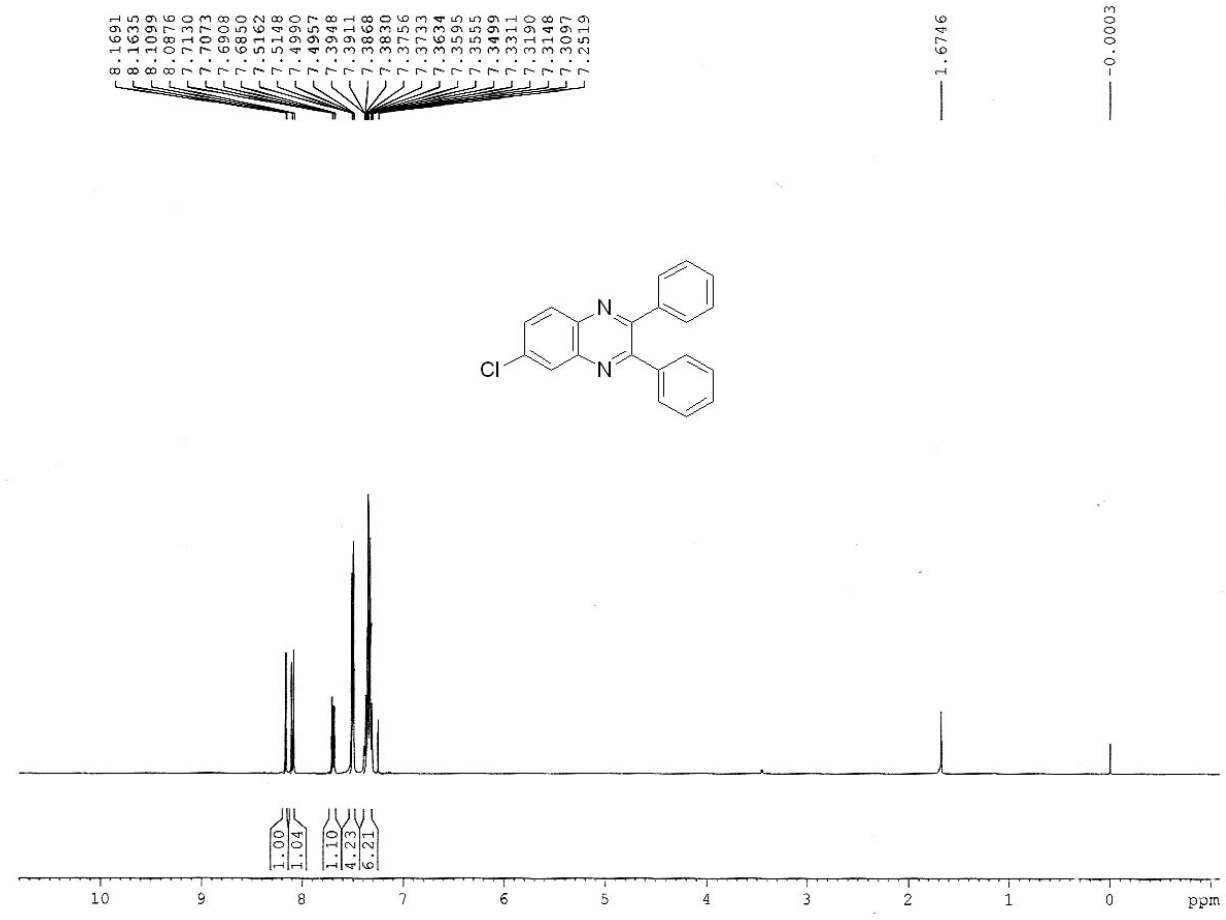
6-Methoxy-2,3-diphenylquinoxaline (entry 3, table 6)



6-Fluoro -2,3-diphenylquinoxaline (entry 4, table 6)



6-Chloro-2,3-diphenylquinoxaline (entry 5, table 6)



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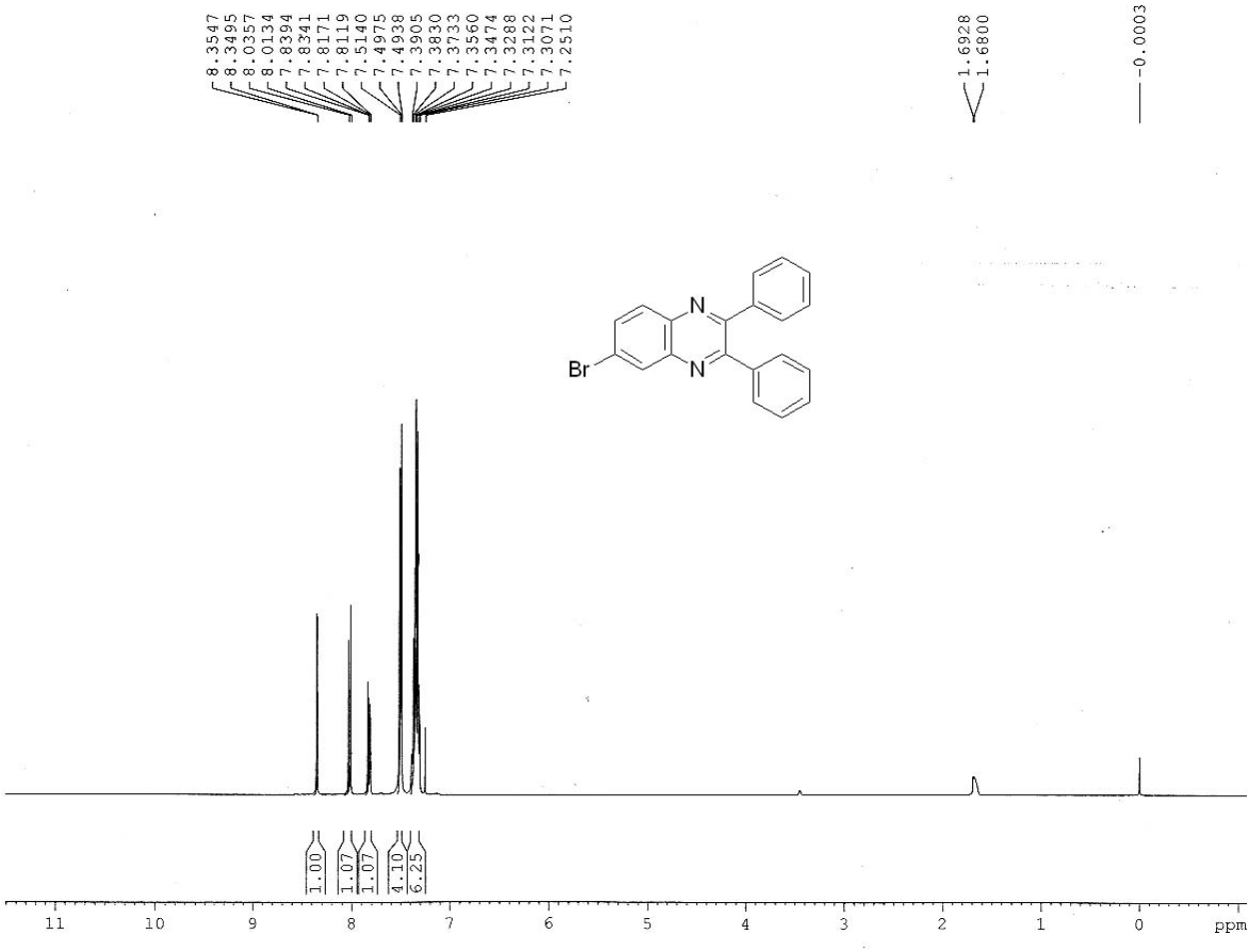
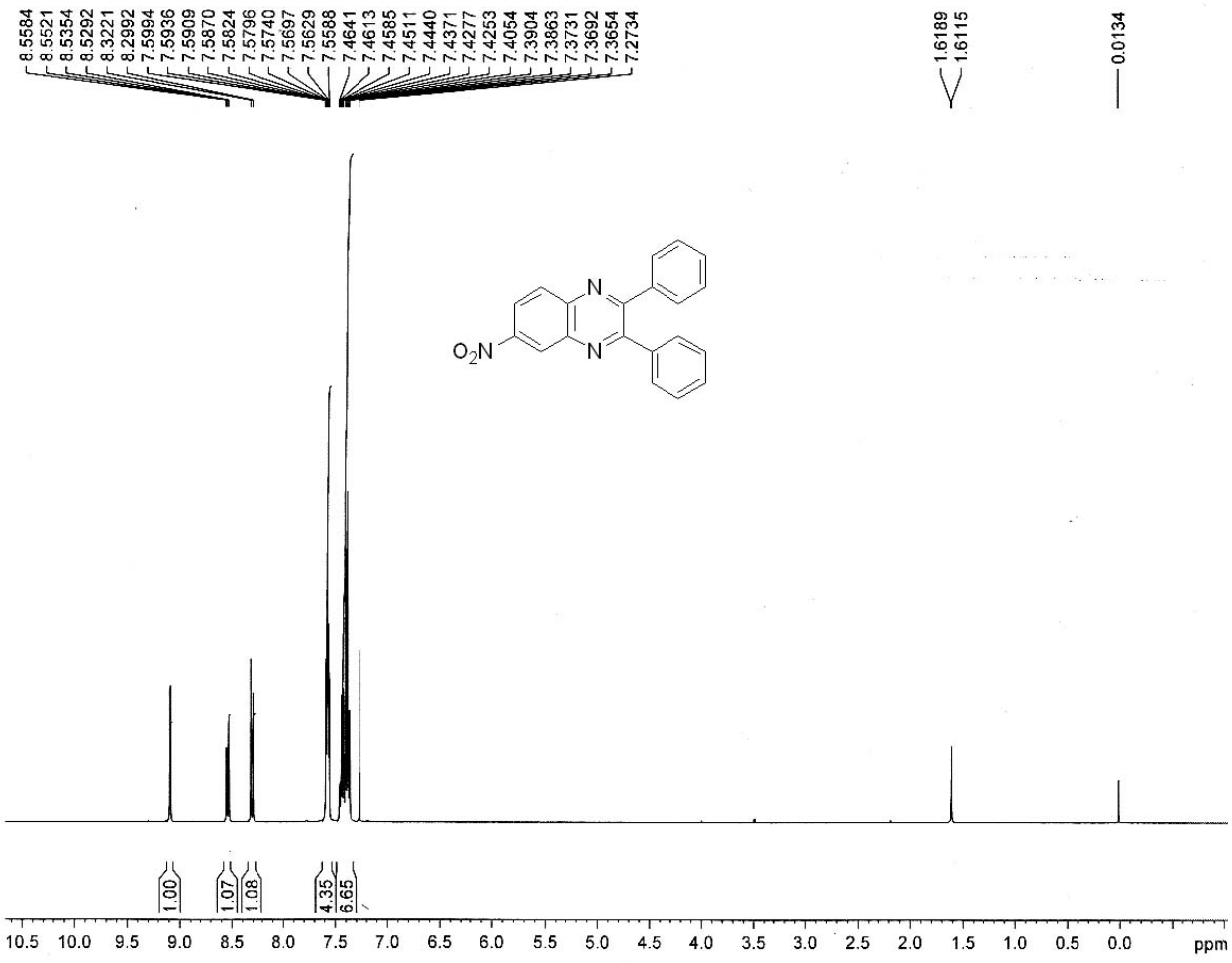
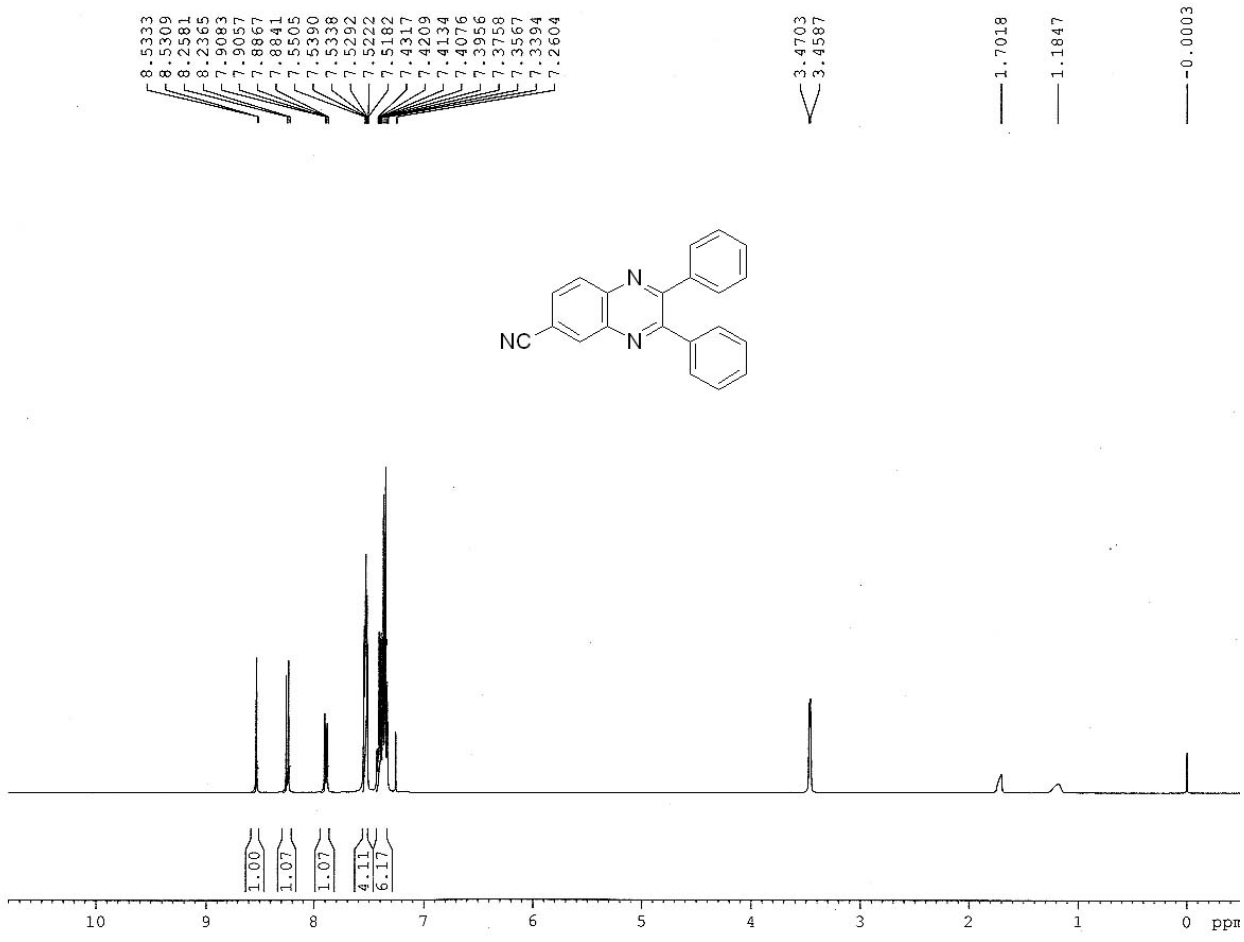


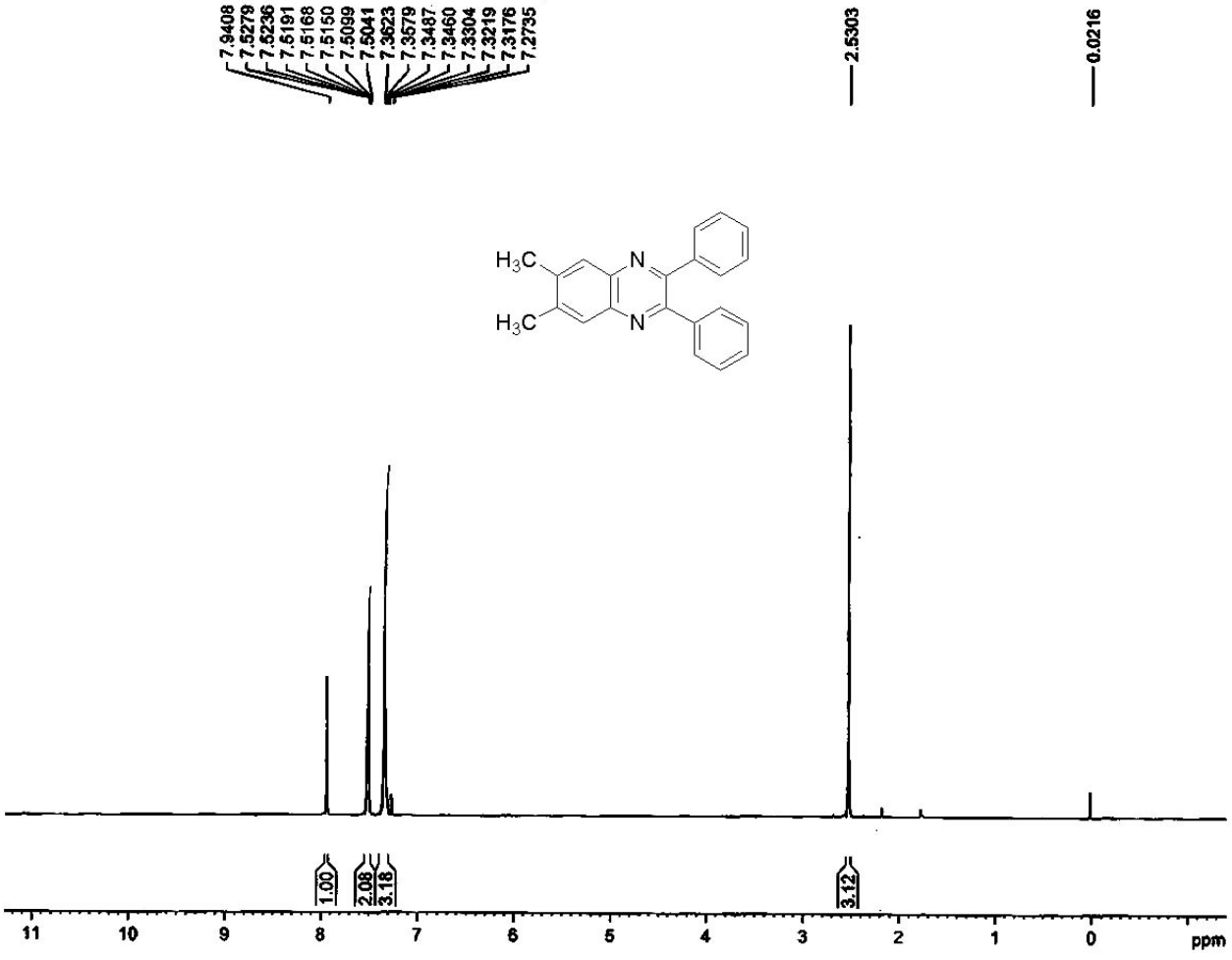
6-Nitro-2,3-diphenylquinoxaline (entry 7, table 6)



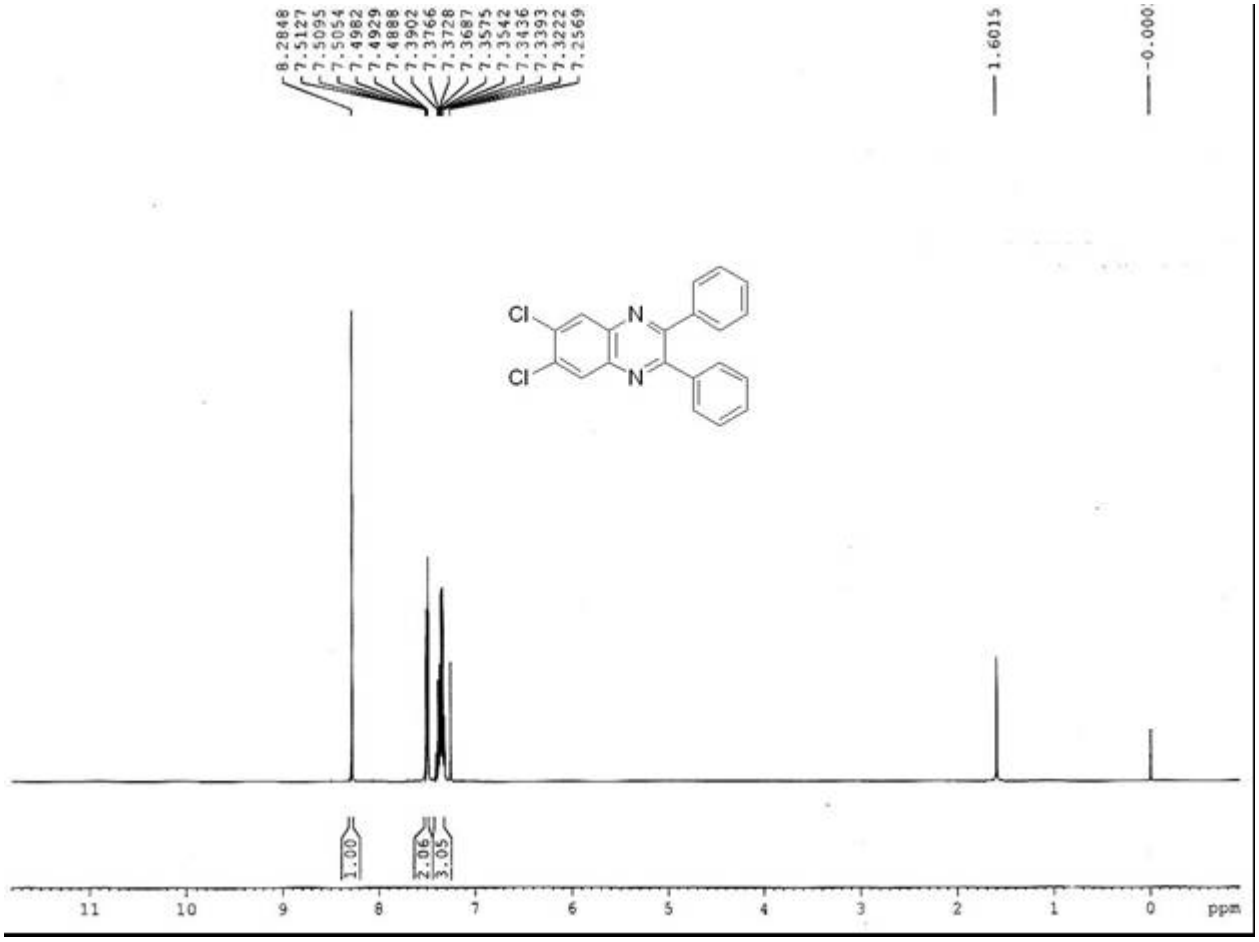
2,3-Diphenylquinoxaline-6-carbonitrile (entry 8, table 6)



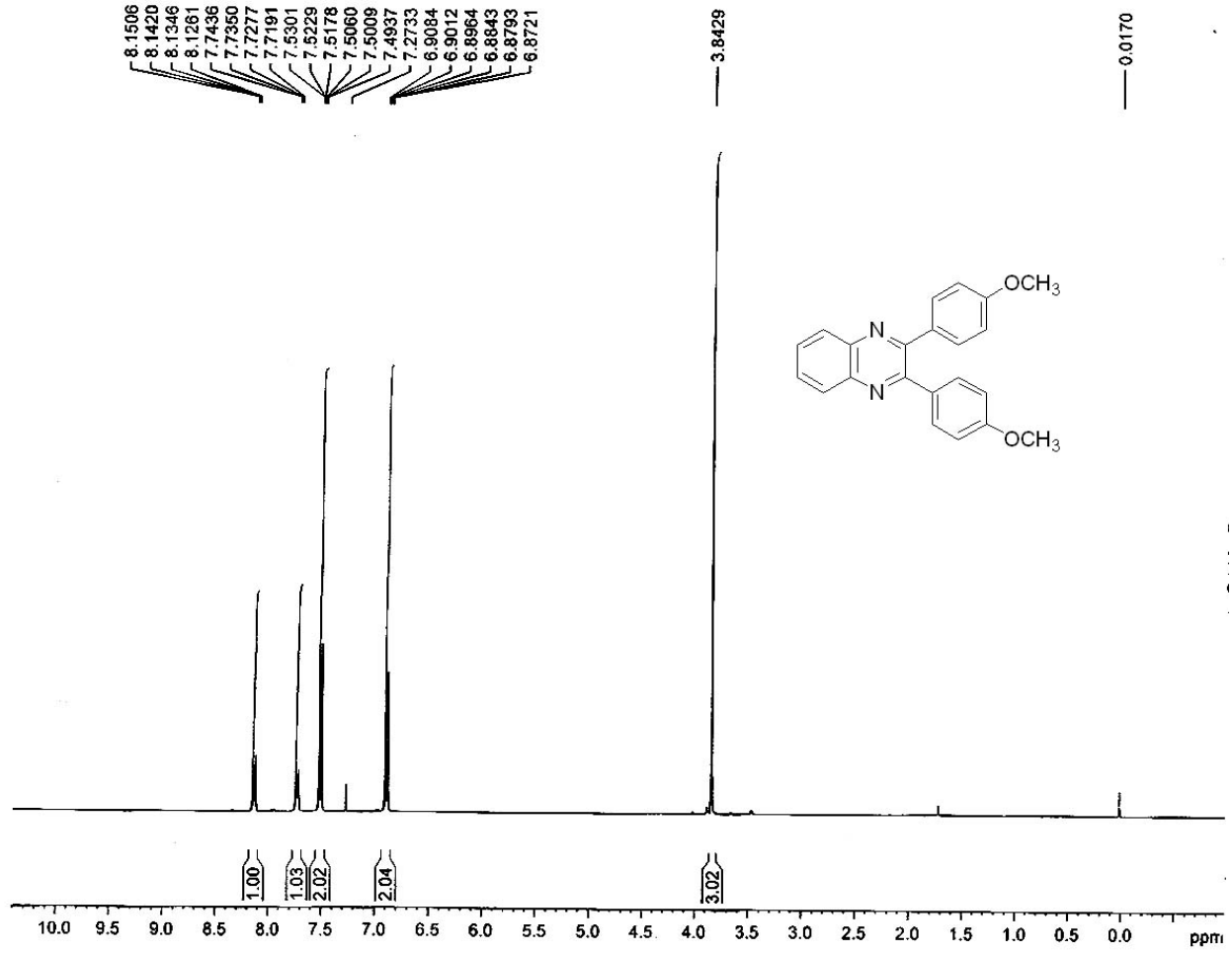
6,7-Dimethyl-2,3-diphenylquinoxaline (entry 9, table 6)



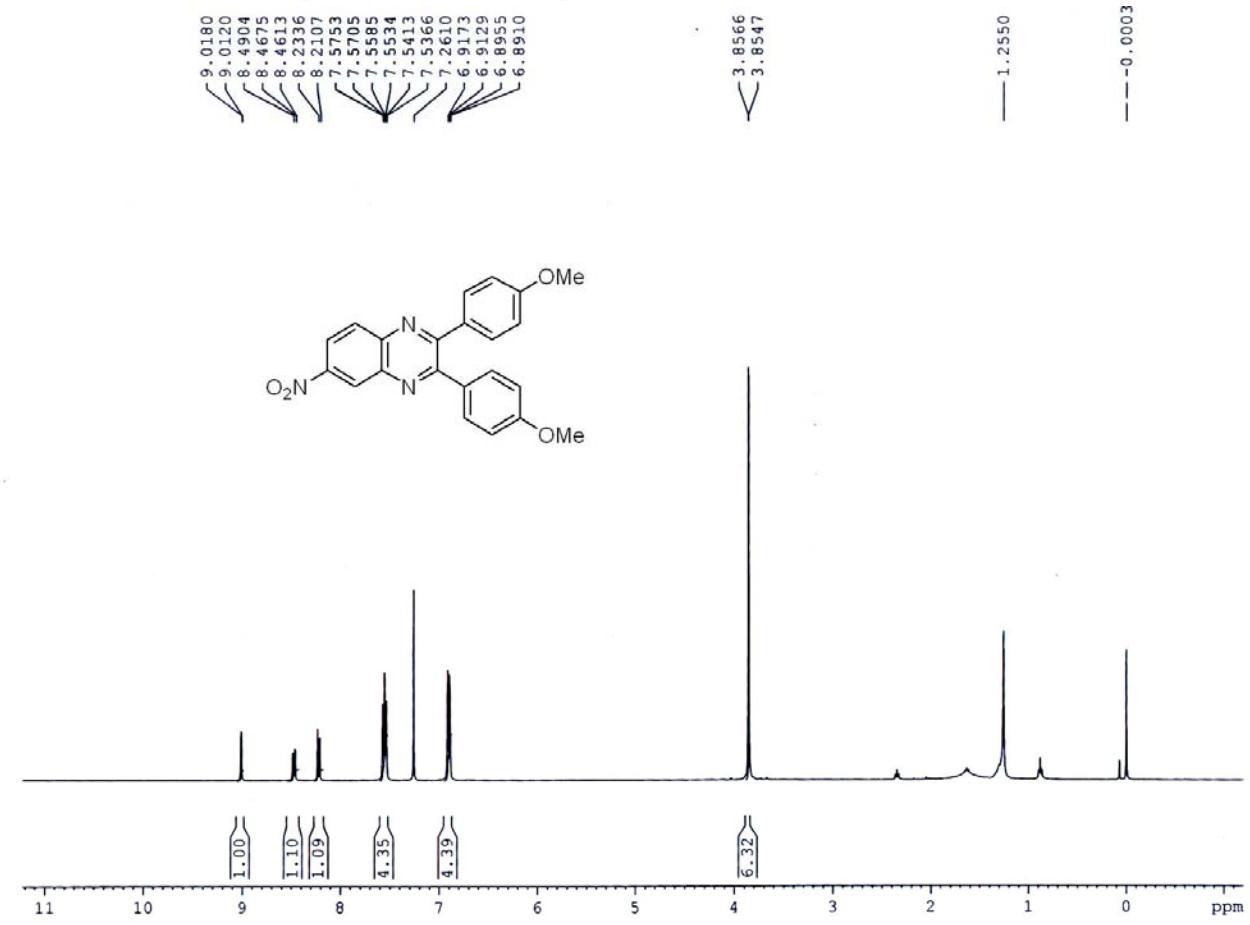
6,7-Chloro-2,3-diphenylquinoxaline (entry 10, table 6)



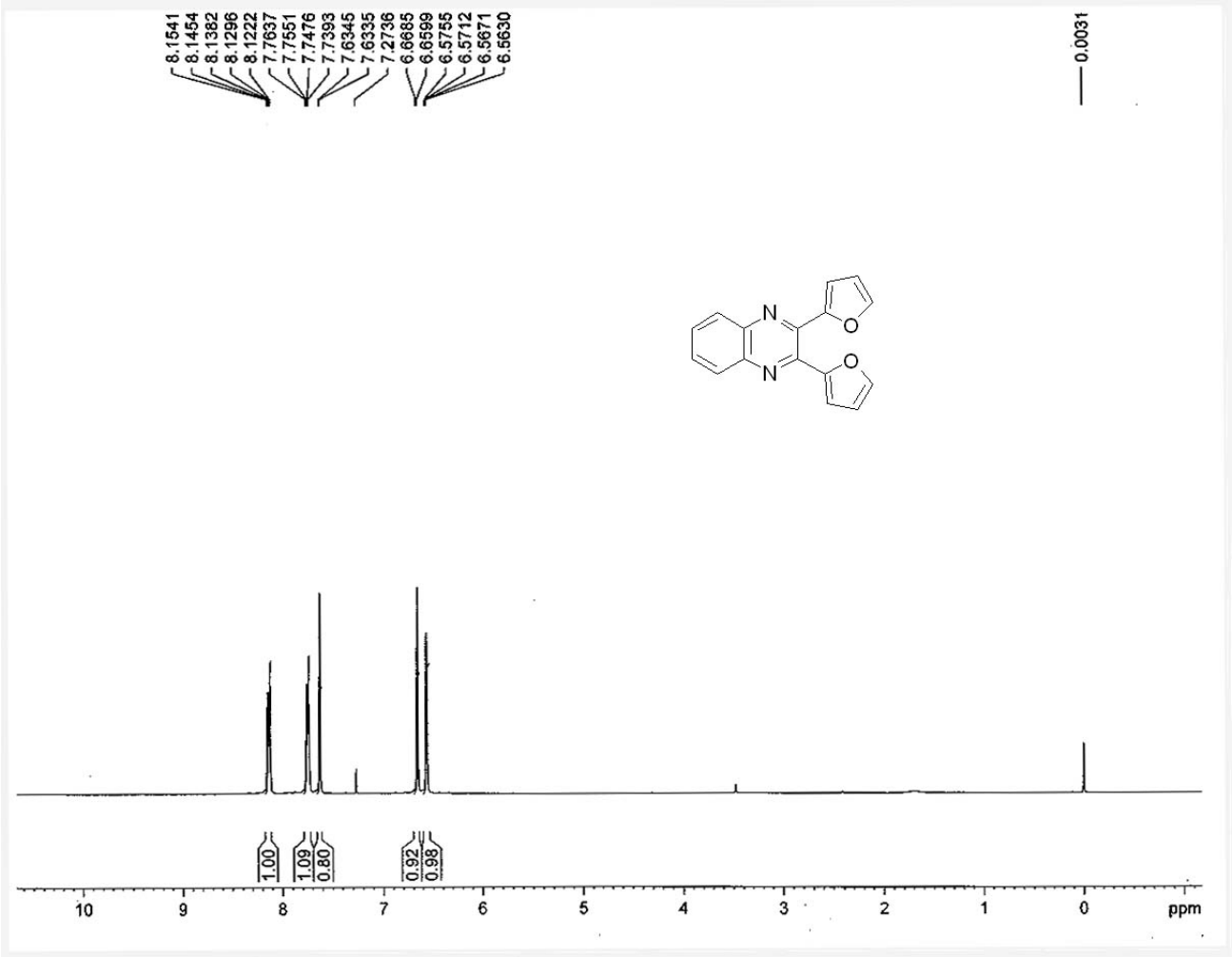
2,3-Bis(4-methoxyphenyl)quinoxaline (entry 11, table 6)



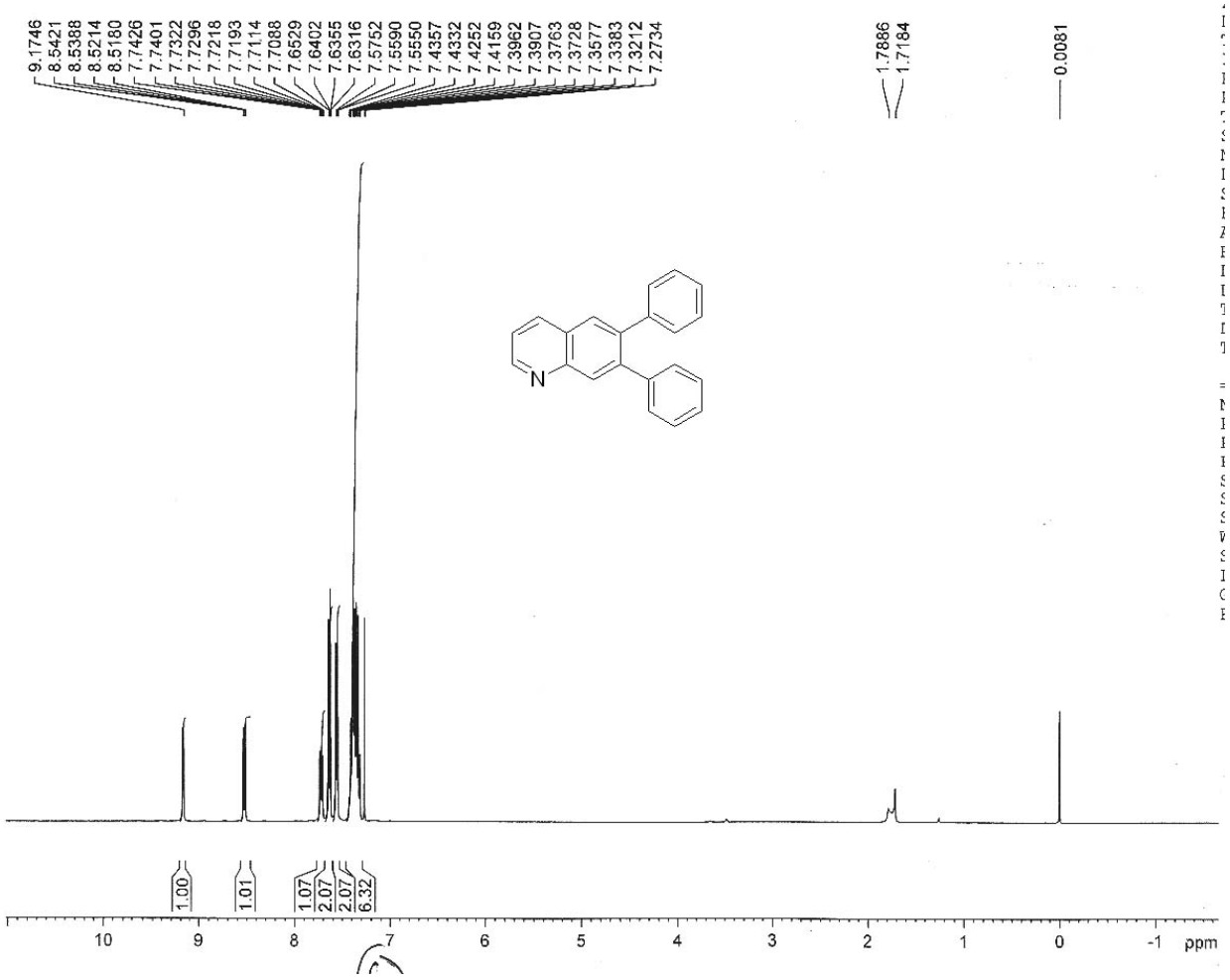
2,3-Bis(4-methoxyphenyl)-6-nitroquinoxaline (entry 12, table 6)



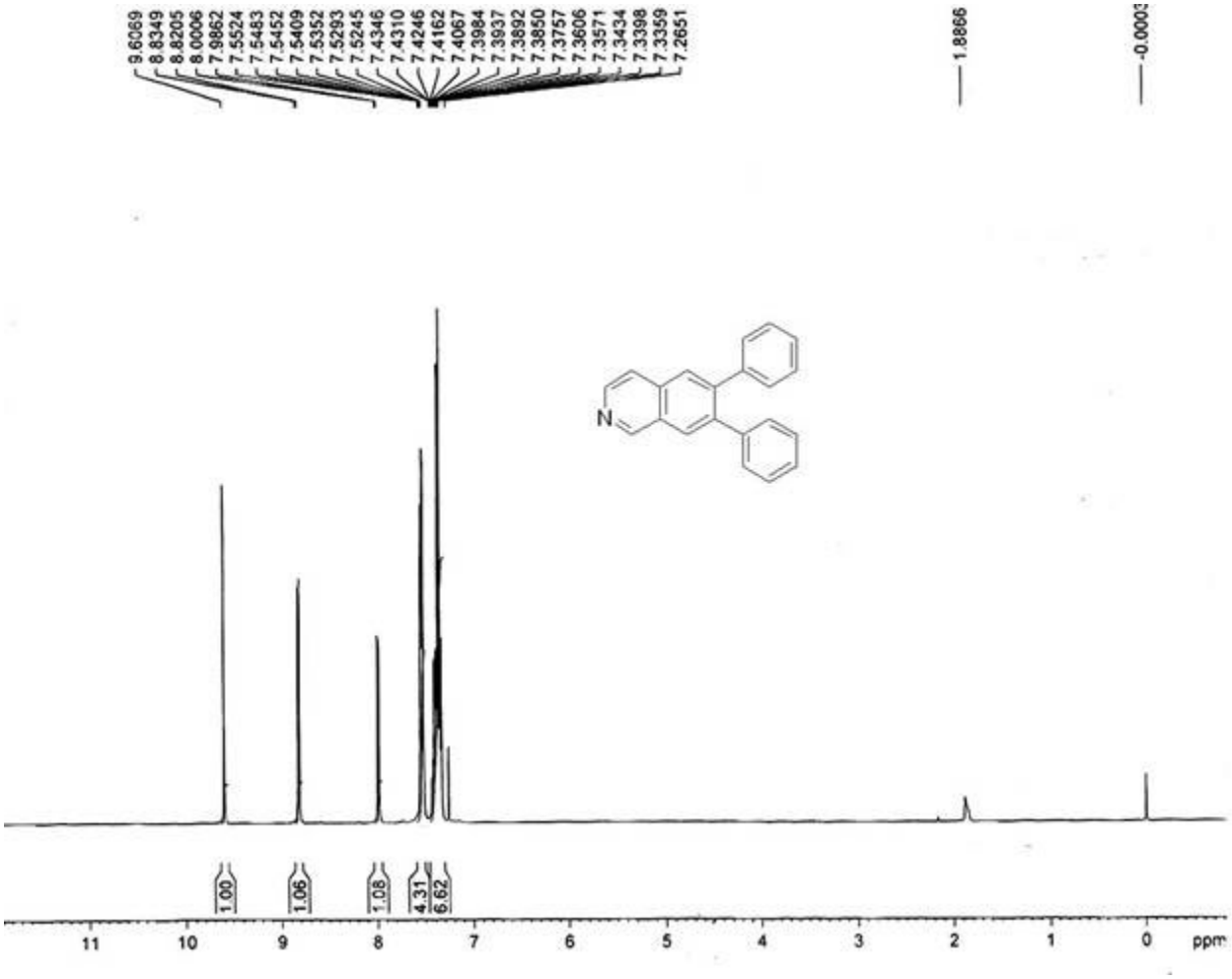
2,3-Di(furan-2-yl)quinoxaline (entry 13, table 6)



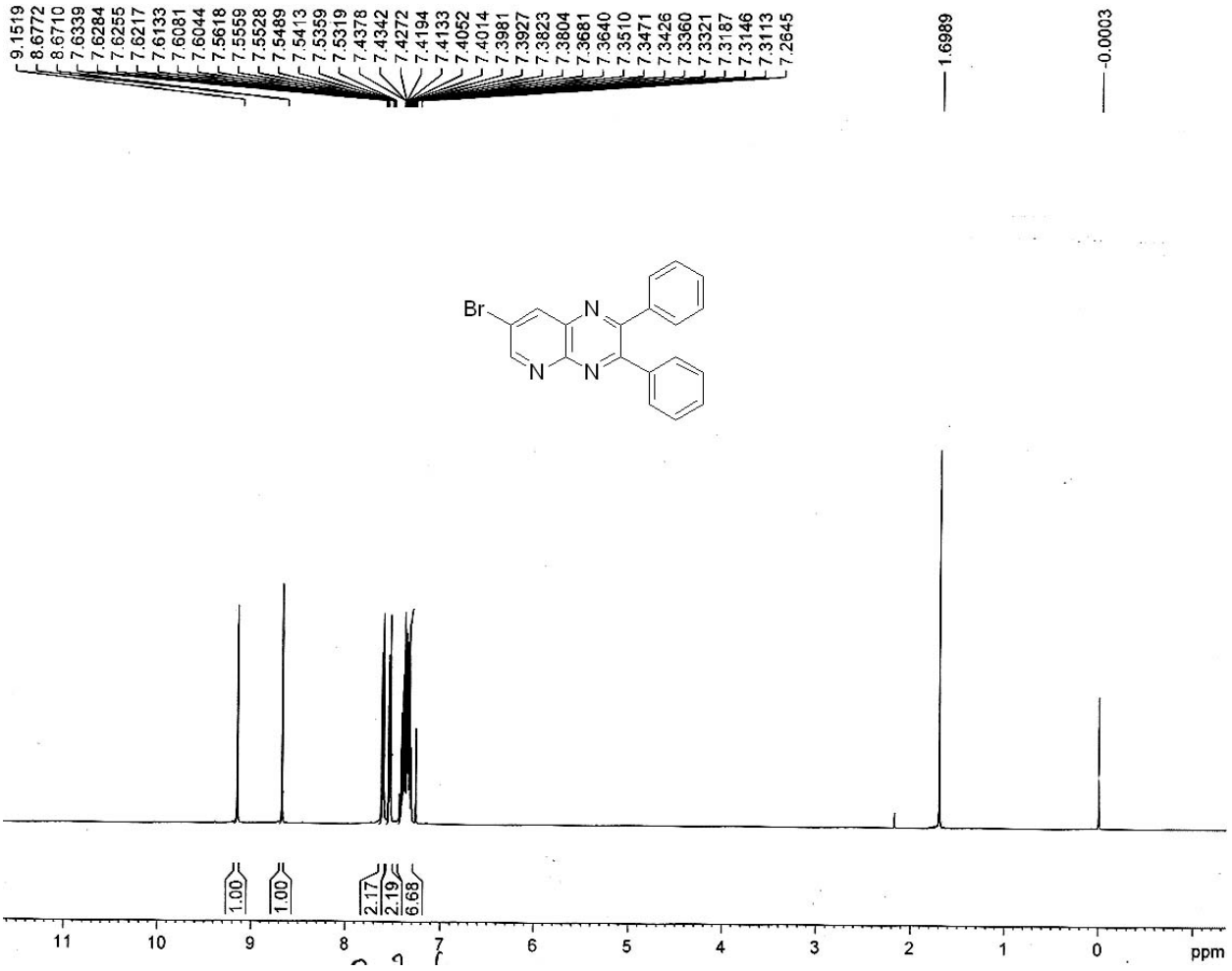
2,3-Diphenylpyrido[2,3-b]pyrazine (entry 14, table 6)



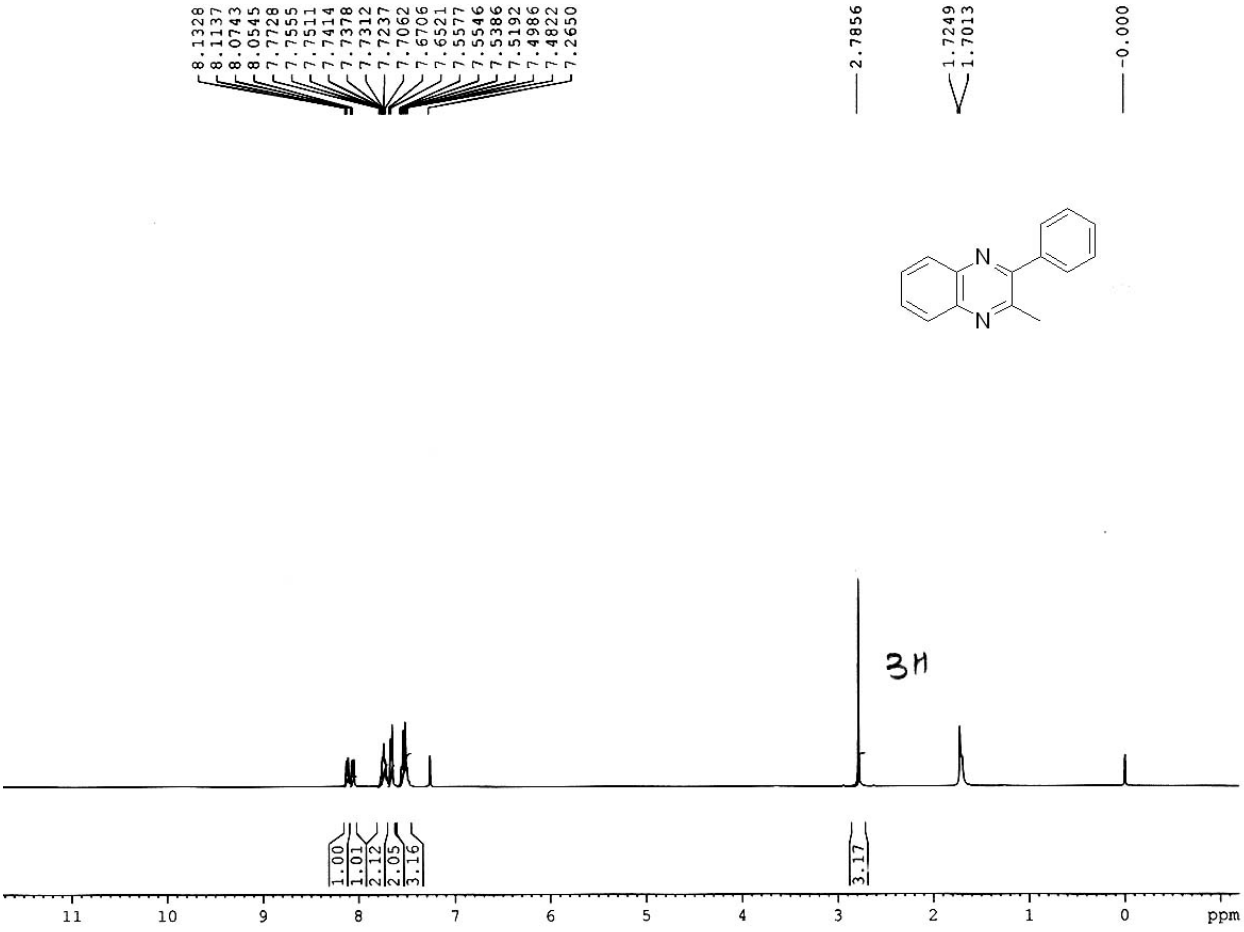
2,3-Diphenylpyrido[3,4-b]pyrazine (entry 15, table 6)



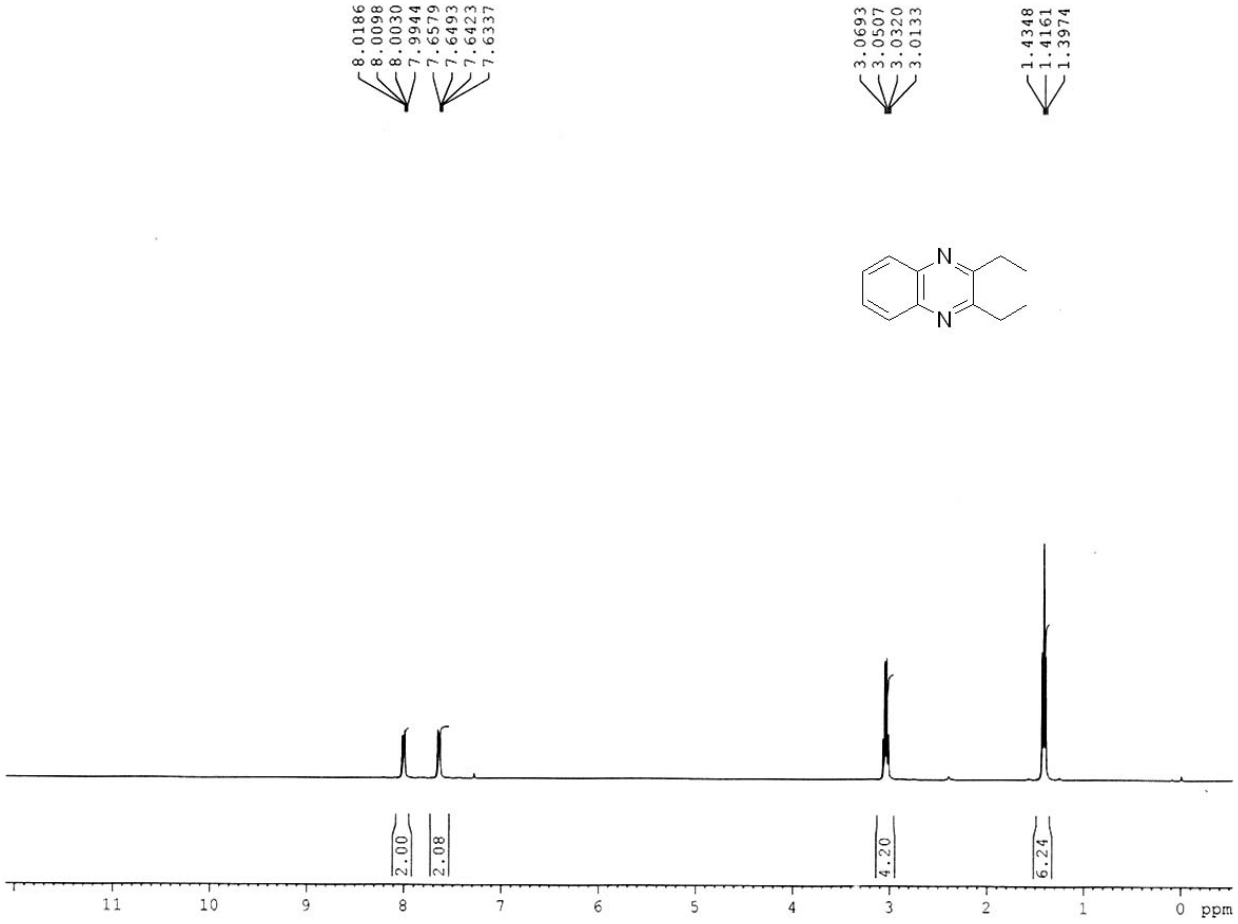
6-Bromo-2,3-diphenylpyrido[2,3-b]pyrazine (entry 16, table 6)



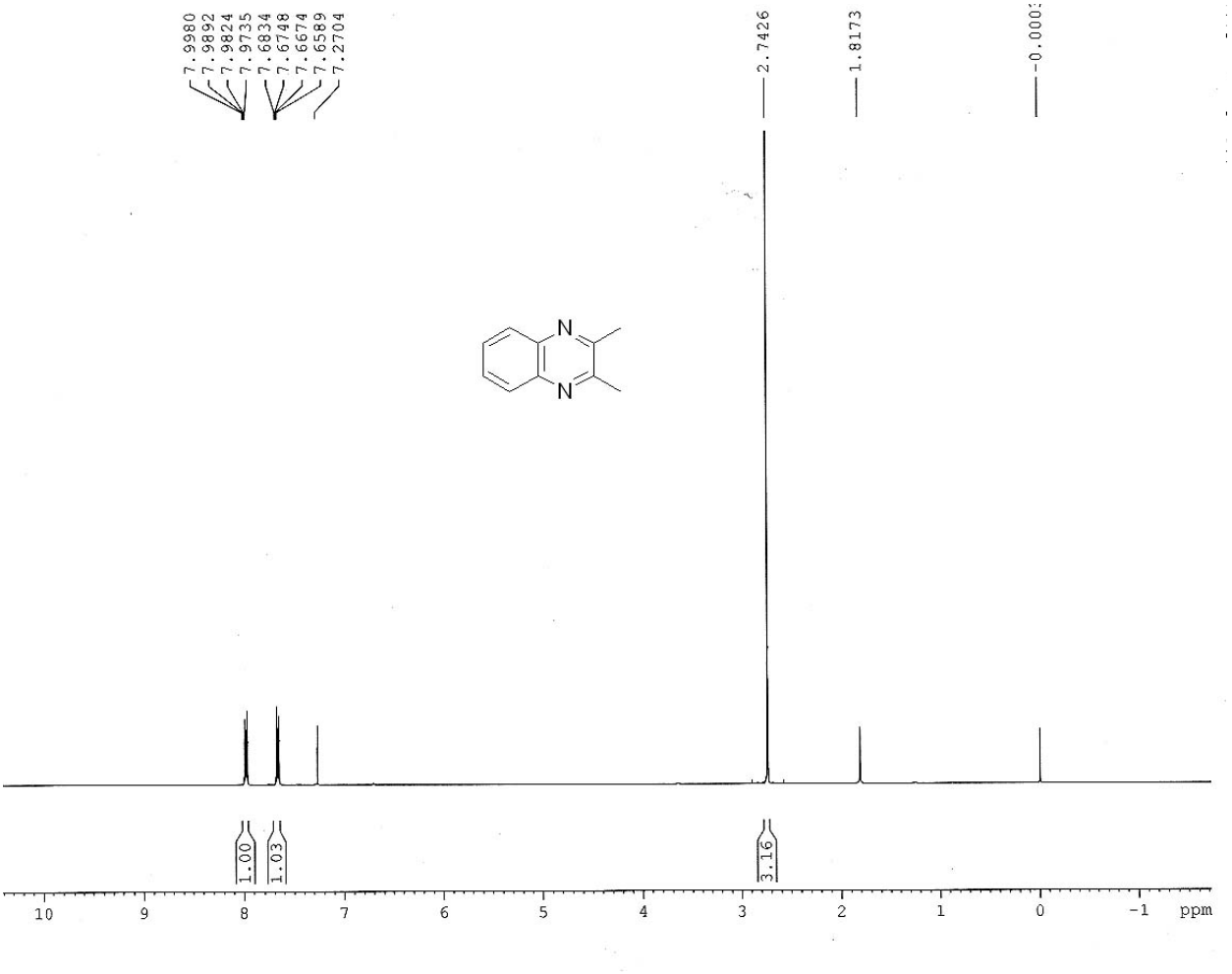
2-Methyl-3-phenylquinoxaline (entry 17, table 6)



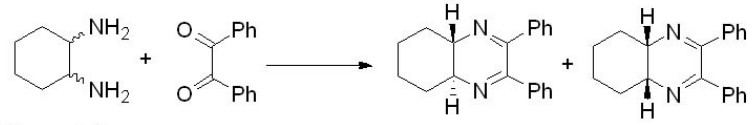
2,3-Diethylquinoxaline (entry 18, table 6)



2,3-Dimethylquinoxaline (entry 19, table 6)

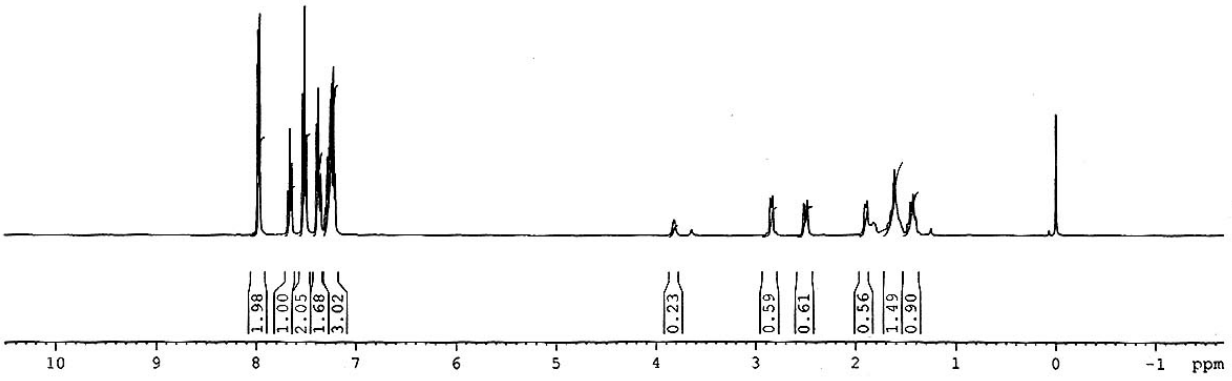


(*cis/trans*) 2,3-diphenyl-5,6,7,8-tetrahydroquinoxaline (entry 20, table 6)

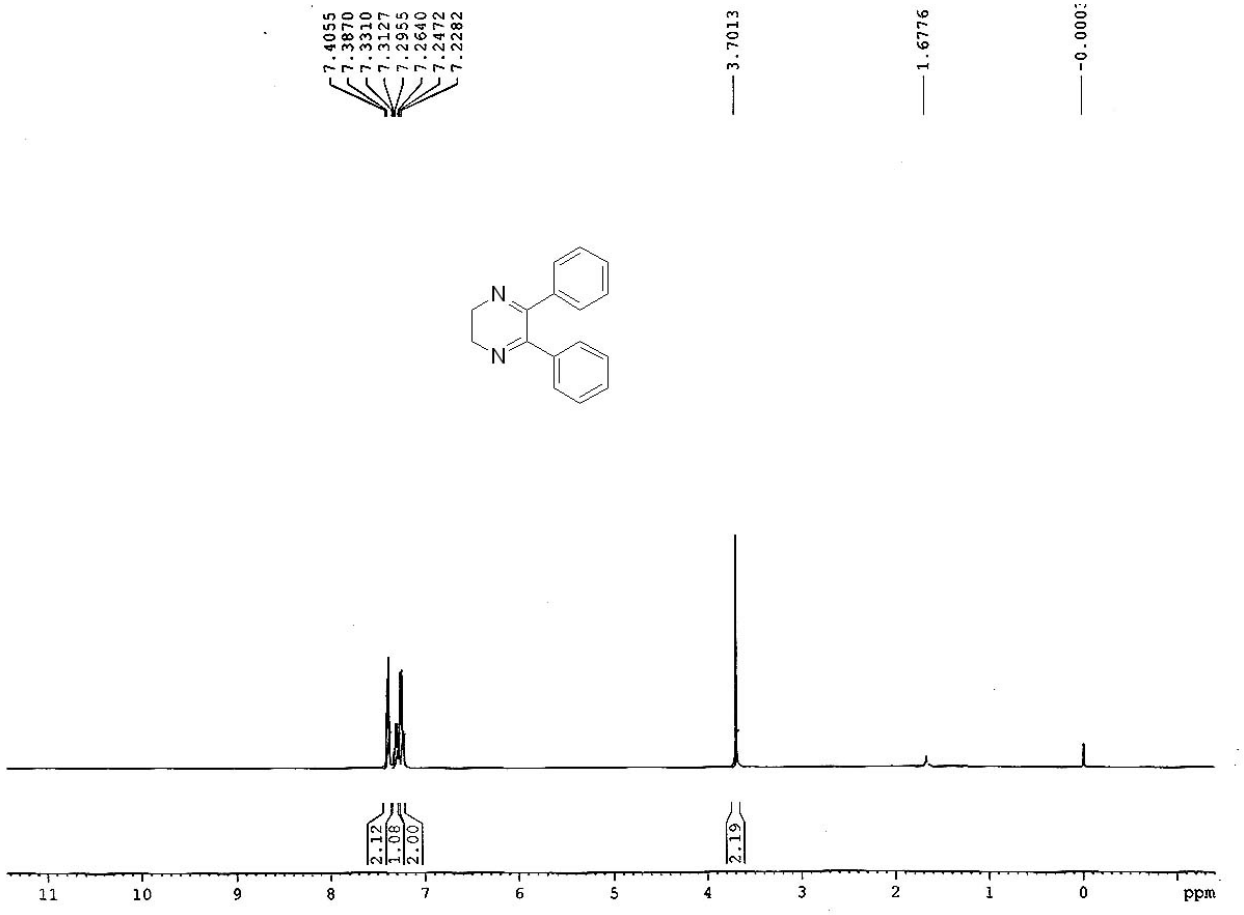


(Racemic)

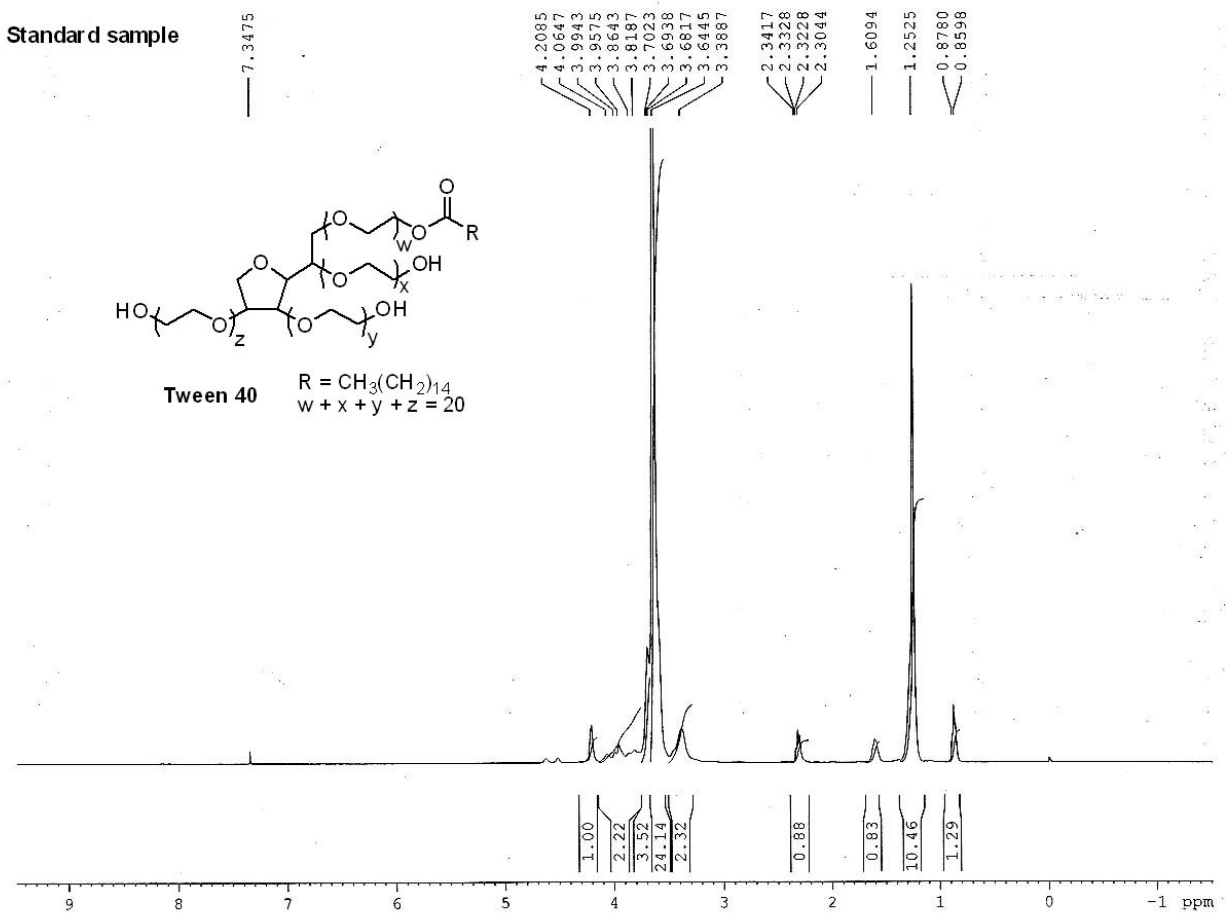
(49 % : 51 %)



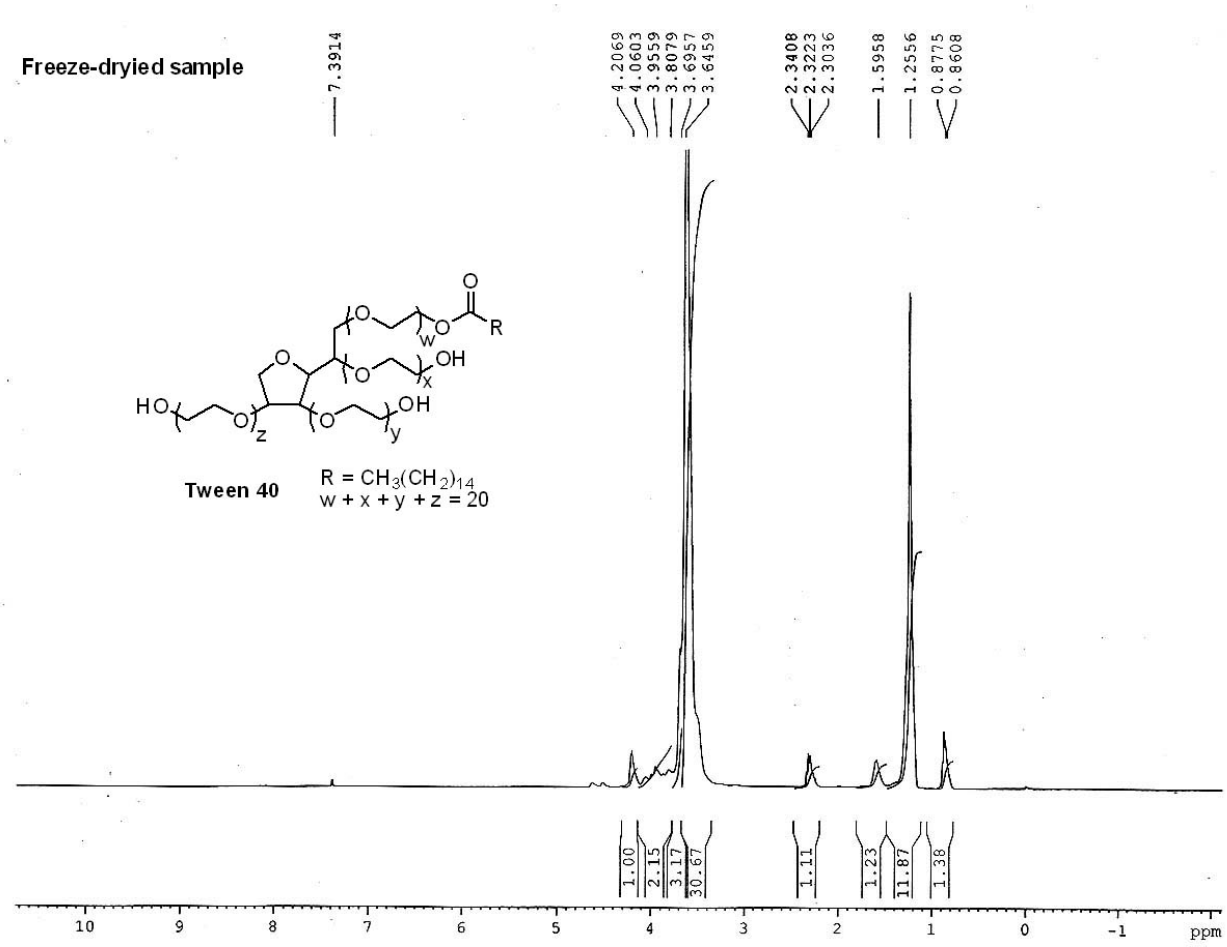
5,6-Diphenyl-2,3-dihydropyrazine (entry 21, table 6)



Authentic/unused sample of Tween 40



Recovered Sample of Tween 40 Obtained after Freeze Drying of the Spent Water Containing the Surfactant after the Quinoxaline Formation



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