Electronic supplementary materials *Mendeleev Commun.*, 2024, **34**, 871–874

Novel synthesis of 1,6- and 1,4-dialkyl glycolurils and their supramolecular organization

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General

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. ^{1}H and ^{13}C NMR were recorded at 23 to 28 °C on a Bruker AM300, Bruker DRX500, and TMS as internal standard. HRMS (ESI) were recorded using Bruker micrOTOF II mass spectrometer. Melting points were determined in a SMP10 instrument (Stuart). Compounds **1a**,**b** and **2a**,**b** were previously described (V. A. Karnoukhova, V. V. Baranov, A. V. Vologzhanina, A. N. Kravchenko and I. V. Fedyanin, *Cryst. Eng. Comm*., 2021, **23**, 4312.).

Synthesis of 1,6- and 1,4-disubstituted 3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-diones 1c,d, 1c•2c, 2d from benzyl 4a and 1-alkylureas 3c,d (approach 1); General procedure

A mixture of the corresponding 1-substituted urea **3c** or **3d** (4 mmol), benzil **4a** (0.420 g, 2 mmol), MeCN (10 ml) and hydrochloric acid (0.12 ml, 35.5%) was heated to boiling, then stirred at reflux for 6 h. The reaction mixture was cooled and the obtained precipitate (mixture of reaction products **1** and **2**) was filtered off and washed with $CHCl_3$ (5 ml). The isolation of the isomers of glycolurils **1c**,**d**, **1c•2c** and **2d** were carried out by fractional crystallization from MeCN.

Synthesis of 1,6- and 1,4-disubstituted 3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-diones 1a-d, 2a-d (approach 2); General procedure

A mixture of imidazolone **4a-d** (1.8 mmol), 1-substituted urea **3a-d** (2 mmol), MeCN ($Pr^{i}OH$) (35 ml) and HCl (35%, 0.18 ml) was refluxed for 20 min with stirring. The reaction mixture was evaporated to dryness. The resulting solid was washed with $CHCl_3$ (4 ml) and H_2O (5 ml). The separation of the isomers of glycolurils **1a-d** and **2a-d** were carried out by fractional crystallization from MeCN.

1,6-Dimethyl-3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (1a)

White powder; yield 41% (0.237 g),† 61% (0.354 g).‡

1,4-Dimethyl-3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (2a).

White powder, yield 27% (0.156 g),† 31% (0.180 g).‡

1,6-Diethyl-3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (1b)

White powder; yield 32% (0.201 g),† 68% (0.428 g).‡

1,4-Diethyl-3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (2b).

White powder; yield 9% (0.057 g),† 20% (0.126 g).‡

† Synthesized by Approach 2, solvent $Pr^{i}OH$

‡ Synthesized by Approach 2, solvent MeCN

3a,6a-Diphenyl-1,6-dipropyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (1c)

Colorless crystals; yield 6% (0.041 g),† 46% (0.313 g),‡ 5% (0.378 g);§ m.p. 224–225 °C (MeCN). ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.81 (t, 6H, J = 6.9 Hz, Me), 1.54–1.78 (m, 4H, CH_2), 2.77–2.92 (m, 2H, CH_2), 3.00–3.14 (m, 2H, CH_2), 6.70–6.83 (m, 2H, Ph), 6.92 – 7.02 (m, 2H, Ph), 7.03 – 7.18 (m, 6H, Ph), 7.98 (s, 2H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 11.37 (Me), 22.60, 43.98 (CH_2), 79.16, 89.95 (C-C), 127.14, 127.48, 127.85, 128.05, 128.13, 128.48 (CH(Ph)), 134.85, 137.49 (C(Ph)), 159.95 (C=O). HRMS, m/z, found: 379.2129 $[M+H]^+$ (calcd for $C_{22}H_{26}N_4O_2$+H 379.2129).

3a,6a-Diphenyl-1,4-dipropyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (2c)

Colorless crystals; yield 2% (0.014 g);‡ m.p. 281–283 °C (MeCN). ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.77 (t, 6H, J = 7.3 Hz, Me), 1.41–1.54 (m, 4H, CH_2), 2.50 – 2.63 (m, 2H, CH_2), 3.12–3.30 (m, 2H, CH_2), 6.92–7.01 (m, 4H, Ph), 7.03–7.13 (m, 6H, Ph), 8.17 (s, 2H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 11.11 (Me), 21.96, 41.94 (CH_2), 83.88 (C-C), 127.19, 127.66, 128.14 (CH(Ph)), 135.71 (C(Ph)), 159.01 (C=O). HRMS, m/z, found: 379.2140 $[M+H]^+$ (calcd for $C_{22}H_{26}N_4O_2$+H 379.2134).

Co-crystal of 3a,6a-diphenyl-1,6-dipropyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione with 3a,6a-diphenyl-1,4-dipropyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (1:1) (1c•2c)

Colorless crystals; yield 26% (0.177 g),† 40% (0.275 g),‡ 37% (0.281 g);§ m.p. 276–278 °C (MeCN). ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.74–0.84 (m, 12H, Me), 1.40–1.57 (m, 4H, CH_2), 1.58–1.80 (m, 4H, CH_2), 2.50–2.63 (m, 2H, CH_2), 2.80–2.92 (m, 2H, CH_2), 3.00–2.15 (m, 2H, CH_2), 3.16–3.30 (m, 2H, CH_2), 6.72–6.80 (m, 2H, Ph), 6.92–7.01 (m, 6H, Ph), 7.03–7.18 (m, 12H, Ph), 8.00 (s, 2H, NH), 8.17 (s, 2H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 11.14, 11.33 (Me), 21.99, 22.55, 41.97, 43.95 (CH_2), 79.18, 83.92, 89.97 (C-C), 127.11, 127.22, 127.42, 127.68, 127.81, 128.00, 128.06, 128.16, 128.42 (CH(Ph)), 133.86, 135.73, 137.54 (C(Ph)), 159.06, 159.94 (C=O). HRMS, m/z, found: 379.2142 $[M+H]^+$ (calcd for $C_{22}H_{26}N_4O_2$+H 379.2134).

1,6-Dibutyl-3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (1d)

Colorless crystals; yield 34% (0.248 g),† 76% (0.555 g),‡ 15% (0.124 g);§ m.p. 200–202 °C (MeCN). ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.84 (t, 6H, J = 7.3 Hz, Me), 1.14–1.33 (m, 4H, CH_2), 1.53–1.79 (m, 4H, CH_2), 2.81–2.96 (m, 2H, CH_2), 3.04–3.19 (m, 2H, CH_2), 6.73–6.81 (m, 2H, Ph), 6.92–7.00 (m, 2H, Ph), 7.01–7.17 (m, 6H, Ph), 7.99 (s, 2H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 13.66 (Me), 19.81, 31.44, 42.11 (CH_2), 79.19, 89.99 (C-C),

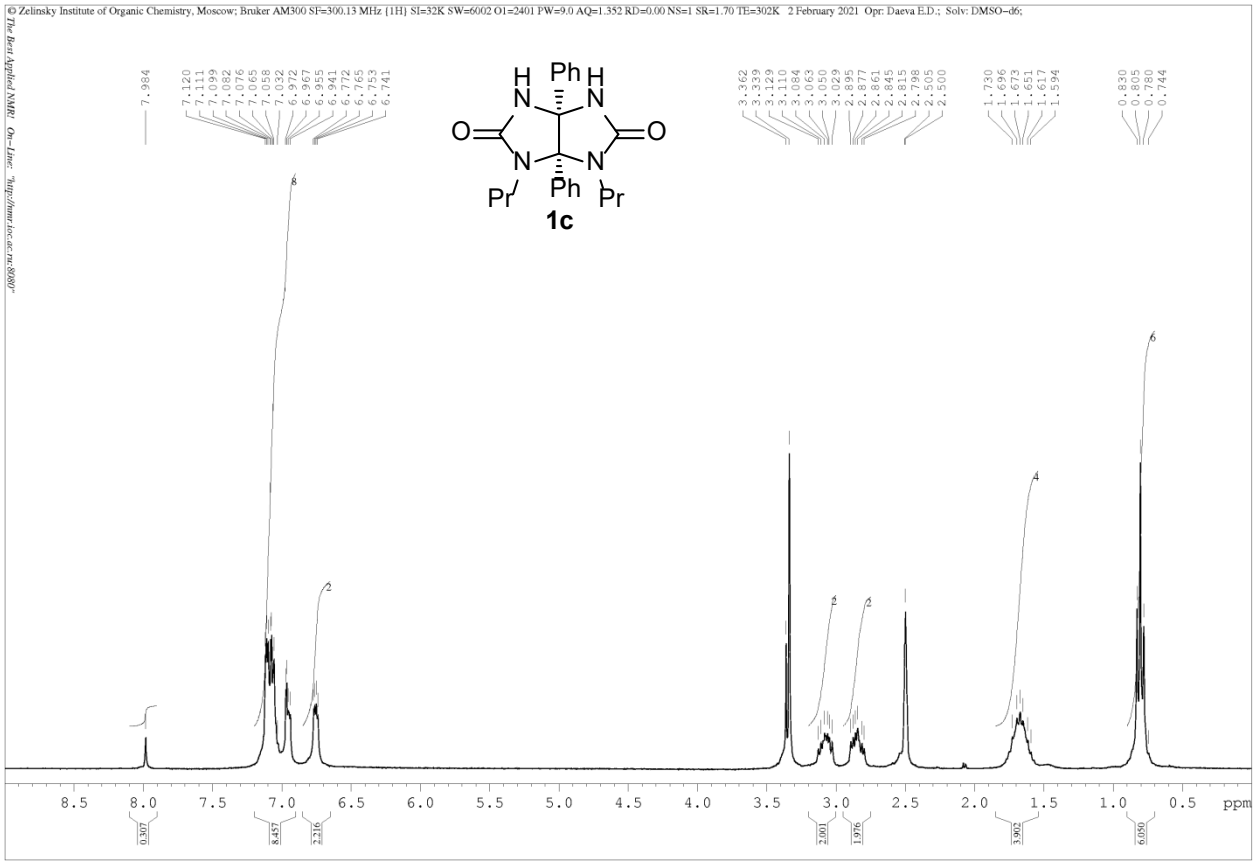
§ Synthesized by Approach 1

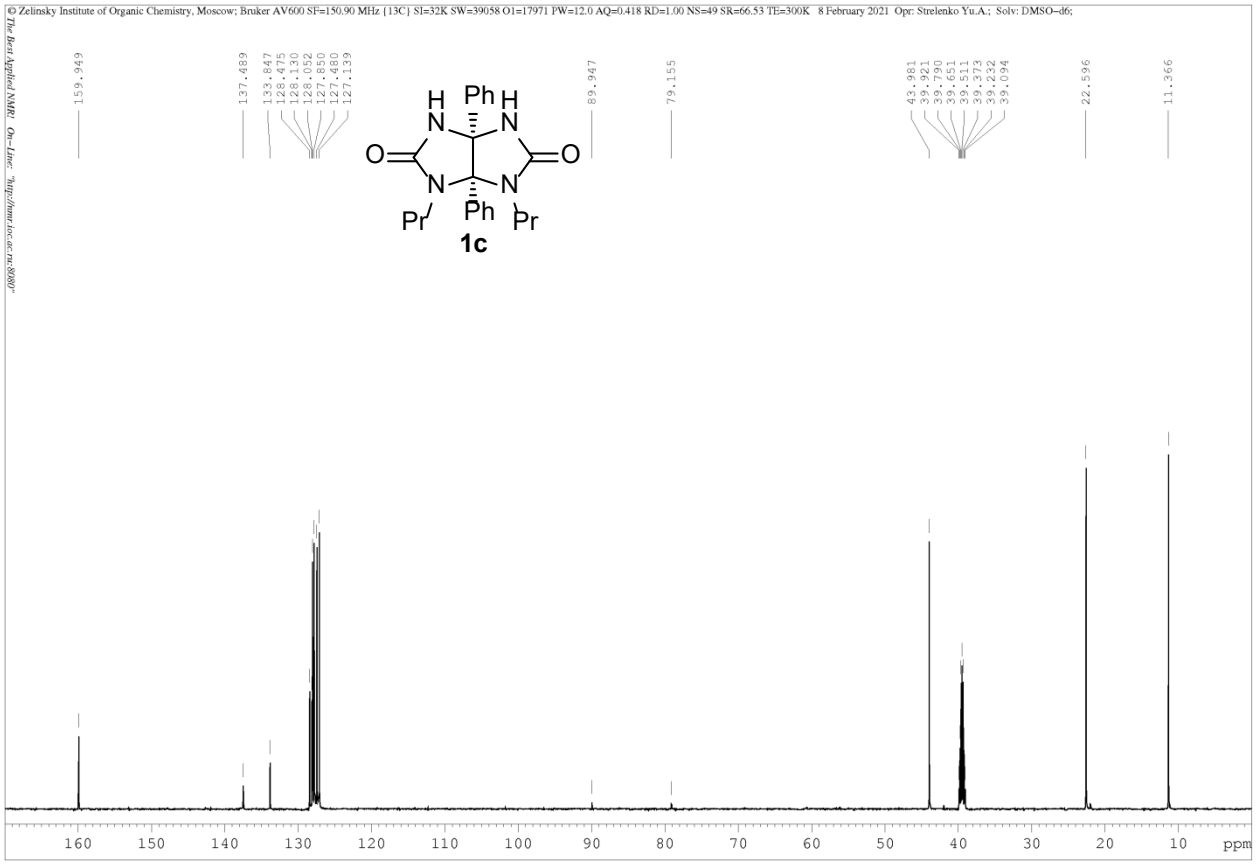
127.11, 127.44, 127.81, 128.03, 128.07, 128.44 (CH(Ph)), 133.83, 137.53 (C(Ph)), 159.92 (C=O). HRMS, m/z, found: 407.2440 $[M+H]^+$ (calcd for $C_{24}H_{30}N_4O_2$+H 407.2447).

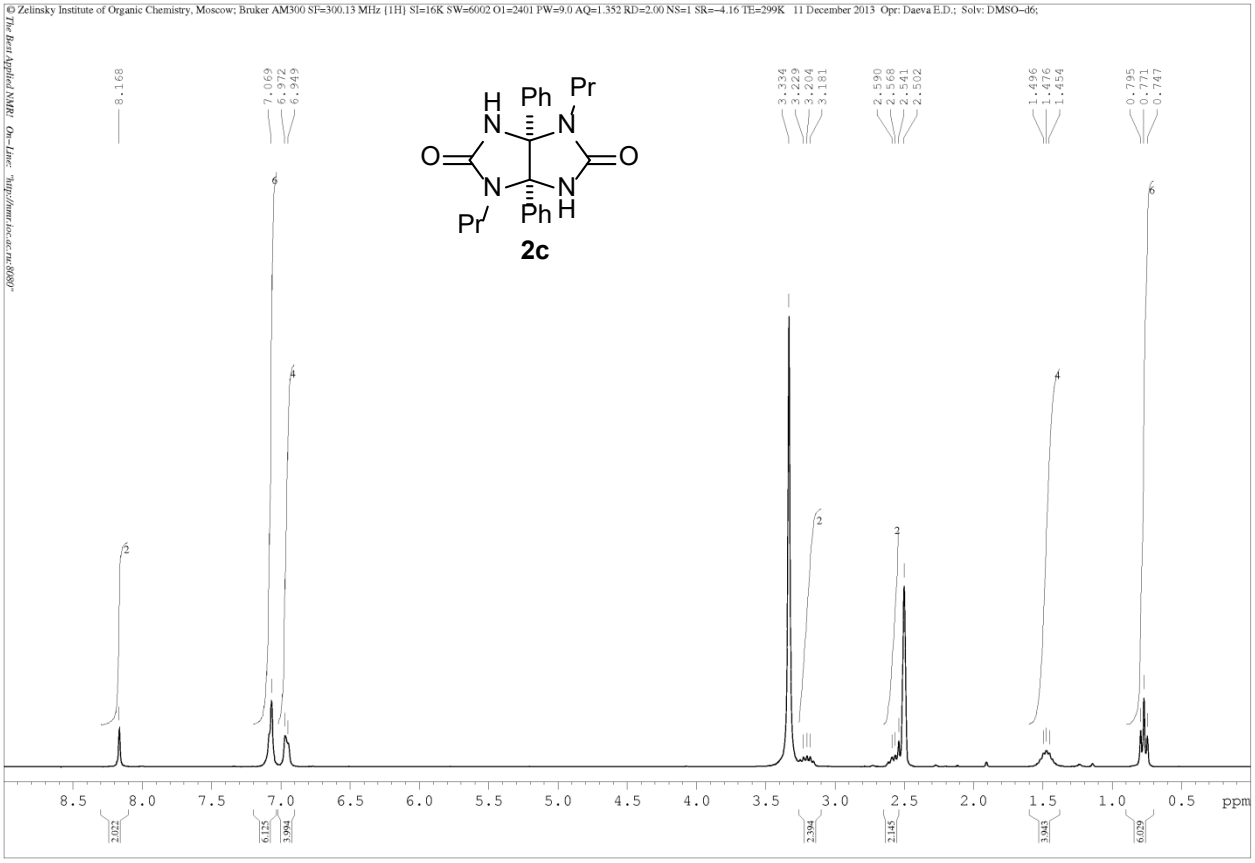
1,4-Dibutyl-3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione (2d)

Colorless crystals; yield 10% (0.073 g),[†] 20% (0.146 g),[‡] 15% (0.121 g);[§]m.p. 307–309 °C (MeCN). ^{1}H NMR (300 MHz, DMSO-d_6): δ 0.81 (t, 6H, J = 7.3 Hz, Me), 1.12–1.29 (m, 4H, CH_2), 1.38–1.52 (m, 4H, CH_2), 2.51–2.69 (m, 2H, CH_2), 3.18–3.33 (m, 2H, CH_2), 6.92–7.01 (m, 4H, Ph), 7.03–7.14 (m, 6H, Ph), 8.18 (s, 2H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 13.69 (Me), 19.63, 30.95, 39.51 (CH_2), 83.92 (C-C), 127.22, 127.68, 128.16 (CH(Ph)), 135.73 (C(Ph)), 159.03 (C=O). HRMS, m/z, found: 407.2443 $[M+H]^+$ (calcd for $C_{24}H_{30}N_4O_2$+H 407.2447).

Copies of NMR spectra for compounds 1c,d, 2a-d.



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3.229
3.204
3.181
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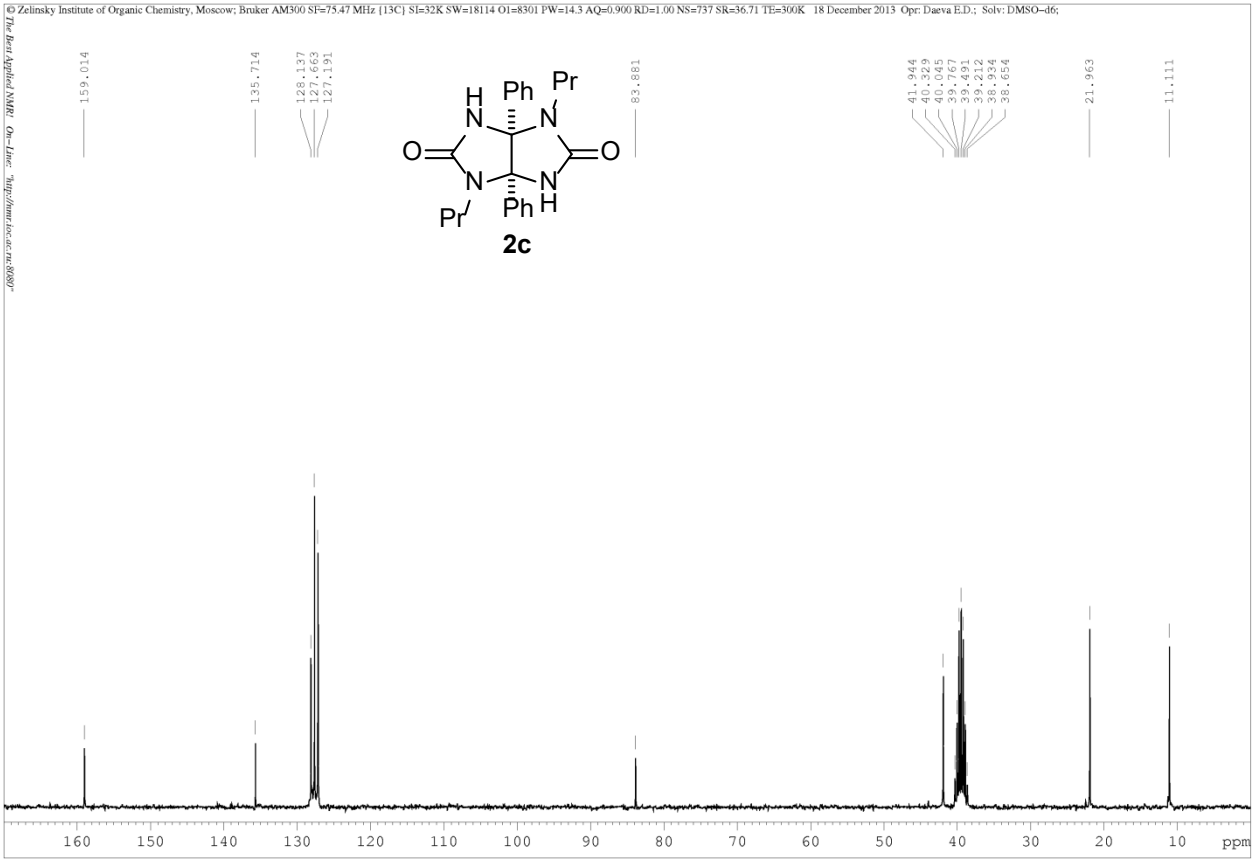
2c
ppm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127.663
127.191
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39.767
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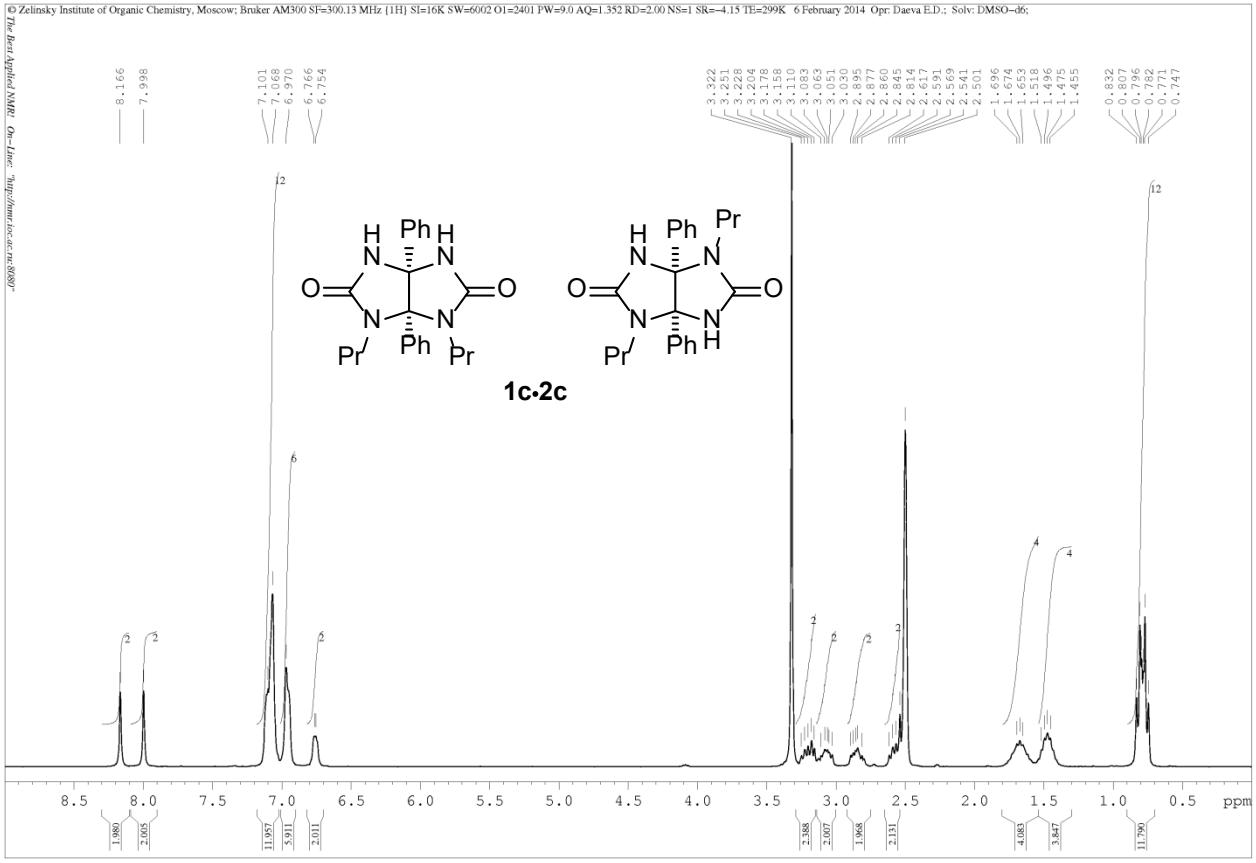
11.111
2c
ppm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7.101
7.068
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6.754
3.322
3.251
3.228
3.204
3.178
3.158
3.110
3.083
3.063
3.051
3.030
2.895
2.877
2.860
2.845
2.814
2.617
2.591
2.569
2.541
2.501
1.696
1.674
1.653
1.518
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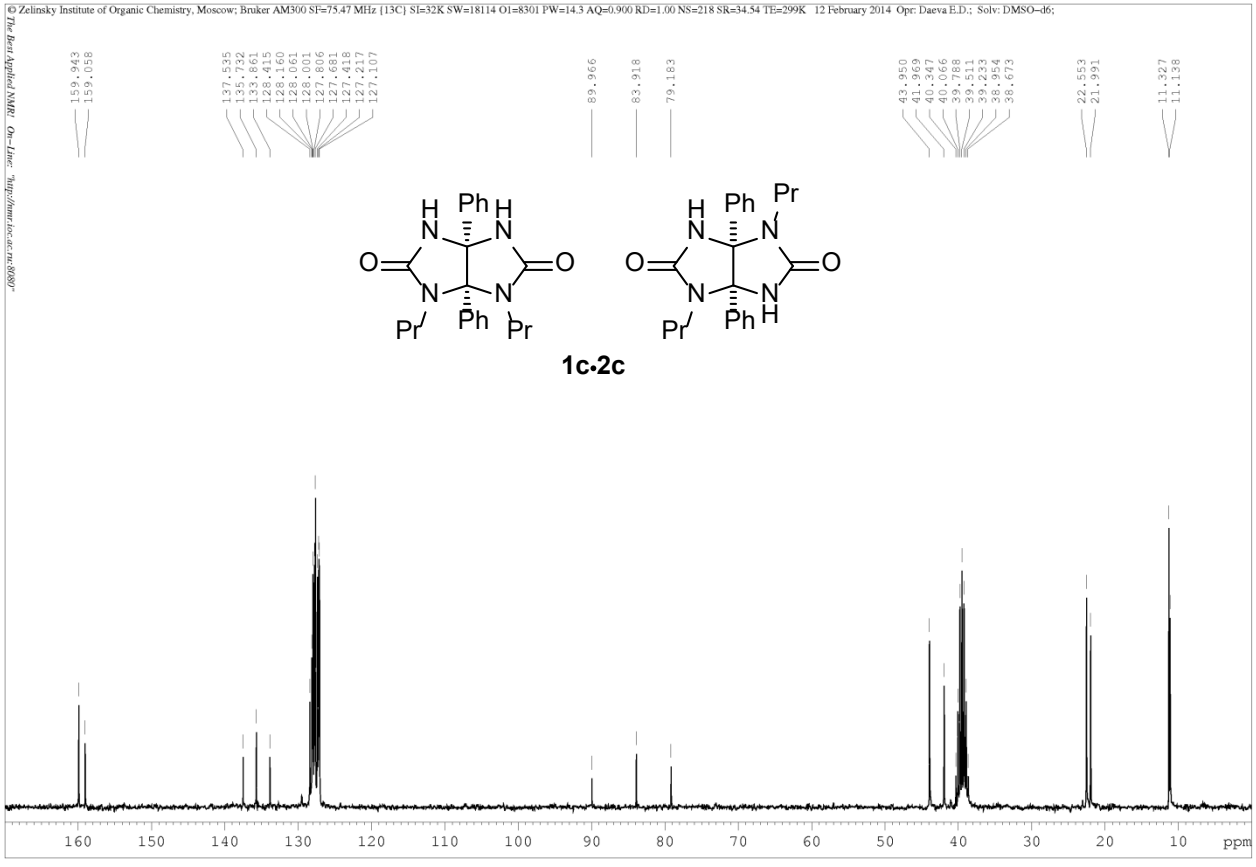
0.747
1c•2c
ppm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127.681
127.418
127.217
127.107
89.966
83.918
79.183
43.950
41.969
40.347
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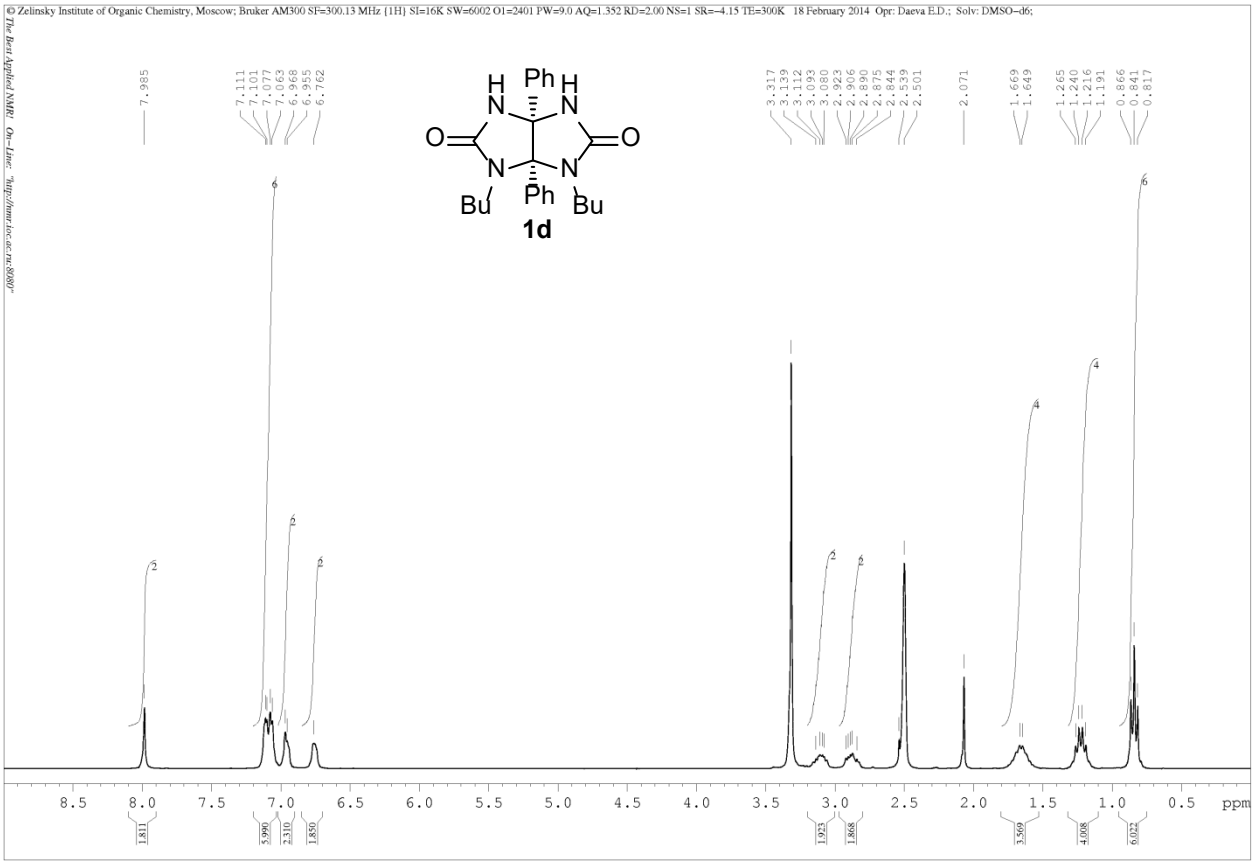
11.138
1c•2c
ppm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7.063
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3.317
3.139
3.112
3.093
3.080
2.923
2.906
2.890
2.875
2.844
2.539
2.501
2.071
1.669
1.649
1.265
1.240
1.216
1.191
0.866
0.841
0.817
1d
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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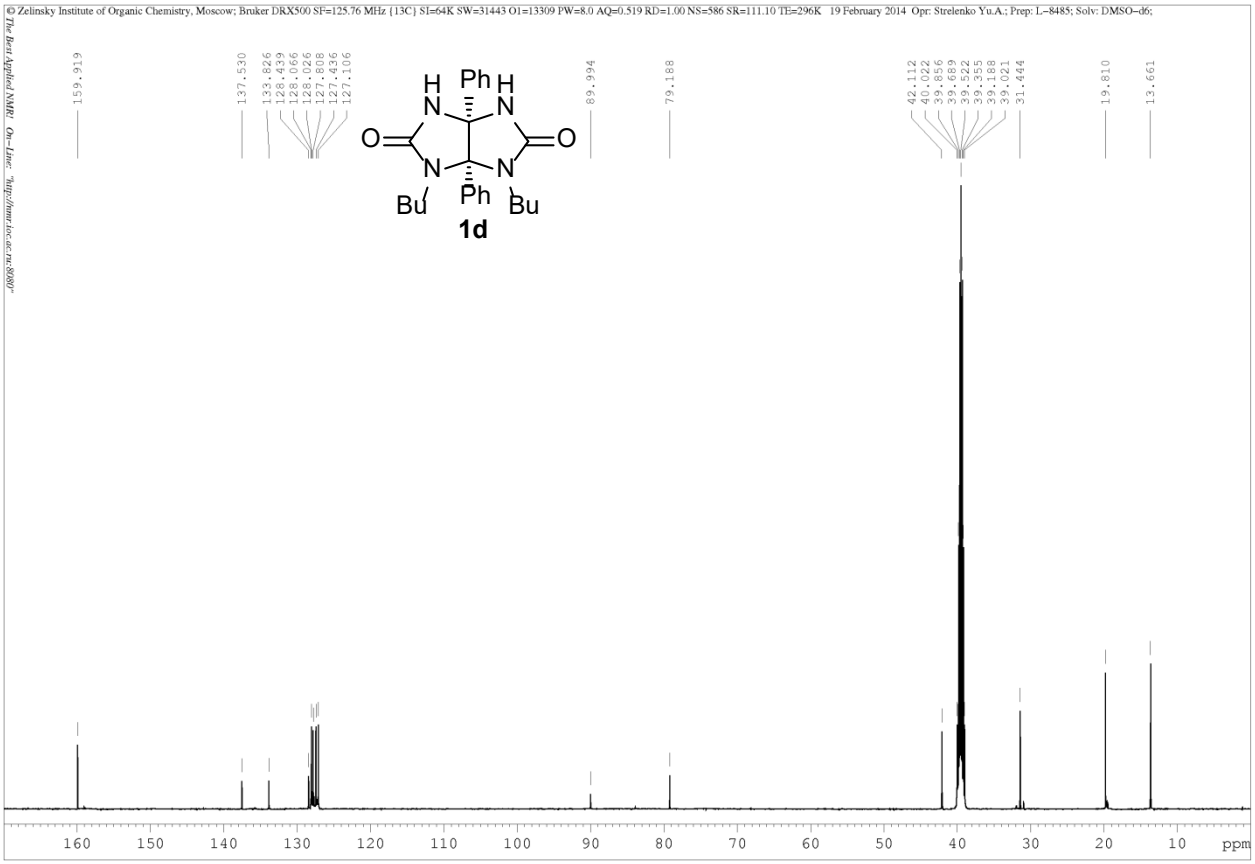
6.025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128.066
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127.106
89.994
79.188
42.112
40.022
39.856
39.689
39.522
39.355
39.188
39.021
31.444
19.810
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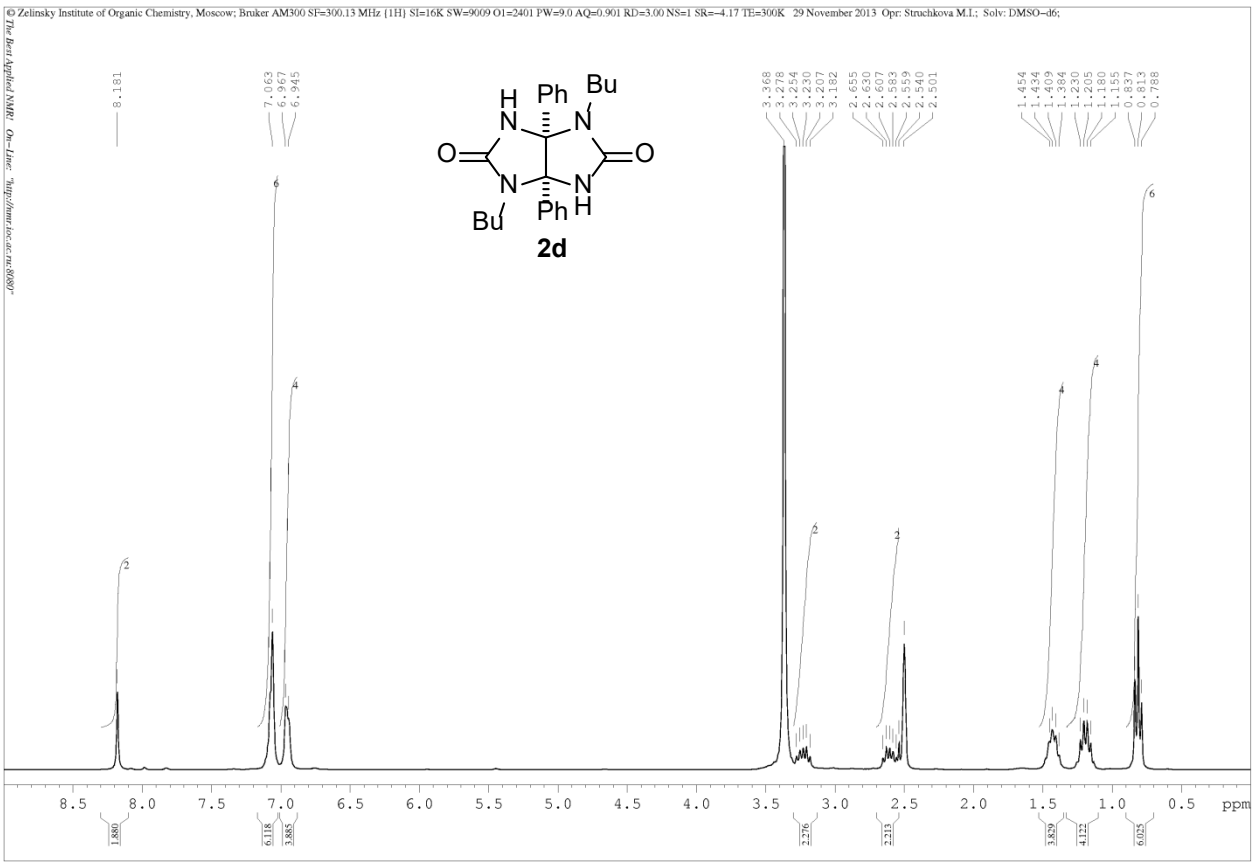
90
80
70
60
50
40
30
20
10
ppm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6.945
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3.230
3.207
3.182
2.655
2.630
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2.583
2.559
2.540
2.501
1.454
1.434
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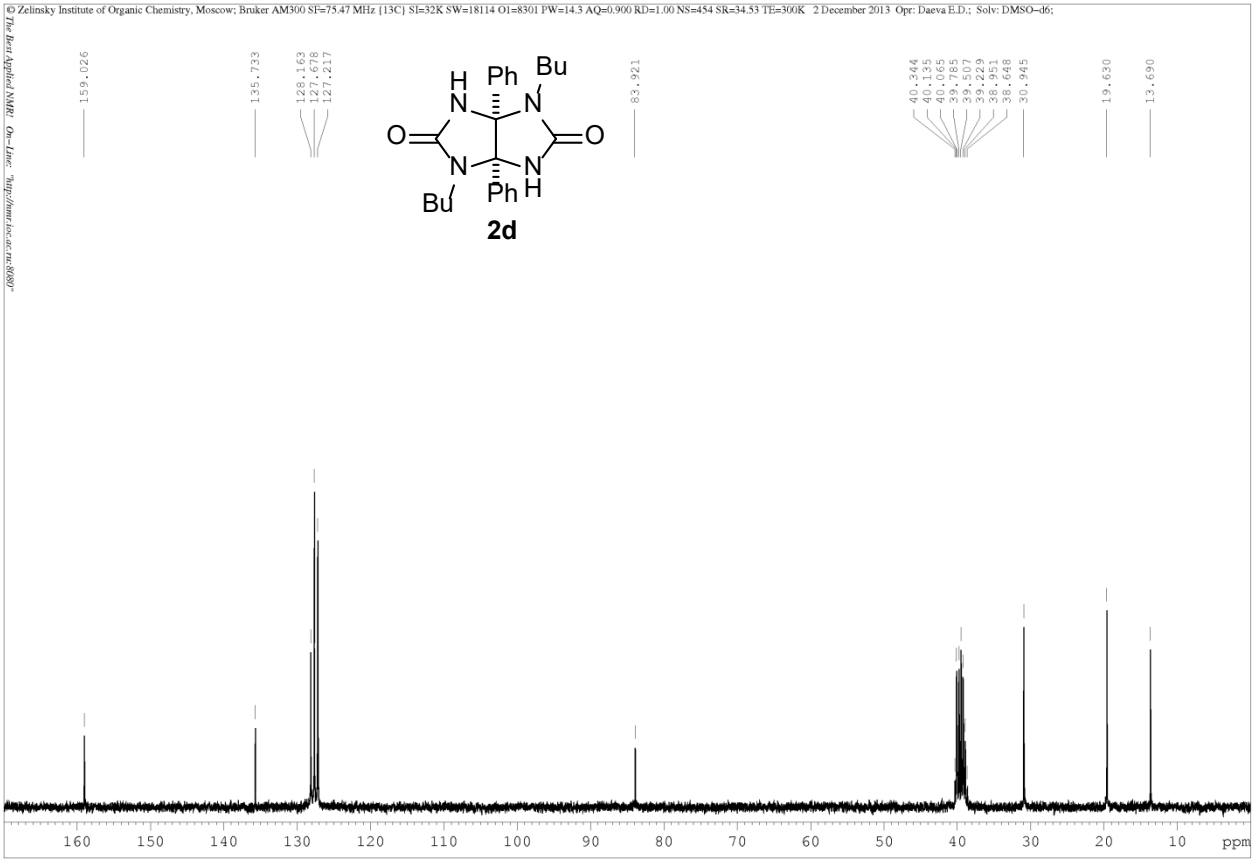
0.788
ppm

2d


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AM300 SF=75.47 MHz {13C} SI=32K SW=18114 O1=8301 PW=14.3 AQ=0.900 RD=1.00 NS=454 SR=34.53 TE=300K 2 December 2013 Opr: Daeva E.D.; Solv: DMSO-d6;
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127.678
127.217
83.921
40.344
40.135
40.065
39.785
39.507
39.229
38.951
38.648
30.945
19.630
13.690
ppm

2d

Table S1. Crystal data and structure refinement parameters for **2c**, **2d**, and **1c•2c**.

Parameter	**2c**	**2d**	**1c•2c**
Empirical formula	$C_{22}H_{26}N_4O_2$	$C_{24}H_{30}N_4O_2$	$C_{44}H_{52}N_8O_4$
Formula weight	378.47	406.52	756.93
T, K	120	120	120
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/c$	C2/c
Z	4	8	8
a, Å	8.8234(7)	16.322(3)	22.830(2)
b, Å	14.8956(11)	17.694(4)	13.5162(14)
c, Å	16.1940(12)	16.240(3)	27.293(3)
α, °	75.029(2)	90	90
β, °	87.532(2)	103.85(3)	107.361(2)
γ, °	84.045(2)	90	90
V, Å^3	2044.7(3)	4553.5(17)	8038.4(14)
D_{calc} (g cm^{-1})	1.229	1.186	1.251
Linear absorption, μ (cm^{-1})	0.81	0.77	0.82
F(000)	808	1744	3232
$2\theta_{max}$, °	56	58	58
Reflections measured	23655	46362	31198
Independent reflections	9868	12097	10635
Observed reflections [$I > 2\sigma(I)$]	7800	9038	7012
Parameters	513	569	509
R1	0.0457	0.1117	0.0557
wR2	0.1224	0.2416	0.1249
GOF	1.027	1.186	1.032
$\Delta\rho_{max}$/ $\Delta\rho_{min}$ (e Å^{-3})	0.540/-0.355	0.370/ -0.382	0.339/-0.323
CCDC	2344098	2344099	2344092