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Dedicated to Full Member of the Russian Academy of Sciences V.I. Minkin on his 70th Anniversary

Tetrazoles: XLVIII.* 3*H*-Naphtho[2,1-*e*]- and 3*H*-Naphtho[1,2-*e*][1,2,4]triazepines from 5-Aryltetrazoles. Physical and Chemical Properties

V. V. Nikulin, T. V. Artamonova, and G. I. Koldobskii

St. Petersburg State Institute of Technology, Moskovskii pr. 26, St. Petersburg, 190013 Russia
e-mail: koldobsk@tu.spb.ru

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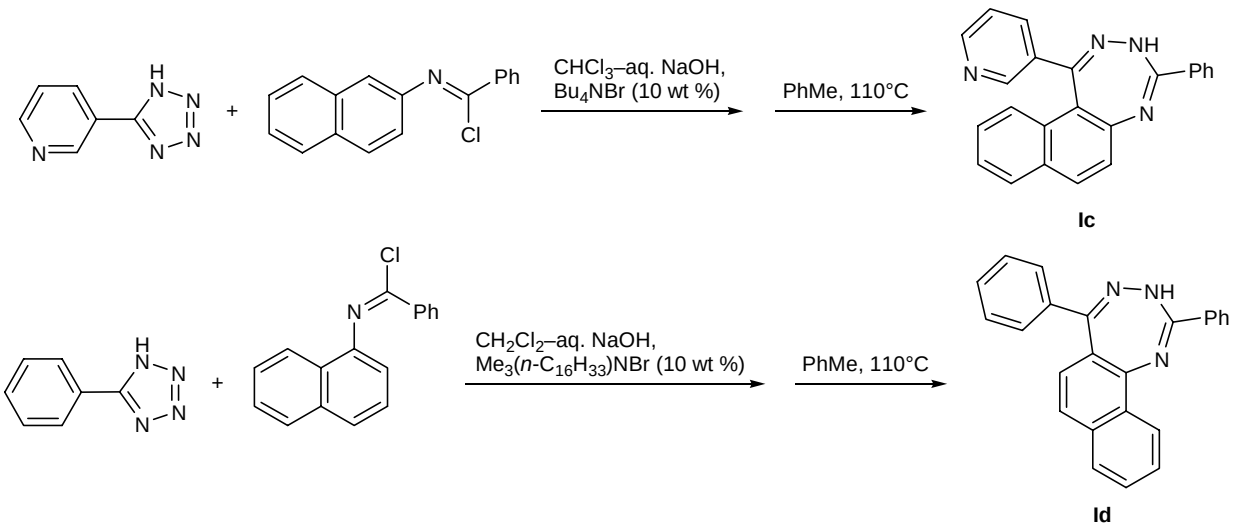
Abstract—Thermolysis of *N*-imidoyltetrazoles generated under conditions of phase-transfer catalysis from 5-aryltetrazoles and *N*-(2-naphthyl)benzimidoyl chloride yields 3*H*-naphtho[2,1-*e*][1,2,4]triazepines, and acid hydrolysis of the latter leads to formation of 3-arylbenz[e]indazoles. Acid hydrolysis of 3*H*-naphtho[1,2-*e*]-[1,2,4]triazepine gives the corresponding amino ketone.

In the past decade, it was convincingly shown that thermal transformation of *N*-imidoyltetrazoles generated under conditions of phase-transfer catalysis from 5-aryltetrazoles and *N*-aryl(or hetaryl)benzimidoyl chlorides provides a universal method for the preparation of various triazepines [2–7]. This procedure was successfully applied to the synthesis of polycyclic compounds in which the triazepine ring is fused to a naphthalene core [8, 9].

While continuing our studies in the field of synthesis and properties of naphthotriazepines, we examined the structure and acid hydrolysis of previously described triazepines, 1,4-diphenyl-3*H*-naphtho[2,1-*e*]-[1,2,4]triazepine (**Ia**) and 1-(4-methoxyphenyl)-4-phenyl-3*H*-naphtho[2,1-*e*][1,2,4]triazepine (**Ib**), as well as of 4-phenyl-1-(3-pyridyl)-3*H*-naphtho[2,1-*e*]-[1,2,4]triazepine (**Ic**) and 2,5-diphenyl-3*H*-naphtho-[1,2-*e*][1,2,4]triazepine (**Id**) which were synthesized

Scheme 1.

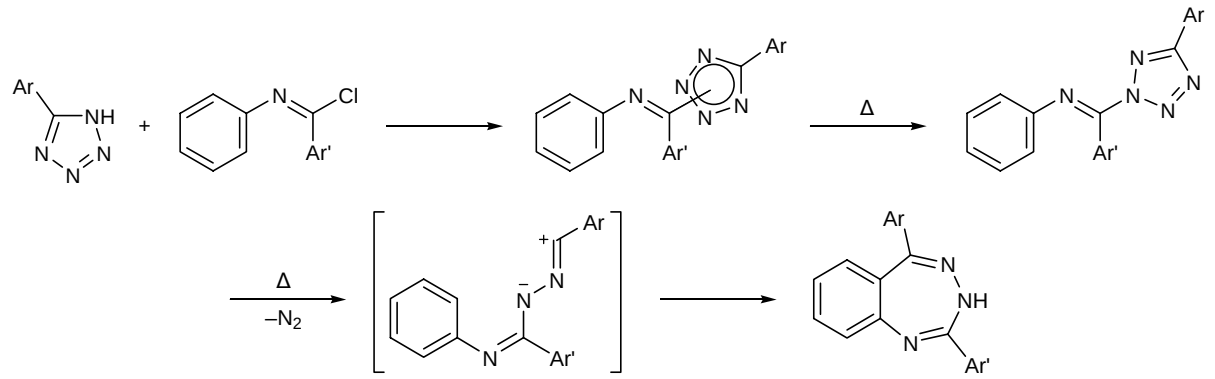


X = N (**c**), CH (**d**).

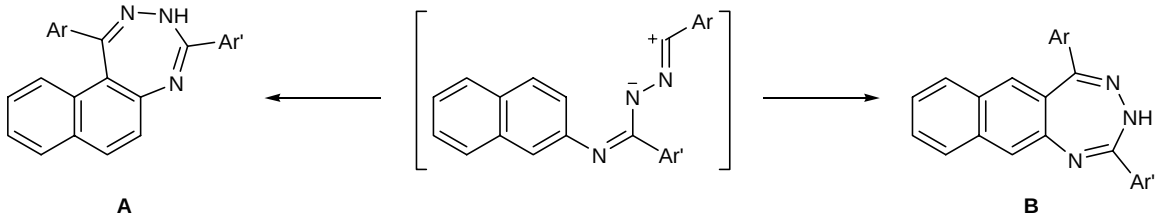
* For communication XLVII, see [1].

1070-4280/05/4103-0444

Scheme 2.



Scheme 3.



A **B**

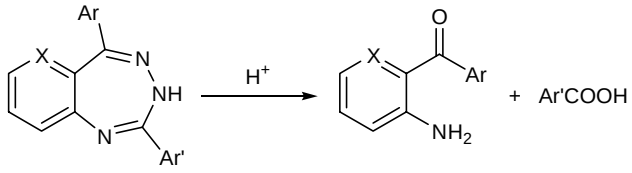
for the first time in the present work. Triazepines **Ic** and **Id** were prepared by the procedure proposed in [9]. Imidoylation of 5-phenyl- and 5-(3-pyridyl)tetrazoles was performed under conditions of phase-transfer catalysis using tetrabutylammonium bromide or cetyl(trimethyl)ammonium bromide. *N*-Imidoyltetrazoles thus obtained were heated in toluene at 110°C. As a result, triazepines **Ic** and **Id** were formed in 21 and 61% yield, respectively (Scheme 1). The structure of compounds **Ia**–**Id** was established by detailed analysis of the mechanism of thermolysis of *N*-imidoyltetrazoles and consideration of the X-ray diffraction data and IR and NMR spectra of both triazepines and their acid hydrolysis products.

Scheme 2 illustrates a plausible mechanism of the thermal transformation of *N*-aryl(or hetaryl)imidoyltetrazoles generated from 5-aryl(or hetaryl)tetrazoles and *N*-aryl(or hetaryl)benzimidoyl chlorides under conditions of phase-transfer catalysis [3]. 5-Substituted tetrazoles react with imidoyl chlorides to give a mixture of isomeric 1- and 2-imidoyltetrazoles. Thermolysis of the latter includes initial transformation of 1-imidoyltetrazoles into thermodynamically more stable 2-substituted isomers which then undergo in succession cleavage of the tetrazole ring and elimination of nitrogen molecule with formation of a 1,3-dipole, the corresponding imidoyl nitrile imide. The process is completed by 1,7-electrocyclization of imidoyl nitrile imide to triazepine.

It should be noted that in the thermolysis of *N*-imidoyltetrazoles derived from *N*-(2-naphthyl)benzimidoyl chloride 1,7-electrocyclization of the intermediate imidoyl nitrile imide can take two pathways leading to structures **A** and **B** (Scheme 3). As a result, isomeric triazepines could be obtained, and their identification may involve some difficulties. Several ways of solving this problem are possible. Among these, the most widespread is acid hydrolysis of the resulting triazepines, which leads to the corresponding amino ketones [2–7] (Scheme 4). In the preceding study, we used this technique to identify triazepines obtained by thermolysis of imidoyltetrazoles which were generated from 5-aryltetrazoles and *N*-(2-naphthyl)benzimidoyl chlorides [9].

The first difficulty encountered while following the hydrolysis technique was that the mechanism of acid hydrolysis of naphthotriazepines differed from the hydrolysis mechanism typical of benzo- and pyridotriazepines. The products of acid hydrolysis of the naphthotriazepine obtained from 5-phenyltetrazole and

Scheme 4.



X = CH, N.

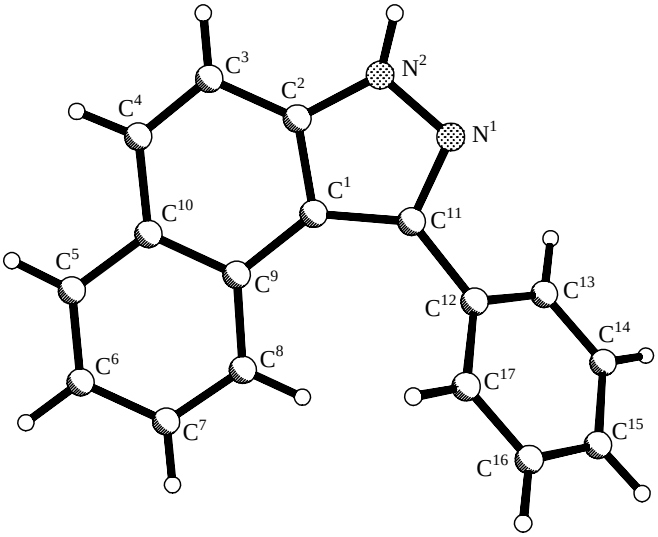


Fig. 1. Structure of the molecule of 3-phenylbenz[*e*]indazole (**IIa**) according to the X-ray diffraction data.

N-(2-naphthyl)benzimidoyl chloride were benzoic acid and a compound whose melting point, molecular weight, elemental composition, and IR and NMR spectra fully coincided with the corresponding data for 3-phenylbenz[*f*]indazole which was synthesized previously from 2-azido-3-benzoylnaphthalene [10]. Therefore, we concluded that naphthotriazepines obtained from 5-aryltetrazoles and *N*-(2-naphthyl)benzimidoyl chloride have structure **B** [9]. However, X-ray diffraction study of the hydrolysis products showed that the compound identified previously as 3-phenylbenz[*f*]indazole is in fact its isomer, 3-phenylbenz[*e*]indazole (Figs. 1, 2; Tables 1, 2). This means that the structure of naphthotriazepines synthesized previously from 5-aryltetrazoles and *N*-(2-naphthyl)benzimidoyl chlorides corresponds to isomer **A**, for 3-phenylbenz[*e*]indazole can be formed only by hydrolysis of naphthotriazepine like **A** (Scheme 5).

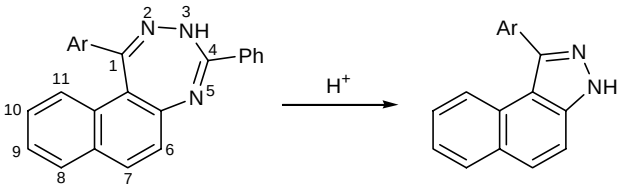
Table 1. Principal bond lengths *d* and bond angles ω in the molecule of 3-phenylbenz[*e*]indazole (**IIa**)

Bond	*d*, Å	Angle	ω, deg
N^1–C^{11}	1.3381(16)	$C^{11}N^1N^2$	106.48(11)
N^1–N^2	1.3497(16)	$C^2N^2N^1$	111.53(11)
N^2–C^2	1.3470(18)	$C^2N^2H^2$	130.9(11)
C^1–C^2	1.3952(18)	$N^1N^2H^2$	117.2(11)
C^1–C^{11}	1.4224(19)	$C^2C^1C^{11}$	104.23(11)
C^1–C^9	1.4451(18)	$C^2C^1C^9$	118.60(12)
C^2–C^3	1.413(2)	$C^{11}C^1C^9$	137.16(12)
N^2–H^2	0.901(18)	$N^2C^2C^1$	107.56(12)
		$N^2C^2C^3$	128.33(13)
		$C^1C^2C^3$	124.09(13)

Table 2. Hydrogen bond parameters in the crystalline structure of 3-phenylbenz[*e*]indazole (**IIa**)

Bond (D–H···A)	*d*(D-H), Å	*d*(H···A), Å	*d*(D···A), Å	ω(DHA), deg
N^2–H^2···N^{1B}	0.901(18)	2.070(18)	2.9622(18)	170.4(15)
N^{2A}–H^{2A}···N^1	0.947(19)	1.992(19)	2.934(3)	172.8(16)
N^{2B}–H^{2B}···N^{1A}	0.918(17)	1.979(17)	2.8830(19)	168.0(14)

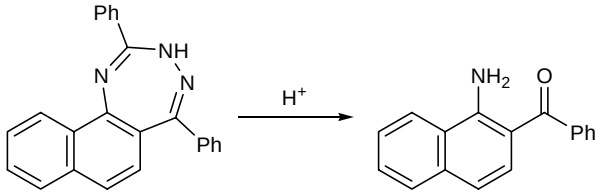
Scheme 5.



R = Ph (**a**), 4-$MeOC_6H_4$ (**b**), 3-pyridyl (**c**).

We cannot still propose a rigorous mechanism of this reaction. On the other hand, our experimental data allow us to draw the following preliminary conclusions. In all cases, ring contraction in naphthotriazepines during their acid hydrolysis is likely to involve elimination of the N^5–C^4–Ph fragment with subsequent ring closure to 3-arylbenz[*e*]indazole. This assumption is supported by the fact that the hydrolysis of 1,4-diphenyl-3*H*-naphtho[2,1-*e*][1,2,4]triazepine (**Ia**) labeled with ^{15}N at the 5-position of the heteroring gives 3-phenylbenz[*e*]indazole containing no ^{15}N (according to the mass spectrometric data). Presumably, the reason for the "anomalous" hydrolysis of naphthotriazepines derived from 5-aryltetrazoles and *N*-(2-naphthyl)benzimidoyl chloride should be sought for in the specific electronic and steric structure of these compounds, as compared to analogous benzo and pyrido derivatives.

Scheme 6.



On the other hand, the acid hydrolysis of triazepine **Id** derived from 5-phenyltetrazole and *N*-(1-naphthyl)-benzimidoyl chloride afforded in a good yield the corresponding amino ketone (Scheme 6; Fig. 3; Tables 3, 4) and benzoic acid. Therefore, there are grounds to believe that the hydrolysis of benzo- and pyridotriazepines, as well as of 2,5-diphenyl-3*H*-naphtho[1,2-*e*]-[1,2,4]triazepine (**Id**), follows the same mechanism.

To conclude, it should be emphasized that acid hydrolysis of triazepines derived from 5-aryltetrazoles and *N*-(2-naphthyl)benzimidoyl chloride may be regarded as a synthetic route to previously unknown 3-substituted benz[*e*]indazoles.

EXPERIMENTAL

The IR spectra were recorded on a Shimadzu FTIR-8400s spectrometer from samples prepared as KBr pellets. The ^{1}H NMR spectra were obtained on a Bruker AC-200 spectrometer from solutions in DMSO-d_6. The mass spectra (electron impact, 70 eV) were run on an MKh-1321 instrument. The purity of the products was checked by TLC on Silufol UV-254 plates using chloroform–petroleum ether–ethyl acetate (10:15:3) as eluent.

Triazepines **Ia** and **Ib** were synthesized by the procedure described in [9]. Acid hydrolysis of compounds **Ib**–**Id**, as well as of ^{15}N-labeled triazepine **Ia**, was performed according to the procedure reported in the same publication. 5-[^{15}N]-Triazepine **Ia** was synthesized from ^{15}N-labeled 2-aminonaphthalene.

Crystals of **IIa** suitable for X-ray analysis were obtained by recrystallization from ethanol. Colorless prisms, 0.54×0.43×0.28 mm, mp 197–199°C. The unit cell parameters and reflection intensities were measured on an Enraf–Nonius CAD-4 difractometer (MoK_α irradiation, θ/2θ scanning). Triclinic crystals: a = 12.524(3), b = 13.351(3), c = 13.882(3) Å; α = 109.60(3), β = 101.33(3), γ = 108.96(3)°; V = 1942.7(8) Å^3; d_{calc} 1.253 g/cm^3; space group P-1; Z = 6. The structure was solved by the direct method; R = 0.0283, R_w = 0.0742 [6885 reflections with $I > 2\sigma(I)$].

Crystals of **III** were obtained by recrystallization from ethanol. Light yellow prisms, 0.42×0.33×0.16 mm, mp 106–108°C. Triclinic crystals: a = 9.486(2), b = 15.583(3), c = 15.628(3) Å; α = 63.12(3), β = 73.92(3), γ = 72.35(3)°; V = 1936.8(7) Å^3; d_{calc} = 1.272 g/cm^3; space group P-1; Z = 6. The structure was solved by the direct method; R = 0.0273, R_w = 0.0656 [6883 reflections with $I > 2\sigma(I)$].

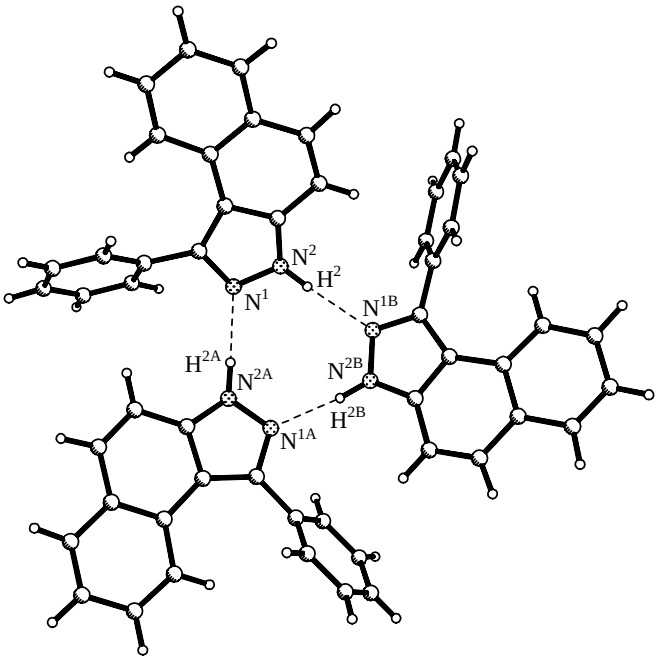


Fig. 2. Hydrogen bonds in the crystalline structure of 3-phenylbenz[*e*]indazole (**IIa**).

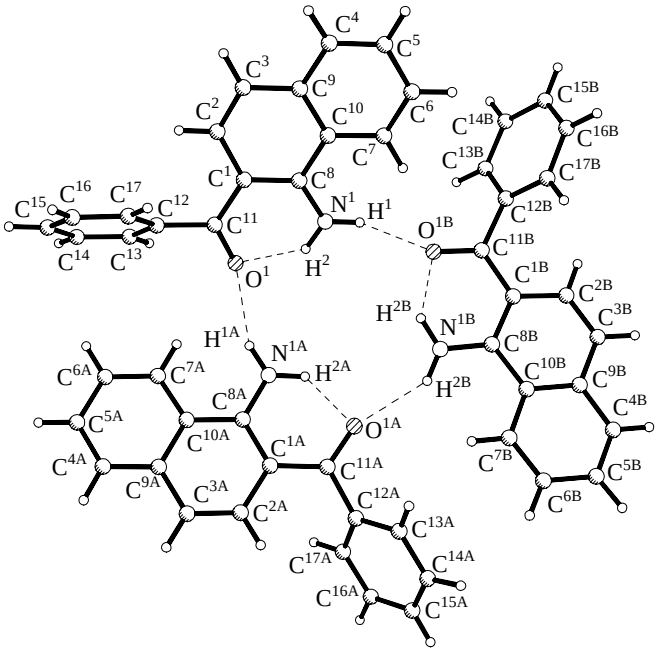


Fig. 3. Structure of the molecule and hydrogen bonds in crystal of 1-amino-2-benzoylnaphthalene (**III**).

4-Phenyl-1-(3-pyridyl)-3*H*-naphtho[2,1-*e*][1,2,4]-triazepine (Ic). A solution of 0.01 mol of *N*-(2-naphthyl)benzimidoyl chloride in 10 ml of chloroform was added over a period of 30 min under stirring at 20°C to a mixture of 0.01 mol of 5-(3-pyridyl)tetrazole, 0.001 mol of tetrabutylammonium bromide, 10 ml of 10% aqueous sodium hydroxide, and 30 ml of chloro-

Table 3. Principal bond lengths *d* and bond angles ω in the molecule of 1-amino-2-benzoylnaphthalene (**III**)

Bond	*d*, Å	Angle	ω, deg
O^1–C^{11}	1.2437(17)	$C^8N^1H^1$	120.6(12)
N^1–C^8	1.345(2)	$C^8N^1H^2$	117.4(11)
N^1–H^1	0.894(19)	$H^1N^1H^2$	121.9(17)
N^1–H^2	0.94(2)	$C^8C^1C^2$	118.40(15)
C^1–C^8	1.405(2)	$C^8C^1C^{11}$	121.30(14)
C^1–C^{11}	1.451(2)	$C^2C^1C^{11}$	120.29(14)
C^{11}–C^{12}	1.497(2)	$N^1C^8C^{10}$	119.57(14)
C^1–C^2	1.431(2)	$C^1C^8C^{10}$	119.12(14)
C^8–C^{10}	1.448(2)	$O^1C^{11}C^{12}$	117.15(15)
		$C^1C^{11}C^{12}$	119.97(14)

Table 4. Hydrogen bond parameters in the crystalline structure of 1-amino-2-benzoylnaphthalene (**III**)

Bond (D–H···A)	*d*(D–H), Å	*d*(H···A), Å	*d*(D···A), Å	ω(DHA), deg
N^1–H^2···O^1	0.94(2)	1.88(2)	2.620(2)	133.6(16)
N^1–H^1···O^{1B}	0.894(19)	2.059(19)	2.915(2)	160.2(16)
N^{1A}–H^{2A}···O^{1A}	0.95(2)	1.92(2)	2.693(2)	136.7(17)
N^{1A}–H^{1A}···O^1	0.94(2)	2.21(2)	3.094(2)	156.1(17)
N^{1B}–H^{2B}···O^{1B}	0.957(18)	1.831(18)	2.627(2)	138.7(14)
N^{1B}–H^{1B}···O^{1A}	0.894(17)	2.174(18)	2.941(2)	143.5(14)

form. The mixture was stirred for 4 h at 20°C, and the organic phase was separated, washed with 1% aqueous sodium hydroxide and water (2×10 ml), and dried over magnesium sulfate. The solvent was removed under reduced pressure, 20 ml of toluene was added to the solid residue, the mixture was heated for 1 h at 110°C and cooled, and the precipitate was filtered off and dried in air. Yield 0.73 g (21%), mp 293–295°C (from DMF–acetonitrile–water, 6:2:1). IR spectrum, ν, cm^{-1}: 911, 940, 960, 995, 1002, 1025, 1064, 1081, 1094, 1147, 1157, 1170, 1181, 1194, 1213, 1221, 1256, 1283, 1304, 1328, 1373, 1416, 1435, 1447, 1470, 1477, 1494, 1503, 1510, 1546, 1567, 1573, 1591, 1601, 1623, 3012, 3024, 3049, 3064, 3326. ^{1}H NMR spectrum, δ, ppm: 7.00–8.51 m (16H, H_{arom}, NH). Found, %: C 79.25; H 4.72; N 16.02. $C_{23}H_{16}N_4$. Calculated, %: C 79.31; H 4.60; N 16.09.

2,5-Diphenyl-3*H*-naphtho[1,2-*e*][1,2,4]triazepine (Id). A solution of 0.01 mol of *N*-(2-naphthyl)benzimidoyl chloride in 10 ml of chloroform was added over a period of 30 min under stirring at 20°C to a mixture of 0.01 mol of 5-phenyltetrazole, 0.0002 mol of cetyl(trimethyl)ammonium bromide, 10 ml of 10% aqueous sodium hydroxide, and 30 ml of chloroform. The mixture was stirred for 4 h at 20°C, and the organic phase was separated, washed with 1% aqueous sodium hydroxide and water (2×10 ml), and dried over magnesium sulfate. The solvent was removed under reduced pressure, 20 ml of toluene was added to the solid residue, the mixture was heated for 2 h at 110°C and cooled, and the precipitate was filtered off and dried in air. Yield 2.12 g (61%), mp 222–224°C (from DMF–acetonitrile, 1:3). IR spectrum, ν, cm^{-1}: 917, 927, 947, 961, 992, 1003, 1023, 1054, 1077, 1104, 1146, 1159, 1181, 1202, 1255, 1281, 1304, 1313, 1336, 1371, 1391, 1450, 1472, 1491, 1501, 1565, 1580, 1595, 1608, 1618, 1631, 3030, 3048, 3056, 3084, 3239, 3264. ^{1}H NMR spectrum, δ, ppm: 6.96–8.80 m (16H, H_{arom}), 9.44 s (1H, NH). Found, %: C 83.17; H 4.92; N 12.00. $C_{24}H_{17}N_3$. Calculated, %: C 83.00; H 4.90; N 12.10.

5-[^{15}N]-1,4-Diphenyl-3*H*-naphtho[2,1-*e*][1,2,4]-triazepine (^{15}N-Ia) was synthesized in a similar way. Yield 0.714 g (36%), mp 300–302°C (from DMF). IR spectrum, ν, cm^{-1}: 920, 940, 949, 959, 977, 993, 1026, 1075, 1101, 1144, 1154, 1170, 1179, 1210, 1227, 1256, 1287, 1303, 1313, 1339, 1378, 1395, 1418, 1438, 1445, 1449, 1473, 1495, 1508, 1560, 1578, 1600, 1624, 2853, 2925, 3023, 3049, 3080, 3313. ^{1}H NMR spectrum, δ, ppm: 7.05–8.08 m (16H, H_{arom}), 8.31 s and 8.73 s (1H, NH). Mass spectrum, *m*/*z*: 348 $[M]^+$. Found, %: C 82.95; H 4.92; N 12.27. $C_{24}H_{17}N_3$. Calculated, %: C 82.76; H 4.88; N 12.36.

Acid hydrolysis of 5-[^{15}N]-1,4-diphenyl-3*H*-naphtho[2,1-*e*][1,2,4]triazepine (^{15}N-Ia). A mixture of 5 mmol of triazepine ^{15}N-**Ia** and 30 ml of concentrated hydrochloric acid was heated for 5 h at 100°C. The mixture was cooled to 20°C, and the precipitate was filtered off and mixed with 50 ml of 10% aqueous potassium carbonate. The mixture was stirred for 30 min at 50°C, cooled to 20°C, and the precipitate was filtered off and dried in air. We thus isolated 1.044 g (86%) of 3-phenylbenz[*e*]indazole, mp 195–196°C (from ethanol). IR spectrum, ν, cm^{-1}: 921, 971, 1001, 1029, 1049, 1071, 1089, 1130, 1159, 1177, 1204, 1259, 1270, 1286, 1325, 1367, 1418, 1436, 1445, 1451, 1468, 1485, 1510, 1544, 1601, 1621, 2754, 2849, 2913, 2944, 2992, 3042, 3117, 3139, 3174, 3193, 3197. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 7.42–8.20 m (11H, H_{arom}), 12.76 s (1H, NH). Mass spectrum, *m*/*z*: 244 $[M]^+$.

Acid hydrolysis of triazepines **Ib**–**Id** was carried out in a similar way.

3-(4-Methoxyphenyl)benz[*e*]indazole (IIb). Yield 0.13 g (85%), mp 232–233°C (from ethanol). IR spectrum, ν, cm^{-1}: 973, 1033, 1049, 1089, 1106, 1126, 1181, 1204, 1245, 1295, 1325, 1437, 1455, 1459, 1528, 1544, 1613, 2760, 2835, 2853, 2901, 2934, 2950, 2997, 3043, 3109, 3139, 3192. ^{1}H NMR spectrum, δ, ppm: 3.93 s (3H, CH_3), 7.12–8.22 m (10H, H_{arom}), 12.63 s (1H, NH). Found, %: C 78.83; H 4.90; N 10.14. $C_{18}H_{14}N_2O$. Calculated, %: C 78.83; H 5.11; N 10.22.

3-(3-Pyridyl)benz[*e*]indazole (IIc). Yield 0.52 g (92%), mp 212–213°C (from ethanol). IR spectrum, ν, cm^{-1}: 967, 1029, 1038, 1059, 1090, 1105, 1135, 1178, 1193, 1204, 1261, 1283, 1320, 1331, 1409, 1425, 1440, 1448, 1501, 1571, 1596, 1619, 2718, 2754, 2806, 2843, 2879, 2896, 2998, 3042, 3105, 3193. ^{1}H NMR spectrum, δ, ppm: 7.37–9.10 m (10H, H_{arom}), 11.95 s (1H, NH). Found, %: C 78.41; H 4.58; N 17.10. $C_{16}H_{11}N_3$. Calculated, %: C 78.37; H 4.49; N 17.14.

1-Amino-2-benzoylnaphthalene (III). Yield 0.65 g (88%), mp 107–108°C (from ethanol). IR spectrum, ν, cm^{-1}: 944, 962, 1015, 1094, 1100, 1145, 1175, 1212, 1242, 1260, 1307, 1411, 1458, 1485, 1500, 1546, 1597, 3058, 3277, 3390. ^{1}H NMR spectrum, δ, ppm: 6.96–7.99 m (13H, H_{arom}, NH_2). Found, %: C 82.65; H 5.20; N 5.50. $C_{17}H_{13}NO$. Calculated, %: C 82.59; H 5.26; N 5.67.

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