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Synthesis of 3,7-Disubstituted Hexahydro- and Tetrahydro-2*H*-indazoles from Cross-Conjugated Dienones

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Abstract—The oxidation of 3,7-disubstituted hexahydroindazoles with potassium hexacyanoferrate(III) afforded previously unknown tetrahydro-2*H*-indazole derivatives. A novel ring contraction reaction leading to 2,3-diazaspiro[4.4]non-3-en-1-one derivatives was discovered. The product structure was proved by NMR spectroscopy, mass spectrometry, and X-ray analysis.

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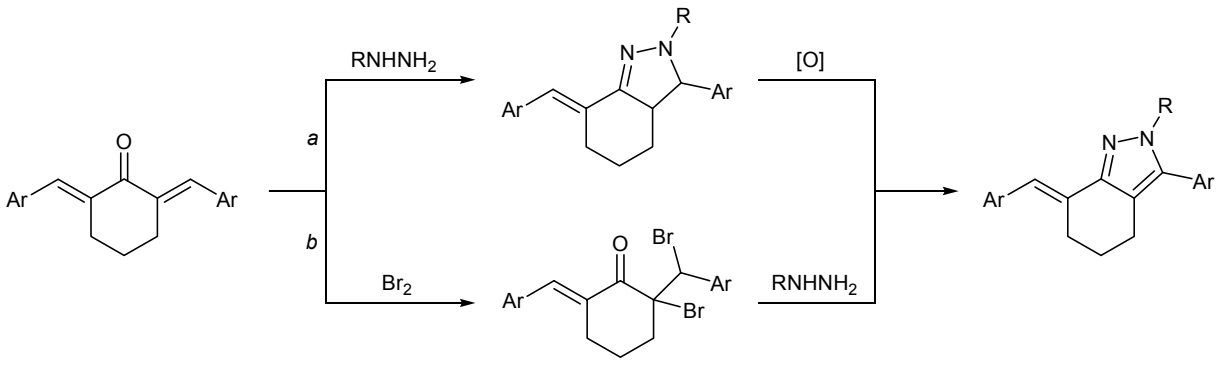
In recent years, organic and hybrid molecular systems have attracted keen interest of researchers [1]. Development of rational approaches for the target-oriented synthesis of organic molecules constitutes the basis for the preparation of such systems [2]. A huge number of successful strategic and tactical solutions, as well as synthetic techniques, have firmly become routine tools of organic chemists [3].

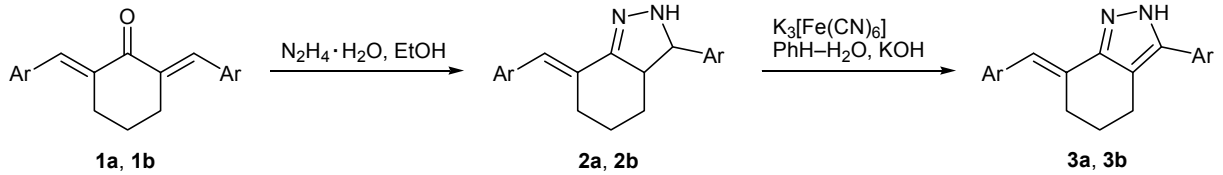
However, a synthetic scheme that seemed to be faultless at the design step often appears to be inappropriate for the preparation of target compounds or leads to unpredictable structures. We have encountered with analogous problem while trying to synthesize 3,7-disubstituted hexahydro- and tetrahydroindazoles used as ligands for the preparation of coordination polymers [4–7], as well as of biologically active compounds [8, 9].

Two pathways can be proposed for the synthesis of tetrahydroindazoles from cross-conjugated dienones (Scheme 1). The first pathway (*a*) is based on the addition of hydrazine or substituted hydrazines to the enone fragment of cross-conjugated dienone, followed by oxidation (dehydrogenation) of cyclohexane-fused dihydropyrazole thus formed. The second path (*b*) involves addition of hydrazine to the dienone adduct with bromine, by analogy with the data of [10]. In addition, syntheses of structurally related pyrazoles via heterocyclization of epoxy ketones [11] and oxidative heterocyclization of dienone hydrazones [12] have been reported. Despite long-term extensive studies,

Scheme 1.



Scheme 2.



1a, **1b** **2a**, **2b** **3a**, **3b**

Ar = Ph (**a**), 4-$MeOC_6H_4$ (**b**).

arylmethylidene-substituted tetrahydro-2*H*-indazoles with no substituent on the nitrogen atom have not been described so far (according to SciFinder).

While planning the synthesis, we presumed that the corresponding reactions or their analogs have already been reported in the literature. However, our experiments showed that the results obtained according to pathway *b* essentially differ from those expected. Path *a* was explored using phenyl-substituted dienone **1a** and its *p*-methoxy derivative **1b** (Scheme 2). The reaction of substituted hydrazines with dienones was described previously [13].

Aromatization of fused heterocyclic systems structurally related to **2** has been the subject of a number of studies. For this purpose, oxidation with bromine [14, 15], heating with elemental sulfur [16], oxidation with singlet oxygen [16], or oxidation with potassium hexacyanoferrate(III) in alkaline medium [17] was generally used. In some cases, aromatization of binucleophile adducts occurred even during their purification [16]. Potassium hexacyanoferrate(III) turned out to be the most efficient oxidant [17–19].

We tried to accomplish aromatization of **2** with 2,3,5,6-tetrachloro-1,4-benzoquinone, 5,6-dichloro-2,3-dicyano-1,4-benzoquinone, and potassium hexacyanoferrate(III). The oxidation with quinones in boiling benzene afforded no desired results. 5,6-Dichloro-2,3-dicyano-1,4-benzoquinone as stronger oxidant induced decomposition of the dihydropyrazole system to initial dienone, while the reaction with 2,3,5,6-tetrachloro-1,4-benzoquinone did not involve the dihydropyrazole fragment.

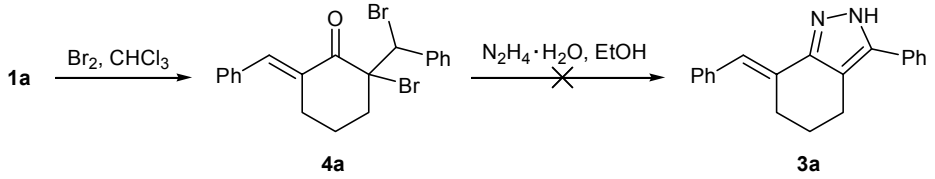
We succeeded in oxidizing compounds **2a** and **2b** in good yields only with potassium hexacyanoferrate(III) in alkaline medium (Scheme 2). The ^{1}H NMR spectra of oxidation products **3a** and **3b** lacked doublet signal typical of 3-H in initial compounds **2**. In addition, the NH singlet appeared in the spectra of **3a** and **3b** in a considerably weaker field (δ 9.9–10.1 ppm against δ 5.58 and 7.22 ppm in the spectra of **2a** and **2b**, respectively).

The dihydropyrazole ring in *N*-phenyl-substituted derivatives remained unchanged in the reaction with potassium hexacyanoferrate(III) [13]. *N*-Substituted dihydropyrazoles are more resistant to oxidation. They do not react with quinones and potassium hexacyanoferrate(III), and their oxidation may be achieved only with the use of lead tetraacetate. Presumably, the oxidation with $K_3[Fe(CN)_6]$ primarily involves the NH group. This follows from the instability of **2a** and **2b** on storage in air or in solution at room temperature, as well as from the formation of complex mixtures of oxidation products. However, crystalline compounds **2a** and **2b** can be stored for a fairly long time at 5°C. Compounds **2a** and **2b** show yellow–green luminescence.

Thus, pathway *a* (Scheme 1) leads to previously unknown tetrahydroindazoles **3** which can be readily subjected to further functionalization at the NH group or double bond. It is known that the C=C double bond in dienones readily takes up bromine on treatment with 1 equiv of Br_2 in $CHCl_3$ [20]. We have reproduced the described procedure, and the spectral parameters of the resulting dibromo derivatives coincided with published data. Moreover, we succeeded in obtaining single crystals of dibromide **4a** and showed that the addition of bromine is stereospecific (*trans*-1,2-addition). However, the quality of crystals of **4a** did not allow satisfactory estimation of bond lengths, bond angels, and intermolecular interactions therein. The bromination of *p*-methoxy derivative **1b** was accompanied by electrophilic substitution in the aromatic rings. Nevertheless, the corresponding dibromide **4b** was isolated in 38% yield.

At first glance, the synthesis of tetrahydroindazoles according to pathway *b* should not involve difficulties. Taking into account high reactivity of bromine in the β-position with respect to the carbonyl group, the major product of the reaction of hydrazine hydrate with dibromides derived from dienones should be pyrazole **3a** (Scheme 3). However, physical and spectral properties of the product isolated in the reaction of **4a** with hydrazine hydrate differed from those of com-

Scheme 3.



pound **3a** obtained by oxidation of **2a** (Scheme 2). In particular, it melted at 161°C against mp 85–86°C of pyrazole **3a**.

According to the MS data, compound **5** obtained by reaction of **4a** with hydrazine contained no bromine, but its molecular ion $[M]^+$, *m*/*z* 302 (I_{rel} 36%) did not match the composition of **3a** ($C_{20}H_{18}N_2$). The ^{1}H NMR spectrum of **5** in $CDCl_3$ contained upfield multiplet signals from six nonequivalent methylene protons (cycloalkane) and CH= group (δ 6.15 ppm, br.s,), unresolved signals from two nonequivalent phenyl substituents, and an acidic proton signal at δ 8.91 ppm (δ 11.5 ppm in DMSO-d_6). In the ^{13}C NMR spectrum of **5** we observed four aliphatic carbon signals, signals from two nonequivalent benzene rings and one C=C bond in the aromatic region, and a separate signal at δ_C 144.4 ppm; also, signals at δ_C 180.5 and 160.3 ppm were present, which may be assigned to amide C=O and C=N carbon atoms, respectively.

The following conclusions can be drawn on the basis of the above data. First, there are no bromine atoms in molecule **5**. Second, the elemental composition of **5** corresponds to the formula $C_{20}H_{18}N_2O$. Third, molecule 5 contains a fairly acidic NH proton (δ 8.5 ppm in $CDCl_3$; νN–H 3200 cm^{-1}) and an amide carbonyl group (δ_C 180.5 ppm; νC=O 1700 cm^{-1}). However, it became possible to unambiguously determine the structure of **5** only when its crystals suitable for X-ray analysis were obtained. Transparent yellow plates with mp 161°C were grown by crystallization of **5** from benzene and from methylene chloride. Better single crystals were obtained from benzene.

The X-ray diffraction study showed that molecules of **5** have bicyclic structure and are composed of spiro-fused cyclopentane and pyrazole rings (Fig. 1). A unit cell of **5** contains two crystallographically independent molecules (see table) differing by the conformation of the carbocycle. These molecules are linked to each other by two hydrogen bonds formed between the NH group of one molecule and carbonyl oxygen atom of the other (Fig. 2), N···O 2.8638(16) and 2.9056(16) Å, ∠NHO 167°. As shown by ESI MS, the H-bonded dimers are also retained in solution.

A probable scheme of the reaction of **4a** with hydrazine includes a step analogous to the Favorskii rearrangement (Scheme 4). Initial Michael-type nucleo-

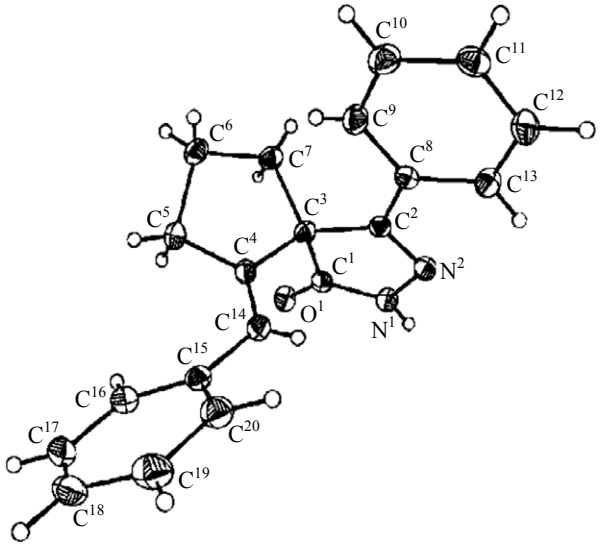


Fig. 1. Structure of the molecule of 6-benzylidene-4-phenyl-2,3-diazaspiro[4.4]non-3-en-1-one (**5**) according to the X-ray diffraction data. Non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

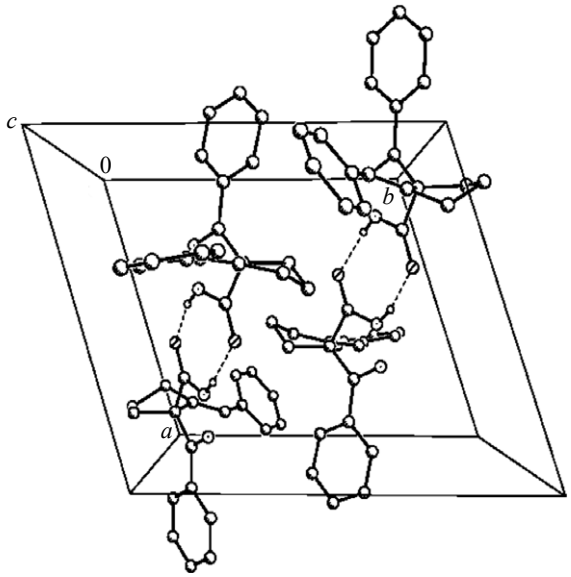
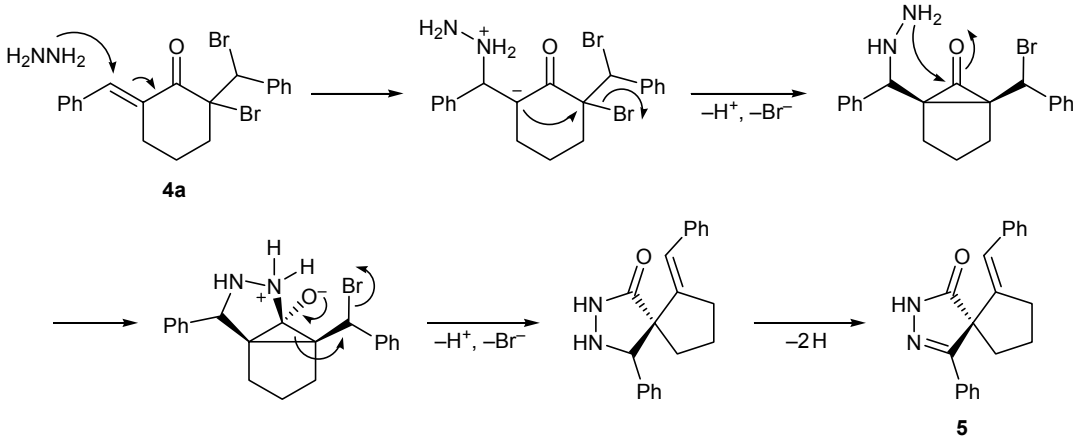


Fig. 2. Packing of H-bonded dimers of compound **5** in a unit cell.

Scheme 4.



philic attack by hydrazine molecule on the double bond conjugated with the carbonyl group leads to the corresponding enolate. Next follows intramolecular substitution of the bromine atom attached to the endocyclic carbon atom. The ring contraction step is likely to involve heterocyclization through the primary amino group and carbonyl group. The tetrahedral intermediate is stabilized via nucleophilic replacement of the second bromine atom. Taking into account stereochemical structure of the initial dibromide, this step may be regarded as a concerted fragmentation as shown in Scheme 4. Dehydrogenation of the intermediate product may be achieved by the action of atmospheric oxygen. However, the low yield of **5** does not rule out disproportionation path.

In order to improve the yield and obtain an analytically pure sample **5** directly from the reaction mixture, the reaction of **4a** with hydrazine was carried out in other solvents, such as DMF, toluene, and THF. The progress of the reactions was monitored by TLC. The reaction in toluene on heating was complete in 7 h. Five products were detected in the reaction mixture by TLC, one of which was compound **5**. The reaction mixture was treated with water and extracted with an organic solvent, the extract was dried and evaporated, and the residue was analyzed by NMR. Apart from signals belonging to **5**, signals from a large number of unidentified compounds were present.

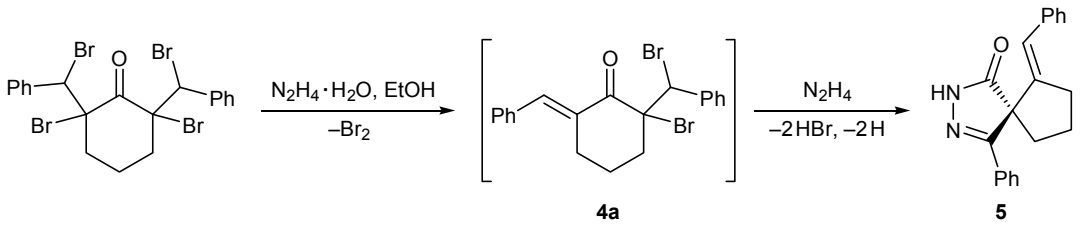
The addition of hydrazine hydrate to a solution of **4a** in THF was accompanied by gas evolution, and the reaction mixture turned bright yellow. The mixture was treated with ice, and the precipitate was filtered off. The ^{1}H NMR spectrum of the product showed signals of compound **5** together with unidentified compounds; however, the number of impurities was lower than in the preceding case.

The reaction of **4a** with excess hydrazine hydrate as reaction medium afforded compound **5** in a low yield.

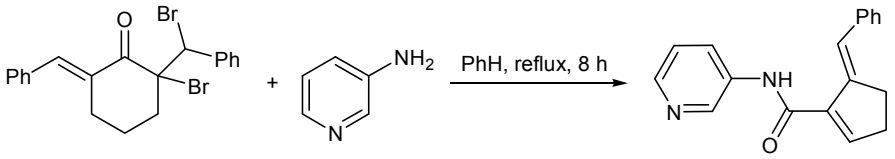
Bond lengths and bond angles in two independent molecules (separated by a slash) of compound **5** according to the X-ray diffraction data

Bond	*d*, Å	Bond angle	ω, deg
O^1–C^1	1.2360(16) / 1.2349(15)	$N^1C^1C^3$	106.07(10) / 105.77(10)
N^1–C^1	1.3581(17) / 1.3592(17)	$N^2C^2C^3$	113.01(11) / 113.23(11)
N^1–N^2	1.4022(15) / 1.4075(15)	$C^2C^3C^1$	99.54(10) / 99.93(10)
N^2–C^2	1.3048(17) / 1.3060(17	$C^2C^3C^4$	114.89(10) / 115.49(10)
C^1–C^3	1.5448(18) / 1.5423(18)	$C^1C^3C^4$	108.94(10) / 111.25(10)
C^2–C^3	1.5233(17) / 1.5187(17)	$C^2C^3C^7$	118.29(11) / 117.37(10)
C^3–C^4	1.5454(18) / 1.5428(17)	$C^1C^3C^7$	110.36(10) / 108.41(10)
C^3–C^7	1.5733(17) / 1.5612(17)	$C^4C^3C^7$	104.61(10) / 104.32(10)
C^4–C^5	1.5202(18) / 1.5221(17)	$C^5C^4C^3$	107.19(11) / 108.70(10)
C^5–C^6	1.539(2) / 1.5449(18)	$C^4C^5C^6$	102.76(11) / 104.74(10)
C^6–C^7	1.5492(19) / 1.5426(18)	$C^6C^7C^3$	105.91(11) / 103.43(10)

Scheme 5.



Scheme 6.



The reaction of **4a** with hydrazine hydrate in DMF on heating was complete in 7 h. The product was precipitated by addition of ice. In this case, pure compound **5** was isolated in a satisfactory yield (39%). Compound **5** can also be obtained by treatment of tetrabromo derivative of dienone **1a** with excess hydrazine hydrate (Scheme 5). Presumably, the process involves intermediate formation of dibromide **4a**. No satisfactory results were obtained in the reactions of hydrazine hydrate with dibromides derived from five- or seven-membered cyclic dienones.

We also examined reactions of dibromide **4a** with nitrogen nucleophiles, in particular with those capable of simultaneously acting as bases. Compound **4a** was inactive toward aniline on heating in boiling DMF, benzene, or ethanol. On heating in boiling pyridine, compound **4a** lost bromine molecule with formation of dienone **1a**; analogous results were obtained when compound **4a** was heated in triethylamine and pyridin-4-amine. Partial debromination of **4a** was observed in the reaction with hydroxylamine in ethanol, and the product was a mixture of dienone **1a** and unreacted dibromide **4a**.

By heating dibromide **4a** with pyridin-3-amine in benzene we obtained 41% of a compound which was assigned structure **6** on the basis of spectral data and the results of the reaction of **4a** with hydrazine (Scheme 6). Compound **6** showed in the aliphatic region of the ^{1}H NMR spectrum two two-proton signals at δ 3.07 and 2.52 ppm, which were assigned to methylene protons in the five-membered carbocycle. Protons on the double bonds resonated at δ 7.76 (exocyclic) and 6.48 ppm (endocyclic). In the aromatic region we observed signals from one phenyl ring and one 3-substituted pyridine ring. The NH signal appeared as a broadened singlet at δ 6.70 ppm. The ^{13}C NMR spectrum of **6** contained signals from the amide carbonyl carbon atom (δ_C 184.7 ppm), aromatic carbons of the benzene and pyridine rings, and two pairs of double-bonded carbon atoms. Methylene carbon signals were located at δ_C 23.4 and 26.5 ppm. A fairly intense molecular ion peak (*m*/*z* 276 $[M]^+$, I_{rel} 25%) was present in the mass spectrum of **6**. At present, we cannot propose a satisfactory mechanism to rationalize loss of Ph–C fragment during the formation of compound **6**.

Searching in the CAS database showed that the closest structural analogs of compound **5** are cardiotonic agents [21] and SIRT1 inhibitors for nontoxic oncotherapy [22]. These compounds are synthesized by reaction of hydrazine with keto esters [23, 24] which are prepared in turn by double alkylation (with cyclization) of benzoylacetic acid esters. We have discovered a simple and cost-efficient synthetic route to such compounds via ring contraction. The presence of an arylmethylidene group and an NH hydrazide fragment in molecule **5** provides the possibility of its further functionalization.

EXPERIMENTAL

The IR spectra were recorded on UR-20 and Specord 75 IR instruments. The ^{1}H NMR spectra were measured on a Bruker Avance 400AMX spectrometer at 27°C. The mass spectra were obtained on an Agilent 1100 Series LC/MSD Tramp SL system. The melting points were determined in open capillaries and are uncorrected (as are boiling points too). The elemental analyses were obtained using a Carlo Erba ER-20 CHN analyzer.

The X-ray analysis of compound **5** was performed at 100 K on a Bruker SMART APEX2 CCD diffractometer (MoK_α radiation, graphite monochromator, ω-scanning). The structure was solved by the direct method and was refined against F^2_{hkl} by the least-squares procedure in full-matrix anisotropic approximation. The NH hydrogen atoms were localized from the difference Fourier maps, and the other hydrogen atoms were placed in geometrically calculated positions. The positions of all hydrogen atoms were refined according to the riding model. All calculations were performed using SHELXTL PLUS package [25].

Initial dienones **1a** and **1b** were synthesized according to the procedures described in [5].

Heterocyclization of dienones 1a and 1b with hydrazine hydrate (*general procedure***).** A mixture of 2.5 mmol of dienone **1a** or **1b** and 10 mmol of hydrazine hydrate in 15 mL of ethanol was stirred for several hours on heating. The progress of the reaction was monitored by TLC. When the reaction was complete, the mixture was cooled, and the precipitate was filtered off and recrystallized from ethanol.

(7*E*)-7-Benzylidene-3-phenyl-3,3a,4,5,6,7-hexahydro-2*H*-indazole (2a) was synthesized from 0.68 g of (2*E*,6*E*)-2,6-dibenzylidenecyclohexan-1-one (**1a**) and 0.5 mL of hydrazine hydrate. Yield 0.48 g (70%), mp 119°C (from EtOH); published data [26]: mp 121°C. IR spectrum (mineral oil): ν 3225 cm^{-1} (N–H). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.32–1.49 m (1H, 5-H), 1.54 d.d (1H, 4-H, *J* = 10.1, 12.1), 1.90–1.99 m (1H, 5-H), 2.08–2.12 m (1H, 4-H), 2.35–2.50 m (1H, 6-H), 2.77–2.87 m (1H, 3a-H, *J* = 6.6, 2.1), 3.05 d (1H, 6-H, *J* = 15.5), 4.88 d (1H, 3-H, *J* = 13.9), 7.22 s (1H, NH), 7.31–7.45 m (9H, H_{arom}, CH=), 7.52 d (2H, *o*-H, *J* = 7.8). Mass spectrum (EI, 70 eV), *m*/*z* (I_{rel}, %): 287 (100) $[M - 1]^+$, 182 (16), 115 (13), 91 (12).

(7*E*)-3-(4-Methoxyphenyl)-7-[(4-methoxyphenyl)-methylidene]-3,3a,4,5,6,7-hexahydro-2*H*-indazole (2b) was synthesized from 0.84 g of (2*E*,6*E*)-2,6-bis-[(4-methoxyphenyl)methylidene]cyclohexan-1-one (**1b**) and 0.5 mL of hydrazine hydrate. Yield 0.90 g, mp 84–86°C (from EtOH) [26]. IR spectrum (mineral oil): ν 3320 cm^{-1} (N–H). ^1H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.38–1.60 m (2H, 4-H, 5-H), 1.89–1.98 m and 2.02–2.11 m (1H each, 4-H, 5-H), 2.35–2.48 m and 2.72–2.84 m (1H each, 3a-H, 6-H), 3.05 d (1H, 6-H, *J* = 15.5), 3.85 br.s (6H, OCH_3), 4.47 d (1H, 3-H, *J* = 13.9), 5.58 s (1H, NH), 6.85–7.00 m (4H, *o*-H), 7.18 s (1H, CH=), 7.32 d and 7.47 d (2H, *m*-H, *J* = 8.4), 7.42 d (2H, *m*-H, *J* = 8.4). Mass spectrum (EI, 70 eV), *m*/*z* (I_{rel}, %): 349 (100) $[M + 1]^+$, 348 (87) $[M]^+$, 333 (56), 214 (57), 212 (34), 147 (78), 134 (39), 121 (72), 91 (67).

Aromatization of the heterocycle in compounds 2a and 2b (*general procedure***).** Compound **2a** or **2b**, 0.001 mol, was dispersed in a mixture of 10 mL of benzene and 10 mL of water, 0.002 mol (0.1 g) of potassium hydroxide and 0.0021 mol (0.84 g) of $K_3[Fe(CN)_6]$ were added, and the mixture was stirred for 16 h at room temperature. The organic phase was separated, and the aqueous phase was extracted with benzene (2×10 mL). The extracts were combined with the organic phase, washed with water until neutral washings, dried over sodium sulfate, filtered, and evaporated, and the residue was recrystallized from appropriate solvent.

(7*E*)-7-Benzylidene-3-phenyl-4,5,6,7-tetrahydro-2*H*-indazole (3a) was obtained from 0.29 g of **2a**. Yield 0.23 g (82%), mp 85–86°C (from THF). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.22–2.29 m (2H, 5-H), 2.54–2.59 m (2H, 4-H), 3.01–3.06 m (2H, 6-H), 7.11–7.53 m (9H, H_{arom}, CH=), 7.96 d (2H, *o*-H, *J* = 7.5 Hz), 10.04 s (1H, NH). Found, %: C 83.99; H 6.22; N 8.91. $C_{20}H_{18}N_2$. Calculated, %: C 83.88; H 6.34; N 8.78.

(7*E*)-3-(4-Methoxyphenyl)-7-[(4-methoxyphenyl)methylidene]-4,5,6,7-tetrahydro-2*H*-indazole (3b) was obtained from 0.35 g of **2b**. Yield 0.15 g (43%), mp 79–82°C (from THF). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.62–1.98 m (2H, 5-H), 2.10–2.28 m (2H, 4-H), 2.73–2.84 m (2H, 6-H), 3.83 br.s (6H, OCH_3); 6.77–7.09 m, 7.21–7.69 m, and 7.76–8.15 m (8H, H_{arom}); 7.86 s (1H, CH=), 9.91 s (1H, NH).

Bromination of dienones 1a and 1b (*general procedure***).** A solution of 5 mmol (0.8 g) of bromine in 5 mL of carbon tetrachloride was slowly added dropwise under vigorous stirring to a solution of 5 mmol of dienone **1a** or **1b** in 30 mL of carbon tetrachloride. When the bromine color disappeared, the mixture was stirred for 15 min, the solvent was distilled off, and the residue was recrystallized from ethanol.

(6*E*)-6-Benzylidene-2-bromo-2-[bromo(phenyl)-methyl]cyclohexan-1-one (4a) was obtained from 1.36 g of **1a**. Yield 1.66 g (77%), mp 122–124°C [20]. IR spectrum (mineral oil): ν 1680 cm^{-1} (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.75–1.90 m and 1.94–2.04 m (1H each, 5-H), 2.21–2.29 m and 2.69–2.81 m (1H each, 4-H), 2.96–3.11 m (2H, 6-H), 6.10 br.s (1H, CHBr), 7.37–7.79 m (11H, H_{arom}, CH=). ^{13}C NMR spectrum, δ_C, ppm: 19.6, 27.8, 33.0, 57.2,

71.0, 128.3, 129.1, 129.3, 129.9, 130.7, 131.1, 131.4, 133.5, 135.5, 140.2, 192.0.

(6*E*)-2-Bromo-2-[bromo(4-methoxyphenyl)-methyl]-6-[(4-methoxyphenyl)methylidene]cyclo-hexan-1-one (4b) was synthesized from 1.30 g of **1b**. Yield 0.75 g (38%), mp 139–143°C. IR spectrum (mineral oil): ν 1680 cm^{-1} (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.82–1.99 m (2H, 5-H), 2.29 q.d (1H, 4-H, *J* = 6.0, 3.1), 2.64–2.71 m (1H, 4-H), 3.37–3.42 m (2H, 6-H), 3.81 s and 3.84 s (3H each, OCH_3), 5.21 s (1H, CHBr), 7.87 d (2H, *o*-H, *J* = 8.4), 6.92 d (2H, *o*-H, *J* = 8.6), 7.42 d (2H, *m*-H, *J* = 8.4), 7.55 d (2H, *m*-H, *J* = 8.6), 7.79 s (1H, CH=). Found, %: C 57.14; H 4.63. $C_{22}H_{22}Br_2O$. Calculated, %: C 57.17; H 4.80.

6-Benzylidene-4-phenyl-2,3-diazaspiro[4.4]non-3-en-1-one (5). Hydrazine hydrate, 0.31 g (6 mmol), was added to a solution of 0.68 g (1.6 mmol) of compound **4a** in 15 mL of ethanol. The mixture was heated for 6 h under reflux, cooled, and diluted with 10 mL of water, and the precipitate was filtered off and recrystallized from ethanol. Yield 0.23 g (48%), mp 159–163°C. IR spectrum (mineral oil), ν, cm^{-1}: 3200 (N–H), 1700 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.08–2.19 m (1H, 4-H), 2.21–2.29 m (2H, 4-H, 5-H); 2.39–2.51 m, 2.96–3.08 m, and 3.08–3.18 m (1H each, 5-H, 6-H); 6.15 s (1H, CH=), 7.19–7.43 m (9H, H_{arom}, CH=), 7.56 d.d (2H, *o*-H, *J* = 7.8, 2.2), 7.76 d (1H, *o*-H, *J* = 7.8), 8.91 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 25.2, 32.3, 34.3, 62.4, 125.4, 126.7, 127.4, 128.7, 128.9, 129.3, 130.1, 137.1, 144.4, 160.3, 180.5. Mass spectrum (EI, 70 eV), *m*/*z* (I_{rel}, %): 302 (36) $[M]^+$, 211 (17), 128 (48), 115 (65), 91 (46), 77 (100), 51 (61).

Crystallographic data. Triclinic crystal system, space group *P*-1; $C_{20}H_{18}N_2O$; unit cell parameters: *a* = 10.393(2), *b* = 12.279(3), *c* = 13.182(3) Å; α = 87.90(3), β = 86.43(3), γ = 71.68(3)°; *V* = 1593.6(7) $Å^3$; *Z* = 4, d_{calc} = 1.260 g/cm^3; μ = 0.79 cm^{-1}; *F*(000) = 640. Intensities of 18065 reflections were measured, including 7660 independent reflections and 6162 reflections with $I > 2\sigma(I)$. Final divergence factors: R_1 = 0.0419 [for reflections with $I > 2\sigma(I)$], R_w = 0.1108 [for all reflections]; goodness of fit 1.002. The complete set of crystallographic data for compound **5**, including coordinates of atoms, was deposited to the Cambridge Crystallographic Data Centre (entry no. CCDC 1436168).

(5*E*)-5-Benzylidene-*N*-(pyridin-3-yl)cyclopent-1-ene-1-carboxamide (6). Pyridin-3-amine, 0.31 g (1.3 mmol), was added to a solution of 0.15 g (3.5 mmol) of compound **4a** in 15 mL of anhydrous benzene. The mixture was heated for 8 h under reflux and cooled, and the precipitate was filtered off. The filtrate was evaporated, and the residue was subjected to column chromatography on silica gel using ethyl acetate–petroleum ether (1:3) as eluent. Yield 0.04 g (41%). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 2.53 d.d (2H, 4-H, *J* = 6.2, 4.8), 3.07 t (2H, 5-H, *J* = 6.2), 6.48 t (2H, 3-H, *J* = 4.8), 6.69 br.s (1H, NH), 7.19–7.47 m (7H, Ph, 4′-H, 5′-H), 7.76 br.s (1H, CH=), 8.20 d (1H, 2′-H, *J* = 4.7), 8.47 d (1H, 6′-H, *J* = 2.4). ^{13}C NMR spectrum, δ_C, ppm: 23.4, 26.5, 116.1, 123.7, 125.0, 128.5, 128.6, 129.8, 134.4, 135.6, 136.6, 136.7, 138.5, 141.2, 142.3, 184.7. Mass spectrum (EI, 70 eV), *m*/*z* (I_{rel}, %): 367 (25) $[M]^+$, 247 (10), 155 (81), 115 (61), 91 (44), 78 (77), 51 (88), 43 (100).

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