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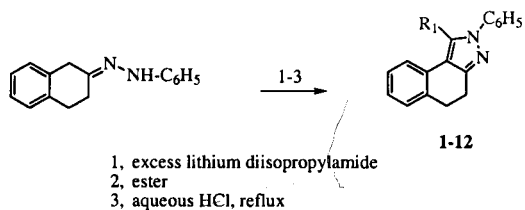
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The phenylhydrazone of 2-tetralone was dilithiated with excess lithium diisopropylamide followed by condensation with several aromatic esters, and the resulting intermediates were acid cyclized to 4,5-dihydro-2*H*-benz[e]indazoles.

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The preparations and uses of 2*H*-indazoles and related indazoles have been well investigated [1], however, the reports dealing with the preparations of 2*H*-benz[e]indazoles and 4,5-dihydro-2*H*-benz[e]indazoles are quite limited [2-5]. Related fused-ring 2*H*-benz[e]indazoles have been prepared or studied as a part of more extensive investigations [6], and in general, these compounds also have additional potential as pharmaceuticals, dyes, and in photography [2-6]. Three synthesis reports of the latter 4,5-dihydro-2*H*-benz[e]indazoles deal with the treatment of 1-acetyl-2-tetralone or related materials with hydrazine [2-4], and another preparation involves the treatment of 1-formyl-2-tetralone with semicarbazide [5].

In earlier studies, we prepared related 4,5-dihydro-2*H*-benz[g]indazoles where dilithiated 1-tetralone carboalkoxyhydrazones or phenylhydrazone were condensed/cyclized with aromatic esters, lithiated ethyl benzoylacetate, or a carboxylic acid anhydride [7]. Since then, additional studies by others with 2,3-diphenyl- and similarly substituted 4,5-dihydro-2*H*-benz[g]indazoles and other 4,5-dihydro-2*H*-benz[g]indazoles have also been reported [8-10]. They were prepared by an unrelated method.



During the current investigation, 2-tetralone was transformed into its phenylhydrazone [11] and dilithiated with excess lithium diisopropylamide [12]. The 1,4-dianion type intermediate underwent a Claisen-type condensation with a variety of aromatic esters ranging from methyl benzoate to methyl 4-hydroxybenzoate to methyl isonicotinate followed by acid cyclization of resulting *C*-acylated intermediates (not isolated) to the expected 4,5-dihydro-2*H*-benz[e]indazoles **1-12** in yields (see Table) ranging from 54-92%.

The actual deprotonation of the benzyl C1-H proton of 2-tetralone phenylhydrazone to the 1,4-dianion-type intermediate with excess lithium diisopropylamide is compared to the possible but less likely deprotonation of a C3-H proton, and this has been established by related precedents in addition to the results obtained in this study. For example, 2-tetralone underwent apparent exclusive deprotonation at C1-H followed by condensation with an electrophilic reagent, such as methyl formate [5,13]. The ¹H nuclear magnetic resonance spectra of compounds **1-12** clearly indicates the coupling of adjacent methylene hydrogens as complex multiplets ranging from δ 2.83-3.11 ppm and establishes the lithiation occurring at C1-H instead of C3-H [14]. Other pendant proton absorptions were noted as singlets at δ 1.35 ppm for the *tert*-butyl group in **10**; ArCH₃; absorptions in **5** and **9** were displayed as singlets δ 2.27-2.39 ppm; ArOCH₃; in **3**, **7**, **8** and **12** were noted as singlets ranging from δ 3.68-3.92 ppm, and ArOH recorded as a singlet at δ 9.83 ppm in **6**. In the ¹³C nuclear magnetic resonance spectra, the C-4 and C-5 carbons of the dihydrobenzindazole were displayed from δ 29.3-30.6 and 21.5-22.6 ppm, respectively. The heteroaromatic (using 1*H*-pyrazole numbering with *N*-phenyl as position N-1) C-4 carbons were noted from δ 114.4-117.0 ppm. The C-3 and C-5 carbons of the heteroaromatic ring were not differentiated [15]. Pendant methoxy carbons in **3**, **7**, **8**, and **12** were observed at δ 55.4-61.2 ppm [16a], the 4-methyl carbon in **5** and the 3,5-dimethyl carbons in **9** were located at δ 30.5 ppm, the methyl carbons of the *tert*-butyl group of **10** were found at δ 31.6 ppm, and the remaining carbon of this pendant group was located at δ 35.1 ppm. There were numerous additional aromatic absorptions noted, and each molecule reported had the predicted number of carbons resonances [16b].

The yields of products **1-12** reported may not be optimal for a particular compound, but the current general procedure readily affords multi-gram quantities of pure fused-ring heterocyclic products resulting from recrystallization from routine solvents, which are in sufficient amounts for spectral characterization and other uses. The experimental procedure is straightforward so that someone not necessarily familiar with strong base procedures can be successful with

Table
 4,5-Dihydro-2*H*-benz[*e*]indazoles

No	R ₁	Molecular Formula	% Yield/ MP, °C	Analyses		
				C	H	N
1	C ₆ H ₅	C ₂₃ H ₁₈ N ₂	76	85.68	5.63	8.69
			138-141 [a, f]	85.56	5.58	8.73
2	4-ClC ₆ H ₄	C ₂₃ H ₁₇ ClN ₂	92	77.41	4.80	7.85
			166-168 [a, g]	77.47	4.87	7.64
3	4-CH ₃ OC ₆ H ₄	C ₂₄ H ₂₀ N ₂ O	57	81.79	5.72	7.95
			162-163 [b, h]	81.52	5.73	7.59
4	3-ClC ₆ H ₄	C ₂₃ H ₁₇ ClN ₂	89	77.41	4.80	7.85
			127-130 [c, i]	77.36	4.67	7.74
5	4-CH ₃ C ₆ H ₄	C ₂₄ H ₂₀ N ₂	54	85.68	5.99	8.33
			166-169 [b, j]	85.54	5.82	8.10
6	4-HOC ₆ H ₄	C ₂₃ H ₁₈ N ₂ O	91	81.63	5.36	8.28
			254-257 [a, k]	81.55	5.42	8.14
7	3,4,5-(CH ₃ O) ₃ C ₆ H ₂	C ₂₆ H ₂₄ N ₂ O ₃	68	75.71	5.86	6.79
			157-159 [b, l]	75.42	5.93	6.69
8	3,5-(CH ₃ O) ₂ C ₆ H ₃	C ₂₅ H ₂₂ N ₂ O ₂	57	78.51	5.80	7.32
			107-109 [b, m]	78.36	5.87	7.18
9	3,5-(CH ₃) ₂ C ₆ H ₃	C ₂₅ H ₂₂ N ₂	79	85.68	6.32	7.99
			145 [b, n]	85.52	6.36	7.73
10	4-(CH ₃) ₃ CC ₆ H ₄	C ₂₇ H ₂₆ N ₂	85	85.68	6.92	7.40
			154-156 [b, o]	85.36	6.92	7.17
11	C ₅ H ₄ N 4-pyridinyl	C ₂₂ H ₁₇ N ₃	51	81.56	5.30	12.99
			199-203 [d, p]	81.15	5.04	12.87
12	3,4-(CH ₃ O) ₂ C ₆ H ₃	C ₂₅ H ₂₂ N ₂ O ₂	63	78.51	5.80	7.32
			169-171 [e, q]	78.22	5.81	7.06

[a] Recrystallized from benzene/ethanol. [b] Recrystallized from 95% ethanol. [c] Recrystallized from ethanol/benzene/xylenes. [d] Recrystallized from toluene/ethanol. [e] Recrystallized from benzene/hexanes. [f] Compound 1. ir: 1593 cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.97-3.11 (m, 4H, CH₂CH₂) [14], 6.94-7.44 (m, 14H, ArH); ¹³C nmr (deuteriochloroform): δ 22.6, 30.5, 116.6, 123.1, 125.0, 126.0, 126.6, 128.6, 128.7, 128.8, 128.9, 130.3, 130.4, 131.1, 135.6, 137.9, 139.9, and 151.5 [g] Compound 2. ir: 1597 cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.95-3.10 (m, 4H, CH₂CH₂) and 6.93-7.39 (m, 13H, ArH); ¹³C nmr (deuteriochloroform): δ 22.5, 30.4, 116.8, 123.0, 125.1, 126.1, 126.6, 127.2, 128.7, 128.9, 129.3, 129.5, 130.1, 131.6, 134.9, 135.7, 136.6, 139.9, and 151.6. [h] Compound 3. ir: 1592 cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.96-3.11 (m, 4H, CH₂CH₂), 3.71 (s, 3H, ArOCH₃), 6.88-7.40 (m, 13H, ArH); ¹³C nmr (deuteriochloroform): δ 22.5, 30.5, 55.4, 114.4, 123.0, 123.1, 125.0, 125.8, 126.5, 126.8, 128.6, 128.7, 128.8, 130.6, 131.5, 135.6, 137.8, 139.9, 151.4, and 159.8. [i] Compound 4. ir: 1595 cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.96-3.11 (m, 4H, CH₂CH₂), 6.92-7.41 (m, 13H, ArH); ¹³C nmr (deuteriochloroform): δ 22.5, 30.5, 117.0, 123.1, 125.1, 126.3, 126.8, 127.3, 128.7, 128.8, 129.0, 129.2, 130.1, 130.2, 130.3, 133.0, 134.8, 135.8, 136.4, 139.6, and 151.7. [j] Compound 5. ir: 1593 cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.39 (s, 3H, CH₃), 2.95-3.10 (m, 4H, CH₂CH₂), and 6.94-7.39 (m, 13H, ArH); ¹³C nmr (deuteriochloroform): δ 21.7, 22.6, 30.5, 116.4, 123.1, 125.0, 125.8, 126.5, 126.8, 128.0, 128.5, 128.7, 129.6, 130.1, 130.6, 135.6, 138.1, 138.7, 140.0, and 151.4. [k] Compound 6. ir: 3111 and 1612 cm⁻¹; ¹H nmr (dimethyl-d₆ sulfoxide): δ 2.83-3.01 (m, 4H, CH₂CH₂), 6.81-7.37 (m, 13H, ArH), and 9.83 (s, 1H, ArOH); ¹³C nmr (dimethyl-d₆ sulfoxide): δ 21.8, 29.5, 115.6, 115.8, 120.7, 122.0, 124.5, 125.6, 126.3, 126.7, 128.5, 128.6, 130.0, 131.3, 134.9, 137.8, 139.2, 150.0, and 157.7. [l] Compound 7. ir: 1585 cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.96-3.11 (m, 4H, CH₂CH₂), 3.68 (s, 6H, ArOCH₃), 3.92 (s, 3H, ArOCH₃), 6.53 (s, 2H, ArH), and 7.03-7.33 (m, 9H, ArH); ¹³C nmr (deuteriochloroform): δ 22.5, 30.4, 56.3, 61.2, 107.4, 116.2, 123.2, 125.0, 126.0, 126.1, 126.5, 127.0, 128.6, 128.8, 130.3, 135.6, 137.7, 138.3, 139.9, 151.4, and 153.4. [m] Compound 8. ir: 1597 cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.96-3.08 (m, 4H, CH₂CH₂), 3.69 (s, 6H, ArOCH₃), 6.49 (s, 3H, ArH), and 7.01-7.29 (m, 9H, ArH); ¹³C nmr (deuteriochloroform): δ 22.5, 30.4, 55.6, 101.4, 108.1, 116.5, 123.3, 124.8, 126.0, 126.6, 126.9, 128.6, 128.7, 129.4, 132.8, 135.6, 137.7, 139.9, 151.4, and 160.9. [n] Compound 9. ir: 1595 cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.27 (s, 6H, ArCH₃), 2.95-3.10 (m, 4H, CH₂CH₂), and 6.83-7.35 (m, 12H, ArH); ¹³C nmr (deuteriochloroform): δ 21.5, 22.5, 30.5, 116.4, 123.2, 124.8, 125.8, 126.5, 126.7, 127.9, 128.5, 128.6, 130.5, 130.6, 130.9, 135.6, 138.3, 138.4, 140.0, and 151.3. [o] Compound 10. ir: 1592 cm⁻¹; ¹H nmr (deuteriochloroform): δ 1.35 (s, 9H, (CH₃)₃CAr), 2.98-3.08 (m, 4H, CH₂CH₂), and 7.00-7.40 (m, 13H, ArH); ¹³C nmr (deuteriochloroform): δ 22.6, 30.6, 31.6, 35.1, 116.5, 123.2, 125.1, 125.8, 125.9, 126.6, 126.8, 128.0, 128.6, 128.7, 129.9, 130.7, 135.7, 138.2, 140.1, 151.5, and 152.0. [p] Compound 11. ir: 1598 cm⁻¹; ¹H nmr (dimethyl-d₆ sulfoxide): δ 2.86-3.06 (m, 4H, CH₂CH₂), 6.80-7.41 (m, 9H, ArH), and 8.65-8.67 (m, 2H, ArH); ¹³C nmr (dimethyl-d₆ sulfoxide): δ 21.5, 29.3, 116.3, 122.1, 124.8, 125.1, 126.2, 126.6, 127.5, 128.7, 128.8, 129.0, 134.8, 135.3, 138.5, 138.8, 150.2, and 150.5. [q] Compound 12. ir: 1593 cm⁻¹; ¹H nmr (deuteriochloroform): δ 2.95-3.09 (m, 4H, CH₂CH₂), 3.69 (s, 3H, OCH₃), 3.91 (s, 3H, OCH₃) and 6.81-7.30 (m, 12H, ArH); ¹³C nmr (deuteriochloroform): δ 22.6, 30.4, 56.0, 56.1, 111.3, 113.0, 116.3, 123.0, 123.1, 123.2, 124.9, 125.9, 126.5, 126.8, 128.6, 128.7, 130.5, 135.6, 137.8, 140.0, 149.0, 149.2, and 151.4.

the reactions, and the experimental set-up does not require an elaborate apparatus (see Experimental).

EXPERIMENTAL

Melting points were obtained with a Mel-Temp II melting point apparatus in open capillary tubes and are uncorrected. Fourier

Transform infrared spectra were obtained with a Nicolet Impact 410 FT-IR. Proton and ¹³C magnetic resonance spectra were obtained with a Varian Associates Mercury Oxford 300 MHz, nuclear magnetic resonance spectrometer, and chemical shifts are recorded in δ ppm downfield from an internal tetramethylsilane standard. Combustion analyses were performed by Quantitative Technologies, Inc., P.O. Box 470, Salem Industrial Park, Bldg. 5, Whitehouse, NJ 08888.

General Procedure for Preparation of 4,5-Dihydro-2H-benz[e]-indazoles **1-12**. (Ratio of reagents - base:hydrazone: ester - 1:3:1; except for **6**, 1:4:1).

In a typical reaction sequence, lithium diisopropylamide 0.0315 mole (or 0.0420 mole for **6**) was prepared by the addition of 20.0 ml (or 27.0 ml for **6**) of 1.6 M *n*-butyllithium 0.0315 mole (or 0.0420 mole for **6**) to a three-neck round-bottomed flask (e.g., 500 ml) equipped with a nitrogen inlet tube, a side-arm addition funnel, and a stir bar. The flask was cooled in an ice bath and 3.21 g (0.0315 mole) or 4.28 g (0.0420 mole for **6**) of diisopropylamine, dissolved in 25-30 ml of dry tetrahydrofuran (sodium/ benzophenone - ketyl) (0°, nitrogen), was added from the funnel (e.g., 125-ml side arm addition) at a fast dropwise rate during 5 minutes. The solution was stirred for an additional 15-20 minutes, and then treated via the addition funnel with 2.36 g of 2-tetralone phenylhydrazone (0.0100 mole) dissolved in 35-45 ml of tetrahydrofuran. After 45-60 minutes of dilithiation, 0.0105 mole ester, dissolved in 25-35 ml of tetrahydrofuran, was added to the dilithiated intermediate, and the solution was stirred for 45-60 minutes for the preparation of **1, 2, 4, 5, 8-11**, 1.25- 1.5 hours for the preparation of **3, 7, and 12** and 2 hours for the preparation of **6** (0°, nitrogen). Next, 100 ml of 3N hydrochloric acid was added, and the two-phase mixture was stirred and heated under reflux for approximately one hour. At the end of this period, the mixture was poured into a large flask containing ice (ca., 100 g) followed by 100 ml of solvent grade ether or tetrahydrofuran. The mixture was then neutralized with solid sodium bicarbonate and the layers separated. The aqueous layer was extracted with ether or tetrahydrofuran (2 x 75 ml), and the organic fractions were combined, evaporated, and recrystallized (see footnote of Table).

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- [14] Several 60 MHz ¹H nmr spectra obtained with a Varian Associates EM 360L Nuclear Magnetic Resonance Spectrometer displayed a broad isochronous absorption for the adjacent methylene protons. When multiple scans on several compounds were made with the 300 MHz spectrometer, the apparent initial triplets were displayed as more complex multiplets. For example, compound **1** displayed twelve absorptions from δ 2.95-3.10 ppm with specifically displayed resonance absorptions noted at δ 2.97, 2.97, 2.99, 2.99, 3.00, 3.01, 3.02, 3.06, 3.08, 3.11, and 3.11 ppm, with each geminal proton being coupled with the other geminal proton and then each of these protons with each of the adjacent methylene protons. Even with multiple scans, a consistent number of resonance absorptions for other compounds in the study was not obtained, as evidenced by the display of eleven lines for compound **2**, twelve lines for compound **3**, eight lines for compound **4** and ten lines for compound **5**. The data establishes the presence of adjacent methylene protons, and they are reported as a multiplet in this study (footnote of Table). It is unclear at this time whether a higher field (> 300 MHz) nuclear magnetic resonance investigation of these compounds would give data with sufficient novelty to warrant a separate spectral study.
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- [16a] The further downfield absorptions ca. δ 57 ppm were assigned to the methoxy carbon bonded to the oxygen bonded to the carbon in the 4-position of the aromatic ring. [b] Summary of the number of unique carbons displayed: **1**, 19; **2**, 19; **3**, 20; **4**, 21; **5**, 20; **6**, 19; **7**, 21; **8**, 20; **9**, 20; **10**, 21; **11**, 18; **12**, 23.