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N-Methyl-*N*-2-propynyl-1-naphthalenecarboxamide, *N*-methyl-*N*-2-propynyl-1-naphthaleneacetamide, and *N*-methyl-*N*-3-butynyl-1-naphthalenecarboxamide undergo intramolecular Diels-Alder reactions at 190°, 250°, and 270° to give lactams **1**, **6**, and **9**, respectively. The cyclization temperatures are higher by 80-120° as compared to those of the corresponding anthracene derivatives. Elaboration of lactam **6** gave the *trans*-4a-aryldecahydroisoquinoline derivative **7a** which, as the (-) isomer, was shown to have the same absolute stereochemistry as morphine.

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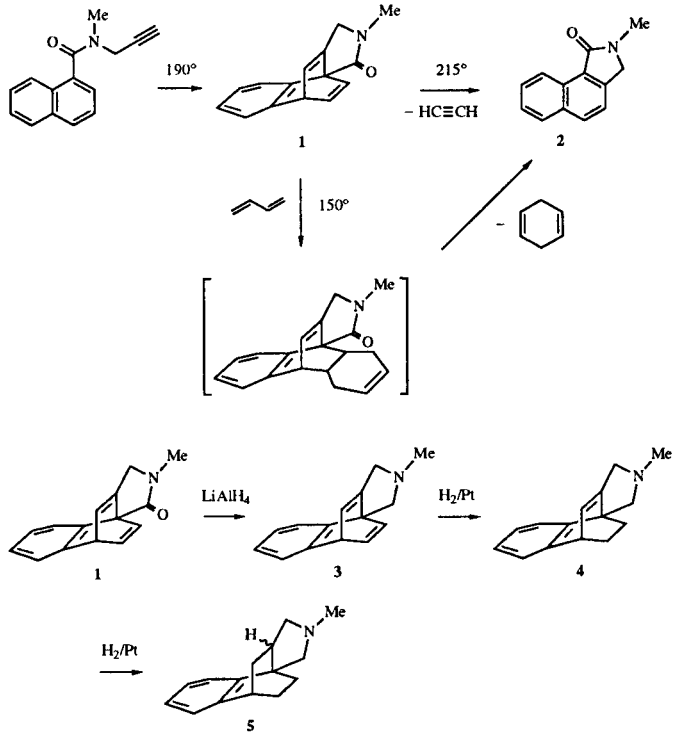
Previous papers in this series described intramolecular Diels-Alder reactions [3] to anthracenes and acridines [4] and to isoindoles [1] as routes to compounds having potential interest as therapeutics. The present paper describes the extension of this work to naphthalenes. Compared to anthracenes, naphthalenes are much poorer dienes in the intermolecular Diels-Alder reaction [5] and this relative order of reactivity was expected to hold true for the intramolecular version as well. Indeed, the few examples of intramolecular Diels-Alder reactions to naphthalenes that have appeared in the literature [6] required cyclization temperatures in excess of 200° except in cases where very reactive dienophiles such as benzyne were involved.

Results and Discussion

Thermolysis of *N*-methyl-*N*-2-propynyl-1-naphthalenecarboxamide in toluene at 190° for 17 hours gave the adduct **1** in 65% yield (Scheme I). By comparison, *N*-methyl-*N*-2-propynyl-9-anthracenecarboxamide cyclizes rapidly at 110° [4]. At 215°, 2,3-dihydro-2-methyl-1*H*-benz[*e*]isoindol-1-one (**2**) was obtained in addition to lactam **1**. The most plausible mechanism for the formation of product **2** involves loss of acetylene by a reverse Diels-Alder reaction. Such a reaction was also observed when the intramolecular Diels-Alder adduct **1** was heated with butadiene to 150° for 20 hours; lactam **2** and unreacted **1** were obtained in a ratio of 3:2. Reduction of lactam **1** with lithium aluminum hydride furnished the amine **3** which was also obtained in low yield by heating *N*-methyl-*N*-2-propynyl-1-naphthalenemethanamine to 210°; preliminary experiments indicated that cyclization of this amine as the hydrochloride salt in water proceeded somewhat more rapidly at that temperature [7]. Catalytic

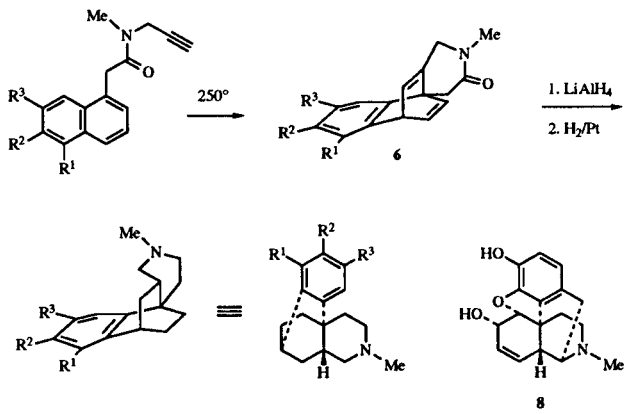
Scheme I



hydrogenation of amine **3** could be directed to give either the dihydro derivative **4** or a single tetrahydro compound **5**; the stereochemistry of the latter was not determined.

Cyclization of the next higher homolog, *N*-methyl-*N*-2-propynyl-1-naphthaleneacetamide, required heating to 250°; nevertheless, the adduct **6** was obtained in 49% yield (Scheme II). Reverse Diels-Alder reaction in this system thus occurs at considerably higher temperature as compared to lactam **1**. The corresponding anthracene

Scheme II

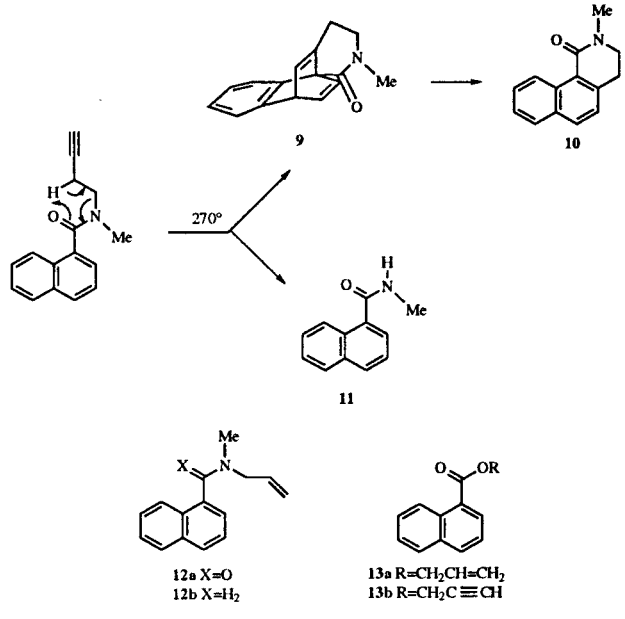


7a: R^1,R^2,R^3 = H
7b: R^1=OMe; R^2,R^3=H
7c: R^1=OH; R^2,R^3=H
7d: R^2=OMe; R^1,R^3=H
7e: R^2=OH; R^1,R^3=H
7f: R^3=OMe; R^1,R^2=H
7g: R^3=OH; R^1,R^2=H

derivative cyclizes cleanly at 140° [4]. Reduction of lactam **6** with lithium aluminum hydride followed by catalytic hydrogenation gave the amine **7a** exclusively; addition of hydrogen to the trisubstituted double bond thus occurred specifically from the less hindered side. Amine **7a** can be viewed as a derivative of the morphine fragment 4a-aryl-*trans*-decahydroisoquinoline for which analgesic activity has been reported [8]. Amine **7a** was therefore resolved and an X-ray structure determination was carried out on the *l*-dibenzoyltartarate of the (-) isomer. This not only elucidated the stereochemistry but also showed that (-)-**7a** has the same absolute configuration as morphine (**8**). The ORTEP drawing, of the base only, is shown in Figure 1. We have also prepared a number of derivatives **7b-g** containing methoxy or hydroxy groups in the aromatic ring. Such groups are known to enhance potency in opioid analgesics [9,10].

The isomeric *N*-methyl-*N*-3-butynyl-1-naphthalenecarboxamide also underwent intramolecular Diels-Alder reaction (Scheme III). However, even higher temperatures were required and retro Diels-Alder cleavage of the product **9** to give lactam **10** was a major side reaction. Under optimal condidtions (270°, 5 hours) the adduct **9** was obtained in 19% yield in addition to unreacted substrate (25%), lactam **10** (7%) and *N*-methyl-1-naphthalenecarboxamide (**11**, 3%). The latter was possibly formed by a mechanism similar to an ester elimination (arrows, Scheme III).

Scheme III



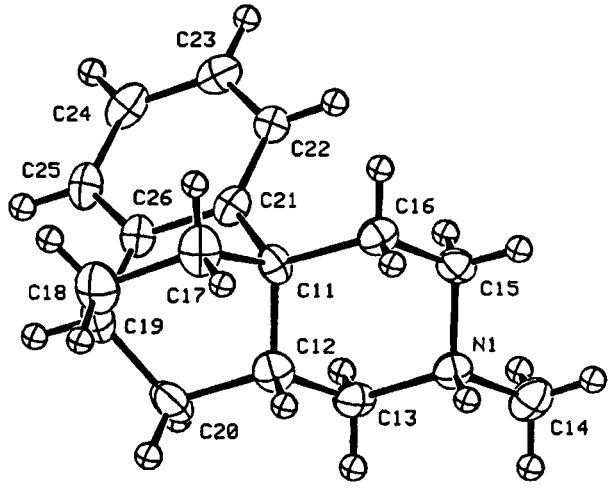
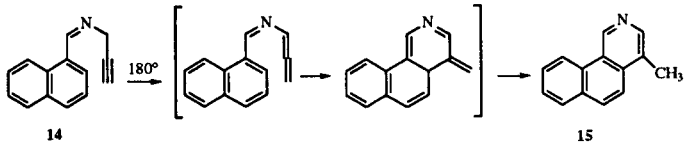


Figure 1. ORTEP drawing of the **7a** cation. The absolute configuration of the asymmetric carbon labelled as C(11) is (*R*).

N-2-propenyl-*N*-methyl-1-naphthalenecarboxamide (**12a**) failed to undergo the intramolecular Diels-Alder reaction at temperatures of up to 300°, as did *N*-2-propenyl-*N*-methyl-1-naphthalenemethanamine (**12b**) at 180°, either as the free base or the hydrochloride. By comparison, the corresponding anthracene derivatives cyclize rapidly at 140° [4]. Partial decomposition and no cyclization was observed when 2-propenyl or 2-propynyl 1-naphthalenecarboxylate **13a,b** were heated to 250°. 2-Propynyl 9-anthracenecarboxylate undergoes the intramolecular Diels-Alder reaction at 140° [4]. *N*-2-Propynyl-1-naphthalenemethylenimine (**14**) at 180° gave a product believed to be 4-methylbenz[*h*]isoquinoline (**15**) in low yield, presumably by isomerization to the allene followed by electrocyclization and aromatization (Scheme IV). The corresponding anthracene derivative

Scheme IV



14 15

undergoes clean intramolecular Diels-Alder addition at 140° [4].

In summary, intramolecular Diels-Alder additions to naphthalenes parallel those to anthracene in that substrates with 3-atom chains cyclize more readily than those with 4-carbon chains. However, as expected, the cyclizations require temperatures that are higher by about 80-120° if they proceed at all.

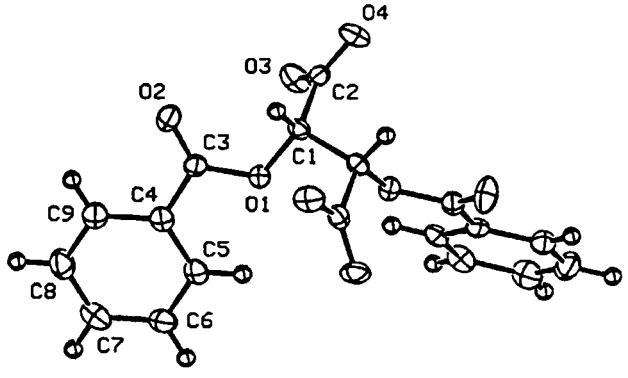


Figure 2. ORTEP drawing of the **7a** anion.

EXPERIMENTAL

Melting points are uncorrected. Proton magnetic resonance spectra were recorded at 60 or 220 MHz in deuteriochloroform using tetramethylsilane as internal standard.

3,5-Dihydro-2-methyl-5,9b-etheno-9b*H*-benz[*e*]isoindol-1(2*H*)-one (**1**).

To a mixture of 20 g (0.29 mole) of *N*-methyl-2-propynylamine, 60 ml of triethylamine, and 200 ml of methylene chloride, 60 g (0.31 mole) of 1-napthalenecarbonyl chloride was added below 25°. The mixture was concentrated after stirring at 25° for 1 hour, the residue was dissolved in methylene chloride and washed sequentially with dilute hydrochloric acid, water, and dilute sodium hydroxide solution. Concentration of the dried solution and crystallization of the residue from 130 ml of 2-propanol gave 57.7 g (89%) of *N*-methyl-*N*-propynyl-1-naphthalenecarboxamide; ^{1}H nmr: ∂ 2.3 (m, 1H), 2.8 (s, 1.8 H), 3.3 (s, 1.2 H), 6.2 (d, J = 2.5 Hz, 0.8 H), 4.5 (d, J = 2.5 Hz, 1.2 H), 7.2-7.9 (m, 7H); the spectrum indicates the presence of two rotamers in the ratio of 3:2. A mixture of this product (24 g) and 45 ml of toluene, contained in an evacuated, sealed Carius tube, was heated to 190° for 17 hours and the residue left after removal of the solvent was crystallized from 50 ml of ethyl acetate to give 16.93 g (65%) of **1** in two fractions, mp 154-155°, unchanged on recrystallization. ^{1}H nmr: ∂ 3.0 (s, 3 H), 4.0 (AB q, split into doublets, J = 14/2 Hz, 2H), 4.9 (t/d, J = 6/1.5 Hz, 1 H), 6.6 (d/t, J = 6/2 Hz, 1 H), 6.9 (m, 3 H), 7.0 (d/d, J = 7/1.5 Hz, 1 H), 7.2 (m, 1 H), 2.6 (m, 1 H).

Anal. Calcd. for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.65; H, 6.01; N, 6.50.

2,3-Dihydro-2-methyl-1*H*-benz[*e*]isoindolone (**2**).

This compound was formed, in addition to **1** and intractable tar, when the above cyclization was carried out at 215°. It was purified by chromatography (Florisil, 9:1 methylene chloride/THF) and crystallization from ethyl acetate, mp 135-136° (lit [11] 130-130.5°); ^{1}H nmr: ∂ 3.1 (s, 3 H), 4.2 (s, 2 H), 7.3 (d, J = 8 Hz, 1 H), 7.5 (m, 2 H), 7.8 (m + d, J = 8 Hz, 2 H), 9.1 (d, split further, J = 8 Hz, 1 H).

Anal. Calcd. for $C_{13}H_{11}NO$: C, 79.16; H, 5.62; N, 7.10. Found: C, 78.95; H, 5.51; N, 7.03.

Reaction of 3,5-Dihydro-2-methyl-5,9b-etheno-9b*H*-benz[*e*]-isoindol-1(2*H*)-one (**1**) with Butadiene.

A mixture of 0.1 g of **1**, 0.5 ml of toluene, and 0.5 g of butadiene, contained in an evacuated, sealed Carius tube, was heated to 150° for 20 hours. The nmr spectrum of the product obtained on evaporation, showed the presence of 2,3-dihydro-2-methyl-1*H*-benz[*e*]isoindolone (**2**) and unreacted **1** in a ratio of 3:2.

2-Methyl-1,2,3,5-tetrahydro-5,9b-etheno-9b*H*-benz[*e*]isoindole (**3**).

A mixture of 4.00 g (17.9 mmoles) of **1**, 50 ml of ether, and 0.88 g (23.0 mmoles) of lithium aluminum hydride was stirred at 25° for 3 hours. Conventional isolation (0.9 ml of water, 0.9 ml of 15% aqueous sodium hydroxide, 2.7 ml of water) and short-path distillation of the crude product (0.0005 mm, 160° bath temperature) gave 3.05 g (77%) of **3** as a solid. The mp of a sample crystallized from hexane was 69-70°; ^{1}H nmr: ∂ 2.7 (s, 3 H), 3.2 (d, J = 2 Hz, 2 H), 3.3 (d, J = 10 Hz, 1 H), 3.7 (d, J = 10 Hz, 1 H), 4.9 (t/d, J = 5/2 Hz, 1 H), 6.3-7.4 (m, 7 H).

Anal. Calcd. for $C_{15}H_{15}N$: C, 86.06; H, 7.22; N, 6.69. Found: C, 85.75; H, 7.29; N, 6.65.

This product was also obtained in low yield on heating *N*-methyl-*N*-2-propynyl-1-naphthalenemethylamine in toluene to 210°. Cyclization of the hydrochloride in water proceeded more rapidly at that temperature.

2-Methyl-1,2,3,5-tetrahydro-5,9b-ethano-9b*H*-benz[*e*]isoindole (**4**).

A mixture of 1.03 g of **3**, 0.16 g of prereduced platinum dioxide, and 10 ml of ethyl acetate was stirred under hydrogen at room temperature and ambient pressure until 131 ml (1.1 molar equivalents) had been taken up (55 minutes). The filtered solution was concentrated and the residue was crystallized from 2-propanol to give 0.53 g (50%) of **4**, mp 92-93°. ^{1}H nmr: ∂ 1.3-2.0 (m, 4 H), 2.5 (s, 3H), 2.8-3.7 (m, 4 H), 4.0 (d/t, J = 6/1.5 Hz, 1 H), 6.2 (d/t, J = 6/2 Hz, 1H), 7.0-7.5 (m, 4H).

Anal. Calcd. for $C_{15}H_{17}N$: C, 85.26; H, 8.11; N, 6.63. Found: C, 85.37; H, 8.12; N, 6.57.

1,2,3,3a,4,5-Hexahydro-2-methyl-5,9b-ethano-9b*H*-benz[*e*]-isoindole (**5**).

A mixture of 1.39 g of **3**, 0.21 g of prereduced platinum dioxide, and 10 ml of ethyl acetate was stirred under hydrogen at room temperature and ambient pressure for 18 hours; 314 ml (2 molar equivalents) of hydrogen were taken up. The product was short-path distilled (0.001 mm, 80-110° bath temperature) to give 1.02 g (72%) of **5**; ^{1}H nmr: ∂ 0.7-3.0 (m, 10 H), 2.4 (s, 3 H), 2.6 (d, J = 10 Hz, 1 H), 3.5 (d, J = 10 Hz, 1 H), 7.0-7.5 (m, 4 H).

Anal. Calcd. for $C_{15}H_{19}N$: C, 84.45; H, 8.98; N, 6.57. Found: C, 83.94; H, 9.09; N, 6.93.

4,6-Dihydro-3-methyl-6,10b-ethenobenz[*f*]isoquinolin-2(3*H*)-one (**6**).

The starting material, *N*-methyl-*N*-2-propynyl-1-naphthaleneacetamide, was prepared from 1-naphthaleneacetyl chloride and *N*-methyl-*N*-2-propynylamine as described above for the preparation of the lower homolog. The crude product was purified by short-path distillation (0.001 mm, 180-200° bath temperature). A solution of 23.7 g of the amide in 150 ml of toluene, contained in a number of Carius tubes, was deoxygenated by three freeze-thaw cycles, and the tubes were sealed under 0.001 mm pressure and heated to 250° for 5 hours. Removal of the solvent and crystallization of the residue from 2-propanol gave 11.53 g (49%) of **6** in two fractions, mp 156-158°; ^{1}H nmr: ∂ 2.9 (s, 3 H), 3.1 (d, J = 15 Hz, 1 H), 3.5 (d, J = 15 Hz, 1 H), 3.9 (m, 2 H), 4.9 (t/d, J = 6/2 Hz, 1 H), 6.4-7.3 (m, 7 H).

Anal. Calcd. for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.76; H, 6.47; N, 5.89.

2,3,4,4a,5,6-Hexahydro-3-methyl-1*H*-6,10b-ethanobenz[*f*]isoquinoline (**7a**).

A solution of 4.14 g (17.5 mmoles) of **6** in 50 ml of dry tetrahydrofuran was added to a stirred slurry of 1.15 g (43.7 mmoles) of lithium aluminum hydride in 80 ml of dry tetrahydrofuran. The mixture was heated under reflux for 4 hours, treated sequentially with 1.15 ml of water, 1.15 ml of 15% aqueous sodium hydroxide solution, and 3.45 ml of water, magnesium sulfate, and methylene chloride. Evaporation of the filtered mixture gave 3.24 g of 2,3,4,6-tetrahydro-3-methyl-1*H*-6,10b-ethenobenz[*f*]isoquinoline. Catalytic hydrogenation of 6.79 g of this product (0.95 g of pre-reduced platinum oxide, 75 ml of tetrahydrofuran, Parr shaker, 2 hours) gave 6.82 g of crude **7a**. Crystallization from acetone at 4° gave 5.34 g (64%) of purified **7a** in three crops, mp 86-91°. An analytical sample had mp 91-92°; ^{1}H nmr: ∂ 2.2 (s, 3 H), 0.6-3.1 (m, 14 H), 7.1-7.3 (m, 4 H).

Anal. Calcd. for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16. Found: C, 84.92; H, 9.13; N, 6.12.

A solution of 1.00 g (4.41 mmoles) of **7a** and 0.83 g (2.21 mmoles) of dibenzoyl-*l*-tartaric acid in 25 ml of absolute ethanol, on standing at room temperature, deposited 0.76 g of a salt which was rebasified and crystallized from acetone to give 0.31 g of (-)-**7a**, mp 120-120.5°, α_D -32° (c = 1 in ethanol). The mother liquors from the diastereomeric salt crystallization were subjected to the same procedure to give 0.32 g of (+)-**7a**, mp 120.5-121°, α_D +31° (c = 1 in ethanol).

A colorless crystal of (-)-**7a** dibenzoyltartarate with approximate dimensions of 0.08 x 0.23 x 0.50 mm was placed in a glass capillary and mounted on a Syntex R3 diffractometer equipped with Mo radiation (λ = 0.71069 Å). A cold stream of nitrogen was applied to the crystal which slowly cooled it to -100°. The unit cell parameters were refined using the Bragg angles of 50 computer-centered reflections. Crystallographic information: $C_{50}H_{56}N_2O_8$, FW = 813.00, monoclinic, space group C2, with a = 18.632(5), b = 7.346(2), c = 15.991(3) Å, V = 2164.0 Å^3, Z = 2, Dc = 1.247 g cm^{-3}, μ = 0.79 cm^{-2}. The intensities of 5533 reflections, comprised of two full quadrants from 4° < 2θ < 55°, were collected using 1.0° ω-scans. The equivalent reflections were averaged and yielded an R(merge) of 0.028. Standard reflections showed an intensity variation of less than 1% over the course of the data collection. No absorption correction was applied. The structure was solved by direct methods (MULTAN). The (-)-dibenzoyltartrate anion is situated on a crystallographic two-fold axis; the two asymmetric centers, C(1) and C(1)', were known to have an (*S*,*S*) configuration and the enantiomorph of the crystal was thus determined. The hydrogen atoms were placed in idealized positions and fixed except for the hydrogen atom bound to N1 which was allowed to refine. The refinement of 274 variables using 1441 reflections with I > 2σ(I) converged at R = 0.038 and Rw = 0.030. The largest peak in the final difference map had a magnitude of 0.17 e A^{-3}.

The methoxy- and hydroxy-substituted derivatives **7b-f** of **7a** were prepared analogously from the corresponding methoxy-1-naphthaleneacetic acids. The latter were obtained by an improved procedure illustrated for the preparation of 5-methoxy-1-naphthaleneacetic acid.

Table 1

Fractional Coordinates and Isotropic (refined or equivalent) Thermal Parameters (Å^2) for all of the Atoms which were Refined.

Atom	X	Y	Z	$B_{iso/eq}$
O(1)	0.0133(1)	0.3868	-0.0800(1)	1.8(1)*
O(2)	0.0684(1)	0.5048(5)	-0.1840(2)	3.0(1)*
O(3)	0.1478(1)	0.4200(5)	0.0083(1)	2.6(1)*
O(4)	0.1210(1)	0.6822(5)	0.0684(1)	2.5(1)*
N(1)	0.2730(2)	0.4361(6)	0.1133(2)	2.0(1)*
C(1)	0.0282(2)	0.5480(6)	-0.0291(2)	1.6(1)*
C(2)	0.1061(2)	0.5500(7)	0.0210(2)	1.9(1)*
C(3)	0.0367(2)	0.3796(7)	-0.1554(2)	1.9(1)*
C(4)	0.0171(2)	0.2048(7)	-0.1990(2)	1.8(1)*
C(5)	-0.0189(2)	0.0684(7)	-0.1619(2)	2.0(1)*
C(6)	-0.0366(2)	-0.0941(7)	-0.2050(2)	2.3(1)*
C(7)	-0.0165(2)	-0.1188(7)	-0.2849(2)	2.9(1)*
C(8)	0.0186(2)	0.0174(7)	-0.3216(2)	2.9(1)*
C(9)	0.0352(2)	0.1795(7)	-0.2792(2)	2.2(1)*
C(11)	0.2300(2)	0.3032(7)	0.2736(2)	1.9(1)*
C(12)	0.2213(2)	0.5037(7)	0.2452(2)	2.4(1)*
C(13)	0.2756(2)	0.5586(7)	0.1877(2)	2.3(1)*
C(14)	0.3259(2)	0.4928(7)	0.0575(2)	2.8(1)*
C(15)	0.2856(2)	0.2429(6)	0.1409(2)	2.2(1)*
C(16)	0.2303(2)	0.1823(7)	0.1961(2)	2.3(1)*
C(17)	0.1634(2)	0.2604(7)	0.3191(2)	3.0(1)*
C(18)	0.1604(2)	0.3951(8)	0.3924(2)	3.3(1)*
C(19)	0.2276(2)	0.5194(7)	0.4037(2)	2.9(1)*
C(20)	0.2266(2)	0.6323(7)	0.3225(3)	3.0(1)*
C(21)	0.2954(2)	0.2809(6)	0.3423(2)	1.9(1)*
C(22)	0.3504(2)	0.1516(6)	0.3457(2)	2.1(1)*
C(23)	0.4035(2)	0.1418(7)	0.4164(2)	2.5(1)*
C(24)	0.4020(2)	0.2589(7)	0.4837(2)	2.5(1)*
C(25)	0.3472(2)	0.3857(7)	0.4820(2)	2.4(1)*
C(26)	0.2934(2)	0.3966(7)	0.4113(2)	2.0(1)*
H(1N)	0.2271(22)	0.4391(62)	0.0808(24)	4.9(11)

*Refined with anisotropic thermal parameters: $B_{eq} = 4/3 \Sigma \Sigma \beta_{ij} a_i a_j$, where a_i and a_j refer to the real lattice constants.

Table 2

Assigned Fractional Coordinates (C-H = 0.95Å) and Isotropic Thermal Parameters (1 + Isotropic Value for Carbon Atom, Å^2) for All of the Hydrogen Atoms Which Bond to Carbon Atoms.

Atom	X	Y	Z	B_{iso}
H(1)	0.0220	0.6532	-0.0639	2.6
H(5)	-0.0315	0.0857	-0.1071	3.0
H(6)	-0.0620	-0.1870	-0.1803	3.3
H(7)	-0.0273	-0.2307	-0.3138	3.9
H(8)	0.0315	0.0003	-0.3763	3.9
H(9)	0.0590	0.2737	-0.3050	3.2
H(12)	0.1740	0.5169	0.2140	3.4
H(13)	0.2663	0.6800	0.1689	3.3
H(13')	0.3232	0.5574	0.2189	3.3
H(14)	0.3229	0.4121	0.0107	3.8
H(14')	0.3736	0.4891	0.0884	3.8
H(14")	0.3150	0.6129	0.0378	3.8
H(15)	0.3332	0.2310	0.1715	3.2
H(15')	0.2823	0.1665	0.0925	3.2
H(16)	0.1833	0.1814	0.1636	3.3
H(16')	0.2401	0.0601	0.2137	3.3
H(17)	0.1673	0.1397	0.3405	4.0
H(17')	0.1200	0.2699	0.2797	4.0
H(18)	0.1588	0.3291	0.4432	4.3
H(18')	0.1178	0.4672	0.3808	4.3
H(19)	0.2287	0.5956	0.4518	3.9
H(20)	0.1858	0.7116	0.3159	4.0
H(20')	0.2698	0.7021	0.3263	4.0
H(22)	0.3515	0.0703	0.2997	3.1
H(23)	0.4411	0.0537	0.4185	3.5
H(24)	0.4391	0.2522	0.5314	3.5
H(25)	0.3459	0.4651	0.5286	3.4

Table 3

Anisotropic Thermal Parameters (Å^2) in the Form exp[-19.739(U_{11}hha*a*...+2(U_{12}hka*b*...))]

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1)	0.023(1)	0.025(2)	0.019(1)	-0.002(1)	0.005(1)	-0.002(1)
O(2)	0.053(2)	0.037(2)	0.030(2)	-0.015(2)	0.019(1)	-0.004(2)
O(3)	0.023(1)	0.039(2)	0.034(2)	0.009(2)	-0.006(1)	-0.006(2)
O(4)	0.025(1)	0.031(2)	0.036(2)	-0.004(1)	-0.005(1)	-0.009(2)
N(1)	0.019(2)	0.032(2)	0.023(2)	0.004(2)	-0.004(1)	0.001(2)
C(1)	0.019(2)	0.023(2)	0.018(2)	-0.001(2)	-0.002(1)	0.000(2)
C(2)	0.018(2)	0.033(3)	0.020(2)	-0.003(2)	0.003(2)	0.006(2)
C(3)	0.015(2)	0.035(3)	0.021(2)	-0.002(2)	0.001(2)	0.001(2)
C(4)	0.017(2)	0.029(2)	0.023(2)	0.006(2)	0.000(2)	0.000(2)
C(5)	0.021(2)	0.030(3)	0.021(2)	0.004(2)	-0.004(2)	0.002(2)
C(6)	0.031(2)	0.026(3)	0.030(2)	-0.005(2)	-0.002(2)	0.003(2)
C(7)	0.039(2)	0.032(3)	0.034(2)	-0.002(2)	-0.005(2)	-0.007(2)
C(8)	0.035(2)	0.046(3)	0.029(2)	0.003(2)	0.008(2)	-0.009(2)
C(9)	0.023(2)	0.034(3)	0.027(2)	0.003(2)	0.003(2)	0.000(2)
C(11)	0.020(2)	0.029(3)	0.023(2)	0.000(2)	-0.002(2)	-0.009(2)
C(12)	0.020(2)	0.039(3)	0.031(2)	0.006(2)	-0.003(2)	-0.002(2)
C(13)	0.031(2)	0.025(2)	0.028(2)	0.000(2)	-0.006(2)	0.000(2)
C(14)	0.026(2)	0.047(3)	0.031(2)	0.003(2)	0.001(2)	0.007(2)
C(15)	0.025(2)	0.027(3)	0.028(2)	0.004(2)	-0.002(2)	-0.001(2)
C(16)	0.027(2)	0.030(2)	0.028(2)	-0.002(2)	0.001(2)	0.002(2)
C(17)	0.025(2)	0.055(3)	0.034(2)	-0.003(2)	0.003(2)	-0.007(2)
C(18)	0.027(2)	0.057(3)	0.041(2)	0.004(3)	0.006(2)	-0.006(3)
C(19)	0.034(2)	0.047(3)	0.026(2)	0.009(2)	0.002(2)	-0.013(2)
C(20)	0.039(2)	0.035(3)	0.038(2)	0.015(2)	0.000(2)	-0.011(2)
C(21)	0.021(2)	0.030(2)	0.023(2)	-0.007(2)	0.003(2)	0.002(2)
C(22)	0.029(2)	0.026(2)	0.023(2)	0.002(2)	0.005(2)	0.000(2)
C(23)	0.027(2)	0.035(3)	0.034(2)	0.000(2)	0.004(2)	0.009(2)
C(24)	0.022(2)	0.046(3)	0.026(2)	-0.007(2)	0.000(2)	0.007(2)
C(25)	0.030(2)	0.039(3)	0.023(2)	-0.007(2)	0.005(2)	-0.005(2)
C(26)	0.022(2)	0.032(2)	0.023(2)	-0.005(2)	0.004(2)	-0.003(2)

Table 4

Interatomic Distances (A) with Estimated Standard Deviations in Parentheses

Atoms	Distance	Atoms	Distance
O(1)-C(1)	1.440 (4)	C(11)-C(12)	1.543 (5)
O(1)-C(3)	1.344 (4)	C(11)-C(16)	1.525 (5)
O(2)-C(3)	1.219 (4)	C(11)-C(17)	1.560 (5)
O(3)-C(2)	1.266 (4)	C(11)-C(21)	1.522 (5)
O(4)-C(2)	1.238 (5)	C(12)-C(13)	1.521 (5)
N(1)-C(13)	1.486 (5)	C(12)-C(20)	1.547 (5)
N(1)-C(14)	1.485 (4)	C(15)-C(16)	1.521 (5)
N(1)-C(15)	1.495 (5)	C(17)-C(18)	1.542 (6)
N(1)-H(1N)	0.932 (41)	C(18)-C(19)	1.539 (6)
C(1)-C(1)a	1.504 (6)	C(19)-C(20)	1.538 (5)
C(1)-C(2)	1.549 (4)	C(19)-C(26)	1.511 (5)
C(3)-C(4)	1.480 (5)	C(21)-C(22)	1.393 (5)
C(4)-C(5)	1.388 (5)	C(21)-C(26)	1.397 (5)
C(4)-C(9)	1.386 (5)	C(22)-C(23)	1.389 (5)
C(5)-C(6)	1.393 (5)	C(23)-C(24)	1.382 (5)
C(6)-C(7)	1.396 (5)	C(24)-C(25)	1.380 (5)
C(7)-C(8)	1.374 (6)	C(25)-C(26)	1.397 (5)
C(8)-C(9)	1.382 (6)		

5-Methoxy-1-naphthaleneacetic Acid.

A mixture of 25.0 g (0.142 mole) of 5-methoxy-1-tetralone, 27.0 g (0.176 mole) of methyl bromoacetate, 12.6 g (0.193 g-atom) of activated zinc [12], and 150 ml of dry benzene was heated to reflux until the exothermic reaction started. After it subsided (ca. 15 minutes), heating under reflux was continued for another hour. Water (250 ml) was added after cooling, and the mixture was acidified with acetic acid and filtered. The aqueous phase was extracted twice with 150-ml portions of benzene and the combined organic phases were washed with 1% ammonium hydroxide solution and water, and dried. Removal of the solvent gave methyl 1-hydroxy-5-methoxy-1-naphthaleneacetate as an oil which was used without purification in the subsequent dehydration [13] step. The crude product was mixed with 1% (by weight) of iodine and heated under *ca.* 250 mm vacuum in an oil bath kept at 205° for 30 minutes. The upper parts of the flask were heated with a heat gun to remove any condensed water. Conventional isolation gave a mixture of unsaturated esters which was dehydrogenated [14] directly by heating with 2.68 g (0.08 g-atom) of sulfur to 205° for 1.5 hours followed by 30 minutes at 235° (**CAUTION**, evolution of hydrogen sulfide). The crude methyl 5-methoxy-1-naphthaleneacetate so obtained was taken up in 55 ml of hot methanol, the solution was decanted from a small amount of insoluble gummy material which was washed with hot methanol. Potassium hydroxide (13.9 g, 0.248 mole) was added to the combined methanol solutions which were then heated under reflux for 2 hours. The solvent was removed under vacuum, the residue was dissolved in 150 ml of hot water and the solution was filtered and acidified to *p*H 2 with hydrochloric acid. The solids were collected by filtration and dissolved in 300 ml of hot saturated aqueous sodium bicarbonate solution. The solution was filtered while hot, cooled, and extract-

Table 5
Intramolecular Angles (Deg) with Estimated Standard Deviations in Parentheses

Atoms	Angle	Atoms	Angle
C(1)-O(1)-C(3)	118.6 (3)	C(12)-C(11)-C(16)	109.2 (3)
C(13)-N(1)-C(14)	111.5 (3)	C(12)-C(11)-C(17)	105.9 (3)
C(13)-N(1)-C(15)	110.7 (3)	C(12)-C(11)-C(21)	110.6 (3)
C(14)-N(1)-C(15)	110.7 (3)	C(16)-C(11)-C(17)	111.2 (3)
C(13)-N(1)-H(1N)	110 (3)	C(16)-C(11)-C(21)	115.1 (3)
C(14)-N(1)-H(1N)	107 (2)	C(17)-C(11)-C(21)	104.4 (3)
C(15)-N(1)-H(1N)	106 (3)	C(11)-C(12)-C(13)	112.4 (3)
O(3)-C(2)-O(4)	127.1 (3)	C(11)-C(12)-C(20)	110.9 (3)
O(1)-C(3)-O(2)	123.2 (4)	C(13)-C(12)-C(20)	110.7 (3)
O(1)-C(1)-C(1)a	104.8 (2)	C(11)-C(16)-C(15)	112.8 (3)
O(1)-C(1)-C(2)	112.7 (3)	C(11)-C(17)-C(18)	110.3 (3)
O(3)-C(2)-C(1)	117.4 (4)	C(17)-C(18)-C(19)	110.4 (3)
O(4)-C(2)-C(1)	115.5 (3)	C(18)-C(19)-C(20)	108.3 (3)
O(1)-C(3)-C(4)	111.5 (3)	C(18)-C(19)-C(26)	106.9 (4)
O(2)-C(3)-C(4)	125.2 (3)	C(20)-C(19)-C(26)	107.3 (3)
N(1)-C(13)-C(12)	112.2 (3)	C(12)-C(20)-C(19)	109.7 (3)
N(1)-C(15)-C(16)	111.0 (3)	C(11)-C(21)-C(22)	127.3 (3)
C(1)a-C(1)-C(2)	111.6 (3)	C(11)-C(21)-C(26)	113.0 (3)
C(3)-C(4)-C(5)	121.7 (3)	C(22)-C(21)-C(26)	119.4 (3)
C(3)-C(4)-C(9)	118.4 (3)	C(21)-C(22)-C(23)	119.8 (4)
C(5)-C(4)-C(9)	119.9 (4)	C(22)-C(23)-C(24)	120.5 (4)
C(4)-C(5)-C(6)	120.1 (3)	C(23)-C(24)-C(25)	120.4 (3)
C(5)-C(6)-C(7)	119.2 (4)	C(24)-C(25)-C(26)	119.6 (4)
C(6)-C(7)-C(8)	120.4 (4)	C(19)-C(26)-C(21)	114.7 (3)
C(7)-C(8)-C(9)	120.2 (3)	C(19)-C(26)-C(25)	125.0 (3)
C(4)-C(9)-C(8)	120.2 (4)	C(21)-C(26)-C(25)	120.2 (4)

ed with three 100-ml portions of ether. Acidification of the aqueous phase with 10% hydrochloric acid at 0° and drying of the water-washed precipitate over phosphorus pentoxide gave 5-methoxy-1-naphthaleneacetic acid (13.0 g and 16.9 g in two runs, 42 and 55% respectively from 5-methoxy-1-tetralone). ^{1}H nmr (DMSO-d_6): ∂ 4.0 (s, 3 H), 4.0 (s, 2 H), 7.0 (d/d, J = 6/3 Hz, 1 H), 7.3-7.6 (m, 4 H), 8.2 (d/d, J = 5/4.5 Hz, 1 H).

2,3,4,4a,5,6-Hexahydro-7-methoxy-3-methyl-1*H*-6,10b-ethanobenz[*f*]isoquinoline (**7b**).

The spectral data of the oily material were as follows: ^{1}H nmr: ∂ 0.7-2.6 (m, 14 H), 2.1 (s, 3 H), 3.8 (s, 3 H), 6.7-7.3 (m, 3 H); hrms m/z Calcd. for $C_{17}H_{23}NO$: 257.1778. Found: 257.1785.

2,3,4,4a,5,6-Hexahydro-3-methyl-1*H*-6,10b-ethanobenz[*f*]isoquinolin-7-ol (**7c**).

An intimate mixture of 0.51 g of **7b** and 2.0 g of pyridine hydrochloride was heated under nitrogen to 190° for 3 hours, partitioned between methylene chloride and water, and the methylene chloride layer was washed with aqueous potassium carbonate solution. Evaporation of the dried organic phase and crystallization of the residue from ethanol gave 0.44 g (90%) of **7c**, mp 206-207°; ^{1}H nmr: ∂ 0.7-2.6 (m, 14 H), 2.2 (s, 3 H), 6.7-7.6 (m, 3 H), hrms Calcd. for $C_{16}H_{21}NO$: 243.1622. Found: 243.1600.

2,3,4,4a,5,6-Hexahydro-8-methoxy-3-methyl-1*H*-6,10b-ethanobenz[*f*]isoquinoline (**7d**).

The compound was obtained as an oil, ^{1}H nmr: ∂ 0.6-3.0, (m, 14 H), 2.1 (s, 3 H), 3.8 (s, 3 H), 6.7-6.9 (m, 2 H), 7.0-7.3 (m, 1 H).

2,3,4,4a,5,6-Hexahydro-3-methyl-1*H*-6,10b-ethanobenz[*f*]isoquinolin-8-ol (**7e**).

The compound was obtained as a solid, mp 247-248°.

Anal. Calcd. for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.59; H, 8.70; N, 6.02.

2,3,4,4a,5,6-Hexahydro-9-methoxy-3-methyl-1*H*-6,10b-ethanobenz[*f*]isoquinoline (**7f**).

The compound was obtained as an oil; ^{1}H nmr: ∂ 1.0-3.0 (m, 14 H), 2.2 (s, 3 H), 3.7 (s, 3 H), 6.5-7.8 (m, 3 H); hrms Calcd. for $C_{17}H_{23}NO$: 257.1778. Found: 257.1782.

2,3,4,4a,5,6-Hexahydro-3-methyl-1*H*-6,10b-ethanobenz[*f*]isoquinolin-9-ol (**7g**).

The compound was obtained as a solid, mp 232-238°; hrms [m+H] Calcd. for $C_{16}H_{22}NO$: 244.1701. Found: 244.1707.

2-Methyl-2,3,4,6-tetrahydro-1*H*-6,10b-ethenobenz[*h*]isoquinolin-1-one (**9**).

N-(3-Butynyl)-*N*-methyl-1-napthalenecarboxamide was prepared from 1-naphthalenecarbonyl chloride and *N*-methyl-3-butynylamine as described above for *N*-methyl-*N*-2-propynyl-1-naphthalenecarboxamide, mp 85-86° (from carbon tetrachloride).

Anal. Calcd. for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 81.17; H, 6.45; N, 6.08.

A deoxygenated solution of 10.61 g of the amide in 150 ml of toluene, contained in a number of evacuated, sealed Carius tubes, was heated to 270° for 5 hours. Separation of the products by hplc (silica, ethyl acetate/hexane 1:1) gave 2.53 g (25%) of unreacted starting material, 2.01 g (19% yield, 25% conversion) of **9**, 0.69 g (7%) of 2-methyl-3,4-dihydrobenz[*h*]isoquinolin-1(2*H*)-one (**10**), and 0.26 g (3%) of *N*-methyl-1-naphthalenecarboxamide.

Compound **9** had mp 116-130° (ethyl acetate); ^{1}H nmr: ∂ 2.3-2.6 (m, 2 H), 3.2 (s, 3 H), 3.2-3.4 (m, 2 H), 4.8 (d/t, J = 6/2 Hz, 1 H), 6.3-7.3 (m, 7 H).

Anal. Calcd. for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.68; H, 6.27; N, 5.69.

Compound **10** had ^{1}H nmr: ∂ 3.0 (t, J = 6.5 Hz, 2H), 3.2 (s, 3H), 3.5 (t, J = 6.5 Hz, split further, 2H), 6.9-7.9 (m, 5H), 9.5 (d, J = 8 Hz split further, 1H); hrms Calcd. for $C_{14}H_{13}NO$: 211.0996. Found: 211.0981.

4-Methylbenz[*h*]isoquinoline (**15**).

A mixture of 5.43 g of 1-naphthalene-carboxaldehyde, 4 ml of 2-propynylamine, and 10 ml of ethanol was heated under reflux for 2 hours. The solvent was removed and the residue was short-path distilled (135° bath temperature, 0.0005 mm) to give 5.36 g (80%) of *N*-2-propynyl-1-naphthalenemethylenimine (**14**) as a solid; ^{1}H nmr ∂ 2.5 (t, J = 2.5 Hz, 1H), 4.5 (d, J = 2.5 Hz, split further, 2H), 7.2-8.0 (m, 6H), 8.7 (m, 1H) and 9.1 (narrow t, 1H). A deoxygenated solution of 0.4 g of **14** in 4 ml of toluene, contained in an evacuated, sealed Carius tube, was heated at 180° for 8 hours. Chromatography of the product on 12 g of Florisil and elution with 9:1 methylene chloride:tetrahydrofuran gave 0.22 g of crude **15** which on crystallization from ethyl acetate gave 0.064 g (16%) of **15**, mp 143-144°; ^{1}H nmr: ∂ 3.5 (s, 3H), 7.4-7.9 (m, 5H), 8.4-8.7 (m+s, 2H).

Anal. Calcd. for $C_{14}H_{11}N$: C, 87.01; H, 5.74; N, 7.25. Found: C, 86.44; H, 5.84; N, 7.07.

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