Synthesis and Spectra of 12-(*o*- and *p*-R-phenyl)-9,9-dimethyl-7,8,9,10,11,12-hexahydro and 8,9,10,11-tetrahydrobenz[*a*]acridin-11-ones. Structure Correction of 1,2,3,4,5,6-Hexahydro and 1,2,3,4-Tetrahydro-2,2-dimethyl-5-aryl-6-aza-9,10-benzophenanthren-4-ones. II

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It has been reported that the reaction of β-naphthylamine, dimedone and the appropriate aromatic aldehyde in ethanol gave 1,2,3,4,5,6-hexahydro-2,2-dimethyl-5-aryl-6-aza-9,10-benzophenanthren-4-ones, **III**, which upon treatment with chromic anhydride, yielded the corresponding tetrahydro derivatives, **IV**. However, the attempted preparation of these compounds resulted instead of the formation of isomeric acridin-11-ones, **V** and **VI**. Structures were confirmed by ir, ^{1}H nmr, ms and X-ray spectroscopy.

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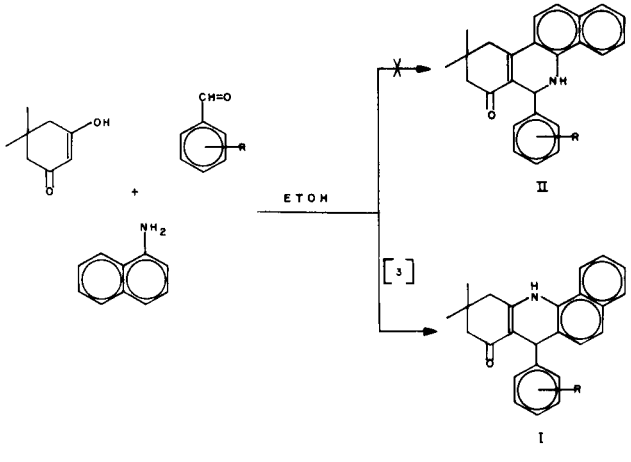
As a part of a program directed towards the synthesis and spectral properties of heterocyclic derivatives with possible pharmacological activity, we have reported recently that the dimedone addition to α-arylidenenaphthylamines [3] affords benzo[*c*]acridines **I** instead of benzo[*c*]-phenanthridines **II** (Scheme 1).

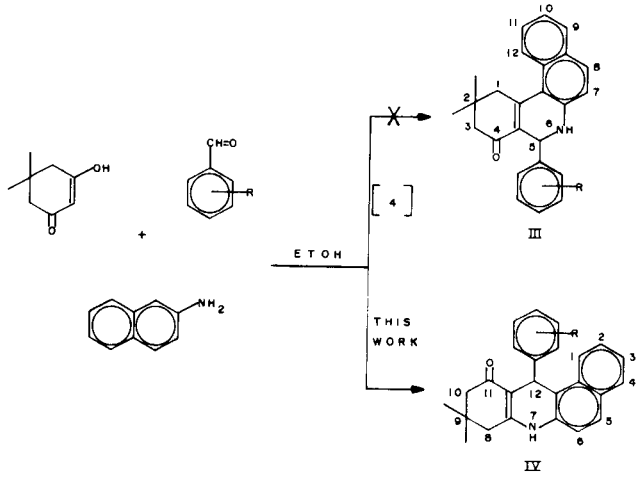
Scheme 1



Since Lielbriedis [4] has been reported also that the reaction of β-naphthylamine, an aromatic aldehyde and dimedone yields the 9,10-benzophenanthren-4-ones **III** (Scheme 2), it was considered of interest to study this reaction and the results examined in light of those obtained earlier for the α-naphthylamine.

When β-naphtylamine, dimedone and the corresponding aromatic aldehydes were refluxed in ethanol, were isolated the compounds **IV** (Scheme 2). The ir spectra (nujol)

Scheme 2



for all the compounds showed very strong bands at 1580, 1520 (vinylogous amide) [5], 1490 and 3260 cm^{-1} secondary amine (Table 1). The ^{1}H nmr data for these compounds are not given due to their insolubility in solvents normally used in these analyses; however, that the compounds **IV** are benz[*a*]acridin-11-ones and not benzophenanthren-4-ones **III** was proved unequivocally by means of X-ray crystallography.

The compound **IVe** (Figure 1) crystallized as the hydrochloride of the iminoenol tautomer (Tables 2 and 3). The acridine moiety is essentially planar with the atoms C(9) and C(12) showing the maximum deviation (.4159 and .7638 Å, respectively) and lying on opposite sides from the best mean plane. The dihydropyridine ring adopts a

Table 1

Physical and Spectral Data for Compounds IV

Compound No.	R	Mp °C	Yield %	Molecular Formula	Spectral Data
a	H	336-337	46.0	$C_{25}H_{23}NO$	ir (nujol): 3240, 3173, 1597, 1580, 1520 cm^{-1} ; ms: M at m/z 353, m/z 276 (100%)
b	*o*-Me	391-392	74.0	$C_{26}H_{25}NO$	ir (nujol): 3236, 3172, 1578, 1520, cm^{-1} ; ms: M at m/z 367, m/z 276 (100%)
c	*o*-OMe	312-313	88.0	$C_{26}H_{25}NO_2$	ir (nujol): 3257, 3186, 1600, 1521 cm^{-1} ; ms: M at m/z 383, m/z 276 (100%)
d	*o*-NO_2	280-281	63.0	$C_{25}H_{22}N_2O_3$	ir (nujol): 3265, 3168, 1582, 1527 cm^{-1} ; ms: M at m/z 398, m/z 276 (100%)
e	*p*-OH	315-316	50.0	$C_{25}H_{23}NO_2$	ir (nujol): 3303, 3240-2480, 1578, 1500 cm^{-1} ; ms: M at m/z 369, m/z 276 (100%)
f	*p*-OMe	297-298	67.0	$C_{26}H_{25}NO_2$	ir (nujol): 3268, 3192, 1600, 1522 cm^{-1} ; ms: M at m/z 383, m/z 276 (100%)
g	*p*-$N(Me)_2$	346-347	35.0	$C_{27}H_{28}N_2O$	ir (nujol): 3247, 3168, 1598, 1520 cm^{-1} ; ms: M at m/z 396, m/z 276 (100%)

Table 2

Bonds Lengths (Å)

O(1)-C(11)	1.312(7)	O(2)-C(18)	1.377(7)
C(1)-C(2)	1.368(10)	C(1)-C(1a)	1.405(9)
C(2)-C(3)	1.386 (10)	C(3)-C(4)	1.378(11)
C(4)-C(4a)	1.392(10)	C(4a)-C(5)	1.399(10)
C(4a)-C(1a)	1.444(9)	C(5)-C(6)	1.366(10)
C(6)-C(6a)	1.428(9)	C(6a)-N(7)	1.395(8)
C(6a)-C(1b)	1.379(9)	N(7)-C(7a)	1.330(8)
C(7a)-C(8)	1.488(9)	C(7a)-C(11a)	1.395(8)
C(8)-C(9)	1.530(9)	C(9)-C(10)	1.554(9)
C(9)-C(13)	1.521(9)	C(9)-C(14)	1.535(10)
C(10)-C(11)	1.497(9)	C(11)-C(11a)	1.358(8)
C(11a)-C(12)	1.528(8)	C(12)-C(1b)	1.518(8)
C(12)-C(15)	1.527(7)	C(1a)-C(1b)	1.432(9)
C(15)-C(16)	1.379(8)	C(15)-C(20)	1.368(9)
C(16)-C(17)	1.385(8)	C(17)-C(18)	1.371(10)
C(18)-C(19)	1.373(9)	C(19)-C(20)	1.397(8)

flattened sofa conformation, meanwhile the tetrahydrocyclohexenol ring is best described as a distorted sofa conformation. The *p*-hydroxyphenyl substituent at C(12) lies almost perpendicular to the plane of acridine, dihedral angle 83.5°.

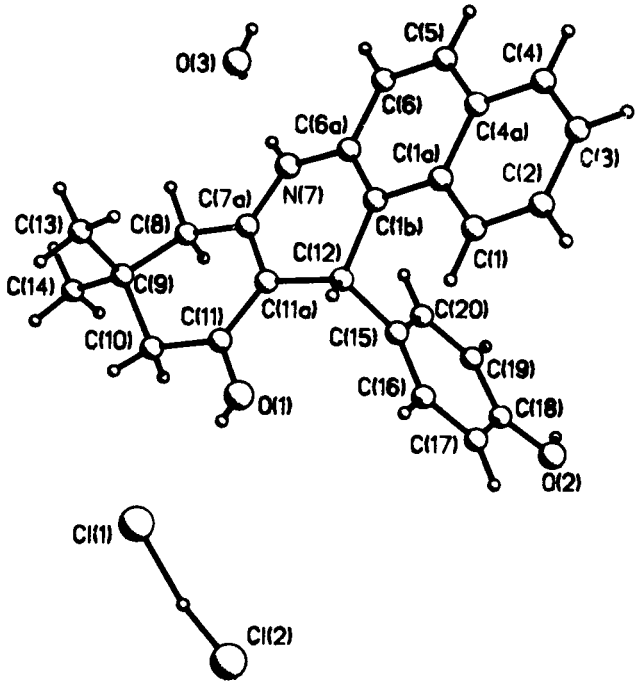


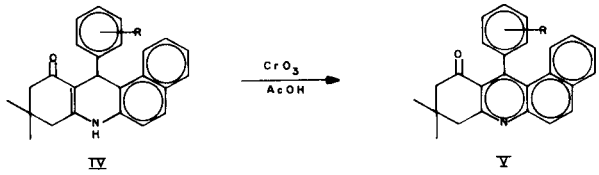
Figure 1

The molecules are held together in the crystal by intra and intermolecular hydrogen bonds (Table 4).

Oxidation of compounds **IV** with chromic anhydride in acetic acid afforded benzo[*a*]acridin-11-ones **V** (Scheme 3). In agreement with the suggested structure, the ir spectra (chloroform) of all the compounds **V** exhibited a strong ketone carbonyl band at 1690-1680 cm^{-1}. Its ^1H nmr spec-

trum showed a singlet at δ 1.15 for the methyl protons of C_9 as well as two singlets of the methylene protons joined to C_8 and C_{10} at δ 3.25-3.61 and δ 2.50-2.63, respectively. The remaining aromatic protons in compounds **V** appeared as a unresolved multiplet at δ 9.3-6.70 (Table 5). Further evidence concerning the structure of the acridinones **V** has been derived from their mass spectral data: while the *ortho*-R-compounds yield an intense ion at m/z [M-(*ortho*-R)]$^+$, base peak; the mass spectra of the *para*-R-compounds lacked this ion completely. These fragmentations supported the structural assignment, as similar features have been observed in the mass spectra of benzo[*c*]-acridin-8-ones [6].

Scheme 3



As shown by investigations of the mechanism of the reaction of α-arylidennaphthylamines with dimedone [3], this reaction may take place through the intermediate **VI** (Scheme 4); therefore the formation of benz[*a*]acridin-11-ones **IV** is consistent with the intermediary of aminoketone **VII** (Scheme 4).

Scheme 4

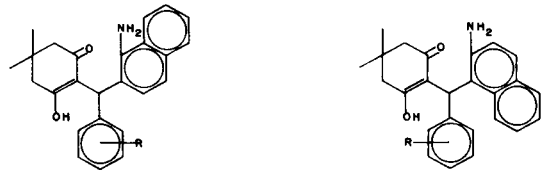


Table 3

Bond Angles (degrees)

C(2)-C(1)-C(1a)	120.8(6)	C(1)-C(2)-C(3)	121.4(7)
C(2)_C(3)-C(4)	119.6(7)	C(3)-C(4)-C(4a)	121.1(6)
C(4)-C(4a)-C(5)	122.0(6)	C(4)-C(4a)-C(1a)	119.3(6)
C(5)-C(4a)-C(1a)	118.7(6)	C(4a)-C(5)-C(6)	122.3(6)
C(5)-C(6)-C(6a)	118.9(6)	C(6)-C(6a)-N(7)	117.0(6)
C(6)-C(6a)-C(1b)	122.0(6)	N(7)-C(6a)-C(1b)	121.0(5)
C(6a)-N(7)-C(7a)	123.9(5)	N(7)-C(7a)-C(8)	118.4(5)
N(7)-C(7a)-C(11a)	119.8(5)	C(8)-C(7a)-C(11a)	121.7(5)
C(7a)-C(8)-C(9)	113.2(6)	C(8)-C(9)-C(10)	107.4(5)
C(8)-C(9)-C(13)	111.2(5)	C(10)-C(9)-C(13)	110.5(5)
C(8)-C(9)-C(14)	109.1(6)	C(10)-C(9)-C(14)	109.3(5)
C(13)-C(9)-C(14)	109.4(5)	C(9)-C(10)-C(11)	113.6(5)
O(1)-C(11)-C(10)	118.3(5)	O(1)-C(11)-C(11a)	117.3(5)
C(10)-C(11)-C(11a)	124.3(5)	C(7a)-C(11a)-C(11)	118.2(5)
C(7a)-C(11a)-C(12)	120.9(5)	C(11)-C(11a)-C(12)	120.8(5)
C(11a)-C(12)-C(1b)	111.8 (5)	C(11a)-C(12)-C(15)	111.5(5)
C(1b)-C(12)-C(15)	109.8(4)	C(1)-C(1a)-C(4a)	117.7(6)
C(1)-C(1a)-C(1b)	122.9(6)	C(4a)-C(1a)-C(1b)	119.3(6)
C(6a)-C(1b)-C(12)	119.3(5)	C(6a)-C(1b)-C(1a)	118.7(6)
C(12)-C(1b)-C(1a)	121.6(5)	C(12)-C(15)-C(16)	122.6(5)
C(12)-C(15)-C(20)	119.3(5)	C(16)-C(15)-C(20)	118.0(5)
C(15)-C(16)-C(17)	121.3(6)	C(16)-C(17)-C(18)	119.7(6)
O(2)-C(18)-C(17)	118.3(5)	O(2)-C(18)-C(19)	121.4(6)
C(17)-C(18)-C(19)	120.3(5)	C(18)-C(19)-C(20)	118.8(6)
C(15)-C(20)-C(19)	121.7(6)		

Table 4

Hydrogen-bond Distances (Å) and Angles (°)

D-H··· A	Position of acceptor atom	D··· A	D-H	H··· A	<D-H··· A
N(7)-H(7)··· O(3)	x, y, z	2.92	0.65	2.28	170.0
O(1)-H(1A)··· Cl(1)	x, y, z	2.90	0.62	2.35	173.4
Cl(2)-H(2B)··· Cl(1)	x, y, z	3.00	1.39	1.66	160.4
O(2)-H(2A)··· Cl(2)	0.5 –x, 0.5 + y, z	3.02	0.81	2.22	166.7
O(3)-H(3A)··· Cl(2)	1.5 –x, 0.5 + y, z	3.02	0.69	2.38	154.1

Table 5

Physical, Analytical and Spectral Data for Compounds V

Compound No.	R	Mp °C	Yield %	Molecular Formula	Analyses, % C	H	Spectral Data
a	H	219-221	76.0	$C_{25}H_{21}NO$	85.44 (85.41)	6.02 (6.00)	ir (chloroform): 1690 cm^{-1}; ^1H nmr (deuteriochloroform: δ 8.1-6.85 (m, 11H), 3.25 (s, 2H), 2.55 (s, 2H), 1.15 (s, 6H), ms: M^+ at m/z 351 (100%)
b	*o*-Me	181-183	93.0	$C_{26}H_{23}NO$	85.45 (85.42)	6.34 (6.31)	ir (chloroform): 1690 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.55-6.65 (m, 10H), 3.25 (s, 2H), 2.50 (s, 2H), 1.7 (s, 3H), 1.14 (s, 6H); ms: m/z 350 (M-R, 100%)
c	*o*-OMe	159-161	96.0	$C_{26}H_{23}NO_2$	81.86 (81.80)	6.07 (6.0)	ir (chloroform): 1690 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.1-6.75 (m, 10H), 3.61 (s, 3H), 3.23 (s, 2H), 2.54 (s, 2H), 1.14 (s, 6H); ms: M^+ at m/z 381, m/z 350 (M-R, 100%)
d	*o*-NO_2	194-196	73.0	$C_{25}H_{20}N_2O_3$	75.73 (75.69)	5.08 (5.0)	ir (chloroform): 1686 cm^{-1}; ^1H nmr (deuteriochloroform): δ 9.3-7.8 (m, 10H), 3.53 (s, 2H), 2.63 (s, 2H), 1.10 (s, 6H); ms: m/z 350 (M-R, 100%)
e	*p*-OH	210 dec	100.0	$C_{25}H_{21}NO_2$	81.72 (81.70)	5.76 (5.73)	ir (chloroform): 1689 cm^{-1}; ^1H nmr (deuteriochloroform): δ 9.2 (bs, 1H), 8.0-6.7 (m, 10H), 3.25 (s, 2H), 2.51 (s, 2H), 1.12 (s, 6H); ms: M^+ at m/z 367 (100%)
f	*p*-OMe	187-189	75.0	$C_{26}H_{23}NO_2$	81.86 (81.81)	6.07 (6.0)	ir (chloroform): 1689 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.2-6.85 (m, 10H), 3.9 (s, 3H), 3.25 (s, 2H), 2.55 (s, 2H), 1.15 (s, 6H); ms: M^+ at m/z 381 (100%)
g	*p*-$N(Me)_2$	123-125	95.0	$C_{27}H_{26}N_2O$	82.20 (82.17)	6.64 (6.61)	ir (chloroform): 1680 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.15-6.74 (m, 10H), 3.25 (s, 2H), 2.92 (s, 6H), 2.52 (s, 2H), 1.15 (s, 6H)

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a Nicolet FT-5SX spectrophotometer. The ^1H nmr spectra were recorded on a Varian FT-80 spectrometer operating at 80 MHz, in deuteriochloroform solution containing tetramethylsilane as the internal standard with chemical shifts (δ) expressed downfield from TMS. Mass spectra were obtained with a Hewlett-Packard 59 854-A quadropolo mass spectrometer.

Crystallogrphy.

X-Ray Analysis Data for 12-(*p*-Hydroxyphenyl)-9,9-dimethyl-7,8,-9,10,11,12-hexahydrobenz[*a*]acridin-11-one hydrochloride, **IVe**.

The molecular formula is $C_{25}H_{26}NO_3Cl_2$, M_w = 459, monoclinic, a = 15.132(2), b = 14.282(2), c = 20.904(4)Å, β = 99.00(1), space group $C_{2/c}$, Z = 8, V = 4462(1)Å^3, D_x = 1.366, μ(CuKα) = 28.73 cm^{-1}, Fooo = 1928 e^-, crystal size *c.a.* .18 x .22 x .04 mm (yellow).

The cell dimension and intensities were measured on a Nicolet P3/F automatic diffractometer using Ni-filtered CuKα radiation (λ = 1.54178Å). A total of 2801 reflections were collected using 2θ-θ scan mode in the range $3° < 2\theta < 110°$ and corrected by Lp effects, absorption correction was ignored. Structure was solved by direct methods and refined by least-squares using anisotropic temperature factors for non-H atoms. The final R was .086 (R_w = .096) for 2032 unique observed reflections ($F_o > 3\sigma(F_o)$). Atomic scattering factors from International Tables for X-Ray Crystallography [7] and all calculations were carried out on a Nova 4S computer using the SHELXTL program package [8].

The compounds **IVa-g** and **Va-g** have been prepared following reported procedures [3]. The structures of compounds **IVa-g** and **Va-g** were supported by ir, ^1H nmr, ms and X-ray spectral data. The physical, analytical and spectral data for synthesized compounds **IVa-g** and **Va-g**, are recorded on Tables 1 and 2, respectively.

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[2] Contribution No. 981 from Instituto de Química, UNAM.

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