Synthesis, Structural and Conformational Study of *N*-β(or γ)-Acyloxyalkylnortropinones

M. L. Izquierdo, E. Gálvez* and C. Burgos

Departamento de Química Orgánica, Universidad de Alcalá de Henares, Madrid, Spain

F. Florencio

Instituto Rocasolano, Departamento de Rayos-X, C.S.I.C., Serrano 119, 28006-Madrid, Spain

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A series of *N*-β(γ)-acyloxyalkylnortropinones have been synthesized and studied by ^1H and ^{13}C nmr spectroscopy, and the crystal structure of *N*-[γ-(*p*-chlorophenylcarbonyloxy)propyl]nortropinone **4** has been determined by X-ray diffraction. The compounds studied display in deuteriochloroform solution the same preferred conformation. The pyrrolidine and piperidone rings adopt a flattened N-8 envelope and distorted chair conformation, puckered at N-8 and flattened at C-3 respectively, with the *N*-substituent in axial position with respect to the piperidone ring. These results are in close agreement with that found for compound **4** in the crystalline state.

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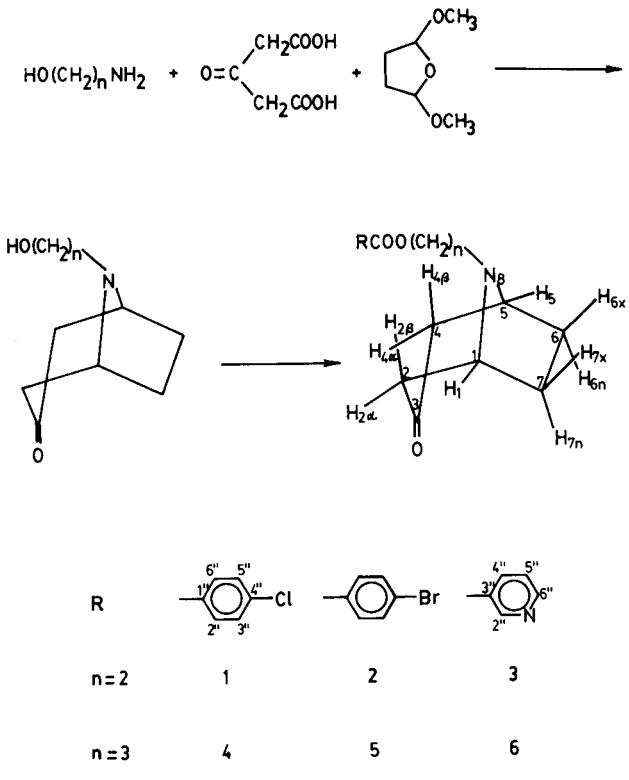
Introduction.

As a part of a research program related to the synthesis and structural study of pharmacologically interesting tropane compounds [1-5], we report in this paper the synthesis and structural analysis with the aid of ^1H and ^{13}C nmr spectroscopy of a series of *N*-β(γ)-acyloxyalkylnortropinones **1-6** (Scheme I) in order to determine their preferred conformation both in solution and in the solid state. The crystal structure of compound **4** has also been determined. The relationship between compounds **1-6** and atropine (a powerful muscarinic antagonist), prompted the synthesis and the conformational study of compounds **1-6** with the objective of establishing a structure-activity relationship.

SCHEME I



Results and Discussion.

Description of the Structure of Compound **4**.

The main crystallographic data and the structure determination conditions are given in Table 1. Table 2 shows the atomic parameters and Tables 3 and 4 show bond lengths, bond and torsion angles respectively. Figure 1 displays the structural formula.

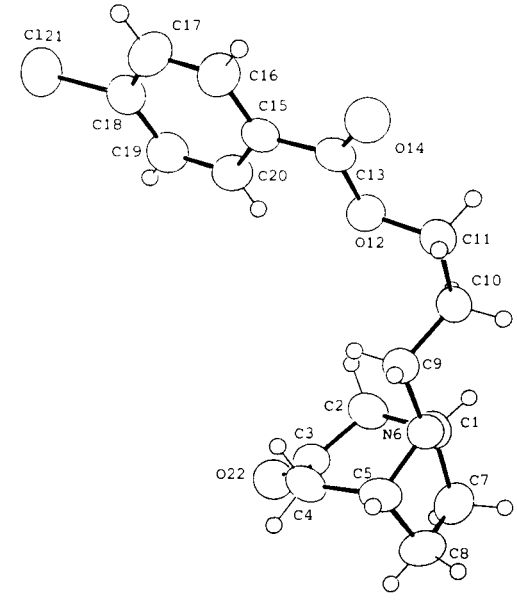


Figure 1

Table 1

Experimental Data and Structure Refinement Procedures

Crystal data	
Formula	$C_{16}H_{18}NO_3Cl$
Crystal habit	Parallelepiped
Crystal size (mm)	0.2 x 0.2 x 0.3
Symmetry	Triclinic P-1
Unit cell determination:	Least-squares fit from 47 reflexions ($\theta < 28°$)
Unit cell dimensions	8.360(4)Å, 9.242(8)Å, 11.229(2)Å 104.65(4), 73.35(3), 99.80(7)°
Packing: V(A³), Z	799.7(8), 4
Dc(g cm^{-3}), M, F(000)	2.3838, 287.005, 992
μ (cm^{-1})	1.519
Experimental data	
Technique	Four circle diffractometer: En Nonius CAD-4
	Bisecting geometry
	Graphite oriented monochromato
	w/2θ scans
	Detector apertures 1.1, up θ max = 1.25 min/reflex
Number of reflexions:	
Measured	4630
Independent	3763
Observed	2896 (2 σ (I) criterion)
Range of hkl	-11 11, -13 13, 0 15, (sin θ/λ)
Standard reflexions:	2 reflexions every 90 minutes
	Variation: no
Max-min transmission factors, [6]:	1.245, 0.612
Solution and refinement	
Solution	Direct methods
Refinement	L.S. on Fobs with 1 Blocks
Parameters:	
Number of variables	278
Degrees of freedom	2618
Ratio of freedom	10.4
H atoms	Difference synthesis
Final shift/error	0.11
w-scheme	Empirical as to give no trends vs $<\|Fobs\|>$ and $<\sin\theta/\lambda>$
Final F peaks	0.3 eA-3
Final R and Rw	0.053 0.065
Computer and programs	Vax 11.750, Multan80, [8], X-Ray 76 [9], Pesos [10]
Scattering factors	Int Tables for X-Ray Crystall [7]
Anomalous dispersion	Int Tables for X-Ray Crystall

Table 2

Coordinates and Thermal Parameters as
Ueq = (1/3).sum(Uij.ai*.aj*.ai.aj.cos(ai,aj)).10**4

Atom	x	y	z	Ueq
C1	0.02803(23)	-0.61986(21)	-0.35238(18)	517(7)
C2	-0.06171(23)	-0.55932(23)	-0.21295(19)	541(7)
C3	-0.01571(22)	-0.63658(19)	-0.12667(17)	496(6)
C4	0.16486(26)	-0.66613(24)	-0.16202(19)	569(8)
C5	0.23580(24)	-0.71176(20)	-0.30719(19)	538(7)
N6	0.21110(17)	-0.60258(15)	-0.37345(13)	465(5)
C7	-0.00917(32)	-0.79103(25)	-0.38972(24)	699(9)
C8	0.13646(32)	-0.85231(23)	-0.36543(24)	701(9)
C9	0.29460(22)	-0.45217(19)	-0.34177(17)	468(6)
C10	0.27409(24)	-0.35090(20)	-0.42281(17)	492(6)
C11	0.39176(26)	-0.20777(20)	-0.41235(17)	523(7)
O12	0.34769(16)	-0.12871(13)	-0.28021(12)	519(5)
C13	0.44598(20)	-0.00399(18)	-0.24784(16)	455(6)
O14	0.56295(18)	0.04549(17)	-0.32304(13)	665(7)
C15	0.39288(19)	0.06578(17)	-0.11055(16)	429(6)
C16	0.48722(24)	0.19341(23)	-0.06243(20)	569(7)
C17	0.44197(26)	0.26390(25)	0.06442(21)	621(8)
C18	0.30253(23)	0.20557(21)	0.14336(17)	508(7)
C19	0.20724(27)	0.07881(24)	0.09765(20)	612(8)
C20	0.25295(25)	0.00873(21)	-0.02891(18)	547(7)
CL21	0.24822(7)	0.29032(7)	0.30429(5)	699(4)
O22	-0.11673(19)	-0.67240(17)	-0.03481(14)	665(7)

Atom	U11	U22	U33	U12	U13	U23
C1	486(9)	548(9)	556(9)	-65(7)	-201(7)	188(8)
C2	413(8)	596(10)	646(11)	80(7)	-88(7)	228(8)
C3	516(9)	450(8)	497(8)	46(7)	-78(7)	122(7)
C4	589(10)	605(11)	599(10)	168(8)	-122(8)	248(9)
C5	504(9)	465(9)	628(10)	112(7)	-32(8)	174(8)
N6	447(7)	432(7)	498(7)	-10(5)	-105(6)	122(5)
C7	741(14)	599(11)	646(12)	-198(10)	-171(10)	123(9)
C8	785(14)	442(9)	713(13)	14(9)	35(11)	125(9)
C9	459(8)	454(8)	510(9)	-18(6)	-164(7)	138(7)
C10	539(9)	476(8)	486(9)	-10(7)	-177(7)	134(7)
C11	601(11)	492(9)	455(8)	-20(7)	-100(7)	156(7)
O12	549(7)	463(6)	487(6)	-56(5)	-88(5)	123(5)
C13	439(8)	419(7)	538(9)	4(6)	-132(7)	177(7)
O14	620(8)	676(8)	582(8)	-154(6)	-52(6)	194(6)
C15	396(7)	415(7)	523(8)	57(6)	-128(6)	167(6)
C16	433(9)	626(11)	595(10)	-70(7)	-129(8)	125(8)
C17	539(10)	620(11)	655(11)	-45(8)	-214(9)	46(9)
C18	516(9)	537(9)	517(9)	163(7)	-164(7)	90(7)
C19	589(11)	614(11)	565(10)	-9(8)	-39(8)	180(9)
C20	561(10)	471(9)	561(10)	-58(7)	-99(8)	149(7)
CL21	738(3)	797(4)	562(3)	238(3)	-184(2)	22(2)
O22	656(9)	664(9)	600(8)	-41(7)	-28(6)	227(7)

Coordinates and Thermal Parameters as
exp(-8.π^2.U.(sin(0/1)**2.10**3)

Atom	x	y	z	U
H11	-0.003(3)	-0.570(2)	-0.407(2)	28(5)
H21	-0.186(3)	-0.579(3)	-0.198(2)	43(6)
H22	-0.026(3)	-0.447(3)	-0.185(2)	38(6)
H41	0.173(3)	-0.738(3)	-0.113(2)	48(7)
H42	0.231(3)	-0.571(3)	-0.126(2)	50(0)
H51	0.362(3)	-0.717(2)	-0.322(2)	37(6)
H71	-0.003(4)	-0.821(3)	-0.483(3)	64(9)
H72	-0.120(4)	-0.828(3)	-0.337(3)	53(7)
H81	0.098(4)	-0.920(3)	-0.305(3)	59(8)
H82	0.216(4)	-0.903(3)	-0.445(3)	58(8)
H91	0.422(3)	-0.460(3)	-0.359(2)	46(7)
H92	0.252(3)	-0.406(2)	-0.252(2)	25(5)
H101	0.153(3)	-0.324(3)	-0.395(2)	42(6)
H102	0.302(3)	-0.399(3)	-0.513(2)	33(6)
H111	0.376(3)	-0.144(3)	-0.464(2)	33(5)
H112	0.509(3)	-0.230(3)	-0.438(2)	38(6)
H161	0.584(3)	0.227(3)	-0.120(2)	48(7)
H171	0.509(4)	0.347(3)	0.096(3)	55(8)
H191	0.112(4)	0.038(8)	0.155(3)	63(8)
H201	0.195(3)	-0.075(3)	-0.062(2)	42(6)

Table 3

Bond Distances (Å)

C1-C2	1.534(3)	C1-N6	1.467(3)
C1-C7	1.532(3)	C2-C3	1.501(3)
C3-C4	1.501(3)	C3-O22	1.210(2)
C4-C5	1.540(3)	C5-N6	1.467(3)
C5-C8	1.523(3)	N6-C9	1.452(2)
C7-C8	1.543(4)	C9-C10	1.519(3)
C10-C11	1.549(3)	C11-O12	1.450(2)
O12-C13	1.331(2)	C13-O14	1.204(2)
C13-C15	1.481(2)	C15-C16	1.382(3)
C15-C20	1.381(3)	C16-C17	1.379(3)
C17-C18	1.368(3)	C18-C19	1.372(3)
C18-CL21	1.738(2)	C19-C20	1.376(3)

Table 4

Bond Angles (°)

N6-C1-C7	101.5(3)	C2-C1-C7	111.1(2)
C2-C1-N6	112.1(2)	C1-C2-C3	110.6(2)
C2-C3-O22	122.5(4)	C2-C3-C4	115.3(2)
C4-C3-O22	122.2(3)	C3-C4-C5	112.0(3)
C4-C5-C8	111.6(2)	C4-C5-N6	112.2(2)
N6-C5-C8	100.8(2)	C1-N6-C5	102.3(3)
C5-N6-C9	115.7(2)	C1-N6-C9	118.1(3)
C1-C7-C8	104.2(3)	C5-C8-C7	103.8(3)
N6-C9-C10	111.9(2)	C9-C10-C11	112.0(2)
C10-C11-O12	106.7(2)	C11-O12-C13	116.5(2)
O12-C13-C15	112.2(3)	O12-C13-O14	123.1(2)
O14-C13-C15	124.7(3)	C13-C15-C20	122.7(3)
C13-C15-C16	118.5(2)	C16-C15-C20	118.8(2)
C15-C16-C17	120.9(3)	C16-C17-C18	119.3(3)
C17-C18-CL21	119.6(3)	C17-C18-C19	120.8(2)
C19-C18-CL21	119.6(3)	C18-C19-C20	119.7(3)
C15-C20-C19	120.6(3)		

Torsion Angles (°)

N6-C1-C7-C8	26.4(3)	C2-C1-C7-C8	-92.9(3)
C2-C1-N6-C9	-58.5(4)	C7-C1-N6-C5	-48.8(3)
C2-C1-N6-C5	69.8(3)	N6-C1-C2-C3	-57.43(4)
C7-C1-C2-C3	55.4(4)	C7-C1-N6-C9	-177.1(3)
C1-C2-C3-C4	39.4(4)	C1-C2-C3-O22	-140.7(4)
C2-C3-C4-C5	-38.0(4)	O22-C3-C4-C5	142.2(4)
C3-C4-C5-N6	53.6(4)	C3-C4-C5-C8	-58.7(4)
C4-C5-N6-C1	-67.3(3)	C4-C5-C8-C7	86.2(3)
C4-C5-N6-C9	62.4(4)	C8-C5-N6-C1	51.6(3)
N6-C5-C8-C7	-33.2(3)	C8-C5-N6-C9	-178.7(3)
C5-N6-C9-C10	175.2(3)	C1-N6-C9-C10	-63.2(4)
C1-C7-C8-C5	4.2(4)	N6-C9-C10-C11	-166.8(3)
C9-C10-C11-O12	-62.0(4)	C10-C11-O12-C13	174.7(3)
C11-O12-C13-O14	2.2(5)	C11-O12-C13-C15	-178.5(3)
O12-C13-C15-C16	177.7(3)	O12-C13-C15-C20	-2.4(5)
O14-C13-C15-C16	-3.0(5)	O14-C13-C15-C20	176.9(4)
C13-C15-C20-C19	-179.1(3)	C13-C25-C16-C17	179.2(3)
C16-C15-C20-C19	0.8(5)	C20-C15-C16-C17	-0.7(5)
C15-C16-C17-C18	0.5(5)	C16-C17-C18-C19	-0.4(5)
C16-C17-C18-CL21	178.0(3)	C17-C18-C19-C20	0.5(5)
CL21-C18-C19-C20	-178.0(3)	C18-C19-C20-C15	-0.7(5)

The piperidine ring adopts a distorted chair conformation in good agreement with the results found in previous compounds [2-4]. The deviations of C(3) and N(6) from the mean plane through the remaining atoms of the ring are -0.470 (4) and 0.786(4)Å. The asymmetry parameters [11] are ΔCs(3) = 0.017(2), ΔC2(1-6) = 0.051(2), ΔC2(1-2) = 0.310. Consequently, a mirror symmetry is dominant with an approximate Cs plane passing through C3 and N6.

The five membered ring of the bicyclo system shows a *N*-envelope conformation. The asymmetry parameter is ΔCs(N6) = 0.033(1) and the deviation of the N6 atoms from the plane through C1, C5, C7 and C8 is 0.715(2)Å. Consequently, the bicyclo system adopts a boat-chair conformation with an approximate mirror plane defined by N6, C3 and O22 atoms. The acyloxy group occupies an axial position with respect to the piperidone ring being displaced from the mirror plane.

The intermolecular contacts correspond to Van der Waals interactions.

NMR Spectra.

The ^1H and ^{13}C nmr data of **1-6** are summarized in Tables 5 and 6. Assignments of proton and carbon resonances were made from the literture data of several

Table 5

^1H NMR Chemical Shifts (δ, ppm) and Multiplicities (J, Hz) for Compounds **1-6** [a,b]

Compound	**1**	**2**	**3**	**4**	**5**	**6**
H-1(5)	3.5 (brs)	3.3 (brs)	3.6 (brs)	3.5 (brs)	3.5 (brs)	3.4 (brs)
	w½ 10.5	w½ 9.5	w½ 10	w½ 10	w½ 10.5	w½ 10
H-2(4)$_\beta$	2.7 (dd)	2.5 (dd)	2.7 (dd)	2.7 (dd)	2.6 (dd)	2.7 (dd)
	^2J 15.5	^2J 15	^2J 14	^2J 15	^2J 15	
	^3J 4.5	^3J 4.5	^3J 3.5	^3J 4	^3J 3.6	^3J 4
H-2(4)$_\alpha$	2.2 (dd)	2.0 (dd)	2.2 (d)	2.2 (dd)	2.2 (d)	2.1 (dd)
	^3J 1.2	^3J 1.6		^3J 1.2		^3J 1.5
H-6(7)$_x$	2.0 (m)	1.8 (m)	2.0 (m)	2.0 (m)	2.0 (m)	2.2 (m)
H-6(7)$_n$	1.7 (m)	1.5 (m)	1.6 (m)	1.6 (m)	1.5 (m)	1.7 (m)
H-α	2.9 (t)	2.7 (t)	2.9 (t)	2.7 (t)	2.7 (t)	2.7 (t)
	^3J 6	^3J 6	^3J 6	^3J 6.6	^3J 6	^3J 6
H-β	4.5 (t)	4.3 (t)	4.5 (t)	2.0 (q)	2.0 (q)	2.0 (q)
				^3J 6.6	^3J 6	^3J 6
H-γ				4.5 (t)	4.5 (t)	4.4 (t)
H-2''	7.9 (d)	7.2 (brs)	9.2 (d)	7.9 (d)	7.9 (d)	9.2 (d)
	^3J 8.4		^4J 1.5	^3J 8.4	^3J 8	^4J 1.5
H-3''	7.4 (d)	7.2 (brs)		7.4 (d)	7.6 (d)	
H-4''			8.30 (dt)			8.27 (dt)
			^3J 7			^3J 7
			^4J 1.5			^4J 1.5
H-5''	7.4 (d)	7.2 (brs)	7.4 (dd)	7.4 (d)	7.6 (d)	7.4 (dd)
			^3J 4.2			^3J 4
			^3J 7			^3J 7
H-6''	7.9 (d)	7.2 (brs)	8.7 (dd)	7.9 (d)	7.9 (d)	8.7 (dd)
			^3J 4.2			^3J 4
			^4J 1.5			^4J 1.5

[a] Spectra recorded in deuteriochloroform. [b] Abbreviations: brs, broad singlet; d, doublet; dd, doublet of doublets; dt, doublet of triplets; m, multiplet, t, triplet.

tropane systems [1-5]. In the case of ^{13}C nmr assignments, substituent steric and electronic effects on ^{13}C chemical shifts [12,13] and signal multiplicity obtained from off-resonance decoupled spectra were taken into consideration.

Table 6

Carbon-13 Chemical Shifts (δ [a], ppm) for Compounds **1-6**

Compound	1	2	3	4	5	6
C-1(5)	59.62	59.59	59.58	58.89	58.79	58.78
C-2(4)	47.66	47.61	47.65	47.64	47.57	47.54
C-6(7)	27.96	27.92	27.87	27.92	27.88	28.23
C-3	209.21	209.12	209.20	209.27	209.46	209.40
C-α	49.40	49.35	49.37	47.18	47.08	47.04
C-β	64.50	64.42	64.55	28.49	28.39	27.80
C-γ				63.52	63.50	63.63
C=O(0)	165.54	165.85	165.09	165.58	165.71	165.15
C-1″	128.76	129.14		129.00	129.32	
C-2″	130.93	131.76 [b]	153.39	130.93	131.69 [b]	153.32
C-3″	128.76	131.06 [b]	126.09	128.71	131.04 [b]	126.22
C-4″	139.42	128.10	136.97	139.32	127.96	136.93
C-5″	128.76	131.06 [b]	123.35	128.71	131.04 [b]	123.29
C-6″	130.93	131.76 [b]	150.71	130.93	131.69 [b]	150.74

[a] Directly measured on the spectra, ±0.05 ppm. [b] Values may be interchanged.

From the ^1H and ^{13}C nmr data of **1-6**, the following general features for the bicycle system were deduced: a) The pyrrolidine and piperidone rings in these compounds all have a flattened *N*-8 envelope and distorted chair conformation puckered at N8 and flattened at C3, similar to that observed in the crystal structure of **4**. b) The *N*-group is attached in axial position with respect to the piperidone ring, this group has not a preferred conformation in deuteriochloroform solution and, finally, the carbonyl group is conjugated with the phenyl ring. No difference was observed between the compounds with n = 2 and n = 3.

These conclusions are supported by the following:

a) In the ^1H nmr spectra, the $w_{1/2}$ value for the H-1(5) hydrogen signals of ~10 Hz corresponds to a tropane system with the piperidine ring in a flattened chair conformation [1,2,5,14]. The JH2(4)-H1(5) values (Table 5) correspond to dihedral angles of ~60°. In all cases $JH2(4)_\beta$-H1(5) is greater than $JH2(4)_\alpha$-H1(5), consequently, the dihedral angle $H2(4)_\alpha$-C-C-H1(5) is greater than $H2(4)_\beta$-H1(5). The regularity of the $^3JH2(4)_\beta$-H1(5) values in **1-6** reveals that the piperidone ring conformation is not appreciably influenced by the shape and size of the group attached to the piperidone nitrogen atom. In the ^{13}C nmr spectra, the chair conformation adopted by the piperidone ring is confirmed by the C2(4) values (Table 6). For a boat conformation, these carbon signals would be shifted to higher field because of the steric compressing effect due to the eclipsing between the $C2(4)_\beta$ and C1(5) hydrogen atoms [1,2,15,16].

b) For compounds **1-6**, δ C2(4) values are nearly the same. The chemical shifts of C6(7) are not affected by the substituents on the nitrogen atom. These facts can be justified by considering that the conformer with the nitrogen substituent in an axial position with respect to the piperidone ring is the most favourable, in agreement with previous observations [16-18]. The patterns of the CH_2-O and CH_2-N triplets and the aromatic protons in the ^1H nmr spectra of **1-6** accounts for several preferred conformations for the acyloxyalkyl group, as it can be seen with molecular models. The conjugation between the carbonyl and the phenyl group in **1-6** is confirmed by the δ C aromatic values.

The results obtained by X-ray diffraction of **4** are in good agreement with the ^1H and ^{13}C nmr conclusions although in the crystalline state; the acyloxyalkyl group has a fixed conformation, due probably to packing forces.

With the objective to establish a possible structure-activity relationship, the parameters established by Schulman *et al* [19] for a model of agonist recognition by the muscarinic receptor (P-Q distance and P-N-O-Q angle) have been calculated from the X-ray coordinates of **4** (P-Q:5.847 Å, P-N-O-Q:160.65°) with the assumption, that in solution, one of the preferred conformations of the *N*-group is that found in the crystalline state.

EXPERIMENTAL

All melting points were taken in open capillary tubes and are uncorrected. Infrared spectra were determined using a Perkin-Elmer 1310 spectrophotometer. The ^1H nmr spectra were recorded using a Varian EM390 operating at 90 MHz. The ^{13}C nmr spectra were determined on a Varian FT 80 spectrometer operating at 20 MHz. Noise decoupled and single frequency off resonance decoupled spectra were obtained. The elemental analysis were made in a Perkin-Elmer Elemental Analizer model 240B.

N-B-Hydroxyethyl and *N*-γ-hydroxypropylnortropinones were obtained by the Robinson-Schöpf method [20] modified by Finlay [21].

Synthesis of the Esters (**1-6**). General Procedures.

Method A.

A solution of the acyl chloride (3.5 mmoles), triethylamine (3.5 mmoles) and the corresponding *N*-substituted-nortropinone (3.5 mmoles) in anhydrous methylene chloride (20 ml) were stirred at room temperature for 3 hours. The reaction mixture was washed with water. The organic layer was separated, dried (magnesium sulfate) and the solvent evaporated under reduced pressure. The residual oil was purified on a silica gel column prepacked in ethylacetate-hexane. Elution of the column with ethyl acetate-hexane (7:3 v/v) gave an homogeneous residue which was crystallized from hexane.

Method B.

To a stirred solution of the corresponding *N*-substituted-nortropinone (4 mmoles) and the acid (4 mmoles) in anhydrous methylene chloride (10 ml), was added dropwise a solution of DCC (*N,N'*-Dicyclohexylcarbodiimide) (5 mmoles) and DMAP (4-(Dimethylamino)pyridine) (0.4 mmole) in anhydrous methylene chloride (5 ml). The mixture was stirred at room

temperature for 3 hours. The mixture was filtered under reduced pressure. The filtrate was concentrated *in vacuo*, ether was added to the resulting oil, the mixture was filtered and the filtrate was evaporated under reduced pressure. The residual oil was purified on a silica gel column prepacked in acetone. Elution of the column with acetone gave the desired ester as an oil.

N-[β(4-Chlorobenzoyloxy)ethyl]nortropinone (**1**).

This compound was obtained (Method A) in 74% yield, mp 65-67°; ir (potassium bromide): ν CO 1720 cm^{-1}; pmr: (see Table 5); cmr: (see Table 6).

Anal. Calcd. for $C_{16}H_{18}ClNO_3$: C, 62.44; H, 5.85; N, 4.55. Found: C, 62.46; H, 5.97; N, 4.50.

N-[β(4-Bromobenzoyloxy)ethyl]nortropinone (**2**).

This compound was obtained (Method A) in 65% yield, mp 52-54°; ir (potassium bromide): ν CO 1710 cm^{-1}; pmr: (see Table 5); cmr: (see Table 6).

Anal. Calcd. for $C_{16}H_{18}BrNO_3$: C, 54.56; H, 5.15; N, 3.97. Found: C, 54.90; H, 5.26; N, 3.67.

N-[β(3-Pyridyncarbonyloxy)ethyl]nortropinone (**3**).

This compound was obtained (Method B) in 70% yield; ir (film) ν CO 1715 cm^{-1}; pmr: (see Table 5); cmr: (see Table 6).

The tetrafluoroborate derivative had mp 144-146°.

Anal. Calcd. for $C_{15}H_{20}B_2F_8N_2O_3$: C, 40.04; H, 4.48; N, 6.22. Found: C, 40.02; H, 4.40; N, 6.43.

N-[γ(4-Chlorobenzoyloxy)propyl]nortropinone (**4**).

This compound was obtained (Method A) in 63% yield, mp 75-77°; ir (potassium bromide): ν CO 1710 cm^{-1}; pmr: (see Table 5); cmr: (see Table 6).

Anal. Calcd. for $C_{17}H_{20}ClNO_3$: C, 63.45; H, 6.22; N, 4.35. Found: C, 63.56; H, 6.33; N, 4.29.

N-[γ(4-Bromobenzoyloxy)propyl]nortropinone (**5**).

This compound was obtained (Method A) in 56% yield, mp 86-88°; ir (potassium bromide): ν CO 1710 cm^{-1}; pmr: (see Table 5); cmr: (see Table 6).

Anal. Calcd. for $C_{17}H_{20}BrNO_3$: C, 55.75; H, 5.50; N, 3.82. Found: C, 55.88; H, 5.17; N, 3.77.

N-[γ(3-Pyridyncarbonyloxy)propyl]nortropinone (**6**).

This compound was obtained (Method B) in 81% yield; ir (film): ν CO 1710 cm^{-1}; pmr: (see Table 5); cmr: (see Table 6).

The tetrafluoroborate derivative had mp 150-152°.

Anal. Calcd. for $C_{16}H_{22}B_2F_8N_2O_3$: C, 41.72; H, 4.77; N, 6.03. Found: C, 42.00; H, 5.01; N, 5.92.

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