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Substituent-dependent Asymmetric Induction in the Ring Transformation of 2,3-Dihydroimidazo[2,1-*a*]phthalazin-4-ium-6-olates Effected by Acetic and Propionic Anhydrides

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Abstract: On the effect of acetic and propionic anhydrides 2,3-dihydroimidazo[2,1-*a*]phthalazin-4-ium-6-olates (**1c-j**) underwent ring transformation (**1** → **7,8**). Alternative mechanisms are applied to reason the characteristic substituent-dependent asymmetric induction observed for the transformations of the 2-monosubstituted precursors. The structures of products were determined by IR, MS, ^{1}H- and ^{13}C-NMR (1D- and 2D) measurements supported by single crystal X-ray analysis.

Introduction

Owing to their mechanistic and synthetic interest, backbone rearrangements effected by anhydrides represent a very intriguing and widely investigated area of heterocyclic chemistry[1]. It is generally accepted that the size of the ring involved in a rearrangement has significant control over both the rate and the direction of the reaction studied[2], but the lack of satisfactory interpretation often makes it difficult to extend the application of the experimental findings in planned synthetic routes. For instance, a highly remarkable and - at first glance - not too easily interpretable difference has been observed between the reactivities of 2,3-dihydroimidazo[2,1-*a*]phthalazin-4-ium-6-olate (**1a**) and its ring homologue 3,4-dihydro-2*H*-pyrimido[2,1-*a*]phthalazin-5-ium-7-olate (**2**) toward refluxing acetic anhydride[3]: the imidazo derivative underwent a Bamberger-like ring cleavage resulting in 2-(2-diacetylaminoethyl)-4-acetoxyphthalazin-1(2*H*)-one (**7a**)[3a], while the ring homologue afforded a fundamentally changed ring system (**3**), containing an asymmetry centre at the C11b atom (Scheme 1). Moreover, the reaction of the latter substrate with propionic anhydride produced the same triazaindenoindanone skeleton with an additional asymmetry centre at the C1 atom (**4**). No formation of the sterically more crowded C1-epimer ("*endo*") has been reported[3b]. In a particular case the imidazo[2,1-*a*]phthalazin-4-ium-6-olate ring system could also be forced to undergo similar a transformation, constructing a triazapentalenoindanone skeleton (**1b** → **8b**, Scheme 1)[4]. On the other hand, when dichloroacetic anhydride was replaced by acetic anhydride, the zwitterionic **5b** could only be obtained as the sole product. In contrast to **5a**, the isolated intermediate of ring fission reaction leading to **7a** (Scheme 1)[3a], **5b** proved to be stable even on prolonged heating in acetic anhydride[4]. All these previous findings prompted us to start a systematic study to

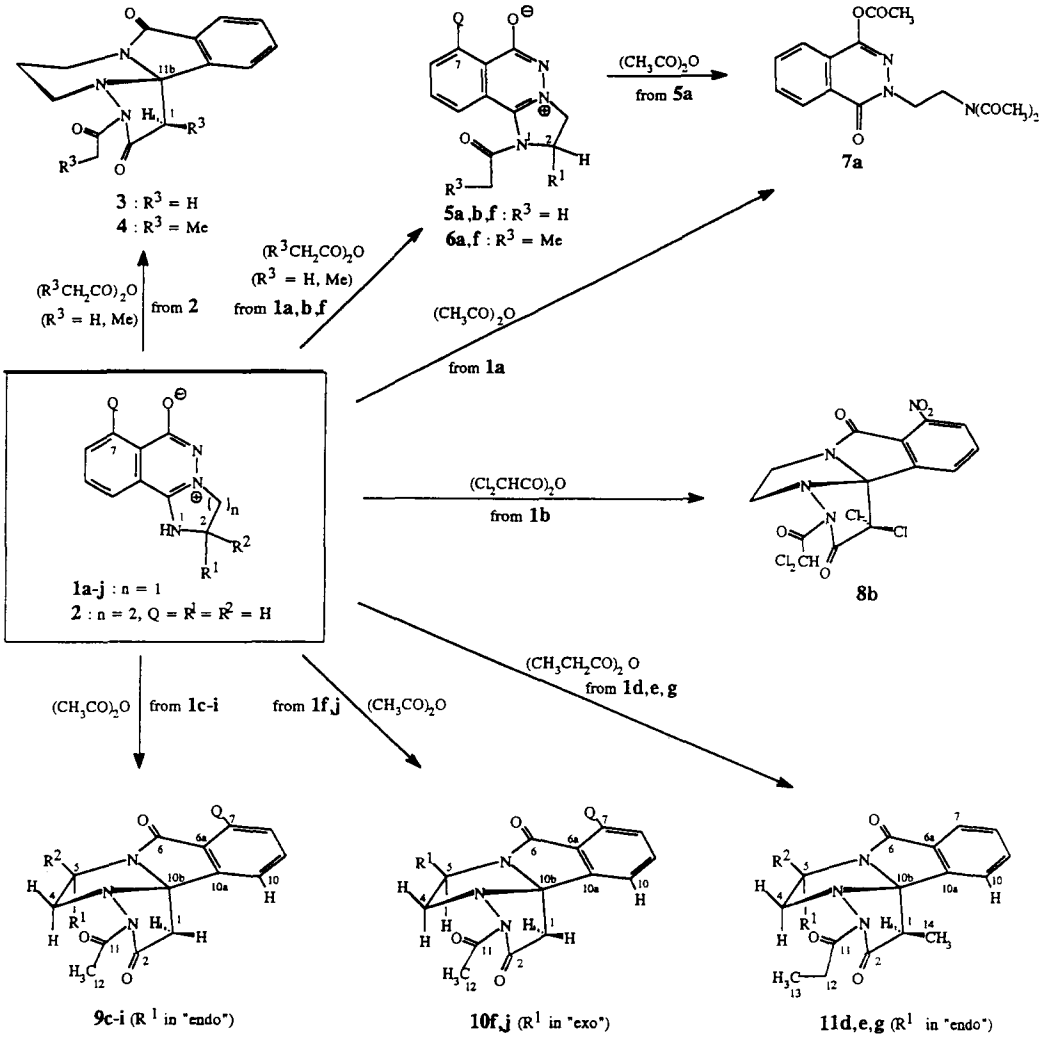
collect more information about the structural features and other conditions controlling direction and stereochemistry of the ring transformations when the easily available[5] precursors of types **1** and **2** are treated with anhydrides containing at least one hydrogen in the α-position relative to the carbonyl group.

Results and Discussion

First of all we aimed to find suitable modes of substitution that, suppressing the fission of the condensed ring, facilitate the ring transformation of the 2,3-dihydroimidazo[2,1-*a*]phthalazin-4-ium-6-olate skeleton when simply acetic or propionic anhydride is used as a reagent. It seemed reasonable that the introduction of bulky substituent(s) into position 2 prevents the acylation of the N1 atom, the first step of the conversions of type **1** → **7**[3a] and, consequently, increases the chance of the desired ring transformation. As described in Experimental, starting from phthalic- or 3-nitrophthalic anhydride and the corresponding 2-aminoalcohols, we prepared a series of new 2-alkyl-substituted tricyclic model compounds (**1c-j**) among which **1c,g-j** are optically active. The previously reported conversions of **1a,b** and **2** together with the reactions of the extended group of model compounds, discussed in this contribution, are summarized in Scheme 1.

Pointing to the efficiency of steric hindrance at the N1 atom, on treatment with acetic anhydride **1c-j** afforded triazapentalenoindanones (**9c-i**, **10f,j**) in moderate to good yields. Quite interestingly, after the reactions of the monoalkyl-substituted precursors **1c,e,g,h** and the 2-phenyl derivative **1i** the sterically more crowded 5-*endo*-monosubstituted diastereomers **9c,e,g-i** could only be isolated, while the 2-benzyl derivative **1j** was converted into the 5-*exo*-monosubstituted analogue **10j**. In the last case we could neither isolate nor detect the corresponding 5-*endo* isomer. The reaction of **1f** (Q = NO_2, R^1 = Et) yielded a mixture of zwitterion **5f** and both diastereomers of the corresponding tetracycle (**9f** and **10f**) with characteristic dominance of the *endo* isomer (**5f** : **9f** : **10f** ≈ 1 : 2 : 1). The appearance of **5f** is in accordance with the previous findings[4] mentioned in the Introduction, which in the absence of the alkyl group at C2-position N1-acylation is practically the only process taking place on the 7-nitro-substituted precursor **1b**. No formation of other poorly soluble zwitterions of type **5** was detected after the reactions of **1c-j** with acetic anhydride.

Using propionic anhydride additional experiments were performed with the selected model compounds **1a,d-g**. In these cases each reaction afforded single products: the unsubstituted **1a** and the 2-ethyl-7-nitro derivative **1f** were acylated on the N1 atom to give **6a** and **6f**, respectively; in diastereoselective processes **1d,e,g** were converted into the appropriate triazapentalenoindanones **11d,e,g**, in which the 1-methyl substituent is *exo*-oriented relative to the ring system. The latter observations are in keeping with the outcome of the aforementioned reaction of **2** with propionic anhydride affording the 1-*exo* diastereomer **4** as the only isolated product[3b]. On the other hand, at C5 position of tetracycles **11e,g** containing three asymmetry centres, the alkyl group is again *endo*-oriented relative to the ring system.



1,5-11	a	b	c*	d	e	f	g*	h*	i*	j*
Q	H	NO_2	H	H	H	NO_2	H	H	H	H
R^1	H	H	Me	Me	Et	Et	^iPr	^tBu	Ph	CH_2Ph
R^2	H	H	H	Me	H	H	H	H	H	H

*Configurations: "*S*" at C2 for **1c,g-j** (**1e,f** are racemates); **9c,g-i**, **10g** and **11j** are presented with their absolute configuration (**9d-f**, **10d,e** and **11f** are racemates).

Scheme 1

The structures of the novel compounds formed in the reactions investigated were determined by IR, MS, ^{1}H- and ^{13}C-NMR spectroscopy including 2D-techniques (COSY, HSC and HMBC). The assignments of NMR spectra are listed in Table 1. The relative configuration of the tetracycles was established by ^{1}H-DNOE measurements. First of all, the *exo*-positioned H and Me (in **9**, **10** and **11**, resp.) were identified *via* its space-transmitted dipolar interaction with H10 being in steric proximity on the aromatic ring. After identification of these resonances, assignation of the signal due to the *endo*-positioned H1 was straightforward. Characteristic spatial interactions between $H1_{endo}$ and R^1 (in **9c,e-i** and **11e,g**) as well as between $H1_{endo}$ and H5 (in **10f,j**) were detected by a series of irradiations resulting in enhancements at least of 4% on the resonances involved. Further NOEs (4-12%) observed for the pairs of nuclei $H1_{endo}$-$H4_{endo}$ and $H4_{exo}$-H5 serve as additional evidences for the unexpected 5-*endo* substitution of tetracycles **9c,e-i** and **11e,g**. The structure of **9h** carrying the bulky R^1 = ^{t}Bu group in *endo* position was also confirmed by single-crystal X-ray analysis.

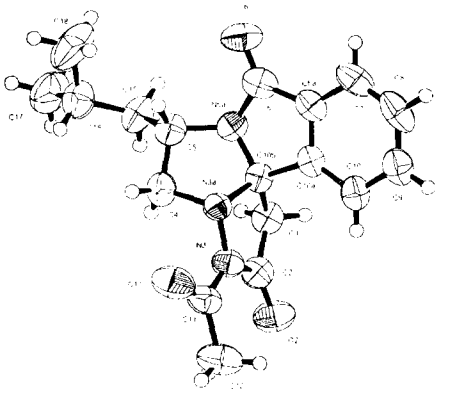
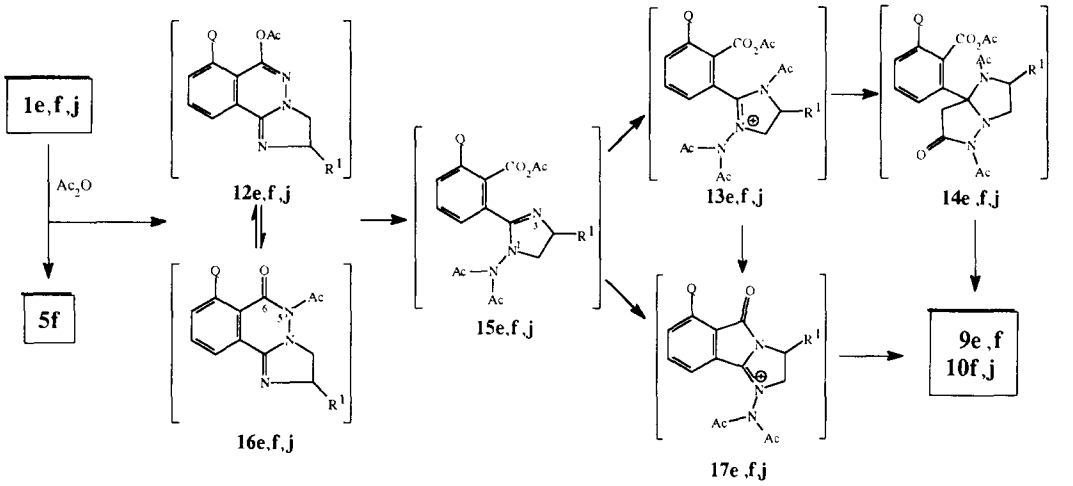


Figure: ORTEP drawing of **9h**

On the basis of the experimental findings summarized in Scheme 1 alternative mechanisms accounting also for the observed stereocontrol are proposed for the ring transformation reactions (Scheme 2). For the sake of simplicity the assumed pathways are presented only on the conversions of model compounds **1e,f,j** with acetic anhydride representing different regio- and diastereoselectivities (**1e** → **9e**; **1f** → **5f**, **9f**, **10f**; **1j** → **10j**). According to our view, due to the steric hindrance at the N1 atom, the primary acetylation takes place preferably on the amidate moiety to give intermediate O-acetyl-(**12**)- and/or N-acetyl (**16**) isomers being in equilibrium by O⇌N acyl migration[6]. In the presence of nitro group in position 7, however, the nucleophilicity of the adjacent amidate function is significantly decreased, as reflected from the formation of the poorly soluble and not reactive zwitterionic product **5f** in 18% yield. Consequently, the cleavage of the pyridazine ring at N5-C6 bond producing bicyclic intermediates (**15e,f,j**), which must be postulated to the ring transformation studied, is preceeded by the acetylation of the amidate moiety. The imidazolines **15e,f,j** produced in the ring

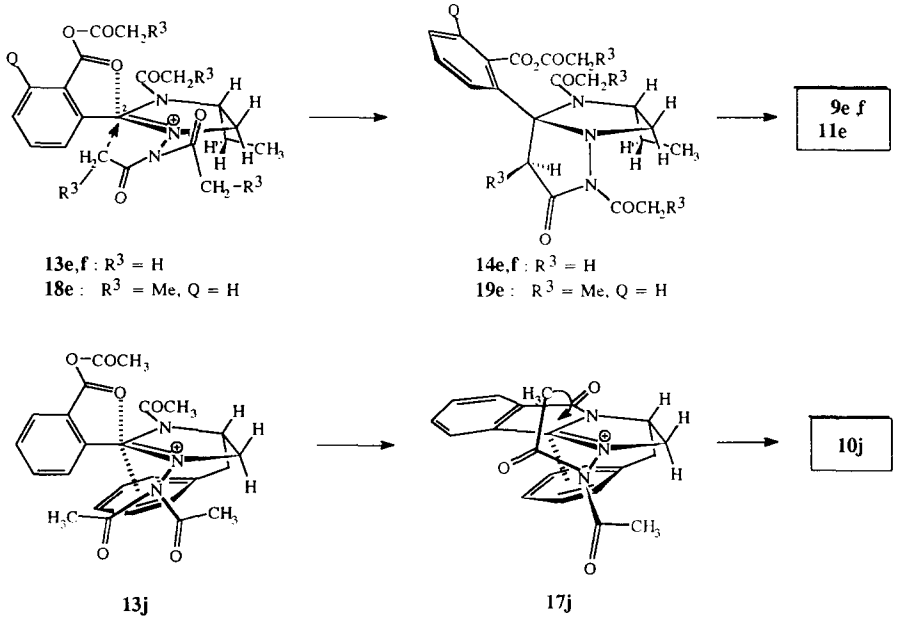
fission step can be acylated either by the reagent (**15** → **13**) or the acyloxycarbonyl group being inside the molecule (**15** → **17**). The tricyclic cations resulted from the intramolecular process can cyclize to yield the corresponding tetracyclic end-products (**17** → **9**, **10**) directly while the analogous ring closure of the bicyclic amidinium cations (**13** → **14**) must be followed by the loss of a molecule of acetic anhydride to furnish the same skeleton. Finally, the sequence including both bicyclic and tricyclic cations (**15** → **13** → **17** → **9**, **10**) can also be considered to build up triazapentalenoindanones.



Scheme 2 : **e**: Q = H R^1 = Et; **f**: Q = NO_2 R^1 = Et; **i**: Q = H R^1 = CH_2Ph

Each particular sequence staring from **15e,f,j** is consistent with the formation of particular diastereomers which can be shown in the following manner. Bicyclic intermediates of types **13** and **15** adopt the less crowded staggered conformations in which the bulky R^1 group and acyloxycarbonyl group are situated on the opposite sides of the five-membered ring. Especially in the cationic intermediates **13** (Scheme 3) such an arrangement can be stabilised by a stereoelectronic interaction[7] producing a weak bond between C2 atom of the imidazolinium ring and the oxygen of the carbonyl group attached to the aromatic ring. It follows that the formation of the C-C bond, the crucial step determining the stereostructure of triazapentalenoindanones, is allowed to take place from the opposite side. Consequently, in the resulting *cis*-fused bicyclic intermediates **14e,f** the ethyl group gets into *endo* position, which conformation is retained in **9e,f** formed in the last step. Due to the presence of donor benzene ring capable of occupying the opposite side relative to the carbonyl oxygen, an additional stereoelectronic interaction is supposed to exist in the benzyl-substituted cation **13j** (Scheme 3). Therefore, in this intermediate the formation of the C-C bond is prevented from either sides but, following the ring closure associated with the loss of acetic anhydride, the resulting tricyclic cation **17j**, which has a free side opposite to the interacting benzyl group, can cyclize to give selectively 5-*exo*-substituted

tetracycle **10j**. This special directing effect of the benzyl substituent is indirectly evidenced by reaction **1i** → **9i** (Scheme 1), in the course of which the phenyl group bonded directly to skeletal carbon atom is not able to get close to the electron–deficient part in the corresponding cationic intermediate, thus allowing the intermolecular nucleophilic attack from the same side (type **13** → **14**) finally leading to 5-*endo* substitution. On the other hand, it also means that the pathway including the same sequence (**15** → **13** → **14**) can generally be applied to the interpretation of the transformation yielding selectively 5-*endo* products of type **9**. In the course of reactions effected by propionic anhydride a simultaneous development of two asymmetry centres is assumed to take place in a similar cyclization of the appropriate staggered bicyclic intermediates (e. g. **18e** → **19e**; Scheme 3). In such cases R^1 substituent, being on the same side of the molecular plane, directs methyl group into the *exo* position of the resulting *cis*-fused system.



Scheme 3

Formation of the isomeric mixture of 5-ethyl-7-nitrotriazapentalenoindanones (**9f** : **10f** ≈ 2 :1) can be explained as follows. The intermolecular acylation of the imidazoline intermediate (**15f** → **13f**) leading finally to **9f** is probably accompanied by the intramolecular process (**15f** → **17f**) promoted by the electron-withdrawing group (Q = NO_2), and the ring closure of the resulting tricyclic cation takes place mainly from the site opposite to the ethyl group (**17f** → **10f**, Scheme 2). Nevertheless, according to modelling studies, the ethyl group in **17f** is too far from the cationic centre to have significant control over the final cyclization which, therefore, can also give **9f**.

Table 1: ^{1}H- and ^{13}C-NMR data[a,b] (δ in ppm, J in Hz) of compounds **9c-i**, **10f,j** and **11d,e,g** in $CDCl_3$ solution (δ_{TMS}=0 ppm)[c].

	$H1_{endo}$[d]	$H4_{endo}$[e]	H5[f]	H13[g]	H7[h]	H8[i]	C1	C4	C6	C6a	C7	C8	C11	C13
	$H1_{exo}$[j]	$H4_{exo}$[e]	H12[k]	H14[l]	H10[h]	H9[m]	C2	C5	C10a	C10b	C10	C9	C12	C14
9c	3.52	2.92	4.35	-	7.70	7.48	40.5	66.7	173.3	130.9	124.5	130.6	166.6	-
	3.04	4.39	2.51	-	7.31	7.53	170.8	51.8	146.6	85.5	120.9	133.7	24.6	-
9d	3.65	3.28	-	-	7.75	7.52	41.1	73.5	170.8	132.2	124.1	130.3	166.4	-
	2.93	4.17	2.47	-	7.38	7.59	170.2	60.7	146.7	86.7	120.4	133.4	24.6	-
9e	3.57	3.02	4.23	-	7.77	7.55	40.2	65.3	173.2	130.8	124.4	130.6	166.5	-
	3.10	4.45	2.58	-	7.40	7.61	170.7	57.4	146.6	85.4	120.8	133.6	24.6	-
9f	3.52	2.95	4.20	-	-	7.55	40.0	65.2	167.6	123.5	148.9	124.9	166.3	-
	3.04	4.38	2.51	-	7.85	7.69	169.9	58.1	146.1	84.6	125.2	134.6	24.6	-
9g	3.49	2.98	3.88	-	7.70	7.47	39.9	64.4	173.3	130.8	124.4	130.6	166.6	-
	3.02	4.36	2.50	-	7.31	7.53	170.8	62.2	146.5	85.5	120.8	133.6	24.6	-
9h	3.51	2.98	4.38	-	7.75	7.54	40.4	65.9	173.2	130.8	124.4	130.6	166.6	-
	3.11	4.42	2.57	-	7.39	7.60	170.8	54.6	146.7	85.5	120.9	133.7	24.6	-
9i	3.42	3.37	5.46	-	7.77	7.52	39.9	65.8	173.2	130.8	124.6	130.8	166.6	-
	3.01	4.64	2.44	-	7.38	7.58	170.2	58.2	146.4	85.9	121.2	133.9	24.6	-
10f	3.45	3.33	3.87	-	-	7.75	40.4	65.8	168.2	123.6	148.2	124.6	166.4	-
	3.09	3.50	2.52	-	7.60	7.69	169.3	58.7	146.2	85.3	125.0	134.4	24.7	-
10j	3.42	3.07[n]	4.15	-	7.70	7.48	40.6	65.7	170.0	131.9	124.1	130.4	166.4	-
	3.07[n]	3.64	2.44	-	7.38	7.55	169.4	57.2	145.9	86.4	121.3	133.6	24.6	-
11d	3.62	3.39	-	1.21	7.77	7.53[n]	42.7	72.5	170.4	133.4	124.4	130.2	173.0	8.9
	-	4.20	2.94	0.87	7.20	7.53[n]	170.5	61.1	142.6	91.1	121.8	132.3	30.3	8.3
11e	3.52	3.06	4.22	1.14	7.78	7.53[n]	42.1	64.6	173.5	131.9	124.9	130.4	173.0	9.0
	-	4.52	2.94	0.96	7.19	7.53[n]	170.6	57.8	142.5	89.9	122.1	132.6	30.3	8.3
11g	3.52	3.11	3.97	1.21	7.78	7.53[n]	41.8	63.7	173.4	131.8	124.8	130.4	173.0	8.9
	-	4.49	2.94	1.02	7.19	7.53[n]	170.6	62.5	142.3	89.9	122.1	132.5	30.4	8.3

[a] The numbering of atoms is shown in Scheme 1. [b] Assignments are supported by DEPT, D-NOE, 2D-COSY, 2D-HSC and 2D-HMBC measurements. [c] ^{1}H/^{13}C-NMR signals of R^1 and R^2=CH_3 groups: CH_3: 1.50 (3H, d, J=6.7)/22.1 for **9c**; 1.68 (6H, s)[n]/29.7, 25.4 for **9d**, **11d**. CH_2CH_3: 1.91, 180 (2x1H, 2m)/29.8 and 1.12 (3H, t, J=7.4)/11.0 for **9e,f**; 2.57 (2H, qi, J=7.3)/30.2 and 1.01 (3H, t, J=7.3)/11.7 for **10f**; 1.88, 1.72 (2x1H, 2m)/30.3 and 1.04 (3H, t, J=7.3)/11.0 for **11e**. $CH(CH_3)_2$: 1.85 (1H, m)/35.1 and 1.12, 0.94 (2x3H, 2d, J=6.9)/20.4, 19.0 for **9g**; 1.94 (1H, m)/35.6 and 1.20, 1.00 (2x3H, 2d, J=6.9)/20.5, 18.9 for **11g**. $CH_2CH(CH_3)_2$: 1.80, 1.53 (2H+1H, 2m)/46.2, 25.9 and 1.08, 1.01 (2x3H, 2d, J=6.3)/22.9, 22.3 for **9h**. C_6H_5: 7.30-7.24 (4H, m)/139.7, 129.0, 128.4, 125.2 for **9i**; 7.25-7.18 (4H, m)/137.8, 128.9, 128.8, 126.9 for **10j**. $\underline{CH_2}C_6H_5$: 4.19 (1H, dd, J=13.1, 4.2), 2.88 (1H, dd, J=13.1, 10.5)/35.2 for **10j**. [d] d (J=18.4±0.2) for **9**, **10** and qa (J=7.3) for **11**. [e] dd (J=10.3±0.2, 7.5±0.3) for **9c,e-i**, **10**, **11e,g** and d (J=10.5) for **9d**, **11d**. [f] sex (J=7.6) for **9c**, qi (J=7.5±0.2) for **9e,f,h**, **10**, **11e**, qa (J=7.8) for **9g**, **11g** and t (J=7.6) for **9i**. [g] t (J=7.3) for **9**, **10** and unresolved for **11**. [h] t (J=7.8) for **9c-e**, **g-i**, **10j**, d (J=7.8) for **9f**, **10f** and unresolved for **11**. [j] d (J=18.4±0.3). [k] s for **9**, **10** and qa (J=7.3) for **11**. [l] d (J=7.3). [m] t (J=7.8±0.2) for **9**, **10** and unresolved for **11**. [n] Overlapping signals.

Concluding Remarks

As discussed above, in the course of the ring transformations leading to **9-11**, development of the asymmetry centres at positions C10b and C1 is strongly influenced by the first asymmetry centre originally present in the tricyclic precursors. It follows that, starting from optically active tricyclic compounds of type **1** containing side chains of chiral aminoalcohols (as in **1c,g-j**; cf. Experimental), the asymmetric synthesis[8] of further optically active triazapentalenoindanones with two or more chirality centres can probably be achieved. Besides their preparative and stereochemical aspects, these reactions may be of pharmaceutical interest, as the triazapentalenoindenone skeleton incorporates the tricyclic tetrahydroimidazo[1,2-*a*]isoindolone as a main structural element of which aryl-substituted derivatives proved to be active inhibitors of HIV-1 reverse transcriptase[9].

Experimental

General: Melting points (uncorrected) were determined with a Boetius apparatus. Optical rotations were measured with a Zeiss POLAMAT A polarimeter. The IR spectra were recorded in KBr pellets with a BRUKER IFS 55 spectrometer. MS spectra were obtained with a KRATOS MS 50 double focused high resolution spectrometer (EI 70 eV). ^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 (internal reference TMS) at 500.13 and 125.77 MHz by a BRUKER DRX 500 instrument. The e.e. (>98%) for **9c,g–i**, **10j** and **11g** was determined by using Eu(hfc)$_3$.

2,3-dihydroimidazo[2,1-*a*]phthalazin-4-ium-6-olates (1a–j). Compounds 1a[5] and 1b[4] are described. Preparation of **1c-j** was carried out in two steps.

i) Applying the general method starting from phthalic or 3-nitrophthalic anhydride and the corresponding aminoalcohols[3a] a series of novel hydroxyalkylaminophthalazin-1(2*H*)-ones were synthetized as the precursors of **1c-j** in 50-70% overall yield.

(*S*)-4-(1-Hydroxy-2-propyl)aminophthalazin-1(2*H*)-one: mp 231-234°C; $[\alpha]_D^{20}$ -17.4° (c 0.005, EtOH); IR (cm^{-1}) 3340, 3145, 3300-2400 and 1648; ^{1}H-NMR (DMSO-d_6) 11.56 (1H, s), 8.23 (1H, d, J=7.8), 8.18 (1H, J=7.8), 7.89 (1H, t, J=7.8), 7.82 (1H, t, J=7.8), 6.14 (1H, d, J=7.3), 4.68 (1H, t, J=5.5), 3.92 (1H, sept, J=6.8), 3.58 (1H, dt, J=10.5, 5.5), 3.42 (1H, dt, J=10.5, 6.0), 1.21 (3H, d, J=6.4); ^{13}C-NMR (DMSO-d_6) 158.6, 145.2, 133.5, 131.9, 129.1, 127.1, 126.0, 65.0, 49.1, 18.0; Anal. Calcd for $C_{11}H_{13}N_3O_2$ (219.2): C, 60.26; H, 5.98; N, 19.17; Found: C, 60.15; H, 5.84; N, 19.10.

4-(2-Butyl-1-hydroxy)amino-8-nitrophthalazin-1(2*H*)-one: mp 221-224°C; IR (cm^{-1}) 3323, 3190, 3300-2400 and 1659; ^{1}H-NMR (DMSO-d_6) 11.89 (1H, s), 8.5 (1H, dd, J=6.9, 2.3), 8.12-8.07 (2H, m), 6.33 (1H, d, J=7.3), 4.63 (1H, t, J=5.5), 3.78 (1H, m), 3.56 (1H, dt, J=10.5, 5.5), 3.48 (1H, dt, J=10.5, 5.5), 1.73 (1H, m), 1.58 (1H, m), 0.93 (3H, t, J=7.3); ^{13}C-NMR (DMSO-d_6) 154.9, 149.7, 144.8, 134.6, 127.3, 126.9, 125.8, 119.4, 62.9, 55.1, 24.3, 11.5; Anal. Calcd for $C_{12}H_{14}N_4O_4$ (278.3): C, 51.80; H, 5.07; N, 20.13; Found: C, 51.60; H, 5.22; N, 20.02.

(*S*)-4-(2-Butyl-1-hydroxy-3-methyl)aminophthalazin-1(2*H*)-one: mp 240-241°C; $[\alpha]_D^{20}$ -171.4° (c 0.021, EtOH); IR (cm^{-1}) 3380, 3145, 3300-2400 and 1648; ^{1}H-NMR (DMSO-d_6) 11.52 (1H, s), 8.29 (1H, d, J=8.2), 8.24 (1H, d, J=7.8), 7.89 (1H, t, J=7.8), 7.82 (1H, t, J=7.8), 6.03 (1H, d, J=8.3), 4.52 (1H, t, J=5.5), 3.76 (1H, qi, J=6.0), 3.65-3.54 (2H, m), 2.07 (1H, m), 0.96 (3H, d, J=6.9), 0.94 (3H, d, J=6.9); ^{13}C-NMR (DMSO-d_6) 158.1, 145.3, 133.0, 131.4, 128.6, 126.6, 125.5, 123.6, 60.8, 57.9, 28.7, 19.7, 19.6; Anal. Calcd for $C_{13}H_{17}N_3O_2$ (247.3): C, 63.14; H, 6.93; N, 16.99; Found: C, 62.96; H, 6.99; N, 16.84.

(*S*)-4-(1-Hydroxy-4-methyl-2-pentyl)aminophthalazin-1(2*H*)-one: mp 208-11°C; $[\alpha]_D^{20}$ -68.6° (c 0.019, EtOH); IR (cm^{-1}) 3315, 3150, 3300-2400 and 1645; ^{1}H-NMR (DMSO-d_6) 11.48 (1H, s), 8.21 (2H, d, J=8.0), 7.86 (1H, t, J=5.6), 3.96, 3.50, 3.39, 1.72, 1.53 and 1.48 (6x1H, 6xm), 0.90 and 0.85 (2x3H, 2d, J=6.6) ; ^{13}C-NMR (DMSO-d_6) 157.6, 144.5, 132.6, 128.2, 126.2, 125.0, 123.1, 63.0, 50.3, 24.5, 23.3, 22.2; Anal. Calcd for $C_{14}H_{19}N_3O_2$ (261.3): C, 64.35; H, 7.33; N, 16.08; Found: C, 64.37; H, 7.16; N, 16.23.

(*S*)-4-(2-Ethyl-1-hydroxy-2-phenyl)aminophthalazin-1(2*H*)-one: mp 208-208.5°C; $[\alpha]_D^{20}$ -110.0° (c 0.0014, EtOH); IR (cm^{-1}) 3185, 3150, 3300-2400 and 1699; ^{1}H-NMR (DMSO-d_6) 11.49 (1H, d, J=8.2), 8.23 (1H, d, J=7.8), 7.96 (1H, t, J=7.8), 7.84 (1H, t, J=7.8), 7.41 (2H, d, J=7.3), 7.29 (2H, t, J=7.3), 7.20 (1H, t, J=7.3), 6.76 (1H, d, J=6.9), 4.97-4.91 (2H, m), 3.80-3.67 (2H, m); ^{13}C-NMR (DMSO-d_6) 158.1, 144.5, 142.4, 133.2, 131.6, 128.6, 128.3, 127.3, 126.9, 126.7, 125.4, 123.6, 57.9; Anal. Calcd for $C_{16}H_{15}N_3O_2$ (281.3): C, 68.31; H, 5.37; N, 14.94; Found: C, 68.21; H, 5.49; N, 14.78.

(*S*)-4-(1-Hydroxy-3-phenyl-2-propyl)aminophthalazin-1(2*H*)-one: mp 182.5-183°C; $[\alpha]_D^{20}$ -257.7° (c 0.016, EtOH); IR (cm^{-1}) 3370, 3330, 3300-2400 and 1652; ^{1}H-NMR (DMSO-d_6) 11.55 (1H, s), 8.22 (2H, d, J=7.8), 7.9 (1H, t, J=7.8), 7.81 (1H, t, J=7.8), 7.31 (2H, d, J=6.9), 7.25 (2H, t, J=7.3), 7.15 (1H, t, J=7.3), 6.29 (1H, d, J=7.8), 4.78 (1H, t, J=5.5), 4.05 (1H, m), 3.57 and 3.49 (2x1H, 2dt, J=11.0, 5.5), 2.97 and 2.93 (2H, A and B parts of an ABX spin system, J_{AB}=13.8, J_{AX}=6.4, J_{BX}=7.8); ^{13}C-NMR (DMSO-d_6) 158.1, 144.7, 140.4, 133.1, 131.5, 129.6, 128.6, 128.4, 126.6, 126.2, 125.4, 123.5, 62.2, 54.8, 36.8; Anal. Calcd for $C_{17}H_{17}N_3O_2$ (295.3): C, 69.14; H, 5.80; N, 14.23; Found: C, 69.03; H, 5.85; N, 14.18.

ii) **Cyclization of the precursors**. The preparation of **1a** and **1b** are described in Refs. 5 and 4, respectively. The 2-substituted analogues **1c-i** were synthetized by a general procedure as follows: To a solution of the corresponding precursor described above (0.01 mol) in dry pyridine (10 cm^3) cooled to 0°C was added *p*-tosyl chloride (5.72g, 0.03 mol). The reaction mixture was allowed to warm to room temperature, stirred overnight and diluted with water (50 cm^3) then stirred with chloroform (30 cm^3). The organic layer was separated,

washed with 3x50 cm^3 water and dried over anhydrous Na_2SO_4. After evaporation the oily residue was dissolved in abs. ethanol (20 cm^3) containing piperidine (2.0 cm^3, 0.02 mol). The resulting mixture was refluxed for 1 hour, then evaporated in *vacuo*. The residue was dissolved in dry acetonitril (10 cm^3) and the solution was allowed to stand in refrigator. The next day the precipitated yellow cubic crystals were filtered off, washed with acetonitril and dried. Recrystallization from ethanol gave **1c-i**. Yield: 50-85%.

(*S*)-2,3-Dihydro-2-methyl-imidazo[2,1-*a*]phthalazin-4-ium-6-olate (1c): mp 215-19°C (dec); $[\alpha]_D^{20}$ -44.1° (c 0.011, 5N HCl); IR (cm^{-1}) 3400-2200, 1620 and 1570; ^{1}H-NMR (DMSO-d_6) 8.81 (1H, br s), 8.27 (1H, d, J=7.9), 8.02 (1H, d, J=7.9), 7.90 (1H, t, J=7.3), 7.84 (1H, t, J=7.3), 4.52 (1H, dd, J=11.6, 8.2), 4.32 (1H, m), 4.14 (1H, dd, J=11.6, 8.2), 1.42 (3H, d, J=6.3); ^{13}C-NMR (DMSO-d_6) 162.9, 146.6, 134.6, 132.0, 130.6, 128.0, 125.3, 120.4, 60.8, 50.1, 21.8; Anal. Calcd for $C_{11}H_{11}N_3O$ (201.2): C, 65.66; H, 5.51; N, 20.88; Found: C, 64.97; H, 5.65; N, 20.75.

2,3-Dihydro-2,2-dimethylimidazo[2,1-*a*]phthalazin-4-ium-6-olate (1d): mp 260-65°C (dec); IR (cm^{-1}) 3400-2200, 1620 and 1570; ^{1}H-NMR (DMSO-d_6) 8.77 (1H, br s), 8.23 (1H, d, J=7.8), 8.01 (1H, d, J=7.8), 7.91 (1H, t, J=7.3), 7.84 (1H, t, J=7.3), 4.17 (2H, s), 1.47 (6H, s); ^{13}C-NMR (DMSO-d_6) 163.7, 144.7, 134.5, 131.8, 129.9, 128.1, 125.3, 119.6, 66.1, 58.0, 28.8; Anal. Calcd for $C_{12}H_{13}N_3O$ (215.3): C, 66.96; H, 6.09; N, 19.52; Found: C, 66.80; H, 6.02; N, 19.43.

2-Ethyl-2,3-dihydroimidazo[2,1-*a*]phthalazin-4-ium-6-olate (1e): mp 255-260°C (dec); IR (cm^{-1}) 3400-2200, 1620 and 1570; ^{1}H-NMR (DMSO-d_6) 8.83 (1H, br s), 8.23 (1H, d, J=8.0), 8.01 (1H, d, J=7.8), 7.91 (1H, t, J=7.3), 7.84 (1H, t, J=7.3), 4.54 (1H, dd, J=11.0, 9.2), 4.21 (1H, m), 4.11 (1H, dd, J=11.0, 9.2), 1.73 (2H, qi, J=7.3), 0.99 (3H, t, J=7.3); ^{13}C-NMR (DMSO-d_6) 164.1, 144.5, 134.6, 132.0, 130.0, 128.2, 125.3, 121.1, 59.2, 55.7, 28.6, 10.0; Anal. Calcd for $C_{12}H_{13}N_3O$ (215.3): C, 66.96; H, 6.09; N, 19.52; Found: C, 66.84; H, 5.98; N, 19.41.

2,3-Dihydro-2-ethyl-7-nitro-imidazo[2,1-*a*]phthalazin-4-ium-6-olate (1f): mp>350°C; IR (cm^{-1}) 3400-2200, 1611 and 1582; ^{1}H-NMR (DMSO-d_6) 8.83 (1H, br s), 8.27 (1H, d, J=7.8), 8.12 (1H, d, J=7.8), 8.01 (1H, t, J=7.8), 4.55 (1H, dd, J=11.0, 9.2), 4.21 (1H, m), 4.10 (1H, dd, J=11.0, 9.2), 1.73 (2H, qi, J=7.3), 0.99 (3H, t, J=7.3) ; ^{13}C-NMR (DMSO-d_6) 160.7, 145.5, 142.0, 132.8, 128.2, 128.1, 127.6, 122.2, 59.2, 55.7, 28.6, 10.1; Anal. Calcd for $C_{12}H_{12}N_4O_3$ (260.3): C, 55.38; H, 4.65; N, 21.53; Found: C, 55.55; H, 4.67; N, 21.65.

(*S*)-2,3-Dihydro-2-*iso*-propylimidazo[2,1-*a*]phthalazin-4-ium-6-olate (1g): mp 260-265°C (dec); $[\alpha]_D^{20}$ -22.7° (c 0.006, 5N HCl); IR (cm^{-1}) 3200-2200, 1625 and 1578; ^{1}H-NMR (DMSO-d_6) 8.78 (1H, br s), 8.23 (1H, d, J=7.8), 8.18 (1H, d, J=7.8), 7.91 (1H, t, J=7.8), 7.83 (1H, t, J=7.8), 4.49 and 4.13 (2x1H, 2dd, J=11.9, 9.6), 4.04 (1H, m), 1.89 (1H, m), 0.99 and 0.95 (2x3H, 2t, J=6.9); ^{13}C-NMR (DMSO-d_6) 164.8, 146.7, 134.5, 131.8, 130.8, 128.0, 125.6, 120.3, 59.8, 57.3, 33.1, 18.6, 18.5; Anal. Calcd for $C_{13}H_{15}N_3O$ (229.3): C, 68.10; H, 6.59; N, 18.33; Found: C, 67.95; H, 6.69; N, 18.53.

(*S*)-2-*iso*-Butyl-2,3-dihydroimidazo[2,1-*a*]phthalazin-4-ium-6-olate (1h): mp 281-283°C (dec); $[\alpha]_D^{20}$ -56.7° (c 0.006, 5N HCl); IR (cm^{-1}) 3200-2200, 1625 and 1578; ^{1}H-NMR (DMSO-d_6) 8.54 (1H, br s), 8.20 (1H, d, J=7.9), 8.05 (1H, d, J=7.8), 7.89 (1H, t, J=7.7), 7.82 (1H, t, J=7.8), 4.53 (1H, dd, J=11.6, 7.4), 4.28 (1H, qi, J=7.2), 4.02 (1H, dd, J=11.6, 7.4), 1.82 (1H, m), 1.63 (1H, m), 1.53 (1H, m), 0.96 and 0.95 (6H, two overlapping d's, J=5.6); ^{13}C-NMR (DMSO-d_6) 164.7, 146.7, 134.0, 131.3, 130.4, 127.6, 124.9, 120.4, 59.4, 52.2, 44.7, 24.6, 23.2, 22.5; Anal. Calcd for $C_{14}H_{17}N_3O$ (243.3): C, 69.11; H, 7.04; N, 17.27; Found: C, 69.03; H, 6.95; N, 17.20.

(*S*)-2,3-Dihydro-2-phenylimidazo[2,1-*a*]phthalazin-4-ium-6-olate (1i): mp 232-238°C (dec); $[\alpha]_D^{20}$ -19.6° (c 0.010, 5N HCl); IR (cm^{-1}) 3200-2200, 1620 and 1573; ^{1}H-NMR (DMSO-d_6) 9.14 (1H, br s), 8.26 (1H, d, J=8.0), 8.10 (1H, d, J=7.3), 7.52 (2H, d, J=7.3), 7.46 (2H, t, J=7.3), 7.40 (1H, t, J=7.3), 5.40 (1H, t, J=11.0), 4.88 and 4.25 (2x1H, 2t, J=11.0); ^{13}C-NMR (DMSO-d_6) 165.0, 146.4, 141.4, 134.6, 131.9, 131.0, 129.8, 129.2, 128.2, 127.7, 125.4, 120.3, 61.9, 57.2; Anal. Calcd for $C_{16}H_{13}N_3O$ (263.3): C, 72.99; H, 4.98; N, 15.96; Found: C, 72.86; H, 4.95; N, 15.84.

(*S*)-2-Benzyl-2,3-dihydroimidazo[2,1-*a*]phthalazin-4-ium-6-olate (1j): mp 281-83°C (dec); $[\alpha]_D^{20}$ -9.2° (c 0.007, 5N HCl); IR (cm^{-1}) 3200-2200, 1570 and 1545; ^{1}H-NMR (DMSO-d_6) 8.79 (1H, br s), 8.19 (1H, d J=7.8), 8.08 (1H, d, J=7.8), 7.90 (1H, t, J=7.8), 7.83 (1H, t, J=7.8), 7.36 (2H, d, J=7.3), 7.31 (2H, t, J=7.3), 7.23 (1H, t, J=7.3), 4.54 (1H, m), 4.45 (1H, t, J=11.9), 4.13 (1H, dd, J=11.9, 7.9), 3.03 (2H, br d); ^{13}C-NMR (DMSO-d_6) 163.1, 149.2, 137.3, 134.5, 131.9, 130.5, 130.3, 129.3, 128.0, 127.6, 125.4, 120.5, 58.6, 55.0, 41.4; Anal. Calcd for $C_{17}H_{15}N_3O$ (277.3): C, 73.63; H, 5.45; N, 15.15; Found: C, 73.48; H, 5.42; N, 14.99

Reaction of 1a-j with anhydrides. *General procedure*: A mixture of **1** (2 mmol) and the appropriate anhydride (2.0 cm^3) was refluxed for 2 hours. The solvent was evaporated in reduced pressure and water (10 cm^3) was added to the residue. The aqueous solution and the precipitate was extracted with chloroform (10 cm^3). The material insoluble in chloroform was filtered off to give **5b,f** and **6f**. Zwitterion **6a** was obtained by the evaporation of aqueous mother liquor and subsequent crystallization from ethanol. The chloroformic solution was washed with 20 cm^3 water, 2x20 cm^3 of 10% $NaHCO_3$ solution and 2x20 cm^3 water, then dried over anhydrous Na_2SO_4 and evaporated in *vacuo*. The residue was crystallized with ethanol and filtered off to obtain **9c-e,g-i**, **10j** and **11d,e,g** in practically pure form and a 2:1 mixture of **9f** and **10f**. Its repeated recrystallization (2x) from ethanol gave **9f** without being contaminated by **10f** of which attempted isolations have failed so far. Structure determination of **10f** was performed by taking NMR spectra of the 2:1 mixture samples of the two epimers (Table 1). Analitical samples of **9c-e,g-i**, **10j** and **11d,e,g** were also recrystallized from ethanol.

1-Acetyl-2,3-dihydro-2-ethyl-7-nitroimidazo[2,1-*a*]phthalazin-4-ium-6-olate (5f): Yield: 18%; mp>350°C; IR (cm^{-1}) 1693, 1604 and 1568; ^{1}H-NMR (DMSO-d_6) 8.18 (1H, d, J=7.8, H8), 8.14 (1H, d, J=8.3, H10), 7.98 (1H, t, J=8.2, H9), 5.03 (1H, dd, J=13.3, 7.3, H3 *cis* relative to H2), 4.82 (1H, qa, J=6.9, H2), 4.23 (1H, d, J=13.3, H3 *trans* relative to H2), 2.38 (3H, s, $C\underline{H}_3CO$), 1.81 (2H, m, $C\underline{H}_2CH_3$), 0.90 (3H, t, J=7.2, $CH_2C\underline{H}_3$),

diagnostic NOE's proving N1-acylation: [C$\underline{H}_3$CO]-H2 (12.5%), [C$\underline{H}_3$CO]-C$\underline{H}_2$CH$_3$ (17.9%); ^{13}C-NMR (DMSO-d$_6$) 171.0 (CH$_3$$\underline{C}$O), 163.7 (C6), 149.3 (C7), 138.4 (C10b), 132.4 (C9), 131.4 (C10), 128.2 (C8), 124.5 (C6a), 119.5 (C10a), 60.8 (C3), 59.1 (C2), 27.3 (C$\underline{H}_2$CH$_3$), 23.8 (C$\underline{H}_3$CO), 9.1 (CH$_2$C$\underline{H}_3$); Anal. Calcd for $C_{14}H_{14}N_4O_4$ (302.3): C, 55.63; H, 4.67; N, 18.53; Found: C, 55.50; H, 4.51; N, 18.36.

2,3-Dihydro-1-propionylimidazo[2,1-*a*]phthalazin-4-ium-6-olate (6a): Yield: 58%; mp 232-236°C (dec); IR (cm^{-1}) 1695, 1605 and 1590; ^{1}H-NMR (CDCl$_3$-DMSO-d$_6$ 4:1) 8.07 (1H, d, J=7.8, H7), 7.62 (1H, J=7.8, H10), 7.56 (1H, t, J=7.8, H9), 7.35 (1H, t, J=7.8, H8), 4.32 (2H, t, J=8.7, H3), 4.08 (2H, t, J=8.7, H2), 2.32 (2H, qa, J=6.9, CH$_3$C$\underline{H}_2$CO), 0.92 (3H, t, J=6.9, C$\underline{H}_3$CH$_2$CO); **diagnostic NOE proving N1-acylation**: [CH$_3$C$\underline{H}_2$CO]-H2 (13.7%); ^{13}C-NMR (CDCl$_3$-DMSO-d$_6$ 4:1) 171.9 (CH$_3$CH$_2$$\underline{C}$O), 167.1 (C6), 138.9 (C10b), 133.2 (C9), 130.1 (C8), 128.3 (C6a), 127.1 (C7), 126.4 (C10), 121.5 (C10a), 54.8 (C3), 44.1 (C2), 28.4 (CH$_3$$\underline{C}H_2$CO), 8.2 ($\underline{C}H_3CH_2$CO); Anal.Calcd. for $C_{13}H_{13}N_3O_2$ (243.3): C, 64.19; H, 5.39; N, 17.27; Found: C, 64.08; H, 5.46; N, 17.20.

2,3-Dihydro-2-ethyl-7-nitro-1-propionylimidazo[2,1-*a*]phthalazin-4-ium-6-olate (6f): Yield: 63%; mp 229-231°C (dec); IR (cm^{-1}) 1697, 1603 and 1567; ^{1}H-NMR (CDCl$_3$) 7.92 (1H, d, J=7.3, H10), 7.74-7.66 (2H, m, H8 and H9), 4.94 (1H, dd, J=13.8, 7.8, H3 *cis* relative to H2), 4.63 (1H, qa, J=6.9, H2), 4.09 (1H, d, J=13.8 H3 *trans* relative to H2), 2.70 and 2.55 (2x1H, 2dqa, J=16.5, 7.3, CH$_3$C$\underline{H}_2$CO), 1.79 (2H, qi, J=7.0, C$\underline{H}_2$CH$_3$), 1.24 (3H, t, J=7.3, C$\underline{H}_3$CH$_2$CO), 0.91 (3H, t, J=7.3, C2-CH$_2$C$\underline{H}_3$); **diagnostic NOE's proving N1-acylation**: [CH$_3$C$\underline{H}_2$CO]-C$\underline{H}_2$CH$_3$ (18.8% and 25.2%); ^{13}C-NMR (CDCl$_3$) 173.0 (C10b), 131.0 (C9), 130.0 (C10), 127.1 (C8), 124.9 (C6a), 119.8 (C10a), 60.3 (C3), 58.0 (C2), 28.3 (C$\underline{H}_2$CH$_3$), 27.6 (CH$_3$$\underline{C}H_2$CO), 9.0 (CH$_2$$\underline{C}H_3$), 8.4 ($\underline{C}H_3CH_2$CO); Anal. Calcd for $C_{15}H_{16}N_4O_4$ (316.3): C, 56.96; H, 5.10; N, 17.71; Found: C, 56.85; H, 5.03; N, 17.65.

(5*S*,10b*R*)-3-Acetyl-1,2,3,3*a*,4,5,6,6*a*-oktahydro-5-methyl-3,3*a*,5*a*-triazapentaleno[3*a*,3-*a*]inden-2,6-dione (9c): Yield: mp 192-194°C; $[\alpha]_D^{20}$ -65.4° (c 0.005, CCl$_4$); MS m/z 284 (M$^+$); IR (cm^{-1}) 1773, 1732 and 1703; Anal. Calcd for $C_{15}H_{15}N_3O_3$ (285.3): C, 63.15; H, 5.30; N, 14.73; Found: C, 63.07; H, 5.28; N, 14.66.

(10b*R)-3-Acetyl-1,2,3,3*a*,4,5,6,6*a*-oktahydro-5,5-dimethyl-3,3*a*,5*a*-triazapentaleno[3*a*,3-*a*]inden-2,6(3*H*, 5a*H*)-dione (9d)**: Yield: 76%; mp 226-228°C; MS m/z 299 (M$^+$); IR (cm^{-1}) 1744, 1710 and 1708; Anal. Calcd for $C_{16}H_{17}N_3O_3$ (299.3): C, 64.20; H, 5.72; N, 14.04; Found: C, 64.16; H, 5.71; N, 13.96.

(5*R,10b*S**)-3-Acetyl-5-ethyl-1,2,3,3*a*,4,5,6,6*a*-oktahydro-3,3*a*,5*a*-triazapentaleno[3*a*,3-*a*]inden-2,6(3*H*, 5a*H*)-dione (9e)**: Yield: 62%; mp 197-199°C; MS m/z 299 (M$^+$); IR (cm^{-1}) 1745, 1725 and 1713; Anal. Calcd for $C_{16}H_{17}N_3O_3$ (299.3): C, 64.20; H, 5.72; N, 14.04; Found: C, 64.40; H, 5.71; N, 14.15.

(5*R,10b*S**)-3-Acetyl-5-ethyl-1,2,3,3*a*,4,5,6,6*a*-oktahydro-7-nitro-3,3*a*,5*a*-triazapentaleno[3*a*,3-*a*]inden-2,6(3*H*, 5a*H*)-dione (9f)**: Yield: 31%; mp 232-235°C; MS m/z 344 (M$^+$); IR (cm^{-1}) 1748, 1728, 1720, 1535 and 1370; Anal. Calcd for $C_{16}H_{16}N_4O_5$ (344.3): C, 55.81; H, 4.68; N, 16.27; Found: C, 55.73; H, 4.62; N, 16.18.

(5*S*,10b*R*)-3-Acetyl-1,2,3,3*a*,4,5,6,6*a*-oktahydro-5-*iso*-propyl-3,3*a*,5*a*-triazapentaleno[3*a*,3-*a*]inden-2,6(3*H*, 5a*H*)-dione (9g): Yield: 57%; mp 196.5-197.5°C; $[\alpha]_D^{20}$ -176.7° (c 0.005, CCl_4); MS m/z 313 (M^+); IR (cm^{-1}) 1760, 1730 and 1702; Anal. Calcd for $C_{17}H_{19}N_3O_3$ (313.4): C, 65.16; H, 6.11; 13.40; Found: C, 64.99; H, 6.12; N, 13.21.

(5*S*,10b*R*)-3-Acetyl-5-*iso*-butyl-1,2,3,3*a*,4,5,6,6*a*-oktahydro-3,3*a*,5*a*-triazapentaleno[3*a*,3-*a*]inden-2,6(3*H*, 5a*H*)-dione (9h): Yield: 51%; mp 165.5-166.5°C; $[\alpha]_D^{20}$ -163.7° (c 0.006, EtOH); MS m/z 327 (M^+), IR (cm^{-1}) 1749, 1730 and 1715; Anal. Calcd for $C_{18}H_{21}N_3O_3$ (327.4): C, 66.03; H, 6.47 ; N, 12.83; Found: C, 65.96; H, 6.38; N, 12.75.

(5*S*,10b*R*)-3-Acetyl-1,2,3,3*a*,4,5,6,6*a*-oktahydro-5-phenyl-3,3*a*,5*a*-triazapentaleno[3*a*,3-*a*]inden-2,6(3*H*, 5a*H*)-dione (9i): Yield: 48%; mp 241-243°C; $[\alpha]_D^{20}$ -98.1° (c 0.003, CCl_4); MS m/z 323 (M^+); IR (cm^{-1}) 1748, 1728 and 1716; Anal. Calcd for $C_{18}H_{17}N_3O_3$ (323.4): C, 66.86; H, 5.30; N, 13.00; Found: C, 66.79; H, 5.23; N, 13.11.

(5*S*,10b*S*)-3-Acetyl-1,2,3,3*a*,4,5,6,6*a*-oktahydro-5-benzyl-3,3*a*,5*a*-triazapentaleno[3*a*,3-*a*]inden-2,6(3*H*, 5a*H*)-dione (10j): Yield: 44%; mp 253-256°C; $[\alpha]_D^{20}$ +171.5° (c 0.002, $CHCl_3$); MS m/z 361 (M^+); IR (cm^{-1}) 1747, 1710 and 1698; Anal. Calcd for $C_{21}H_{19}N_3O_3$ (361.4): C, 69.79; H, 5.30; N, 11.63; Found: C, 69.63; H, 5.27; N, 11.52.

(1*R,10b*R**)-1,2,3,3*a*,4,5,6,6*a*-Oktahydro-1,5,5-trimethyl-3-propionyl-3,3*a*,5*a*-triazapentaleno[3*a*,3-*a*]inden-2,6(3*H*, 5a*H*)-dione (11d)**: Yield: 75%; mp 209-211°C; MS m/z 327 (M^+); IR (cm^{-1}) 1742, 1710 and 1695; Anal. Calcd for $C_{18}H_{21}N_3O_3$ (327.4): C, 66.04; H, 6.47; N, 12.84; Found: C, 65.93; H, 6.39; N, 12.70.

(1*R,5*S**,10b*R**)-5-Ethyl-1,2,3,3*a*,4,5,6,6*a*-oktahydro-1-methyl-3-propionyl-3,3*a*,5*a*-triazapentaleno[3*a*,3-*a*]inden-2,6(3*H*, 5a*H*)-dione (11e)**: Yield: 64%; mp 201-203°C; MS m/z 327 (M^+); IR (cm^{-1}) 1740, 1722 and 1710; Anal. Calcd for $C_{18}H_{21}N_3O_3$ (327.4): C, 66.04; H, 6.47; N, 12.84; Found: C, 65.90; H, 6.64; N, 12.72.

(1*R*,5*S*,10b*R*)-1,2,3,3*a*,4,5,6,6*a*-Oktahydro-1-methyl-3-propionyl-5-*iso*-propyl-3,3*a*,5*a*-triazapentaleno[3*a*,3-*a*]inden-2,6(3*H*, 5a*H*)-dione (11g): Yield: 55%; mp 185-87°C; $[\alpha]_D^{20}$ -122.0° (c 0.002, CCl_4); MS m/z 341 (M^+); IR (cm^{-1}) 1747, 1729 and 1713; Anal. Calcd for $C_{19}H_{23}N_3O_3$ (341.4): C, 66.84, H, 6.79; N, 12.31; Found: C, 66.75; H, 6.75; N, 12.23.

^1H- and ^{13}C-NMR data of **9**–**11** are listed in Table 1.

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