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Aggregative Activation and Heterocyclic Chemistry I Complex Bases promoted Arynic Cyclisation of Imines or Enaminoketones ; Regiochemical Synthesis of Indoles

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Abstract: The complex base $NaNH_2$-*t*-BuONa allowed expeditious syntheses of indoles by arynic cyclisation of imines or enaminoketones prepared from halogeno anilines and carbonyl derivatives. Unstable imines may be used without purification, complex bases being unsensitive to impurities. It is showed that this kind of reaction may be applied to mixture of substrates suitably halogenated on the benzene ring. Formation of three components aggregates is proposed to explain a number of observations.

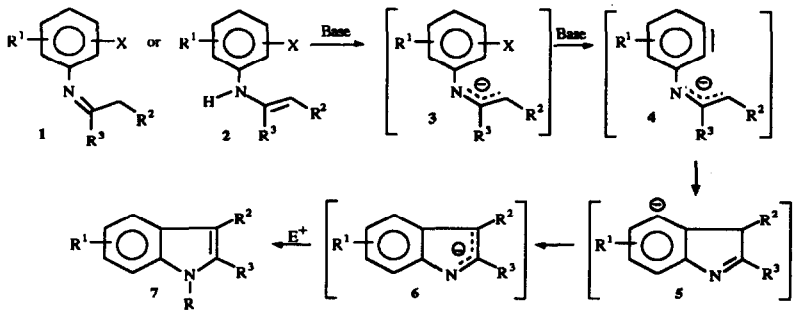
The consequence of the paramount position held by indoles in chemistry of natural products[1] as well as in medicinal chemistry[2] is that numerous synthetic methods were devised in order to reach such kind of heterocycles.[3] However, examination of the abondant literature shows that number of drawbacks of the syntheses described incite organic chemists in continuing to conceive new approaches of these compounds. In other words a need still exists for new and preferentially inexpensive preparation of indoles.

The extended experience of our laboratory in arynic chemistry[4] led us to consider that intramolecular arynic cyclisations of aryl halides bearing appropriate nitrogen functions ought to be of interest in such investigations. We thought that a simple way to perform such syntheses could be the cyclisation of the anionic aryne **4** (Scheme 1) which could be conveniently reached from the simple starting materials **1** or **2**.

Besides the easy accessibility of the starting materials this synthesis presented three interesting characteristics : i) the cyclisation is regiospecific; ii) arynes **4** may be generated from aryl halides bearing halogen atom on the 2 or 3 position relative to the nitrogen allowing, if necessary, the use of a mixture of both halides. A situation met when the aryl halides are obtained by halogenation of aromatic derivatives; iii) N-substituted indoles **7** may be obtained one pot by trapping the anion **6** with appropriate electrophiles.

However to be useful on small as well as large scale the synthesis has to fulfill some conditions.

Scheme 1



The necessary base must be commercially available, inexpensive and easily handled even on large scale. Thus lithium containing bases such as lithium amides sometimes used in arynic reactions[5] should be discarded. Indeed such bases are obtained from expensive lithium alkyl reagents not easily handled on large scale. Moreover lithium amides and their corresponding amines are potential nucleophiles which may compete with the anionic part of **4** for the aryne.[6] Discarded also was the expensive KNH_2 prepared from potassium and generally used in liquid NH_3.[7] Finally $NaNH_2$ appeared as the best base. From our previous works on the activation of bases[4e] we could assert that if **3** was able to aggregate with $NaNH_2$ and thus to activate this base, **4** could be generated. Thus the reaction could be performed with $NaNH_2$ alone in solvents such as THF or DME instead of liquid NH_3. Now if **3** was not a good activating agent, the problem could be solved by using a unimetal superbase[8] such as the non nucleophilic complex bases[9] $NaNH_2$-RONa (where RONa is an alkoxide) in ethereous solvents. It must be incidentally noted that complex bases have already been industrially used.[8]

Last but not least the cyclisation must tolerate the presence of ketones and amines. Indeed it is well known that imines may be unstable. In such cases they must be used as crude products containing more or less large amounts of the starting materials used for their preparation.

A few exploratory experiments[3f,4h] showed that the reactions reported in Scheme 1 seemed to fulfill the conditions above mentioned and appeared as promising as new indole synthesis. Note that a number of arynic synthesis of indole derivatives have been described in the literature and that till our first preliminary publications[3f] none of them used aryl imines enolates as starting material. In fact two main cyclisations were described. The first one deals with the arynic condensations of amine derivatives leading to indoline,[3a,b,e,h,l] the critical oxydation of which is necessary in order to reach the corresponding indoles. The second one, described a long time ago, deals with arynic condensation of amide enolates[3c,d] and led only to the formation of 2-hydroxyindole derivatives. The above synthesis use organolithium compounds or lithium amides or alkali amides in liquid NH_3. Moreover none of them allowed the one pot synthesis of N-substituted indoles.

In the present publication we wished to present more details on our cyclisations and their scope and limitations.

Cyclisation of imines

The most significative results obtained with a number of imines prepared from representative anilines and carbonyl derivatives are reported in Table I.

We devoted a particular attention to the imines coming from the commercially available 3-chloro-4-methoxy aniline which cyclisation should result in the formation of 5-methoxy indoles of special interest in pharmaceutical and medicinal chemistry.[10] Runs 1 to 12 correspond to the main results of a systematic study performed with imines coming from this particular aniline and three cyclanones.

It soon appeared that the imine enolates were not good activating agents for $NaNH_2$ (runs 1, 6). As expected replacement of $NaNH_2$ by the complex base $NaNH_2$-*t*-BuONa (runs 2, 3, 7) considerably improved the results. Note that even in benzene (run 4) the result was better with a complex base than with $NaNH_2$ in the more polar THF. The best ratio substrate/$NaNH_2$/*t*-BuONa was found to be 1/5/2 and a few comments must be given.

It is now firmly established that the efficiency of sodium amide containing complex bases depends on the ratio $NaNH_2$/activating agent and that the best ratio is 2/1.[4, 9, 12] Thus since one equivalent of $NaNH_2$ was used to generate **3** the ratio **3**/$NaNH_2$/*t*-BuONa was 1/4/2 ($NaNH_2$/*t*-BuONa = 2) which corresponds to a ratio **1**/$NaNH_2$/*t*-BuONa equal to 1/5/2 (as mentioned in Table I).

At this point while we *a priori* discarded lithium amides as bases, we wanted to compare the efficiency of the complex base with one of these reagents. LDA, the most commonly used was chosen.

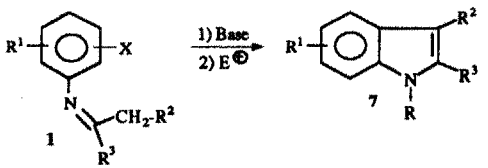
This comparison was performed with the imine of cyclooctanone used in run 10. When this compound was reacted with LDA (2 equivalents) in hexane-THF (1/2) at 0°C and then 45°C no substantial cyclisation was observed after 8 days. In the presence of 5 equivalents no reaction took place at room temperature after 22 hours. At 45°C indole was isolated with 70 % yield after 48 hours. In order of comparing more rigorously, the cyclisation with the complex base was repeated in hexane-THF (1/2). The indole was then obtained with 65% yield after 30 hours at room temperature. In fact according to the reaction performed in pure benzene (run 4) this result was not unexpected. Thus the result obtained in run 10 compare very favorably and shows that LDA may be advantageously replaced by the complex base $NaNH_2$-*t*-BuONa in THF.

In order of obtaining informations about the behaviour of our reaction medium we examined (runs 5, 8, 9, 11, 12) the one pot condensation of a number of representative electrophiles of interest for future pharmaceutical applications. Comparison with the corresponding protonations shows that the condensation of the electrophiles took place with yields varying from 60% to quantitative. The unexpected variation of yields between runs 10 and 11 was due to the fact that the N-methyl indole was more easily isolated than the corresponding protonated one. Note that the addition of DMF to the reaction medium was necessary to conveniently condense the bromoesters. It is noteworthy that the presence of the base sensitive ester group in the electrophile was tolerated under our conditions.

From the Table I it appears that these cyclisations are of general application and may be extended to imines coming from dialkyl (runs 1-17 and 28-37), alkyl aryl or hetero aryl ketones (runs 18-23) as well as from aldehydes (run 27). Potential functional group may be also introduced as illustrated in run 24. It must be underlined that even sensitive derivatives such as the imine of the 3-keto thiopyran may be transformed into the corresponding indole with rather good yields (runs 25, 26).

Finally we examined the sensitivity to impurities of this kind of cyclisation. Thus run 15 was repeated with a mixture of 3-chloro 4-methoxy aniline and the corresponding imine of acetone in 1/1 ratio. Using an excess of complex base (10 $NaNH_2$ / 4 *t*-BuONa) to neutralise the aniline, 85% of the expected indole was obtained, a better yield than starting from the pure imine. In the same way the crude product of the reaction of 3-

Table I



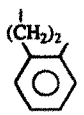
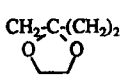
Run a)	R1 b)	X b)	R2 b)	R3 b)	Base NaNH2/t-BuONa	t°C	t (h)	E	R	7 % c)
1	4-MeO	3-Cl	$(CH_2)_4$		5/-	0°-RT	> 48	H_3O^+	H	25
2	4-MeO	3-Cl	$(CH_2)_4$		4/1.5	0°-RT	24	H_3O^+	H	40
3	4-MeO	3-Cl	$(CH_2)_4$		5/2	0°-RT	24	H_3O^+	H	75
4	4-MeO	3-Cl	$(CH_2)_4$		5/2	0°-RT	40	H_3O^+	H	46
5	4-MeO	3-Cl	$(CH_2)_4$		5/2	0°-RT	24	Me_2SO_4 (3eq)	Me	77
6	4-MeO	3-Cl	$(CH_2)_5$		7/-	0°-RT	24	H_3O^+	H	12
7	4-MeO	3-Cl	$(CH_2)_5$		5/2	0°-RT	24	H_3O^+	H	81
8	4-MeO	3-Cl	$(CH_2)_5$		5/2	0°-RT	24	Me_2SO_4 (3eq)	Me	60
9	4-MeO	3-Cl	$(CH_2)_5$		5/2	0°-RT	24	$BrCH_2COOEt$ (4eq) d)	CH_2COOEt	50
10	4-MeO	3-Cl	$(CH_2)_6$		5/2	0°-RT	24	H_3O^+	H	77
11	4-MeO	3-Cl	$(CH_2)_6$		5/2	0°-RT	24	Me_2SO_4 (3eq)	Me	88
12	4-MeO	3-Cl	$(CH_2)_6$		5/2	0°-RT	24	$BrCH_2COOtBu$ (3eq) d)	$CH_2COOtBu$	47
13	4-MeO	3-Cl	$(CH_2)_{10}$		5/2	0°-RT	24	H_3O^+	H	70
14	4-MeO	3-Cl	$(CH_2)_{10}$		5/2	0°-RT	24	Me_2SO_4 (3eq)	Me	62
15	4-MeO	3-Cl	H	Me	5/2	0°-RT	24	H_3O^+	H	66
16	4-MeO	3-Cl	H	2-Norbornyl	5/2	0°-RT	24	H_3O^+	H	75
17	4-MeO	3-Cl	H	2-Norbornyl	5/2	0°-RT	24	Me_2SO_4 (3eq)	Me	67
18	4-MeO	3-Cl	H	Ph	5/2	0°-RT	24	H_3O^+	H	65
19	4-MeO	3-Cl			5/2	-10°-RT	24	H_3O^+	H	60

Table I continued

Run a)	R^1 b)	X b)	R^2 b)	R^3 b)	Base $NaNH_2$/*t*-BuONa	t°C	t (h)	E	R	7 % c)
21	4-MeO	3-Cl	H	2-Furyl	5/2	0°-RT	24	H_3O^+	H	70
22	4-MeO	3-Cl	H	2-Furyl	5/2	0°-RT	24	Me_2SO_4 (3eq)	Me	58
23	4-MeO	3-Cl	H	2-Thienyl	5/2	0°-RT	24	H_3O^+	H	81
24	4-MeO	3-Cl	H	2-Thienyl	5/2	0°-RT	24	Me_2SO_4 (3eq)	Me	76
25	4-MeO	3-Cl			5/2	0°-RT	24	H_3O^+	H	63
26	4-MeO	3-Cl	S-$(CH_2)_3$		5/2	RT	12	H_3O^+	H	53
27	4-MeO	3-Cl	S-$(CH_2)_3$		5/2	RT	12	$BrCH_2COOEt$ (4eq) d)	CH_2COOEt	46
28	4-MeO	3-Cl	$(CH_2)_4CH_3$	H	5/2	0°-RT	48	H_3O^+	H	60
29	H	3-Cl	$(CH_2)_4$		5/2	RT	4 days	H_3O^+	H	70
30	H	2-Cl	$(CH_2)_4$		5/2	60	48	H_3O^+	H	53
31	4-Me	3-Cl	$(CH_2)_4$		5/2	RT	55	H_3O^+	H	60
32	4-Me	3-Cl	$(CH_2)_4$		5/2	RT	55	Me_2SO_4 (3eq)	Me	61
33	4-Me	2-Cl	$(CH_2)_4$		5/2	50-55	5 days	H_3O^+	H	20
34	4-F	3-Cl	$(CH_2)_4$		5/2	RT	2 days	H_3O^+	H	60
35	4-F	2-Cl	$(CH_2)_4$		5/2	0	2	H_3O^+	H	62
36	2-Me	5-Cl	$(CH_2)_4$		5/2	50	24	H_3O^+	H	60
37	2-Me	5-Cl	$(CH_2)_4$		5/2	50	24	Me_2SO_4 (3eq)	Me	65
38	2-MeO	5-Cl	$(CH_2)_4$		5/2	50	5 days	Me_2SO_4 (3eq)	Me	50

a) The reactions were performed in THF as solvent, except run 4 which was performed in C_6H_6 ; b) The index number correspond to the position of the substituant on the starting materials ; c) Isolated yields ; d) Compounds **6** were added to a solution of electrophile in DMF.

chloro 4-methoxy aniline with 3-keto thiopyran in benzene was submitted to the condition of run 25 after simple removing of the solvent under vacuum. The corresponding indole was obtained with 52% yield with respect to the imine containt (evaluated by gpc).

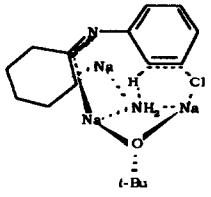
In order to complete our results, we investigated the cyclisation of imines coming from cyclohexanone and anilines variously substituted on the benzene ring.

An interesting observation emerged from the cyclisation of unsubstituted and 4-methyl, 2-and 3-chloroimines. Indeed 3-chloro derivatives were much more reactive and cyclised at room temperature while 50 to 60°C were necessary to cyclise 2-chloroimines. Although 3-benzyne derivative (which cannot cyclise) may be formed in run 28, yield of cyclisation was better than in run 29. Taking account of the mechanism of generation of arynes,[4e] it must be concluded that the hydrogen ortho to the nitrogen in the 3-chloroimine is more easily abstracted.

On the other hand we have previously shown[11] that arynes of salts of halogenated anilines are not generated under mild conditions. This lack of reactivity is of course due to a too large delocalization of the negative charge of the nitrogen on the benzene ring.

The results observed in the present work must then be interpreted as follow. The electronic charge of the imine enolates must be strongly localized on the carbon in such a way that the imine group continue to exert its weak electron withdrawing effect.[13] Moreover according to the principles of the aggregative activation it must be expected that the imine enolates must be included in three components aggregates[8] containing $NaNH_2$ and *t*-BuONa. Such aggregates must contribute to the localization of the charge on the carbon atom and facilitate the abstraction of the proton in the ortho position of the nitrogen as symbolized in Scheme 2.

Scheme 2



Moreover such aggregate may be expected as sterically favoring the condensation of the carbon enolate by directing this reactive center toward the aryne bond.

We shall see later that this hypothesis is supported by results obtained with enaminoketones. Note that directory effects during the generation of arynes and their condensation with nucleophiles has some precedents in the literature.[14]

The important part also played by the acidity of the proton removed during the formation of the benzyne is well illustrated by runs 33 and 34, the 2-chloro 4-fluoroimine being much more reactive than the corresponding 3-chloroimine.

It must be emphasized that runs 28 to 34 show that mixture of 2 and 3-haloarylimines may be used in these cyclisations if needed, although the presence of an 4-alkyl group with 2-chloro derivatives seems unfavorable to these condensations (run 32).

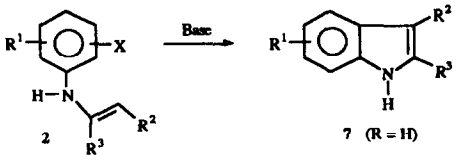
Finally 5-chloro 2-methyl or 2-methoxy imines appeared as less reactive than other 3-chloro imines. Such observation may be attributed to steric hindrance during the enolization step. Moreover a partial complexation of the sodium cation with the methoxy group must be responsible for the very low reactivity observed in run 37.

From the results reported it appears that the proposed cyclisation works well with imines, fulfills the conditions we imposed and is of synthetic interest in the synthesis of indoles.

Cyclisation of enaminoketones

We first studied the behaviour of N-unsubstituted enamino ketones **2**. The main results are reported in Table II. Control experiments showed that the sodium salts of these derivatives did not activate $NaNH_2$ enough. Thus the complex base $NaNH_2$-*t*BuONa was used to perform the cyclisations.

Table II



Run a)	R^1 b)	X b)	R^2	R^3	Base $NaNH_2$/*t*-BuONa	t°C	t (h)	7 R = H % c)
1	4-OMe	3-Cl	-C(O)-CH_2-C(Me)$_2$-CH_2-		5/2	40-50	4	62
2	4-OMe	3-Cl	-C(O)-$(CH_2)_3$-		5/2	40-50	5	60
3	4-Me	3-Cl	-C(O)-CH_2-C(Me)$_2$-CH_2-		5/2	45	4	50
4	4-Me	3-Br	-C(O)-CH_2-C(Me)$_2$-CH_2-		5/2	20	3	45
5	4-F	3-Cl	-C(O)-CH_2-C(Me)$_2$-CH_2-		5/2	20	48	58
6	4-F	2-Cl	-C(O)-CH_2-C(Me)$_2$-CH_2-		5/2	0→20	4	75
7	2-Me	5-Cl	-C(O)-$(CH_2)_3$-		5/2	50	24	30
8	2-Me	5-Cl	-C(O)-CH_2-C(Me)$_2$-CH_2-		5/2	50	4	41

a) All the reactions were performed in THF and hydrolized by H_3O^+. b) The index number correspond to the position of the substituent on the starting materials. c) Isolated yields.

Lower yields of **7** were obtained (unreported experiments) starting from 2-halogeno derivatives corresponding to those of runs 3 and 4. Such a difference may be found in the formation of mixed aggregates ressembling the ones proposed with imine enolates (Scheme 2) favouring the aryne formation step as well as the nucleophilic condensation of the enamino salts.

Comparison of the data of Tables I and II showed that most part of the enamino ketones were less reactive than the corresponding imines and higher reaction temperatures were needed. This behaviour could be due to a looser interaction of the enamine salt in the aggregates leading to a larger electron density delocalized on the benzene ring which consequence is a decrease in the rate of the aryne formation, the rate limitation step.

As mentioned with imines, the acidity of the proton involved in the benzyne generation is also an important factor as illustrated by the higher reactivity of the 2-chloro-4-fluoro enamino ketone compared to the 3-chloro derivative (runs 5, 6).

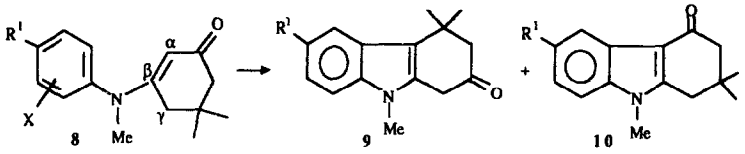
Finally the intriguing spectroscopic properties of the tetrahydrocarbazolones reported in the Table II have to be mentioned. The IR and NMR spectra (see experimental part) indicated that these derivatives should be under enolic form with characteristic absorptions at 3170 cm^{-1} (OH) and 1610 cm^{-1} (C=C). These data agreed with those given in the literature which, curiously, were attributed to the ketonic structure.[15] To clarify the situation we trapped the salt formed in run 7 (Table II) with methanesulfonyl chloride. The N-methanesulfonate

derivative obtained possessed an IR absorption at 1654 cm^{-1} and all the characteristics expected for a keto derivative (see experimental part) supporting thus the enolic form of the N-unsubstituted derivative.

To confirm the enolic form we undertake to compare the electronic spectra (see experimental part) of **7** R^1=4-OMe, R^2R^3=-$COCH_2C(Me)_2CH_2$-, R=H and **7** R^1=4-F, R^2R^3=-$COCH_2C(Me)_2CH_2$-, R=H (Table II) with those of the corresponding N-methylated compound obtained during further condensations (see later **10** R^1=OMe and **10** R^1=F respectively, Table III). In contradiction with what was expected, these data led to conclude that all the products were in the ketonic form. In order to clarify this puzzling situation we undertook X ray diffraction study of the compound prepared in run 7 (Table II) which gave acceptable single crystals. It was found[16] that the data corresponded to a ketonic form. However strong hydrogen bonds between the N-H and the carbonyl group were also evidenced. So we concluded that such strong interactions continued to take place in solution accounting for the IR and ^1H NMR data.

With the above results in hand we decided to briefly examine the behaviour of a few N-substituted enamino ketones and dimedone was chosen as starting diketone. These substrates appeared of interest both from the synthetic and mechanistic point of views more especially as in the presence of lithium amides such cyclisations were unsuccessful.[6] The difference with the cyclisations described above lies on the nature of the nucleophilic parts which are actual enolates of α,β-unsaturated ketones with no potential electron density on the nitrogen. Thus these compounds must be more reactive than N-unsubstituted enaminoketones since the corresponding arynes must be more easily formed. Moreover, according to the results obtained during the arynic condensations of α,β-unsaturated ketones,[17] the formation of two tetrahydrocarbazolones was expected (Scheme 3).

Scheme 3

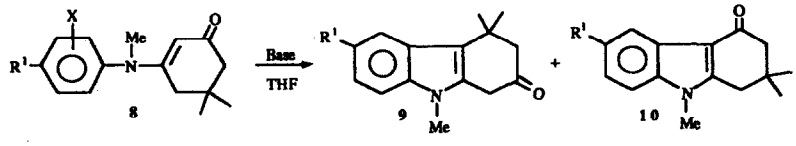


If the hypothesis formulated above and dealing with the formation of aggregates was right we should expected higher ratios **10/9** with 3-halo enaminoketones than with the corresponding 2-halo derivatives. The results obtained with commercially available anilines and reported in the Table III support this hypothesis.

First, as we met with α,β-unsaturated ketones,[17c] $NaNH_2$ may be activated by some corresponding enolates (runs 2 and 3, Table III). However this property is far from being general (runs 6, 8 and 10, Table III) and the use of the complex base $NaNH_2$-*t*-BuONa was prefered.

Second, the formation of aggregates between $NaNH_2$-*t*-BuONa and the enolate which must be more tightly bound with its oxygen containing side (Scheme 4) favour the condensation of the α carbon leading to the expected variation of the **10/9** ratios. We then reasoned that aprotic solvent such as HMPA which strongly solvates cations would strongly loosen the aggregates and thus increase attack on the γ position. This hypothesis was completely verified. Thus the same condensation of run 11 (Table III) performed in THF-HMPA (2/1) led to the corresponding products **9** and **10** with 32 and 35 % yields respectively instead of 5 and 42 % respectively in THF alone. Of course other factors must intervene in the regioselectivity of our reactions, but formation of aggregates appears as essential in the evolution of these condensations.

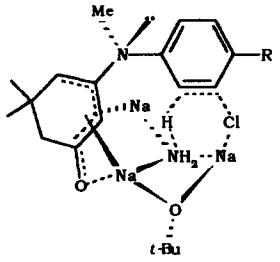
Table III



Run	R1	X	Base NaNH2/t-BuONa	t°C	t (h)	9 a)	10 a)	10/9
1	OMe	3-Cl	5/2	RT	18	15	61	4
2	OMe	3-Cl	7/-	RT	18	8	61	7.6
3	OMe	3-Cl	5/-	RT	18	8	57	7.1
4	H	3-Cl	5/2	RT	48	9	35	3.9
5	H	3-Cl	5/2	30	48	4	24	6
6	H	3-Cl	5/-	30	72	traces	traces	-
7	H	2-Cl	5/2	30	30	20	46	2.3
8	H	2-Cl	5/-	30	54	traces	11.5	∞
9	Me	2-Cl	5/2	30	48	21	46	2.2
10	Me	2-Cl	5/-	30	48	traces	traces	-
11	Me	3-Cl	5/2	RT	66	5	42	8.4
12	F	3-Cl	5/2	RT	5	17	58	3.4
13	F	2-Cl	5/2	RT	2	33	46	1.4

a) Isolated yields.

Scheme 4



Conclusion

From the present work it appears that arynic cyclisations of halogenated imines or enaminoketones in the presence of the complex base $NaNH_2$-*t*-BuONa are well suited for the synthesis of indoles. It must be emphasized that the unexpensive complex base may be easily obtained by simple addition of *t*-BuOH to $NaNH_2$ and may be used on large as well as industrial scale. The arynic cyclisations may be performed with starting materials coming from mixture of 2 and 3-halogeno anilines. With sensitive substrates, imines or enaminoketones may be used as crude materials. In every cases, N-substituted indoles may be obtained one pot by direct trapping of the final anion with electrophiles. Moreover the present indoles synthesis based on anionic chemistry takes benefit of the formation of mixed aggregates. Finally, a number of the compounds presently synthesized showed interesting pharmacological properties which will be published elsewhere.

Experimental

General Methods. Melting points were determined on a Totoli melting point apparatus and a Kofler hot-stage apparatus and are uncorrected. ^{13}C NMR spectra were recorded with a Bruker AM 400 or a Bruker 300 MHz spectrometer (Attached Proton Test method, APT). ^1H NMR spectra were recorded on a Jeol PMX 60 at 60 MHz, or a Brucker AM 400 instrument at 400 MHz: Me_4Si was the internal standard. Infrared (IR) spectra of thin liquid films between NaCl plates or KBr pellets were recorded with a Perkin-Elmer 841 instrument. X ray analysis was performed by Centro di Studio C.N.R. per la Strutturistica Diffractometrica of Parma (Italy). Elemental analyses were performed by CNRS Laboratory (Vernaison) and by E.N.S.C.M. Microanalysis Department of Montpellier. Mass spectra were recorded on Hewlett Packard 5971A instrument.

Thin-layer chromatography (TLC) was performed with plates coated with kieselgel G (Merck). The plates were developed with petroleum ether/EtOAc. The silica gels used for column chromatography and flash chromatography were kieselgels of 0.063-0.2 mm and 0.04-0.063 mm particle size, respectively.

Materials. Sodium amide powder was obtained commercially (Merck). Reagent-grade tetrahydrofuran (THF) (BASF) was distilled from sodium benzophenone ketyl. 1,2-Dimethoxyethane (DME) was distilled from sodium and was stored under sodium until used.

Typical procedures for the preparation of imines 1 and enamines 2 and 8

Imines were prepared from an equimolar mixture of ketone and amine in refluxing benzene or toluene. When necessary, the reaction was catalysed by APTS, BF_3-Et_2O or Zn halide. When the expected H_2O quantity has been collected (in a Dean Stark apparatus), the reaction is stopped, neutralised by a saturated aqueous solution of $NaHCO_3$, and extracted. The organic layer is dried over $MgSO_4$ and solvents removed under vacuum. Crude imines are isolated by rapid distillation under reduced pressure with 40 to 70 % yields.

N-unsubstituted enamines were prepared by azeotropic distillation of an equimolar mixture of amine and 1,3-diketone in benzene with catalytic amount of APTS. When the expected H_2O quantity has been collected (in a Dean Stark apparatus), the reaction mixture is cooled with an ice bath and then filtered. The precipitate is dissolved in EtOAc and neutralised with a solution of $NaHCO_3$. The organic layer is dried over $MgSO_4$ and the solvents evaporated under reduced pressure. The solid is washed with petroleum ether and enamines obtained with 50 to 100 % yields.

N-Methylenaminoketones **8** are obtained by methylation of homologous enamines **2** with NaH (2 eq.) and Me_2SO_4 (3 eq.) in DMF. After completion of the reaction (followed by tlc), the mixture is extracted with NH_4OH/CH_2Cl_2, the organic layer washed with H_2O and dried over $MgSO_4$. After removing of the solvents under reduced pressure, the crude enamines are washed with Et_2O, and obtained with 70-80 % yields.

Typical procedure for the preparation of N-unsubstituted indoles 7: *1,2,3,4,-tetrahydro-6-methoxycarbazole* **7** R^1=4-MeO; R^2R^3=$(CH_2)_4$; R=H

Procedure A: Reaction performed with the complex base $NaNH_2$-*t*-BuONa. a) Preparation of the complex base: to a suspension of the quantity indicated in table of $NaNH_2$ in the reaction solvent (7 ml for 70 mmol of $NaNH_2$) was added dropwise at room temperature the indicated quantity of tBuOH. After completion of the addition, the mixture was warmed at 45°C for 2 hours. b) Condensation: to the complex base prepared as below was added at 0°C 1 eq. of **1** R^1=4-MeO, R^2R^3= $(CH_2)_4$, X=3-Cl. The mixture was allowed to stirr at room temperature for 24 hours. The reaction is monitored by gpc (capillary HP1, 6 m). The reaction was hydrolysed at 0°C and extracted with Et_2O. After drying over $MgSO_4$ and removing of the solvent under vacuum, **7** R^1= 4-MeO; R=H; R^2R^3=$(CH_2)_4$), was isolated by flash chromatography (Kieselgel 40-63 μ) with 5% EtOAc/ petroleum ether as eluant, and identified by the IR, ^1H NMR, ^{13}C NMR, combustion analysis. Yield: 75%.

Procedure B: Reaction performed with $NaNH_2$ alone. 1 eq. of **1** R^1=4-MeO; R^2R^3=$CH_2)_4$; X=3-Cl is added dropwise to a solution of $NaNH_2$ (quantity indicated in the table) in the reaction solvent at 0°C. The condensation is then monitored in the same way than described in procedure A b).

Typical procedure for the preparation of 9 and 10 *1,2,3,9-tetrahydro-6-methoxy-5,5,9-trimethyl-2H carbazol-4-one* **9** R^1=MeO and *1,2,3,9-tetrahydro-6-methoxy-2,2,9-trimethyl-4H-carbazol-4-one* **10** R^1=MeO

Procedure A : Reaction performed with the complex Base $NaNH_2$-*t*-BuONa. a) Preparation of the complex base: see synthesis of **7** R^1=4-MeO; R^2R^3=$(CH_2)_4$; R=H, procedure A a). b) Condensation: to the complex base prepared as below was added at 0°C 1 eq. of **8** R^1=MeO; X=3-Cl. The mixture was allowed to stirr at room temperature for 18 hours. The reaction is monitored by gpc (capillary HP1, 6 m). The reaction was hydrolysed at 0°C and extracted with Et_2O. After drying over $MgSO_4$ and removing of the solvent under vacuum, the indoles **9** and **10** R^1 MeO were separated by flash chromatography (Kieselgel 40-63 μ) with 30% EtOAc/petroleum ether as eluant, and identified by the IR, ^1H NMR, ^{13}C NMR, combustion analysis. Yields: **9** R^1=MeO 15 % ; **10** R^1=MeO 61%.

Procedure B: Reaction performed with $NaNH_2$ alone. 1 eq. of **8** R^1=MeO; X=3-Cl is added dropwise to a solution of $NaNH_2$ (quantity indicated in the table) in the reaction solvent at 0°C. The condensation is then monitored in the same way than described in procedure A b).

Typical procedure for the preparation of N-substituted indoles 7 *1,2,3,4-tetrahydro-6-methoxy-9-methyl carbazole* **7** R^1=4-MeO; R^2R^3=$(CH_2)_4$; R=Me

This compound was prepared as described below (see : **7** R^1=4-MeO; R=H; R^2R^3=$(CH_2)_4$ (procedure A). Upon completion, the reaction mixture was decanted under nitrogen stream. The supernatant liquid was

then added to 3 eq. of Me_2SO_4 at 0°C and then allowed to stir at room temperature. After complete reaction, the mixture was poured on a cold 32 % NH_4OH solution, extracted with CH_2Cl_2, washed twice with water and dried over $MgSO_4$. After evaporation of the solvent under reduced pressure, compound **7** R^1=4-MeO; R=Me; $R^2R^3=(CH_2)_4$, was purified by flash column chromatography (Kieselgel 40-63 μ) with 5 % EtOAc/petroleum ether as eluant, and identified by the IR, ^1H NMR, ^{13}C NMR, combustion analysis. Yield: 77%.

1,2,3,4-Tetrahydro-6-methoxycarbazole **7** R^1=4-MeO; $R^2R^3=(CH_2)_4$; R=H

IR (NaCl) 3395 (NH), 2916-2852 (C-H). ^1H NMR ($CDCl_3$) δ 6.50-7.55 (4 H, m, Arom H + NH); 3.80 (3 H, s, OMe); 2.90-2.50 (4 H, m, 2xCH_2); 2.15-1.60 (4 H, m, 2xCH_2). ^{13}C NMR ($CDCl_3$) δ 153.7 (COMe), 135.1 (Arom C), 130.7 (Arom C), 128.1 (Arom C), 110.9 (Arom CH), 110.4 (Arom CH), 109.8 (Arom C), 100.2 (Arom CH), 55.9 (OMe), 23.2 (CH_2), 23.1 (CH_2), 20.9 (2xCH_2). Totoli m.p. 85°C; Kofler hot-stage m.p. 96°C (lit.[18] Kofler hot-stage m.p. 94-95°C).

1,2,3,4-Tetrahydro-6-methoxy-9-methylcarbazole **7** R^1=4-MeO; $R^2R^3=(CH_2)_4$; R=Me

IR (NaCl) 2993-2930-2833 (C-H). ^1H NMR ($CDCl_3$) δ 7.50-6.60 (3 H, m, Arom H); 3 .80 (3 H, s, OMe); 3.55 (NMe); 3.10-2.50 (4 H, m, 2xCH_2); 2.30-1.70 (4 H, m, 2xCH_2). ^{13}C NMR ($CDCl_3$) δ 153.5 (C-OMe); 136.3 (Arom C), 132.0 (Arom C), 127.2 (Arom C), 109.9 (Arom CH), 108.9 (Arom CH), 108.7 (Arom C), 100.1 (Arom CH), 55.9 (OMe), 28.8 (NMe), 23.1 (2xCH_2), 22.0 (CH_2), 21.0 (CH_2). mp 71°C. Anal. Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.50. Found : C, 78.37; H, 8.10; N, 6.44.

3-Methoxy-5,6,7,8,9,10-hexahydrocyclohept[b]indole **7** R^1=4-MeO; $R^2R^3=(CH_2)_5$; R=H

IR (NaCl) 3405 (NH), 2920-2845 (C-H). ^1H NMR ($CDCl_3$) δ 7.30 (1 H, s, NH); 7.20-6.40 (3 H, m, Arom H); 3.75 (3 H, s, OMe); 3.00-2.50 (4 H, m, 2xCH_2); 2.20-1.50 (6 H, m, 3xCH_2). ^{13}C NMR ($CDCl_3$) δ 153.6 (C-OMe), 138.5 (Arom C), 129.4 (Arom C), 129.3 (Arom C), 113.2 (Arom C), 110.8 (Arom CH), 110.1 (Arom CH), 99.9 (Arom CH), 55.8 (OMe), 31.7 (CH_2), 29.3 (CH_2), 28.6 (CH_2), 27.4 (CH_2), 24.6 (CH_2); mp 113°C. Anal. Calcd for $C_{14}H_{17}NO$ C, 78.10; H, 7.96; N, 6.50; Found : C, 77.92; H, 7.89; N, 6.66.

5-Methoxy-10-methyl-5,6,7,8,9,10-hexahydrocyclohept[b]indole **7** R^1=4-MeO; $R^2R^3=(CH_2)_5$; R=Me

IR (NaCl) 2990-2920-2845 (C-H). ^1H NMR ($CDCl_3$) δ 7.3-6.5 (3 H, m, Arom H); 3.8 (3 H, s, OMe); 3.0-2.5 (4 H, m, 2xCH_2); 2.0-1.5 (6 H, m, 3xCH_2). ^{13}C NMR ($CDCl_3$) δ 153.6 (C-OMe), 139.7 (Arom C), 139.7 (Arom C), 131.2 (Arom C), 127.7 (Arom C), 113.0 (Arom C), 109.9 (Arom CH), 108.9 (Arom CH), 99.8 (Arom CH), 55.9 (OMe), 31.5 (CH_2), 29.3 (NMe), 28.4 (CH_2), 26.9 (CH_2), 26.2 (CH_2), 24.3 (CH_2).mp 48°C. Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.10; Found : C, 78.41; H, 8.51; N, 6.26.

2-(5-Methoxy-5,6,7,8,9,10-hexahydrocyclohept[b]indol-10-yl)ethylacetate **7** R^1=4-MeO; $R^2R^3=(CH_2)_5$; R= CH_2-COO-CH_2-CH_3

IR (NaCl) 2922-2847 (C-H), 1753 (C=O). ^1H NMR ($CDCl_3$) δ 7.0-6.5 (3 H, m, Arom H); 4.6 (2 H, s, CH_2); 4.4-3.8 (2 H, q, CH_2); 3.7 (3 H, s, OMe); 2.9-2.4 (4 H, m, 2xCH_2); 2.0-1.4 (6 H, s, 3xCH_2); 1.4-0.9 (3 H, t, Me). ^{13}C NMR ($CDCl_3$) δ 168.9 (COO), 154.0 (C-OMe), 139.4 (Arom C), 131.0 (Arom C), 128.4 (Arom C), 114.1 (Arom C), 110.2 (Arom CH), 108.8 (Arom CH), 100.3 (Arom CH), 61.2 (OCH_2), 55.8 (OMe),44.7 (NCH_2), 31.4 (CH_2), 28.1 (CH_2), 26.8 (CH_2), 26.3 (CH_2), 24.2 (CH_2), 14.0 (Me). mp 55°C. Anal. Calcd for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.69; N, 4.64. Found : C, 71.62; H, 7.76; N, 4.64.

3-Methoxy-5,6,7,8,9,10,11-heptahydrocyclooct[b]indole **7** R^1=4-MeO; $R^2R^3=(CH_2)_6$; R=H

IR (NaCl) 3405 (NH), 2922-2848 (C-H). ^1H NMR ($CDCl_3$) δ 7.90-6.50 (4 H, m, Arom H + NH); 3.86 (3 H, s, OMe); 3.00-2.50 (4 H m, 2xCH_2); 2.00-1.20 (8 H, m, 4xCH_2). ^{13}C NMR ($CDCl_3$) δ 153.5 (C-OMe), 136.7 (Arom C), 130.1 (Arom C), 128.8 (Arom C), 111.2 (Arom C), 110.9 (Arom CH), 110.0 (Arom CH), 99.9 (Arom CH), 55.8 (OMe), 29.4 (CH_2), 29.4 (CH_2), 25.8 (CH_2), 25.8 (CH_2), 25.6 (CH_2), 22.1 (CH_2). mp 102°C. Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.10. Found : C, 78.65; H, 8.43; N, 6.10.

3-Methoxy-11-methyl-5,6,7,8,9,10,11-heptahydrocyclooct[b]indole **7 R^1=4-MeO; R^2R^3=$(CH_2)_6$; R=Me**

IR (NaCl) 2921-2848 (C-H). ^1H NMR ($CDCl_3$) δ 7.10-6.50 (3 H, m, Arom H); 3.78 (3 H, s, OMe); 3.68 (3 H, s, NMe); 3.00-2.60 (4 H, m, 2xCH_2); 1.90-1.20 (8 H, m, 4xCH_2). ^{13}C NMR ($CDCl_3$) δ 153.5 (C-OMe), 137.7 (Arom C), 131.9 (Arom C), 127.4 (Arom C), 111.1 (Arom C), 109.7 (Arom CH), 109.1 (Arom CH), 99.9 (Arom CH), 55.9 (OMe), 30.4 (CH_2), 29.2 (NMe), 28.7 (CH_2), 25.9 (CH_2), 25.8 (CH_2), 22.9 (2xCH_2). mp 54°C. Anal. Calcd for $C_{16}H_{21}NO$: C, 78.96; H, 8.69; N, 5.75. Found : C, 78.90; H, 8.52; N, 5.82.

2(3-methoxy-5,6,7,8,9,10,11-heptahydrocyclooct[b]indol-11-yl)1-1-dimethyl)ethylacetate **7 R^1=4-MeO; R^2R^3=$(CH_2)_6$; R=CH_2-COO-tBu**

IR (NaCl) 2978-2927-2848 (C-H), 1749 (C=O). ^1H NMR ($CDCl_3$) δ 7.00-6.50 (3 H, m, Arom H), 4.70 (2 H, s, CH_2); 3.65 (3 H, s, OMe); 3.00-2.50 (4 H, m, 2xCH_2); 2.00-1.10 (8 H, m, 4xCH_2); 1.35 (9 H, s, 3xMe). ^{13}C NMR ($CDCl_3$) δ 167.6 (COO), 153.6 (C-OMe), 136.7 (Arom C), 131.5 (Arom C), 127.6 (Arom C), 111.5 (Arom C), 109.7 (Arom CH), 108.5 (Arom CH), 99.7 (Arom CH), 81.2 (C(Me)3), 55.1 (OMe), 44.9 (NCH_2), 29.9 (CH_2), 28.2 (CH_2), 27.4 (3xMe), 25.4 (2xCH_2), 22.5 (CH_2). Anal. Calcd for $C_{21}H_{29}NO_3$: C, 73.43; H, 8.51; N, 4.07. Found : C, 73.19; H, 8.56; N, 4.09.

3-Methoxy-5,6,7,8,9,10,11,12,13,14,15-undecahydrocyclododec[b]indole **7 R^1=4-MeO; R^2R^3=$(CH_2)_{10}$; R=H**

IR (NaCl) 3410 (NH), 2931-2850 (C-H). ^1H NMR ($CDCl_3$) δ 7.5-6.3 (4 H, m, Arom H + NH); 3.7 (3 H, s, OMe), 2.8-2.3 (4 H, m, 2xCH_2); 2.0-1.0 (16 H, m, 8xCH_2). ^{13}C NMR ($CDCl_3$) δ 153.3 (C-OMe), 136.8 (Arom C), 130.8 (Arom C), 128.8 (Arom C), 111.8 (Arom C), 110.7 (Arom CH), 110.1 (Arom CH), 101.3 (Arom CH), 55.9 (OMe), 27.4 (CH_2), 27.2 (CH_2), 24.7 (2xCH_2), 23.8 (CH_2), 22.5 (CH_2), 22.4 (CH_2), 22.0 (CH_2), 21.1 (CH_2). mp 78°C. Anal. Calcd for $C_{19}H_{27}NO$: C, 79.94; H, 9.53; N, 4.90. Found : C, 79.72; H, 9.62; N, 4.97.

3-Methoxy-15-methyl-5,6,7,8,9,10,11,12,13,14,15-undecahydrocyclododec[b]indole **7 R^1=4-MeO; R^2R^3=$(CH_2)_{10}$; R=Me**

IR (NaCl) 2929-2851 (C-H). ^1H NMR ($CDCl_3$) δ 7.00-6.40 (3 H, m, Arom H); 3.75 (3 H, s, OMe); 3.55 (3 H, s, NMe); 2.90-2.50 (4 H, m, 2xCH_2); 2.00-1.10 (16 H, m, 8xCH_2). ^{13}C NMR ($CDCl_3$) δ 153.5 (C-OMe), 138.1 (Arom C), 132.4 (Arom C), 128.0 (Arom C), 111.6 (Arom C), 110.1 (Arom CH), 109.0 (Arom CH), 101.3 (Arom CH), 56.1 (OMe), 29.9 (NMe), 27.8 (CH_2), 27.3 (CH_2), 25.3 (CH_2), 25.0 (CH_2), 24.5 (2xCH_2), 22.3 (CH_2), 22.2 (CH_2), 21.7 (CH_2), 21.6 (CH_2). mp 63°C. Anal. Calcd for $C_{20}H_{29}NO$: C, 80.21; H,9.76; N, 4.67. Found : C, 80.67; H, 9.73; N,4.84.

5-Methoxy-2-methylindole **7 R^1=4-MeO; R^2=H; R^3=Me; R=H**

IR (NaCl) 3396 (NH), 2996-2940-2831 (C-H). ^1H NMR ($CDCl_3$) δ 6.4-7.7 (4 H, m, Arom H), 6.0 (1 H, s, Arom H), 3.8 (3 H, s, OMe), 2.4 (3 H, s, Me). ^{13}C NMR ($CDCl_3$) δ 153.9 (C-OMe), 135.9 (CMe), 131.1 (Arom C), 129.4 (Arom C), 110.8 (Arom CH), 110.5 (Arom CH), 101.8 (Arom CH), 100.1 (Arom CH), 55.8 (OMe), 13.6 (Me). Totoli m.p. 69°C; Kofler hot-stage m.p. 86°C (lit.[19] Kofler hot-stage m.p. 85-86°C).

5-Methoxy-2-(2-norbornyl)indole **7 R^1=4-MeO; R^2=H; R^3=2-Norbornyl; R=H**

IR (NaCl) 3407 (NH), 2952-2871 (C-H). ^1H NMR ($CDCl_3$) δ 7.40 (1 H, s, NH); 7.00-6.20 (3 H, m, Arom H); 5.90 (1 H, s, Arom H), 3.70 (3 H, s, OMe); 2.85-2.60 (1 H, m, CH); 2.60-2.00 (2 H, m, CH_2); 1.80-0.90 (8 H, m, 3xCH_2 + 2xCH). ^{13}C NMR ($CDCl_3$) δ 153.8 (C-OMe), 145.8 (Arom C), 130.9 (Arom C), 128.9 (Arom C), 110.9 (Arom CH), 110.5 (Arom CH), 102.0 (Arom CH), 97.7 (Arom CH), 55.83 (OMe), 42.6 (CH), 41.2 (CH), 37.2 (CH_2), 36.1 (CH), 36.1 (CH_2), 29.6 (CH_2), 28.7 (CH_2). mp 88°C. Anal. Calcd for $C_{16}H_{19}NO$: C, 79.62; H, 7.93; N, 5.80. Found : C, 79.64; H, 7.93; N, 5.96.

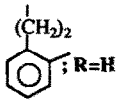
5-Methoxy-1-methyl-2(2-norbornyl)indole **7 R^1=4-MeO; R^2=H; R^3=2-Norbornyl; R=Me**

IR (NaCl) 2951-2871-2827 (C-H). ^1H NMR ($CDCl_3$) δ 7.20-6.40 (3 H, m, Arom H); 6.00 (1 H, s, Arom H), 3.75 (3 H, s, OMe); 3.60 (3 H, s, NMe); 2.90, 2.50 (1 H, m, CH); 2.50-2.10 (2 H, m, CH_2), 1.90-1.00 (8 H, m, 3xCH_2 + 2xCH). ^{13}C NMR ($CDCl_3$) δ 153.8 (C- Me), 146.6 (Arom C), 132.7 (Arom C), 127.8

(Arom C), 110.1 (Arom CH), 109.0 (Arom CH), 102.0 (Arom CH), 96.6 (Arom CH), 55.8 (OMe), 41.7 (CH), 39.6 (CH), 37.4 (CH_2), 36.4 (CH), 35.8 (CH_2), 29.7 (CH_2), 29.5 (NMe), 28.8 (CH_2). mp 68°C. Anal. Calcd for $C_{17}H_{21}NO$: C, 79.95; H, 8.29; N, 5.48. Found : C, 80.05; H, 8.34; N, 5.58.

5-Methoxy-2-phenylindole **7 R^1=4-MeO; R^2=H; R^3=Ph; R=H**

IR (NaCl) 3428 (NH). ^1H NMR ($CDCl_3$) δ 8.2 (1 H, s, NH); 7.8-6.7 (9 H, m, Arom H); 3.9 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ 154.3 (C-OMe), 138.5 (Arom C), 132.3 (Arom C), 131.9 (Arom C), 129.6 (Arom C), 128.9 (2xArom CH), 127.5 (Arom CH), 124.9 (2xArom CH), 112.5 (Arom CH), 111.5 (Arom CH), 102.2 (Arom CH), 99.7 (Arom CH), 55.7 (OMe). mp 154°C. Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.86; N, 6.27. Found : C, 80.58; H, 5.71; N, 6.32.

1,2,3,4-Tetrahydro-6-methoxy-benzo[c]carbazole **7 R^1=4-MeO; R^2R^3=**  **; R=H**

IR (NaCl) 3405 (NH), 2933 (C-H). ^1H NMR ($CDCl_3$) δ 8.10 (1 H, s, NH); 7.35-6.75 (7 H, m, Arom H); 3.85 (3 H, s, OMe); 2.80-3.15 (4 H, m, 2xCH_2). ^{13}C NMR ($CDCl_3$) δ 154.2 (C-OMe), 136.4 (Arom C), 133.8 (Arom C), 132.1 (Arom C), 128.9 (Arom C), 128.4 (Arom CH), 127.7 (Arom C), 126.6 (2 Arom CH), 119.7 (Arom CH), 112.4 (Arom C), 112.3 (Arom CH), 111.7 (Arom CH), 100.5 (Arom CH), 55.8 (OMe), 29.5 (CH_2), 19.6 (CH_2). mp 158°C. Anal. Calcd for $C_{17}H_{15}NO$: C, 81.89; H, 6.06; N, 5.61. Found : C, 81.48; H, 6.20; N, 5.63.

2-(2-Furyl)-5-methoxyindole **7 R^1=4-MeO; R^2=H; R^3=2-Furyl; R=H**

IR (NaCl) 3418-3338 (NH), 2996-2942-2836 (C-H). ^1H NMR ($CDCl_3$) δ 8.2 (1 H, s, NH); 7.5-6.1 (7 H, m, Arom H), 3.7 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ 154.4 (C-OMe), 147.7 (Arom C), 141.5 (Arom CH), 131.3 (Arom C), 129.8 (Arom C), 129.2 (Arom C), 112.6 (Arom CH), 111.7 (Arom CH), 111.5 (Arom CH), 105.1 (Arom CH), 102.2 (Arom CH), 98.6 (Arom CH), 55.7 (OMe). mp 106°C. Anal. Calcd for $C_{13}H_{11}O_2N$: C, 73.22; H, 5.20; N, 6.56. Found : C, 73.20; H, 5.22; N, 6.85.

2-(2-Furyl)-1-methyl-5-methoxyindole **7 R^1=4-MeO; R^2=H; R^3=2-Furyl; R=Me**

IR (NaCl) 2992-2954-2917 (C-H). ^1H NMR ($CDCl_3$) δ 7.51-6.40 (7 H, m, Arom H); 3.85 (3 H, s, OMe); 3.84 (3 H, s, Arom H). ^{13}C NMR ($CDCl_3$) δ 154.3 (C-OMe), 147.4 (Arom C), 142.2 (Arom CH), 133.5 (Arom C), 131.5 (Arom C), 127.8 (Arom C), 112.4 (Arom CH), 111.2 (Arom CH), 110.0 (Arom CH), 107.8 (Arom CH), 102.0 (Arom CH), 100.5 (Arom CH), 55.7 (OMe), 31.4 (NMe). mp 74°C. Anal. Calcd for $C_{13}H_{11}O_2N$: C, 73.98; H, 5.76; N, 6.16. Found : C, 74.11; H, 5.90; N, 6.38.

2-(2Thienyl)-5-methoxyindole **7 R^1=4-MeO; R^2=H; R^3=2-Thienyl; R=H**

IR (NaCl) 3412 (NH). ^1H NMR ($CDCl_3$) δ 7.9 (1 H, s, NH); 7.3-6.4 (7 H, m, Arom H); 3.8 (3 H, s, OMe). ^{13}C NMR ($CDCl_3$) δ 154.5 (C-OMe), 135.6 (Arom C), 133.0 (Arom C), 131.6 (Arom C), 129.5 (Arom C), 127.8 (Arom CH), 124.4 (Arom CH), 122.7 (Arom CH), 112.6 (Arom CH), 111.4 (Arom CH), 102.1 (Arom CH), 100.2 (Arom CH), 55.7 (OMe). mp 124°C. Anal. Calcd for $C_{13}H_{11}NOS$: C, 68.09; H, 4.83; N, 6.10; S, 13.98. Found : C, 67.83; H, 4.98; N, 6.23; S, 14.21.

2-(2-Thienyl)-1-methyl-5-methoxyindole **7 R^1=4-MeO; R^2=H; R^3=2-Thienyl; R=Me**

IR (NaCl) 2932 (C-H). ^1H NMR ($CDCl_3$) δ 7.50-6.40 (7 H, m, Arom H); 3.80 (3 H, s, OMe); 3.75 (3 H, s, NMe). ^{13}C NMR ($CDCl_3$) δ 154.2 (C-OMe), 134.2 (Arom C), 134.1 (Arom C), 133.6 (Arom C), 127.8 (Arom C), 127.4 (Arom CH), 126.3 (2xArom CH), 112.2 (Arom CH), 110.1 (Arom CH), 102.2 (Arom CH), 101.8 (Arom CH), 55.6 (OMe), 30.9 (NMe). mp 89°C. Anal. Calcd for $C_{14}H_{13}NOS$: C, 69.10; H, 5.38; N, 5.75; S, 13.17. Found C, 68.97; H, 5.42; N, 5.70; S, 13.13.

3-Ethylene acetal-1,2,4,9-tetrahydro-6-methoxy-3H-carbazol-3-one **7 R^1=4-MeO; R^2R^3=CH_2-C(OCH_2)$_2$-(CH_2)$_2$; R=H**

IR (NaCl) 3350 (NH), 2892-2833 (C-H). ^1H NMR ($CDCl_3$) δ 7.7 (1 H, s, NH); 7.1-6.6 (3 H, m, Arom H); 4.2-4.0 (4 H, m, 2xCH_2); 3.8 (3 H, s, OMe); 2.9 (2 H, s, CH_2); 2.8 (2 H, m, CH_2), 2.0 (2 H, m, CH_2). ^{13}C NMR ($CDCl_3$) δ 153.7 (COMe), 133.2 (Arom C), 131.6 (Arom C), 127.9 (Arom C), 111.0 (Arom CH), 110.7 (Arom CH), 109.1 (Arom C), 107.8 (O- C- O), 100.0 (Arom CH), 64.5 (2xCH_2), 55.8 (OMe), 31.9

(CH_2), 31.7 (CH_2), 21.4 (CH_2). mp 143°C. Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.47; H, 6.61; N, 5.40. Found C, 69.57; H, 6.78; N, 5.60.

8-Methoxythiopyrano[3,2-b]indole **7 R^1=4-MeO; R^2R^3=S-$(CH_2)_3$; R=H**

IR (NaCl) 3390 (NH), 2999-2938-2834 (C-H). ^1H NMR ($CDCl_3$) δ 7.5 (1 H, s, NH); 7.4-6.7 (3 H, m, Arom H); 3.8 (3 H, s, OMe); 3.2-2.6 (4 H, m, 2xCH_2); 2.5-2.0 (2 H, m, CH_2). ^{13}C NMR ($CDCl_3$) δ 153.7 (COMe), 129.9 (Arom C), 129.6 (Arom C), 126.4 (Arom C), 111.6 (Arom CH), 111.1 (Arom CH), 100.5 (Arom C), 99.6 (Arom CH), 55.6 (OMe), 26.7 (CH_2), 24.0 (CH_2), 22.6 (CH_2). mp 123°C. Anal. Calcd for $C_{12}H_{13}NOS$: C, 65.72; H, 5.97; N, 6.38; S, 14.62. Found C, 65.95; H, 6.03; N, 6.53; S, 14.93.

2-(8-Methoxy-thiopyrano[2,3-b]indol-5-yl)ethylacetate **7 R^1=4-MeO; R^2R^3=S-$(CH_2)_3$; R=CH_2-COO-Et**

IR (NaCl) 2923 (C-H), 1750 (C=O). ^1H NMR ($CDCl_3$) δ 7.2-6.5 (3 H, m, Arom H), 4.5 (2 H, s, NCH_2); 4.3-3.9 (2 H, q, CH_2); 3.8 (3 H, s, OMe); 3.1-2.0 (6 H, m, 3xCH_2); 1.4-1.0 (3 H, t, CH_3). ^{13}C NMR ($CDCl_3$) δ 168.4 (C=O), 154.1 (COMe), 131.3 (Arom C), 130.6 (Arom C), 126.4 (Arom C), 111.7 (Arom CH), 109.0 (Arom CH), 109.0 (Arom CH), 101.2 (Arom C), 100.2 (Arom CH), 61.4 (OCH_2), 55.8 (OMe), 44.5 (NCH_2), 26.6 (CH_2), 24.3 (CH_2), 21.5 (CH_2), 14.0 (CH_3). mp 98°C. Anal. Calcd for $C_{16}H_{19}NO_3S$: C, 62.92; H, 6.27; N, 4.58; S, 10.49. Found C, 62.58; H, 6.32; N, 4.69; S, 10.36.

5-Methoxy-2-pentylindole **7 R^1=4-MeO; R^2=$(CH_2)_4$-CH_3; R^3=H**

IR (NaCl) 3418 (NH), 2929-2855 (C-H). ^1H NMR ($CDCl_3$) δ 7.73 (1 H, s, NH); 7.20-6.70 (4 H, m, Arom H); 3.85 (3 H, s, OMe); 2.80-2.60 (2 H, t, CH_2); 1.80-1.60 (2 H, m, CH_2); 1.50-1.20 (4 H, m, 2xCH_2); 1.00-0.80 (3 H, m, Me). ^{13}C NMR ($CDCl_3$) δ 153.5 (C-OMe), 131.4 (Arom C), 127.8 (Arom C), 121.9 (Arom CH), 116.6 (Arom C), 111.7 (Arom CH), 111.6 (Arom CH), 100.8 (Arom CH), 55.8 (OMe), 31.7 (CH_2), 29.6 (CH_2), 25.0 (CH_2), 22.5 (CH_2), 14.0 (Me). mp 26°C. Anal. Calcd for $C_{14}H_{19}NO$: C, 77.37; H, 8.81; N, 6.44. Found C, 77.21; H, 8.89; N, 6.49.

1,2,3,4-Tetrahydrocarbazole **7 R^1=H; R^2R^3=$(CH_2)_4$; R=H**

IR (NaCl) 3400(NH), 2927-2848 (C-H). ^1H NMR ($CDCl_3$) δ 7.6-6.4 (5 H, m, Arom H + NH); 3.0-2.4 (4 H, m, 2xCH_2); 2.2-1.6 (4 H, m, 2xCH_2). ^{13}C NMR ($CDCl_3$) δ 135.5 (Arom C), 134.0 (Arom C), 127.6 (Arom C), 120.8 (Arom CH), 118.9 (Arom CH), 117.6 (Arom CH), 110.3 (Arom CH), 109.9 (Arom C), 23.2 (CH_2), 23.1 (CH_2), 23.0 (CH_2), 20.8 (CH_2). mp 110°C. Anal. Calcd for $C_{12}H_{13}N$: C, 84.16; H, 7.65. Found : C, 84.09; H, 7.79.

1,2,3,4-Tetrahydro-6-methylcarbazole **7 R^1=4-Me; R^2R^3=$(CH_2)_4$; R=H**

IR (NaCl) 3394 (NH), 2925-2847 (C-H). ^1H NMR ($CDCl_3$) δ 7.40-6.60 (4 H, Arom H + NH); 2.85-2.20 (7 H, m with s at 2.40, 2xCH_2 + Me); 2.20-1.60 (4 H, m, 2xCH_2). ^{13}C NMR ($CDCl_3$) δ 134.2 (Arom CMe), 133.8 (Arom C), 128.1 (Arom C), 127.9 (Arom C), 122.3 (Arom CH), 117.4 (Arom CH), 109.9 (Arom CH), 109.5 (Arom C), 23.2 (CH_2), 23.1 (2xCH_2), 21.4 (Me), 20.8 (CH_2). mp 135°C. Anal. Calcd for $C_{13}H_{15}N$: C, 84.27; H, 8.16. Found : C, 84.58; H, 8.27.

1,2,3,4-Tetrahydro-6,9-dimethylcarbazole **7 R^1=4-Me; R^2R^3=$(CH_2)_4$; R=Me**

IR (NaCl) 2919-2848 (C-H). ^1H NMR ($CDCl_3$) δ 7.2-6.6 (3 H, m, Arom H), 3.4 (3 H, s, NMe), 2.9-2.2 (4 H, m, 2xCH_2); 2.4 (3 H, s, Me); 2.2 -1.5 (4 H, m, 2xCH_2). ^{13}C NMR ($CDCl_3$) δ 135.6 (Arom C), 135.1 (Arom C), 127.5 (Arom C), 127.3 (Arom C), 121.8 (Arom CH), 117.4 (Arom CH), 105.5 (Arom C), 108.0 (Arom CH), 28.7 (NMe), 23.2 (2xCH_2), 21.9 (CH_2), 21.3 (Me), 21.0 (CH_2). mp 80°C. Anal. Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60. Found : C, 84.83; H, 8.79.

6-Fluoro-1,2,3,4-tetrahydrocarbazole **7 R^1=4-F; R^2R^3=$(CH_2)_4$**

IR (NaCl) 3407 (NH), 2932-2850 (C-H). ^1H NMR ($CDCl_3$) δ 7.5 (1 H, s, NH); 7.3-6.6 (3 H, m, Arom H); 2.9-2.5 (4 H, m, 2xCH_2); 2.2-1.7 (4 H, m, 2xCH_2). ^{13}C NMR ($CDCl_3$) δ 159.2-156.1 (C-F), 136.2 (Arom C), 132.0 (Arom C), 128.2-128.1 (Arom C), 110.6-110.7 (Arom CH), 110.3 (Arom C), 108.8-108.5 (Arom CH), 102.9-102.6 (Arom CH), 23.1 (CH_2), 23.1 (CH_2), 23.0 (CH_2), 20.7 (CH_2). mp 97°C. Anal. Calcd for

$C_{12}H_{12}NF$: C, 76.16; H, 6.39; N, 7.40. Found : C, 76.18 ; H, 6.43; N, 7.29.

1,2,3,4-Tetrahydro-8-methylcarbazole **7 R^1=2-Me; R^2R^3=$(CH_2)_4$; R=H**

IR (NaCl) 3403 (NH), 2922-2852 (C-H). ^1H NMR ($CDCl_3$) δ 7.90-7.50 (1 H, s, NH); 7.50-6.65 (3 H, m, Arom H), 2.90-2.50 (7 H, m with s at 2.40, 2xCH_2 + Me); 2.20-1.70 (4 H, m, 2x CH_2). ^{13}C NMR ($CDCl_3$) δ 134.9 (CMe), 133.6 (Arom C), 127.2 (Arom C), 121.6 (Arom CH), 119.3 (Arom C), 111.2 (Arom CH), 115.4 (Arom CH), 110.6 (Arom C), 29.7 (CH_2), 23.3 (2xCH_2), 21.0 (CH_2), 16.6 (Me). mp 102°C. Anal. Calcd for $C_{13}H_{15}N$: C, 84.27; H, 8.16; N, 7.56. Found : C, 84.03; H, 8.23; N, 7.70.

1,2,3,4-Tetrahydro-8,9-dimethylcarbazole **7 R^1=2-Me; R^2R^3=$(CH_2)_4$; R=Me**

IR (NaCl) 2939-2846 (C-H). ^1H NMR ($CDCl_3$) δ 7.3-6.5 (3 H, m, Arom H); 3.8 (3 H, s, NMe), 2.8-2.4 (7 H, m with s at 2.7, 2xCH_2 + Me); 2.2-1.7 (4 H, m, 2xCH_2). ^{13}C NMR ($CDCl_3$) δ 135.9 (C-Me), 135.4 (Arom C), 127.9 (Arom C), 123.5 (Arom CH), 120.3 (Arom C), 118. (Arom CH), 115.6 (Arom CH), 109.3 (Arom C), 31.8 (NMe), 23.4 (CH_2), 23.1 (CH_2), 22.2 (CH_2), 20.9 (CH_2), 20.0 (Me). mp 135°C. Anal. Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60; N, 7.02. Found : C, 84.19; H, 8.81; N, 7.12.

1,2,3,4-Tetrahydro-8-methoxy-9-methyl carbazole **7 R^1=2-OMe; R^2R^3=$(CH_2)_4$; R=Me**

IR (NaCl) 3007-2936-2832 (C-H). ^1H NMR ($CDCl_3$) δ 7.2-6.3 (3 H, m, Arom H); 3.8 (6 H, s, OMe + NMe); 2.9-2.3 (4 H, m, 2xCH_2); 2.1-1.5 (4 H, m, 2xCH_2). ^{13}C NMR ($CDCl_3$) δ 147.1 (C-OMe), 135.7 (Arom C), 129.1 (Arom C), 125.8 (Arom C), 118.6 (Arom CH), 110.6 (Arom CH), 109.2 (Arom C), 101.9 (Arom CH), 55.1 (OMe), 31.6 (NMe), 23.2 (CH_2), 23.0 (CH_2), 21.8 (CH_2), 21.0 (CH_2). mp 87°C. Anal. Calcd for $C_{14}H_{17}ON$: C, 78.10; H, 7.96; N, 6.50. Found : C, 77.89; H, 8.07; N, 6.41.

1,2,3,9-Tetrahydro-6-methoxy-2,2-dimethyl-4H-carbazol-4-one **7 R^1=4-OMe; R^2R^3=CO-CH_2-C(Me)$_2$-CH_2; R=H**

UV (MeOH) λ_{nm} (log ε) 254 (4.27), 276 (4.14), 297 (4.04). IR (NaCl) 3163 (NH), 2951-2916 (C-H), 1611 (C=O). ^1H NMR ($CDCl_3$, DMSO) δ 10.20 (1 H, s, NH); 7.50-6.50 (3 H, m, Arom H); 3.75 (3 H, s, OCH_3); 2.75 (2 H, s, CH_2); 2.25 (2 H, s, CH_2), 1.10 (6H, s, 2xMe). ^{13}C NMR ($CDCl_3$, DMSO) δ 190.5 (C-OH), 153.7 (C-OMe), 149.2 (Arom C), 129.4 (Arom C), 123.5 (Arom C), 110.4 (Arom CH), 109.9 (Arom CH), 109.0 (Arom C), 101.0 (Arom CH), 53.6 (OMe), 50.4 (CH_2), 35.1 (CH_2), 33.6 (Me-C-Me), 26.7 (2xMe). mp 220°C. Anal. Calcd for $C_{15}H_{17}O_2N$: C, 74.04; H, 7.04; N, 5.75. Found : C, 74.09; H, 7.20; N, 5.96.

1,2,3,9-Tetrahydro-6-methoxy-4H-carbazol-4-one **7 R^1=4-OMe; R^2R^3=CO-$(CH_2)_3$; R=H**

IR (NaCl) 3300 to 2800 (NH + C-H), 1619 (C=O). ^1H NMR ($CDCl_3$, DMSO) δ 11.5 (1 H, s, OH); 7.6-6.5 (3 H, m, Arom H); 3.8 (3 H, s, OMe); 3.1-2.7 (2 H, m, CH_2); 2.6-1.9 (4 H, m, 2xCH_2); ^{13}C NMR ($CDCl_3$, DMSO) δ 190.7 (C-OH), 153.2 (C-OMe), 150.2 (Arom C), 128.6 (Arom C), 123.3 (Arom C), 110.1 (Arom CH), 109.8 (Arom C), 109.6 (Arom CH), 100.6 (Arom CH), 53.3 (OMe), 35.9 (CH_2), 21.5 (CH_2), 20.9 (CH_2). mp 290°C. Anal. Calcd for N-tosylate derivative prepared in 80% yield : $C_{20}H_{19}O_4NS$: C, 65.02; H, 5.18; N, 3.79; S, 8.67. Found : C, 65.02; H, 5.24; N, 3.96; S, 8.82.

1,2,3,9-Tetrahydro-2,2,6-dimethyl-4H-carbazol-4-one **7 R^1=4-Me; R^2R^3=CO-CH_2-C(Me)$_2$-CH_2; R=H**

IR (NaCl) 3190 (NH), 2955 (C-H), 1615 (C=O). ^1H NMR ($CDCl_3$, DMSO) δ 11.20 (1 H, s, OH), 7.70 (1 H, s, Arom H); 7.25-6.70 (2 H, m, Arom H); 2.75 (2 H, s, CH_2); 2.40 (3 H, s, Arom CMe), 2.35 (2 H, s, CH_2); 1.10 (6 H, s, 2xMe). ^{13}C NMR ($CDCl_3$, DMSO) δ 190.6 (C-OH), 149.1 (Arom CMe), 132.9 (Arom C), 128.8 (Arom C), 123.1 (Arom C), 121.9 (Arom CH), 118.6 (Arom CH), 109.4 (Arom CH), 108.7 (Arom C), 50.4 (CH_2), 35.1 (Me-C-Me), 33.6 (CH_2), 26.7 (2xMe), 19.6 (Arom CMe). mp 247°C. Anal. Calcd for $C_{15}H_{17}ON$: C, 79.25; H, 7.54; N, 6.16. Found : C, 78.84; H, 7.57; N, 6.42.

1,2,3,9-Tetrahydro-6-fluoro-2,2-dimethyl-4H-carbazol-4-one **7 R^1=4-F; R^2R^3=CO-CH_2-C(Me)$_2$-CH_2; R=H**

UV (MeOH) λ_{nm} (log ε) 247 (4.28), 269 (4.25), 293 (4.12). IR (NaCl) 3174 (NH), 2958 (C-H), 1614 (C=O). ^1H NMR ($CDCl_3$, DMSO) δ 10.90 (1 H, s, OH), 7.90-6.60 (3 H, m, Arom H), 2.80 (2 H, s, CH_2),

2.40 (2 H, s, CH_2), 1.15 (6 H, s, 2xMe). ^{13}C NMR ($CDCl_3$, DMSO) δ 191.0 (C-OH), 158.9-155.7 (C-F), 150.8 (Arom C), 131.4 (Arom C), 123.7-123.6 (Arom C), 110.9-110.7 (Arom CH), 109.6-109.6 (Arom C), 108.7-108.4 (Arom CH), 104.3-104.0 (Arom CH), 50.5 (CH_2), 35.4 (Me-C-Me), 33.9 (CH_2), 26.9 (2xMe). mp 200°C. Anal. Calcd for $C_{14}H_{14}ONF$: C, 72.70; H, 6.10; N, 6.05; F, 8.21. Found : C, 72.58; H, 5.80; N, 6.07; F, 8.23.

1,2,3,9-Tetrahydro-9-methyl-4H-carbazol-4-one **7 R^1=2-Me; R^2R^3=CO(CH_2)3; R=H**

IR (NaCl) 3189 (NH), 2939 (C-H), 1626 (C=O). ^1H NMR ($CDCl_3$, DMSO) δ 11.5 (1 H, s, OH); 7.8-7.5 (1 H, m, Arom H); 7.1-6.7 (2 H, m, Arom H); 3.2-2.8 (2 H, m, CH_2); 2.6-1.9 (7 H, m with s at 2.4, 2xCH_2 + Me). ^{13}C NMR ($CDCl_3$, DMSO) δ 191.0 (C-OH), 150.2 (Arom C), 133.4 (Arom C), 122.4 (Arom C), 121.2 (Arom CH), 119.8 (Arom CH), 118.9 (Arom CMe), 115.9 (Arom CH), 110.2 (Arom C), 36.0 (CH_2), 21.6 (CH_2), 20.9 (CH_2), 14.8 (Me). mp 287°C. X Rays spectroscopic data have been collected.[16]

1,2,3,9-Tetrahydro-9-methylsulfonyl-4H-carbazol-4-one **7 R^1=2-Me; R^2R^3=CO(CH_2)3; R=SO_2Me**

IR (NaCl) 2933-2869 (C-H), 1656 (C=O). ^1H NMR ($CDCl_3$) δ 8.30-8.15 (1 H, m, Arom H); 7.35-7.10 (2 H, m, Arom H); 3.35 (3 H, s, SMe); 3.30-3.20 (2 H, m, CH_2); 2.75 (3 H, s, Me); 2.65-2.55 (2 H, m, CH_2); 2.30-2.15 (2 H, m, CH_2). ^{13}C NMR ($CDCl_3$) δ 195.0 (C=O), 153.6 (Arom C), 136.0 (Arom CMe), 129.5 (Arom CH), 127.5 (Arom C), 125.2 (Arom CH), 124.4 (Arom C), 119.6 (Arom CH), 118.4 (Arom C), 42.8 (SMe), 37.7 (CH_2), 26.0 (CH_2), 23.5 (CH_2), 22.3 (Me). mp 140°C. Anal. Calcd for $C_{14}H_{15}NO_3S$: C, 60.62; H, 5.45; N, 5.05; S, 11.56. Found : C, 60.75; H, 5.38; N, 5.30; S, 11.46.

1,2,3,9-Tetrahydro-2,2,8-trimethyl-4H-carbazol-4-one **7 R^1=2-Me; R^2R^3=CO-CH_2-C(Me)2-CH_2; R=H**

IR (NaCl) 3182 (NH), 2960 (C-H), 1625 (C=O). ^1H NMR ($CDCl_3$, DMSO) δ 11.15 (1 H, s, OH); 7.90-7.50 (1 H, m, Arom H); 7.10-6.70 (2 H, m, Arom H); 2.80 (2 H, s, CH_2); 2.45 (3 H, s, Me), 2.30 (2 H, s, CH_2); 1.15 (6 H, s, 2xMe). ^{13}C NMR ($CDCl_3$, DMSO) δ 190.6 (C=O), 149.0 (Arom CMe), 134.0 (Arom C), 122.4 (Arom C), 121.3 (Arom CH), 119.9 (Arom CH), 119.0 (Arom C), 116.2 (Arom CH), 109.3 (Arom C), 50.4 (CH_2), 34.9 (CH_2), 33.5 (Me-C-Me), 26.6 (2xMe), 15.1 (OMe). mp 228°C. Anal. Calcd for $C_{15}H_{17}ON$: C, 79.25; H, 7.54; N, 6.16. Found : C, 78.92; H, 7.58; N, 6.17.

1,2,3,9-Tetrahydro-6-methoxy-4,4,9-trimethyl-2H-carbazol-2-one **9 R^1=OMe**

IR (NaCl) 2956-2865-2831 (C-H), 1720 (C=O). ^1H NMR ($CDCl_3$) δ 7.15-6.50 (3 H, m, Arom H), 3.75 (3 H, s, OMe); 3.48 (3 H, s, NMe); 3.43 (2 H, s, CH_2); 2.50 (2 H, s, CH_2); 1.40 (6 H, s, 2xMe). ^{13}C NMR ($CDCl_3$) δ 207.1 (C=O), 153.4 (C-OMe), 133.3 (Arom C), 130.7 (Arom C), 124.9 (Arom C), 116.8 (Arom C), 110.2 (Arom CH), 109.5 (Arom CH), 102.9 (Arom CH), 55.9 (OMe), 55.8 (CH_2), 37.7 (CH_2), 35.2 (Me-C-Me), 29.6 (2xMe), 29.2 (NMe). mp 110°C. Anal. Calcd for $C_{16}H_{19}O_2N$: C, 74.67; H, 7.44; N, 5.44. Found : C, 74.24; H, 7.41; N, 5.29.

1,2,3,9-Tetrahydro-6-methoxy-2,2,9-trimethyl-4H-carbazol-4-one **10 R^1=OMe**

UV (MeOH) λ_{nm} (log ε) 257 (4.42), 276 (4.21), 305 (4.18). IR (NaCl) 2997-2961-2873-2835 (C-H), 1651 (C=O). ^1H NMR ($CDCl_3$) δ 7.80-7.45 (1 H, m, Arom H), 7.20-6.55 (2 H, m, Arom H); 3.80 (3 H, s, OMe); 3.45 (3 H, s, NMe); 2.55 (2 H, s, CH_2); 2.25 (2 H, s, CH_2), 1.05 (6 H, s, 2xMe). ^{13}C NMR ($CDCl_3$) δ 192.6 (C=O), 155.9 (COMe), 150.5 (Arom C), 132.2 (Arom C), 124.9 (Arom C), 112.1 (Arom CH), 110.7 (Arom C), 109.6 (Arom CH), 102.8 (Arom CH), 55.5 (OMe), 51.5 (CH_2), 35.6-34.6 (C(Me)2, CH_2), 29.5 (NMe), 28.6 (C(Me)2). mp 133°C. Anal. Calcd for $C_{16}H_{19}O_2N$: C, 74.67; H, 7.44; N, 5.44. Found : C, 74.47; H, 7.35; N, 5.72.

1,2,3,9-Tetrahydro-4,4,9-trimethyl-2H-carbazol-2-one **9 R^1=H**

IR (NaCl) 2974-2954-2868 (C-H), 1722 (C=O). ^1H NMR ($CDCl_3$) δ 7.80-7.70 (1 H, s, Arom H); 7.40-7.00 (3 H, m, Arom H); 3.57 (5 H, s, NMe + CH_2); 2.63 (2 H, s, CH_2); 1.49 (6 H, s, 2xMe). ^{13}C NMR ($CDCl_3$) δ 207.2 (C=O), 137.8 (Arom C), 129.9 (Arom C), 124.7 (Arom C), 121.1 (Arom CH), 119.8 (Arom CH), 119.0 (Arom CH), 117.3 (Arom C), 109.0 (Arom CH), 55.8 (CH_2), 37.7 (Me-C-Me), 35.3 (CH_2), 29.8 (2xMe), 29.1 (NMe). mp 123°C. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.25; H, 7.54; N, 6.16. Found : C, 79.12;

H, 7.40; N, 6.28.

1,2,3,9-Tetrahydro-2,2,9-trimethyl-4H-carbazol-4-one **10 R¹=H**
IR (NaCl) 2958 (C-H), 1643 (C=O). ^{1}H NMR ($CDCl_3$) δ 8.30-8.10 (1 H, m, Arom H); 7.30-7.20 (3 H, m, Arom H); 3.60 (3 H, s, NMe); 2.64 (2 H, s, CH_2); 2.34 (2 H, s, CH_2); 1.12 (6 H, s, 2xMe). ^{13}C NMR ($CDCl_3$) δ 192.9 (C=O), 150.7 (Arom C), 137.5 (Arom C), 124.3 (Arom C), 122.5 (Arom CH), 122.2 (Arom CH), 121.2 (Arom CH), 111.0 (Arom C), 109.0 (Arom CH), 51.7 (CH_2), 35.7 (Me-C-Me), 34.9 (CH_2), 29.6 (NMe), 28.6 (2xMe). mp 115°C. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.25; H, 7.54; N, 6.16. Found : C, 79.20 ; H, 7.58; N, 6.20.

1,2,3,9-Tetrahydro-4,4,6,9-tetramethyl-2H-carbazol-2-one **9 R¹=Me**
IR (NaCl) 2961-2924-2864 (C-H), 1723 (C=O). ^{1}H NMR ($CDCl_3$) δ 7.54 (1 H, s, Arom H); 7.25-7.00 (2 H, m, Arom H); 3.59 (2 H, s, CH_2); 3.57 (3 H, s, NMe); 2.65 (2 H, s, CH_2); 2.49 (3 H, s, Me); 1.52 (6 H, s, 2xMe). ^{13}C NMR ($CDCl_3$) δ 207.3 (C=O), 136.3 (Arom C), 130.0 (Arom C), 128.1 (Arom C), 124.9 (Arom C), 122.6 (Arom CH), 119.6 (Arom CH), 116.8 (Arom C), 108.7 (Arom CH), 55.9 (CH_2), 37.7 (CH_2), 35.3 (Me-C-Me), 29.9 (2xMe), 29.1 (NMe), 21.5 (Me). mp : 170°C. Anal. Calcd for $C_{16}H_{19}NO$: C, 79.62; H, 7.93; N, 5.80. Found : C, 79.64; H, 7.94; N, 5.87.

1,2,3,9-Tetrahydro-2,2,6,9-tetramethyl-4H-carbazol-4-one **10 R¹=Me**
IR (NaCl) 2956-2917-2864 (C-H), 1644 (C=O). ^{1}H NMR ($CDCl_3$) δ 8.03 (1 H, s, Arom H); 7.20-7.00 (2 H, m, Arom H); 3.57 (3 H, s, NMe); 2.61 (2 H, s, CH_2); 2.45 (3 H, s, Me); 2.32 (2 H, s, CH_2); 1.11 (6 H, s, 2xMe). ^{13}C NMR ($CDCl_3$) δ 192.8 (C=O), 150.7 (Arom C), 135.8 (Arom C), 131.8 (Arom C), 124.5 (Arom C), 123.8 (Arom CH), 121.0 (Arom CH), 110.6 (Arom C), 108.7 (Arom CH), 51.7 (CH_2), 35.7 (CH_2), 34.8 (Me-C-Me), 29.6 (NMe), 28.6 (2xMe), 21.2 (Me). mp 183°C. Anal. Calcd for $C_{16}H_{19}NO$: C, 79.62; H, 7.93; N, 5.80. Found : C, 79.69; H, 7.96; N, 5.87.

6-Fluoro-1,2,3,9-Tetrahydro-4,4,9-trimethyl-2H-carbazol-2-one **9 R¹=F**
IR (NaCl) 2944-1873 (C-H), 1722 (C=O). ^{1}H NMR ($CDCl_3$) δ 7.40-6.40 (3 H, m, Arom H); 3.55 (3 H, s, NMe); 3.45 (2 H, s, CH_2); 2.55 (2 H, s, CH_2),1.40 (6 H, s, 2xMe). ^{13}C NMR ($CDCl_3$) δ 206.6 (C=O), 159.1-155.4 (Arom CF), 134.4 (Arom C), 131.8 (Arom C), 124.7-124.6 (Arom C), 117.3-117.2 (Arom C), 109.5-109.4 (Arom CH), 109.3-108.8 (Arom CH), 105.0-104.6 (Arom CH), 55.6 (CH_2), 37.7 (CH_2), 35.0 (Me-C-Me), 29.3 (NMe), 29.6 (2xMe), 29.3 (NMe). mp 141°C. Anal. Calcd for $C_{15}H_{16}NOF$: C, 73.44; H, 6.57; N, 5.71; F, 7.74; Found : C, 73.47; H, 6.75; N, 5.65; F, 7.80.

6-Fluoro-1,2,3,9-Tetrahydro-2,2,9-trimethyl-4H-carbazol-4-one **10 R¹=F**
UV (MeOH) λ_{nm} (log ε) 250 (4.27), 268 (4.17), 296 (4.14). IR (NaCl) 2957 (C-H), 1644 (C=O). ^{1}H NMR ($CDCl_3$) δ 7.90-7.80 (1 H, s. Arom H); 7.20-7.05 (1 H, m, Arom H); 7.00-6.80 (1 H, m, Arom H); 3.62 (3 H, s, NMe); 2.68 (2 H, s, CH_2); 2.33 (2 H, s, CH_2); 1.13 (6 H, s, 2xMe). ^{13}C NMR ($CDCl_3$) δ 192.6 (C=O), 161.3-157.5 (Arom CF), 151.8 (Arom C), 134.0 (Arom C), 125.0-124.8 (Arom C), 111.1-111.0 (Arom C), 110.5-110.1 (Arom CH), 109.8-109.7 (Arom CH), 106.7-106.4 (Arom CH), 51.64 (CH_2), 35.88 (CH_2), 34.87 (Me-C-Me), 29.85 (NMe), 28.62 (2xMe). mp 160°C. Anal. Calcd for $C_{15}H_{16}NOF$: C, 73.44; H, 6.57; N, 5.71; F, 7.74. Found : C, 73.48; H, 6.84; N, 5.81; F, 7.73.

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