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Friedel-Crafts chemistry. Part 60. Concise constructions of bridged polycycles of indanes, pyrido[3,2,1-jk]carbazoles and pyrido[3,2,1-kl]phenothiazines via Friedel-Crafts ring closures

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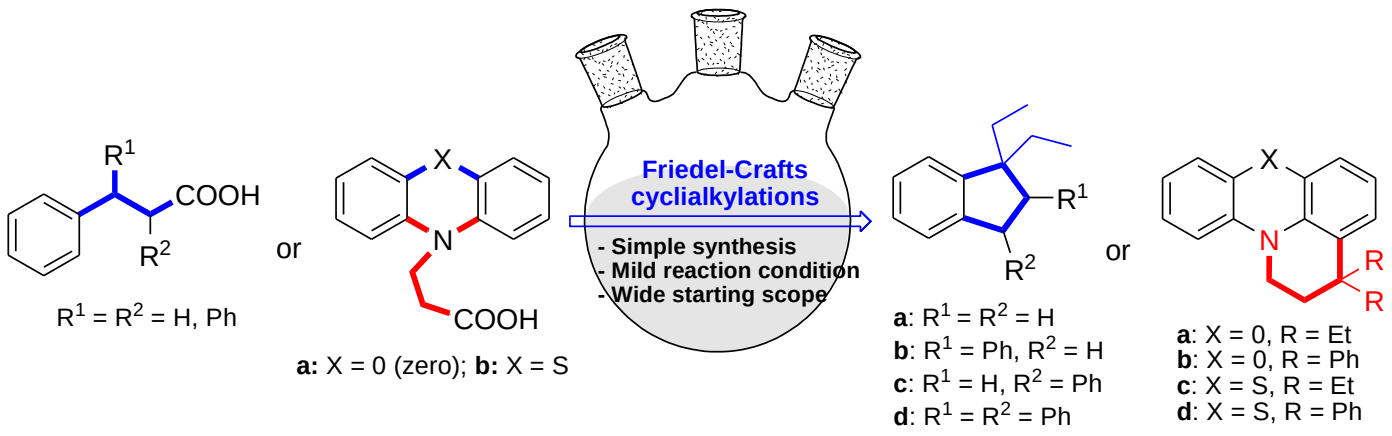
Abstract

Our present study provides expedient methods for the synthesis of novel substituted indanes, pyrido[3,2,1-*jk*]carbazoles and pyrido[3,2,1-*kl*]phenothiazines utilizing intramolecular Friedel-Crafts cyclialkylations of synthesized heteroaryl alcohols. This methodology is realized by a three-step protocol involving first esterification of starting carboxylic acids to the corresponding esters, addition of Grignard reagents to give carbinol precursors and followed by Friedel-Crafts cyclizations of alcohols mediated by $AlCl_3/CH_3NO_2$, PPA or P_2O_5-catalysts to furnish the desired polycycles in good to excellent yields of 65-85%. The designed protocol offers easy access to the pharmaceutically promising templates in good yields. The molecular structural elucidations of all newly obtained compounds have been proved by spectral and elemental analysis.



Keywords: Friedel-Crafts cycliacylations; polycycles; indanes; pyrido[3,2,1-*jk*]carbazoles; carbazoles

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Introduction

Polycycles containing the indane-template are important structural motifs common to biologically active molecules including alkaloids (see examples in Fig. 1).[1] As a result, functionalized indane skeletons have proven utility in the development of pharmaceuticals.[2] For instance, Lubazodone[3] is an antidepressant drug used for the treatments of major depressive disorders and also as a serotonin reuptake inhibitor; Zicronapine[4] is a typical antipsychotic medication showing also potent antagonistic effects at dopamine D1, D2 and serotonin 5HT2A receptor; the sesquiterpenoid taiwaniaquinol B[5] is used for the treatment of Alzheimer's disease and Retosiban[6] is an oral drug which acts as a oxytocin-receptor antagonist for the treatment of preterm labour.

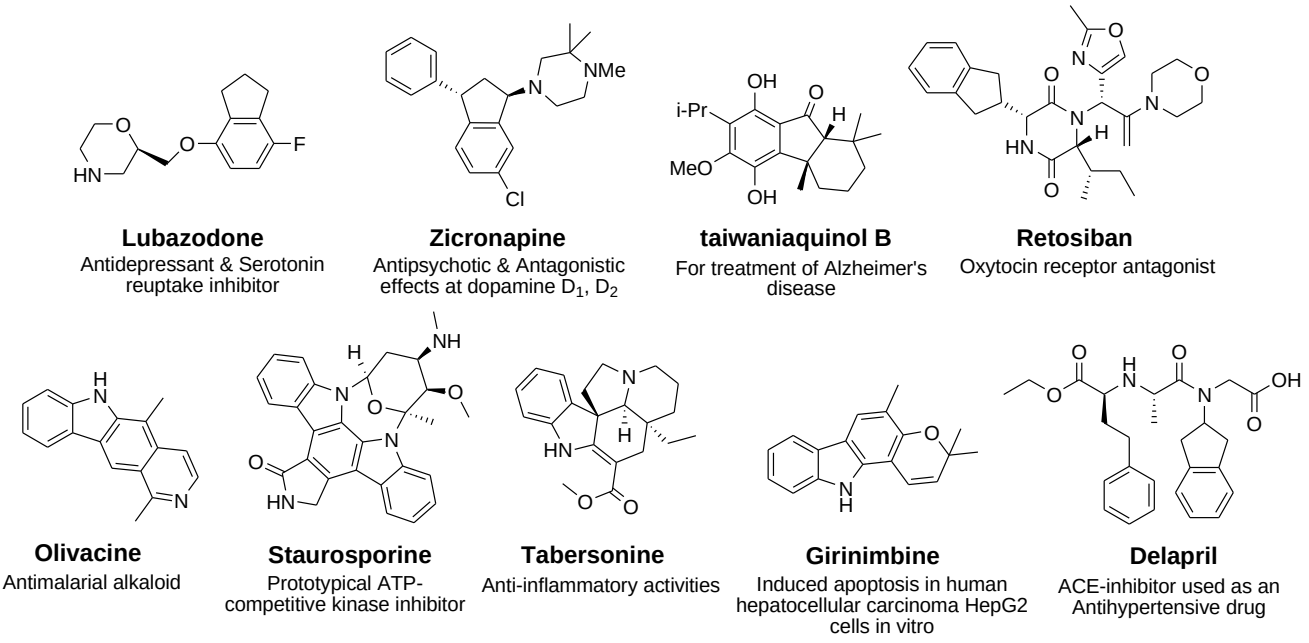


Figure 1. Some indanes and carbazole-based alkaloids used as pharmaceutical drugs

In the literature, numerous strategies for the synthesis of indane derivatives have been reported including: tandem Friedel-Crafts alkylations and acylations,[7] Dieckmann consensations,[8] Diels–Alder reactions,[9] photochemical rearrangements,[10] ring-closing metathesis reactions,[11] transition-metal catalyzed cycloadditions,[12] Cope rearrangements,[13] Aldol condensations,[14] Heck and Larock ring adjustment reactions,[15] palladium-catalyzed cyclization of 2-(2-iodoaryl)propionitriles,[16] Norrish-Yang photochemical cyclizations of 1,2-diketones, enones, enones and ynones,[17] intramolecular Cannizzaro reactions of methyl ketones with phthalaldehydes[18] and Nazarov cyclizations of α-carbonyl dienones using stoichiometric $MeSO_3H$ or $Cu(OTf)_2$ catalysts.[19]

On the other hand, among carbazole-fused polycycles subclasses, in particular, pyrido[3,2,1-*jk*]carbazole scaffolds exemplify a unique class of organic systems that are noted for their interesting biological activities that makes them appealing for the development of industrial applications with respect to optoelectronics,[20] dye-sensitized solar cells (DSCs)[21] and photochromic dyes.[22]

Precedents in the literature have also shown that the synthesis of some pyridocarbazoles have been achieved through thermal condensation of malonates with carbazoles,[23] Diels-Alder reactions of vinylindoles,[24] Graebe-Ullmann reactions via pyrolysis or photolysis of benzotriazoles,[25] photolysis of *N*-

aryltetrahydroquinolines,[26] dimerizations of N-vinylcarbazoles,[27] Fischer reactions of tetrahydroquinolines[28] and intermolecular [4+2] cycloadditions of benzotriazoles with alkenes.[29] It is worth mentioning that for a long time Friedel-Crafts chemistry has provided a reliable means to interesting carb- and heterocyclic scaffolds for materials, petrochemical, agrochemical and pharmaceutical applications. There are thus noteworthy examples in the literature in terms of pyrroloquinolines, pyrido[1,2–*a*]indolones, isoindoloisoquinolinones, indolizinoindolones, hydropyrido[1,2–*a*]indoles, indan–based frameworks, benzodiazocines and tetracyclic thiazocines (see representative examples in Fig. 2).[30-33] Although conventional Friedel-Crafts reactions are usually characterized by harsh conditions and poor to modest yields, this methodology has been extended to readily furnish a wide range of complex structures from simple starting materials in a one-pot fashion.

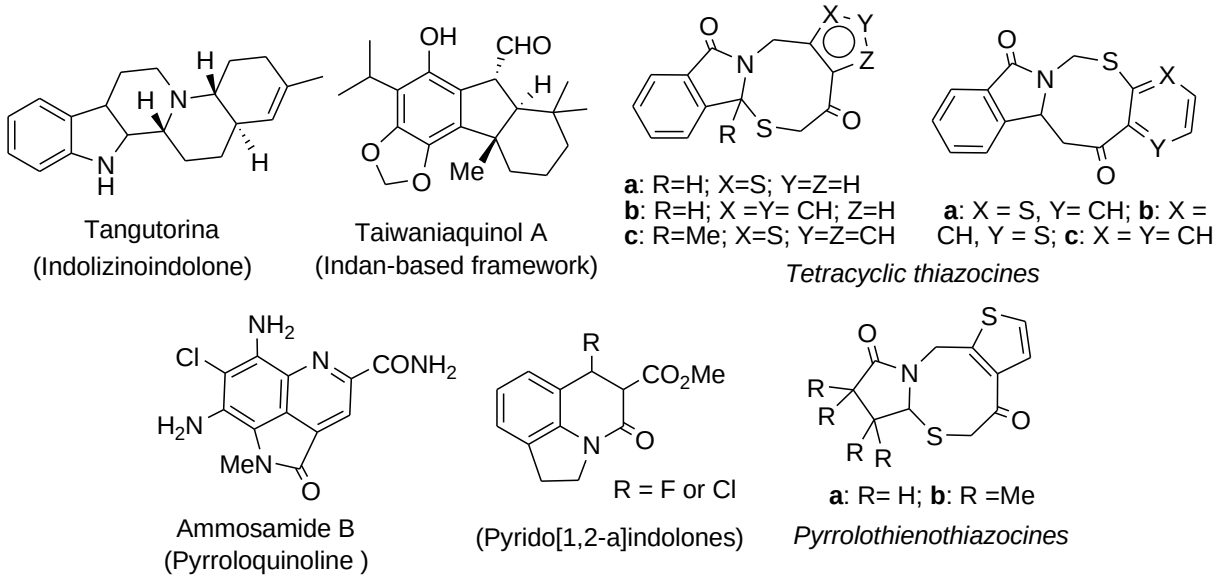


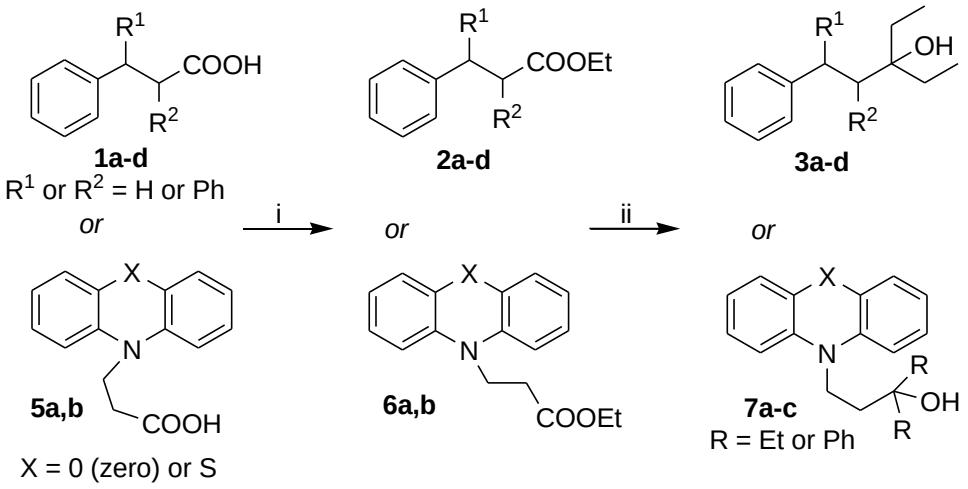
Figure 2. Examples of biologically active heterocycles synthesized by Friedel–Crafts processes

Notably, Friedel-Crafts reactions are generally associated with low enthalpic and relatively high entropic barriers in the transition state.[34] Accordingly, the unfavorable enthalpy and entropy factors independently affect the ease of cyclizations. To fairly assess these prior synthetic approaches in heterocyclic systems, as well as ascertain their strengths and weaknesses, examination of conditions suitable for the Friedel-Crafts in terms of choice and loading of catalysts, harshness of reactions conditions, substrate scope, efficiency, and versatility, needs to be carried out. In light of the above findings, as well as of our ongoing research programs and progresses on Friedel-Crafts reactions,[35-39] that have led to the construction of several condensed drug like homo-and heteropolycyclic systems, herein, we present our endeavors towards the synthesis of a series of indanes, pyridocarbazoles and pyridophenothiazines via cyclizations of some selectively synthesized alcohols in facile quick, one-step reactions resulting in the desired products in moderate to good yields. Our strategy offers easy access to such systems which appear to be attractive and valuable for future medicinal chemistry and drug discovery.

Results and Discussion

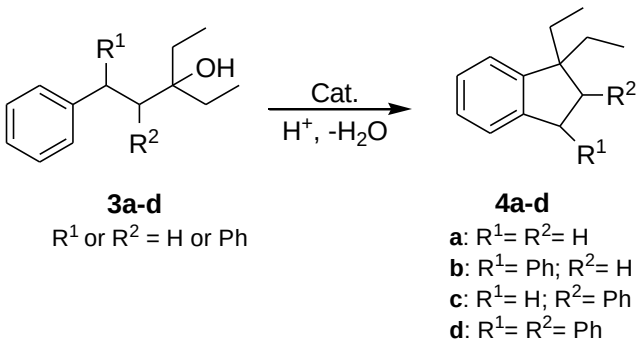
Syntheses of the heteroaryl alcohol **3a-d** & **7a-c** precursors required for this protocol were conducted from easily accessible starting materials as shown in Scheme 1. Firstly, the starting homo-and heteroaromatic carboxylic acids **1a**[40] (R^1 = R^2 = H), **1b**[41] (R^1 = Ph, R^2 = H), **1c**[42] (R^1 = H, R^2 = Ph), **1d**[43] (R^1 = R^2 = Ph), 3-(9H-

carbazol-9-yl)propanoic acid (**5a**)[44] and 3-(10H-phenothiazin-10-yl)propanoic acid (**5b**)[45] were obtained in good yields using indicated literature procedures. Secondly, these acids were esterified under $EtOH/H_2SO_4$ conditions and the resulting ethyl esters were converted into carbinol precursor's **3a-d** and **7a-c** in good yields by addition of the respective Grignard reagents (Scheme 1). Thirdly, our synthetic pathways to the desired indanes **4a-d** and heterocycles **8a-c** are outlined in Schemes 2 and 3. Initial investigations focused on the screening of conditions that would promote the intramolecular Friedel-Crafts cycliacylations of electro-rich benzyl carbinols **3a-d** and **7a-c**. Ring closures of these carbinols were effectively achieved in good yields using various mild Lewis and Brønsted acids such as $AlCl_3/CH_3NO_2$, polyphosphoric acid (PPA) and P_2O_5 under varying conditions.

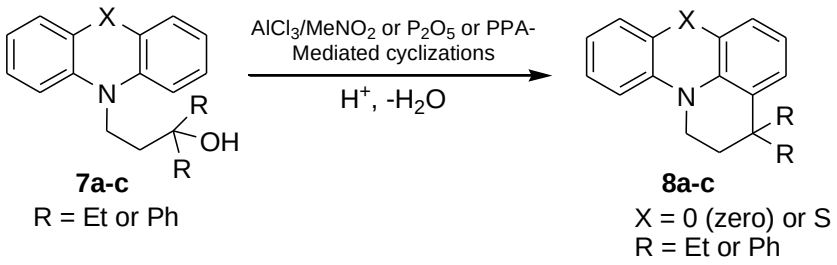


Scheme 1. Reagents and conditions: (i) $EtOH/H_2SO_4$, 8-10 h, reflux, 78-94%, (ii) RMgX, 12-14 h, rt, 75-88%.

The conditions and respective products, namely, indanes **4a-d** (Scheme 2 and Table 1, Entries 1-4), pyrido[3,2,1-*jk*]carbazoles **8a,b** (Scheme 3 and Table 1, Entries 5&6) and pyrido[3,2,1-*kl*]phenothiazine **8c** (Scheme 3 and Table 1, Entry 7) are embedded in Table 1. The structures of synthesized compounds, notably without stereochemical implications, were established using both spectral and analytical data.



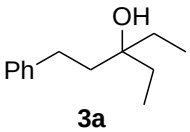
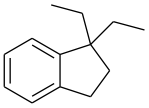
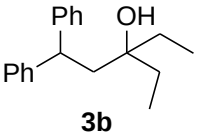
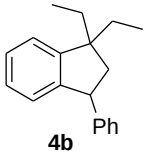
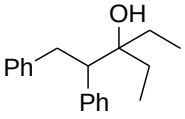
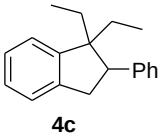
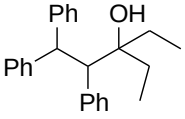
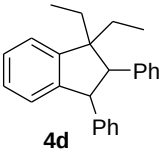
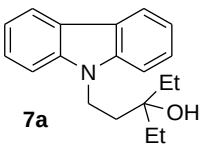
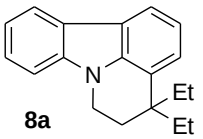
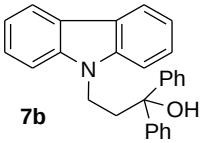
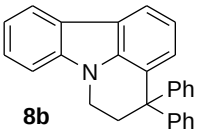
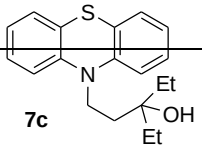
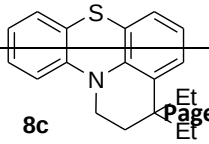
Scheme 2. $AlCl_3/CH_3NO_2$ or PPA or P_2O_5-mediated cyclizations of carbinols **3a-d** (Table 1).



Scheme 3. Lewis and Brønsted acids-catalyzed cyclialkylations of heterocyclic carbinols **7a-c** (Table 1).

Examination of the results compiled in Table 1 reveals that yields vary considerably with reaction conditions, including reaction duration, as well as types of catalyst and solvent. In the first sets of ring closure trials, we attempted cyclization of carbinol precursor **3a** using stoichiometric loading of moderate catalysts under different reaction conditions. This resulted in low conversion of starting material **3a** into cyclic **4a**. Therefore, multiple attempts were conducted to improve closure of **3a** by variations of the catalytic cyclization conditions. The conditions and results depicted on Table 1 thus appeared satisfactory.

Table 1: Optimized conditions and results of cyclization for carbinols **3a-d** and **7a-c**.

Entry	Carbinol	Product	Conditions	Yield (%)[A]
1	 **3a**	 **4a**	$AlCl_3/CH_3NO_2$[B], CH_2Cl_2, 8 h, rt	80
			P_2O_5[C], CH_2Cl_2, 6h, reflux	75
			PPA[D], 2 h, 180–190 °C	73
2	 **3b**	 **4b**	$AlCl_3/CH_3NO_2$, CH_2Cl_2, 10 h, rt	82
			P_2O_5, CH_2Cl_2, 5 h, reflux	80
			PPA, 2 h, 180–190 °C	70
3	 **3c**	 **4c**	$AlCl_3/CH_3NO_2$, CH_2Cl_2, 20 h, rt	78
			P_2O_5, CH_2Cl_2, 10 h, reflux	75
			PPA, 5 h, 180–190 °C	66
4	 **3d**	 **4d**	$AlCl_3/CH_3NO_2$, CH_2Cl_2, 17 h, rt	79
			P_2O_5, CH_2Cl_2, 5 h, reflux	85
			PPA, 5 h, 180–190 °C	72
5	 **7a**	 **8a**	$AlCl_3/CH_3NO_2$, CH_2Cl_2, 17 h, rt	82
			P_2O_5, CH_2Cl_2, 5 h, reflux	80
			PPA, 10 h, 180–190 °C	70
6	 **7b**	 **8b**	$AlCl_3/CH_3NO_2$, CH_2Cl_2, 18 h, rt	77
			P_2O_5, CH_2Cl_2, 20 h, reflux	82
			PPA, 24 h, 180–190 °C	68
7	 **7c**	 **8c**	$AlCl_3/CH_3NO_2$, CH_2Cl_2, 20 h, rt	84

	P_2O_5, CH_2Cl_2, 17 h, reflux	81
	PPA, 18 h, 180–190 °C	65

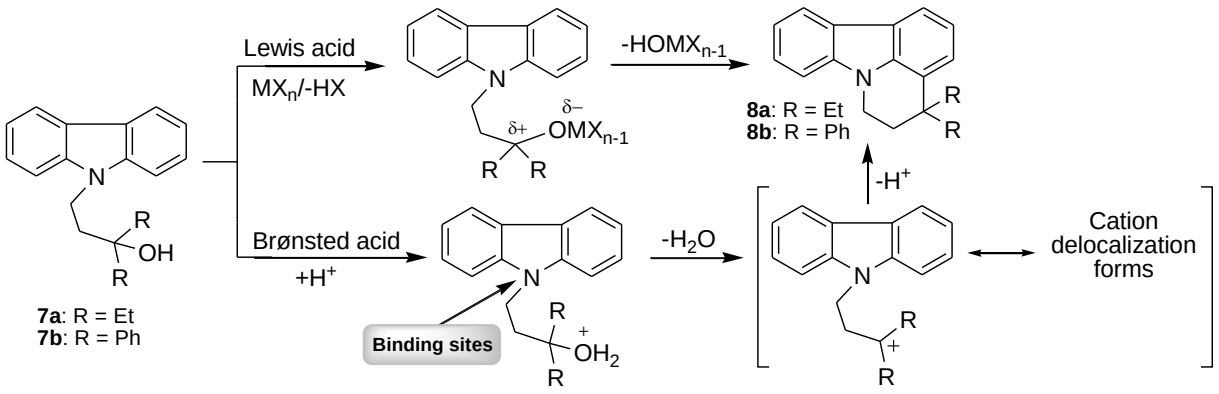
[A]Crude yields. [B]With $AlCl_3/CH_3NO_2$ catalyst reactant proportions were: carbinol (2 mmol), $AlCl_3$ (10 mmol) in CH_3NO_2 (80 mmol), solvent (10 mL). [C]With P_2O_5 catalyst reactant proportions were: carbinol (5 mmol) and P_2O_5 (20 mmol), solvent (15 mL). [D]With PPA catalyst reactant proportions were: acid (5 mmol) and PPA (15 g).

Evidently, steric effects also played a role on the ease of ring closures and increase bulk required harsher conditions. For instance, the steric hindrance caused by the bulky Ph-groups in closure of **7b** to **8b** with PPA required heating at 180-190 °C for 24 h to effect complete conversion. Crude products were purified by flash column chromatography and crystallization. The operational simplicity, optimized conditions and ready availability of all precursors make this methodology a useful tool for the assembly of such substituted indanes and *hetero*-tetracyclic carbazoles and phenothiazine skeletons.

The structures of all compounds obtained were determined by ^1H and ^{13}C NMR spectroscopy, gas chromatography-mass spectrometry (GC-MS), elemental analyses and mass spectrometry (MS). Thus, compound **8c**, was obtained as a yellow solid from methanol. It displayed an M^+ ion at *m/z* 295 consistent with the molecular formula $C_{19}H_{21}NS$ (295). The IR spectrum showed absorption peaks at 3061, 2964 cm^{-1} indicating the presence of aromatic and cyclic aliphatic protons respectively. The presence of methylene groups for cyclic skeleton **8c** at C-1 and C-2 was indicated from the ^1H NMR spectrum by the characteristic triplet at δ 1.84 for shielded C^2H_2 group and downfield triplet at δ 3.93 for deshielded protons of C^1H_2. Increasingly, ^{13}C- and DEPT-NMR spectroscopy showed the presence of seven sp^3-carbons with δ 7.9 (2C) for $2CH_3$-carbons, 31.2 (2C) for $2CH_2$-carbon and 35.3, 42.2, 74.5 corresponding to cyclic C-3, C-2 and C-1, respectively.

Owing to the diastereotopic methylene groups presenting unresolved signals, unlike the other multiplets of the spectrum, the assignment of the methylene groups of indane derivatives (**4b** at C-2 and **4c** at C-3) was made on the basis of *J*-values that were obtained by direct inspection of the ^1H NMR spectrum. Nevertheless, the ^1H NMR spectrum of indane **4c** showed the chemical shifts of the methylene protons of the ring at C-3 (Ha and Hb) to be a characteristic of an AB system appearing as multiplets on average near δ 3.30 ppm and C-2 proton showed as a triplet at δ 3.58 ppm with J 3.5 Hz. In comparison with the compound **4c**, bicyclic **4b** showed ^1H NMR spectroscopy chemical shifts in $CDCl_3$ for the C^2H_2 protons as characteristic multiplets at an average of δ 1.9 ppm, while the C-3 proton showed signals in the shape of triplets at of δ 4.26 ppm with *J* at an average of 4.2 Hz.

In this methodology of catalytic intramolecular Friedel-Crafts reactions, several mechanisms are possible, particularly when either the Brønsted acid or the Lewis acid cases are to be considered. Mechanistically[46] in fact, it is well known that Friedel-Crafts alkylation reactions, for example, are electrophilic aromatic substitutions involving carbocations as intermediates. One method to generate carbocations from alcohols involves the treatment with either Lewis or Brønsted acid catalysts. The steps involved in these operations are illustrated by those formulated in scheme 4. The distinct reactivity of the electron-rich versus the electron-deficient substrates has also been proposed. Operationally, a simple cyclization reaction would be facilitated by the highly electrophilic precursor that is easily prepared and functionalized.



Scheme 4. Proposed mechanism for the Friedel-Crafts cyclization of carbinols **7a,b**.

As postulated in Scheme 4, the treatment of carbinols with acidic catalysts results in stable catalyst-substrate complexes or substrates with protonated heteroatoms in the case of Brønsted-catalysts.[47] Further loss of H_2O or $HOMX_{n-1}$ molecules then generates the carbocation, either in its free form or as an ion pair.[48,49] The generated tertiary carbocations are stabilized by either (or both) resonance delocalizations or hyperconjugative interactions.[50] Subsequently, electrophilic reactions with these carbocations, followed by loss of a ring proton then provided a series of di-and tetracyclic products under Friedel-Crafts conditions.

Conclusions

In conclusion, we have developed a facile and efficient approach to synthesize new substituted indanes, pyrido[3,2,1-*jk*]carbazoles and pyrido[3,2,1-*kl*]phenothiazines via intramolecular Friedel-Crafts reactions. The results presented herein highlighted the operational simplicity by way of optimized conditions and ready availability of all precursors which justifies this approaches synthetic utility as a useful tool for the construction of a wide range of homo-and heterocyclic ring systems.

Experimental Section

General. All chemicals used were of reagent grade and solvents were freshly distilled and dried by standard procedures before use. Melting points were taken on a digital Gallenkamp capillary melting point apparatus. Infrared (IR) spectra were obtained on a on a Mattson 5000 FT-IR spectrophotometer using KBr wafer and thin film techniques (ν cm^{-1}). The ^{1}H- and ^{13}C-NMR spectroscopy measurements were obtained with a Jeol-JNM ECA 400 MHz and on Varian NMR (90 MHz) spectrometers in $CDCl_3$ solution, and chemical shifts are expressed in δ (ppm) with reference to TMS as well as coupling constants (*J*) in Hertz. The ^{13}C-multiplicities were determined by the DEPT pulse sequence (90^o). Mass spectra were measured on a Perkin Elmer PE SCIEX-API 2000 mass spectrometer at an ionizing potential of 70 eV using the direct inlet system. Elemental analyses were performed on a GmbH Vario-EL III, 2400, CHNOS-elemental analyzer. All reactions were monitored by thin layer chromatography (TLC) using aluminum-backed plates coated with Merck Kieselgel 60 GF254. Plates were visualized under UV light (at 254 and/or 360 nm). Flash column chromatography was performed on silica gel and basic alumina.

General procedure for the synthesis of alcohols 3a-d & 7a,c. These cyclization precursors were obtained in two reaction steps starting with carboxylic acids **1a-d** or **5a,b**. A summary of the steps is given in the following:
A. A mixture of acid **1a-d** or **5a,b** (20 mmol), absolute EtOH (30 mL) and concentrated sulfuric acid (3-5 mL) was refluxed for 8-10 h. The excess alcohol was removed in *vacuo* and the residue was diluted with water (50 mL), basified by addition of solid Na_2CO_3 and finally extracted with ether (3×30 mL). The organic layer was separated, washed with water and dried over anhydrous $MgSO_4$. Afterwards, the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (basic alumina, EtOAc/*n*-hexane, 1/1) gave the pure product **2a-d** or **6a,b**. The yields and spectral data are given below:
Ethyl 3-phenylpropanoate (2a). Yellow viscous oil; Yield 90%; n_D^{25} l.5710 (Lit.[40] b.p. 90-94 °C/10 mm)**;** IR (Film, ν_{max}, cm^{-1}): 2982, 1731, 1457, 1373, 1160, 1035, 749, 700. ^{1}H NMR (90 MHz, $CDCl_3$, δ, ppm): δ 1.35 (t, 3H, *J* 7 Hz, $\underline{CH_3}CH_2O$), 2.70 (t, 2H, J 7.5 Hz, $Ph\underline{CH_2}$), 3.25 (t, 2H, *J* 7.5 Hz, $\underline{CH_2}CO$), 4.15 (q, 2H, *J* 7 Hz, $CH_3\underline{CH_2O}$), 7.20-7.60 (m, 5H, ArH). Anal. Calcd. for $C_{11}H_{14}O_2$ (178); C, 74.15; H, 7.86. Found; C, 74.33; H, 7.80.%.
Ethyl 3,3-diphenylpropanoate (2b). Yellowish viscous oil; Yield 88%; n_D^{25} l.5664 (Lit.[41] b.p. 153-154 °C/20 mm); IR (Film, ν, cm^{-1}): 3061, 2981, 2934, 1735, 1599, 1494, 1451, 1371, 1255, 1152, 746, 700. ^{1}H NMR (90 MHz, $CDCl_3$, δ, ppm): 1.15 (t, 3H, *J* 9 Hz, $\underline{CH_3}CH_2O$), 3.2 (d, 2H, *J* 7.5 Hz, CH_2), 3.80 (q, 2H, *J* 9 Hz, $CH_3\underline{CH_2}O$), 4.65 (t, 1H, *J* 7.5 Hz, $(Ph)_2CH$), 7.15-7.60 (m, 10H, ArH). Anal. Calcd. for $C_{17}H_{18}O_2$ (254); C, 80.31; H, 7.08. Found; C, 80.30; H, 7.12%.

Ethyl 2,3-diphenylpropanoate (2c). Pale yellow viscous oil; Yield 92%; n_D^{25} l.6037 (Lit.[42] b.p. 168-170 °C/8 mm); IR (KBr, ν, cm^{-1}): 3086, 2981, 2934, 1731, 1601, 1496, 1451, 1370, 1211, 1152, 748. ^{1}H NMR (90 MHz, $CDCl_3$, δ, ppm): 1.20 (t, 3H, *J* 7.5 Hz, $\underline{CH_3}CH_2O$), 2.90 (t, 1H, *J* 9 Hz, $C^{\beta}Ha$), 3.35 (t, 1H, J 9 Hz, $C^{\beta}Hb$), 3.70 (d, 1H, *J* 9 Hz, CHPh), 4.20 (q, 2H, *J* 7.5 Hz, $CH_3\underline{CH_2}O$), 7.00-7.60 (m, 10H, ArH). Anal. Calcd. for $C_{17}H_{18}O_2$ (254); C, 80.31; H, 7.08. Found; C, 80.51; H, 6.87%.
Ethyl 2,3,3-triphenylpropanoate (2d). White crystals; Yield 78% (cyclohexane); mp 116-18 °C (Lit.[43] mp 119 °C); IR (KBr, ν, cm^{-1}): 3028, 2978, 2931, 1719, 1600, 1496, 1454, 1370, 1298, 1171, 746, 796. ^{1}H NMR (90 MHz, $CDCl_3$, δ, ppm): 0.95 (t, 3H, *J* 7.5 Hz, $\underline{CH_3}CH_2O$), 3.80 (q, 2H, *J* 7.5 Hz, $CH_3\underline{CH_2}O$), 4.40 (d, 1H, J 13.5 Hz, $(Ph)_2C^{\beta}H$), 4.60 (d, 1H, J 13.5 Hz, $PhC^{\alpha}HCO$), 6.80-7.50 (m, 15H, ArH). Anal. Calcd. for $C_{23}H_{22}O_2$ (330); C, 83.63; H, 6.66. Found; C, 83.68; H, 6.59%.
Ethyl 3-(9*H*-carbazol-9-yl)propanoate (6a). Yellow viscous oil; Yield 94%; n_D^{25} 1.5722 (Lit.[44] n_D^{25} 1.5757); IR (Film, ν, cm^{-1}): 3051, 2963, 2935, 1729, 1594, 1485, 1463, 1452, 1350, 1210, 751, 720. ^{1}H NMR (90 MHz, $CDCl_3$, δ, ppm): 1.25 (t, 3H, *J* 9 Hz, $\underline{CH_3}CH_2O$), 2.80 (t, 2H, *J* 7.5 Hz, $C^{\alpha}H_2CO$), 4.20 (q, 2H, *J* 9 Hz, $CH_3\underline{CH_2}O$), 4.27 (t, 2H, *J* 7.5 Hz, $NC^{\beta}H_2$), 6.60-7.60 (m, 8H, ArH). MS (EI, 70 eV) *m/z* (%), 267 (M^+, 22.8), 252 (M^+-CH_3, 46.3), 239 (15.7), 238 (M^+-C_2H_5, 74.5), 222 (100), 208 (9.6), 194 (15.7), 166 (45.6), 91 (8.4), 77 (4.2). Anal. Calcd. for $C_{17}H_{17}NO_2$ (267); C, 76.40; H, 6.36; N, 5.24. Found; C, 76.27; H, 6.30; N, 5.33%.
Ethyl 3-(10*H*-phenothiazin-10-yl)propanoate (6b). Brownish crystals: Yield 84% (cyclohexane); mp 62 °C (Lit.[45] mp 64 °C, bp 263-65°C/20 mm); IR (KBr, ν, cm^{-1}): 3059, 2979, 2915, 1732, 1479, 1455, 1448, 1271, 1025, 773. ^{1}H NMR (90 MHz, $CDCl_3$, δ, ppm): 1.30 (t, 3H, *J* 7.5 Hz, $\underline{CH_3}CH_2O$), 2.80 (t, 2H, *J* 6 Hz, $C^{\alpha}H_2CO$), 4.00-4.40 (m, 5H, $NC^{\beta}H_2$ & $CH_3\underline{CH_2}O$), 6.70-7.50 (m, 8H, ArH). Anal. Calcd. for $C_{17}H_{17}NO_2S$ (299); C, 68.22; H, 5.68; N, 4.68; S, 10.70. Found; C, 68.41; H, 5.62; N, 4.59; S, 10.84%.

B. To an ice-cold Grignard reagent obtained as usual from Mg turnings (8 mmol) and alkyl or aryl halide (8 mmol) in ether (25 ml) was added ester **2a-d** or **6a,b** (3.6 mmol). The reaction mixture was stirred for 12-14 h at room temperature and finally decomposed by saturated NH_4Cl soln. The product was extracted with ether (3×30 mL) and the combined organic phases were washed with water, dried over anhydrous $MgSO_4$ and the

solvent was evaporated in *vacuo*. The residue was purified by flash column chromatography (basic alumina, ethyl acetate/hexane, 1:1) to afford the pure alcohols **3a-d** or **7a-c**. The conditions, yields and spectral data are given as the following:

3-Ethyl-1-phenylpentan-3-ol (3a). Yellow oil; Yield 88%, (Lit.[40] bp 117-119 °C/13 mm); IR (Film, ν, cm^{-1}): 3423, 3085, 2966, 1520, 1496, 1480, 1455, 698. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 0.76 (t, 6H, J 0.7 Hz, $2CH_3$), 1.40 (q, 4H, *J* 1.4 Hz, $2CH_2$), 1.60 & 2.50 (m, AA'XX' system, 2 × 2H), 1.86 (s, 1H, OH exchangeable with D_2O), 6.90-7.70 (m, 5H, ArH). Anal. Calcd. for $C_{13}H_{20}O$ (192); C, 80.25; H, 10.41. Found; C, 80.09; H, 10.42%.

3-Ethyl-1,1-diphenylpentan-3-ol (3b). Reddish oil; Yield 83%; n_D^{25} 1.5528. IR (Film, ν, cm^{-1}): 3568, 3085, 2966, 2879, 1493, 1462, 1451, 1310, 1215, 1080, 745. ^{1}H NMR (90 MHz, $CDCl_3$, δ, ppm): 0.71 (t, 6H, J 0.7 Hz, $2CH_3$), 1.18 (s, 1H, OH exchangeable with D_2O), 1.37 (q, 4H, *J* 1.3 Hz, $2CH_2$), 2.21 (d, 2H, *J* 2.2 Hz, CH_2), 4.08 (t, 1H, *J* 4.0 Hz, CH), 7.02-7.61 (m, 10H, ArH). Anal. Calcd. for $C_{19}H_{24}O$ (268); C, 85.07; H, 8.95. Found; C, 85.13; H, 9.06%.

3-Ethyl-1,2-diphenylpentan-3-ol (3c). Yellow viscous oil; Yield 85%; n_D^{25} 1.5781. IR (Film, ν, cm^{-1}): 3568, 3026, 2967, 1495, 1454, 1381, 1154, 698. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 0.86 (t, 6H, J 0.8 Hz, $2CH_3$), 1.73 (s, 1H, OH exchangeable with D_2O), 1.77 (q, 4H, J 1.7 Hz, $2CH_2$), 3.08-3.45 (m, 2H, CH_2), 4.19 (t, 1H, *J* 4.2 Hz, CH), 7.00-7.54 (m, 10H, ArH). MS (EI, 70 eV) *m/z* (%), 268 (M^+, 88.9), 253 (M^+-15, 25.4), 211 (M^+-57, 19.8), 143 (33), 91 (22.6), 81 (26.2), 55 (30.8), 43 (100). Anal. Calcd. for $C_{19}H_{24}O$ (268); C, 85.07; H, 8.95. Found; C, 85.05; H, 8.82%.

3-Ethyl-1,1,2-triphenylpentan-3-ol (3d). White crystals; Yield 75%; mp 66-67 °C (Petroleum ether 60-80 °C); IR (KBr, ν, cm^{-1}): 3570, 3460, 3050, 2975, 1590, 1540, 1490, 1445, 1340, 1360, 1180, 1065, 740. ^{1}H NMR (90 MHz, $CDCl_3$, δ, ppm): 0.80 (t, 6, J 6Hz, $2CH_3$), 2.00-2.50 (m, 4H, $2CH_2$), 3.30 (s, 1, OH exchangeable with D_2O), 4.55 (d, 1H, J 10.5 Hz, PhCH), 4.80 (d, 1H, J 10.5 Hz, $(Ph)_2CH$), 6.80-7.60 (m, 15, ArH). Anal. Calcd. for $C_{25}H_{28}O$ (344); C, 87.20; H, 8.14. Found; C, 87.37; H, 8.04%.

1-(9*H*-Carbazol-9-yl)-3-ethylpentan-3-ol (7a). White needles; Yield 83% (methanol), mp 106-108 °C; IR (KBr, ν, cm^{-1}): 3652, 3051, 2963, 1470, 1486, 1463, 1350, 1276, 1100, 900, 757. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 0.95 (t, 6H, *J* 0.9 Hz, $2CH_3$), 1.60 (s, 1H, OH exchangeable with D_2O), 1.65 (q, 4H, *J* 1.6 Hz, $2CH_2$), 1.93 (t, 2H, *J* 1.9 Hz, CH_2), 4.45 (t, 2H, *J* 4.4 Hz, CH_2), 6.60-7.54 (m, 8H, ArH). MS (EI, 70 eV) *m/z* (%), 281 (M^+, 20.9), 180 (100), 152 (9), 126 (2), 32 (5). Anal. Calcd. for $C_{19}H_{23}NO$ (281); C, 81.13; H, 8.18; N, 4.98. Found; C, 81.10; H, 8.24; N, 4.90%.

3-(9*H*-Carbazol-9-yl)-1,1-diphenylpropan-1-ol (7b). Yellow crystals; Yield 80% (methanol), mp 160-162 °C; IR (KBr, ν, cm^{-1}): 3545, 3083, 2960, 1498, 1474, 1456, 1345, 1266, 1169, 753, 647. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.20 (s, 1H, OH exchangeable with D_2O), 2.26 (t, 2H, *J* 2.2 Hz, CH_2), 3.80 (t, 2H, *J* 3.8 Hz, CH_2), 6.43-7.87 (m, 18H, ArH). MS (EI, 70 eV) *m/z* (%), 377.1 (M^+, 46), 295 (M^+-18, 2), 180 (100), 167 (22), 152 (15), 105 (30), 77 (13), 40 (7), 32 (68). Anal. Calcd. for $C_{27}H_{23}NO$ (377); C, 85.94; H, 6.10; N, 3.71. Found; C, 86.03; H, 6.17; N, 3.55%.

3-Ethyl-1-(10*H*-phenothiazin-10-yl)pentan-3-ol (7c). Brownish plates; Yield 77%, mp 75-77 °C (methanol); IR (KBr, ν, cm^{-1}): 3452, 3061, 2965, 1520, 1480, 1465, 1250, 741, 1120, 1030, 720. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 0.81 (t, 6H, *J* 0.7 Hz, $2CH_3$), 1.34 (s,1H, OH exchangeable with D_2O), 1.45 (q, 4H, *J* 1.4 Hz, $2CH_2$), 1.83 (t, 2H, *J* 1.8 Hz, CH_2), 3.93 (t, 2H, *J* 3.9 Hz, CH_2), 6.80-7.76 (m, 8H, ArH). MS (EI, 70 eV) *m/z* (%), 313 (M^+, 42), 212 (100), 198 (85), 199 (32), 180 (35), 154 (6), 127 (2), 87 (2), 57 (1), 32 (29). Anal. Calcd. for $C_{19}H_{23}NOS$ (313); C, 72.84; H, 7.34; N, 4.47; S, 10.22. Found; C, 72.77; H, 7.51; N, 4.40; S, 10.28%.

Cyclization procedures. Friedel-Crafts cyclization procedures[36] using $AlCl_3/CH_3NO_2$ or P_2O_5 or PPA were essentially followed. The crude products were purified by flash column chromatography (basic alumina, EtOAc/n-hexane, 1/2) and by crystallization from a suitable solvents. The conditions and

yields for the products 4a-d and 8a-c are shown in Table 1, while the physical and spectral data of the products are given in the following*:*

1,1-Diethyl-2,3-dihydro-1*H*-indene (4a). Yellow viscous oil; Yield 91%, n_D^{25} 1.6704. IR (Film, ν, cm^{-1}): 2961, 2873, 1510, 1490,1476, 1463, 754. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 1.49 (t, 6H, *J* 1.5 Hz, $2CH_3$), 1.71 (q, 4H, *J* 1.7 Hz, $2CH_2$), 2.09 (t, 2H, *J* 2.0 Hz, CH_2), 3.19 (t, 2H, *J* 3.2 Hz, CH_2), 7.20-7.67 (m, 4H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 21.2 (2C), 26.29 (2C), 36.5, 38.2, 42.2, 125.5, 125.8, 129.2, 129.4, 136.3, 143.7. MS (EI, 70 eV) *m/z* (%), 174 (M^+, 56), 159 (M^+-29, 63), 145 (75), 117 (100), 91 (21). Anal. Calcd. for $C_{13}H_{18}$ (174); C, 89.65; H, 10.34. Found; C, 89.52; H, 10.22%.

1,1-Diethyl-2,3-dihydro-3-phenyl-1*H*-indene (4b). Yellow viscous oil; Yield 91%; n_D^{25} 1.5840. IR (Film, ν, cm^{-1}): 3061, 2961, 2875, 1493, 1453, 1374, 1251, 1110, 756, 700. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 0.74 (t, 6H, J 0.7 Hz, $2CH_3$), 1.10 (q, 4H, J 1.0 Hz, $2CH_2$), 1.91 (m, 2H, CH_2), 4.26 (t, 1H, *J* 4.2 Hz, CH), 6.70-7.81 (m, 9H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 14.1, 40.9, 44.3, 49.4, 50.8, 123.4, 125.1, 126.2, 126.5, 127.7, 128.0, 128.4, 128.5 (2C), 128.5, 128.8 (2C), 130.8, 143.6. MS (EI, 70 eV) *m/z* (%), 250 (M^+, 32.7), 235 (M^+-15, 13.5), 180 (100), 131 (21.8), 91 (27.9), 77 (9.5). Anal. Calcd. for $C_{19}H_{22}$ (250); C, 91.20; H, 8.80. Found; C, 91.23; H, 8.75%.

1,1-Diethyl-2,3-dihydro-2-phenyl-1*H*-indene (4c). Brown viscous oil; Yield 93%; n_D^{25} 1.5882. IR (Film, ν, cm^{-1}): 3061, 3026, 2961, 2876, 1494, 1452, 1378, 757, 699. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 0.83 (t, 6H, J 0.8 Hz, $2CH_3$), 1.42 (q, 4H, *J* 1.4 Hz, $2CH_2$), 3.30 (m, 2H, CH_2), 3.58 (t, 1H, *J* 3.5 Hz, CH), 6.75-7.68 (m, 9H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 17.9, 38.8, 48.0, 51.8, 54.2, 124.7, 125.6, 126.3, 126.2, 126.3, 127.2, 127.7 (2C), 127.9, 128.0 (2C), 128.8, 128.9, 144.5. MS (EI, 70 eV) *m/z* (%), 250 (M^+, 77.9), 235 (M^+-15, 25.4), 221 (M^+-29, 95.8), 179 (29.7), 143 (37.5), 128 (27.9), 105 (32), 91(100). Anal. Calcd. for $C_{19}H_{22}$ (250); C, 91.20; H, 8.80. Found; C, 91.31; H, 8.65%.

1,1-Diethyl-2,3-dihydro-2,3-diphenyl-1*H*-indene (4d). Yellow viscous oil; Yield 82%; n_D^{25} 1.6159; IR (Film, ν, cm^{-1}): 3040, 2985, 1595, 1580, 1480, 1445, 1070, 1025, 750, 700. ^{1}H NMR (90 MHz, $CDCl_3$, δ, ppm): 0.9 (t, 6, *J* 7.5 Hz, $2CH_3$), 2.25 (q, 4, *J* 7.5 Hz, $2CH_2$), 3.7 (d, 1, *J* 9 Hz, C^2H), 4.5 (d, 1, *J* 9 Hz, C^3H), 6.6-7.4 (m, 14H, ArH). MS (EI, 70 eV) *m/z* (%), 326 (M^+, 0.3), 311 (M^+-CH_3, 0.2), 297 (M^+-C_2H_5, 3.6), 268 (M^+-$2C_2H_5$, 1.4), 249 (M^+-Ph, 0.9), 234 (M^+-Ph-CH_3, 0.4), 219 (M^+-Ph-C_2H_5-H, 1.2), 172 (M^+-2Ph, 0.2), 167 (45.0), 166 (100), 164 (56.1), 151 (25.1), 143 (M^+-2Ph-C_2H_5-3H, 0.2), 91 (1.8), 90 (16.2), 77 (8.9). Anal. Calcd. for $C_{25}H_{26}$ (326); C, 92.02; H, 7.97. Found; C, 91.14; H, 8.74%.

4,4-Diethyl-5,6-dihydro-4*H*-pyrido[3,2,1-*jk*]carbazole (8a). Green crystals; Yield 85%, mp 80-82°C (methanol); IR (KBr, ν, cm^{-1}): 3052, 2962, 1620, 1493, 1456, 1436, 1330, 1295, 1060, 1025, 749. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 0.75 (t, 6H, J 0.7, $2CH_3$), 1.66 (q, 4H, *J* 1.6, $2CH_2$), 1.94 (t, 2H, J 1.9, CH_2), 4.05 (t, 2H, *J* 4.0, CH_2), 6.90-8.21 (m, 7H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 7.03 (2C), 28.9 (2C), 30.1, 36.7, 37.1, 107.1, 116.6, 117.2, 117.5, 119.6, 119.8, 120.6, 122.1, 124.1, 125.5, 136.2, 138.5. MS (EI, 70 eV) *m/z* (%), 263 (M^+, 43.6), 234 (M^+-29,100), 204 (M^+-59, 17.3), 180 (6.7), 102 (5.4). DEPT-90°: 7.03 (CH_3), 28.9 (CH_2), 30.1 (CH_2), 36.7 (CH_2). Anal. Calcd. for $C_{19}H_{21}N$ (263); C, 86.69; H, 7.98; N, 5.32. Found; C, 86.82; H, 8.07; N, 5.17%.

5,6-Dihydro-4,4-diphenyl-4*H*-pyrido[3,2,1-*jk*]carbazole (8b). Brown plates; 90%, mp 102-103°C (benzene); IR (Film, ν, cm^{-1}): 3053, 2926, 2865, 1492, 1472, 1445, 1294, 1115, 750. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 2.87 (t, 2H, *J* 2.8 Hz, CH_2), 3.83 (t, 2H, *J* 3.8 Hz, CH_2), 6.5-8.0 (m, 17H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 31.3, 34.1, 46.3, 103.5, 106.1, 114.0, 114.6 (2C), 115.5, 116.1, 118.2, 120.4, 120.7, 121.0, 121.8 (2C), 123.4 (4C), 124.0 (4C), 132.7, 135.0, 141.3. MS (EI, 70 eV) *m/z* (%), 359 (M^+, 100), 282 (M^+ -77,83.3), 204 (48.5), 77(9,9). DEPT-90°: 31.3 (CH_2), 34.1 (CH_2). Anal. Calcd. for $C_{27}H_{21}N$ (359); C, 90.25; H, 5.85; N, 3.90. Found; C, 90.24; H, 5.69; N, 4.10%.

3,3-Diethyl-2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazine (8c). Yellow solid; 86%, mp 116-18°C (methanol); IR (KBr, ν, cm^{-1}): 3061, 2964, 2876, 1492, 1472, 1458, 1443, 1429, 747. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 0.78 (t, 6H, J 0.7 Hz, $2CH_3$), 1.44 (q, 4H, *J* 1.4 Hz , $2CH_2$), 1.84 (t, 2H, J 1.8 Hz, CH_2), 3.93 (t, 2H, *J* 3.9 Hz, CH_2), 6.66-7.78 (m, 7H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 7,9 (2C), 31.2 (2C), 35.3, 42.2 ,74.5, 112.8, 115.2, 115.5, 121.5, 122.3, 122.6, 125.1, 125.3, 126.8, 127.3, 127.5, 145.3. MS (EI, 70 eV) *m/z* (%), 295 (M^+, 100), 266 (M^+-29, 93.2), 236 (M^+-32, 40.3), 199 (29), 167 (29.8), 94 (21), 69 (11.7). DEPT-90°: 7.9 (CH_3), 31.2 (CH_2), 34 (CH_2), 42.2 (CH_2). Anal. Calcd. for $C_{19}H_{21}NS$ (295); C, 77.28; H, 7.11; N, 4.74; S, 10.84. Found; C, 77.33; H, 7.19; N, 4.90; S, 10.71%.

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