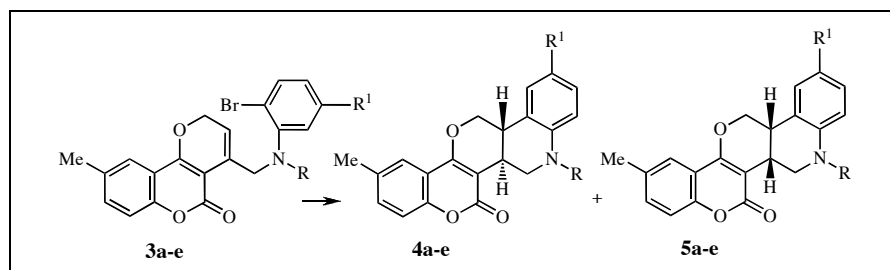


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Regioselective synthesis of a number of coumarin-annulated pentacyclic heterocycles have been achieved by tri-*n*-butyltin hydride-mediated aryl radical cyclization. The products are formed as a mixture of *cis*- and *trans*- forms which were successfully separated by careful silica gel flash chromatography.

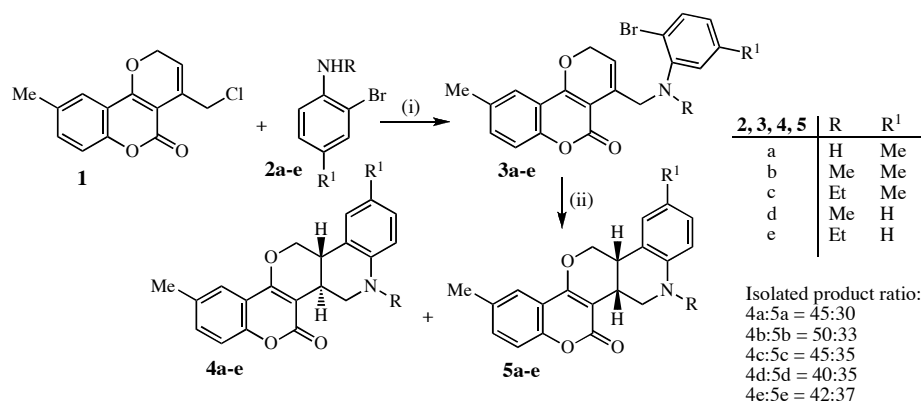
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INTRODUCTION

Organotin-mediated intramolecular free radical cyclization reactions have gained dramatic prominence in the synthesis of carbo- and heterocyclic ring structures [1-6]. The mild reaction conditions with these reagents and normally high levels of chemo-, regio- and often stereocontrol coupled with functional group tolerance allow radical reactions to serve as a powerful method for carbon-carbon bond formations. Contrary to predictions based on thermodynamic criteria, cyclization of 5-hexenyl systems, generally gives cyclopentyl methyl radical *via* a prominent 5-*exo* mode of closure [4,5] and not the more stable cyclohexyl radical *via* 6-*endo* cyclization, a feature that has been rationalized [7] in terms of stereoelectronic control of the reaction. Nevertheless, for stabilized radicals the regiochemistry of ring closure of 5-hexenyl radical is reversed [8]. In continuation of our studies, directed towards the synthesis of heterocycles using

radical cyclization [9], we directed our attention to cyclize 4-arylaminoethylpyrano[3,2-*c*][1]benzopyran-5(2*H*)-ones **3** under radical initiated conditions.

We initiated our investigation by examining the cyclization of **3a-e**. These were readily prepared in 85-90% yields by the reaction of 4-chloromethylpyrano[3,2-*c*][1]benzopyran-5(2*H*)-ones **1** with various *o*-bromoanilines **2a-e** in refluxing acetone in the presence of anhydrous potassium carbonate and catalytic amount of sodium iodide. The amines **3a-e** were treated with ¹⁰Bu₃SnH-AIBN to induce radical cyclization. Compound **3a** was heated in degassed toluene at 80°C under nitrogen with ¹⁰Bu₃SnH and catalytic amount of AIBN to give a mixture of *trans*-fused **4a** and *cis*-fused **5a** cyclized products *via* 6-*endo* cyclization (Scheme 1). Compound **1** was prepared by following the literature procedure [10] *i.e.* by alkylation of 4-hydroxy coumarin with 1,4-dichlorobutene followed by Claisen rearrangement.



Scheme 1. Reagents and Condition: (i) Acetone, K₂CO₃, NaI, reflux, 4 h.
(ii) Bu₃SnH, toluene, 80°C, 1 h.

RESULTS AND DISCUSSION

Determination of relative stereochemistry. The stereochemical assignments of the *trans*- and *cis*-fused cyclized products are based on ^1H NMR, ^{13}C NMR, DEPT, COSY, HETCOR and decoupling experiments. Construction of a Dreiding model revealed a structure for the *trans*- and *cis*- isomer as shown by Fig. I and Fig. II respectively.

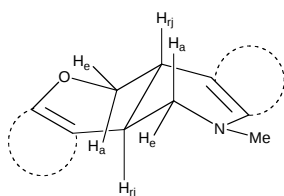


Figure I

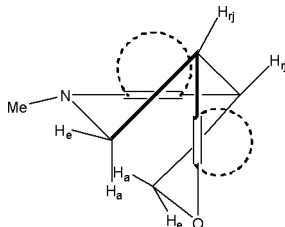


Figure II

Figure I and Figure II represent the part structure of the *trans*-fused and *cis*-fused cyclized product respectively depicted by Dreiding model. H_a , H_e and H_{rj} denote the axial, equatorial and ring juncture hydrogen respectively.

For the *trans*-isomer **4a** (Fig. I), in the ^1H NMR spectroscopy, one proton doublet of a doublet centered at δ 5.26 (dd, $J = 10.8, 3.7$ Hz) and a one proton triplet centered at δ 4.25 ($J = 10.8$ Hz) were assigned to equatorial and axial protons of $-\text{OCH}_2$ respectively. Another one proton doublet of a doublet centered at δ 4.52 ($J = 11.1, 5.2$ Hz) and a one proton triplet centered at δ 3.27 ($J = 11.1$ Hz) were assigned to equatorial and axial protons of $-\text{NCH}_2$ respectively. The ring juncture (rj) protons appear as one proton ddd each at δ 2.90 ($J = 11.2, 11.1, 5.2$ Hz) and δ 3.15 ($J = 11.2, 10.8, 3.7$ Hz) due to $\text{CH}_{rj}\text{CH}_2\text{N}$ and $\text{CH}_{rj}\text{CH}_2\text{O}$ respectively.

That the *trans*-isomer was formed was confirmed on the basis of decoupling experiment. With irradiation at δ 5.26 ($-\text{OCH}_e$), the multiplicity of OCH_a resonance at δ 4.25 was simplified from a triplet to a doublet ($J = 10.9$ Hz) and the ring juncture proton resonance of $\text{CH}_{rj}\text{CH}_2\text{O}$ at δ 3.15 was simplified from ddd to a triplet ($J = 11.3$ Hz). The remaining resonances remain unchanged. With irradiation at δ 4.25 ($-\text{OCH}_a$), the multiplicity of OCH_e resonance at δ 5.26 was transformed from a doublet of doublet to a doublet ($J = 3.7$ Hz) and the ring juncture proton resonance of $\text{CH}_{rj}\text{CH}_2\text{O}$ at δ 3.15 was transformed from ddd to a doublet of doublet ($J = 11.2, 3.7$ Hz). The remaining resonances remain unchanged. The high coupling constant value ($J = 11.2$ Hz) due to the coupling of the two ring juncture protons clearly indicated that a *trans*-isomer was formed *via* 6-*endo*-aryl radical cyclization.

The structure of the *trans*-isomer was further confirmed by the following experiments. Homonuclear correlation

(HOMCOR/COSY) spectrum of the compound **4a** showed that $-\text{OCH}_2$ protons at δ 5.26 and δ 4.25 correlate with each other and $-\text{NCH}_2$ protons at δ 4.52 and δ 3.27 correlate with each other. The ^{13}C chemical shift of the compound **4a** was assigned by DEPT experiment. Distortionless Enhancement by Polarization Transfer (DEPT) showed 13 protonated carbons; two $-\text{CH}_3$, nine $>\text{CH}-$ and two $>\text{CH}_2$. Carbon resonances were established by direct correlation with proton resonances by Heteronuclear correlation (HETCOR) experiment (normal one bond C-H coupling). Methyl proton (ArCH_3 and NCH_3) resonance at δ 2.43 and δ 3.03 were related to carbon resonance at δ 20.95 and δ 38.98 respectively. Methylene proton (OCH_2) resonances at δ 4.25 and δ 5.26 were related to carbon resonance at δ 69.01 and methylene proton (NCH_2) resonances at δ 3.27 and δ 4.52 were related to carbon resonance at δ 54.06. Methine proton resonance ($\text{CH}_{rj}\text{CH}_2\text{N}$ and $\text{CH}_{rj}\text{CH}_2\text{O}$) at δ 2.90 and δ 3.15 were related to carbon resonance at δ 32.99 and δ 36.63 respectively. The mass spectrum of the compound showed molecular ion peak at m/z 333 (M^+).

For the *cis*-isomer **5a** (Fig II), in the ^1H NMR spectroscopy, one proton doublet of a doublet centered at δ 4.54 ($J = 11.5, 4.5$ Hz) and a one proton triplet centered at δ 4.15 ($J = 11.5$ Hz) were assigned to equatorial and axial protons of $-\text{OCH}_2$ respectively. Another one proton doublet of a doublet centered at δ 3.74 ($J = 11.2, 4.0$ Hz) and a one proton triplet centered at δ 3.08 ($J = 11.2$ Hz) were assigned to equatorial and axial protons of $-\text{NCH}_2$ respectively. The ring juncture (rj) protons appear as one proton ddd each at δ 3.31 ($J = 11.5, 5.3, 4.5$ Hz) and δ 3.42 ($J = 11.5, 5.3, 4.0$ Hz) due to $\text{CH}_{rj}\text{CH}_2\text{O}$ and $\text{CH}_{rj}\text{CH}_2\text{N}$ respectively.

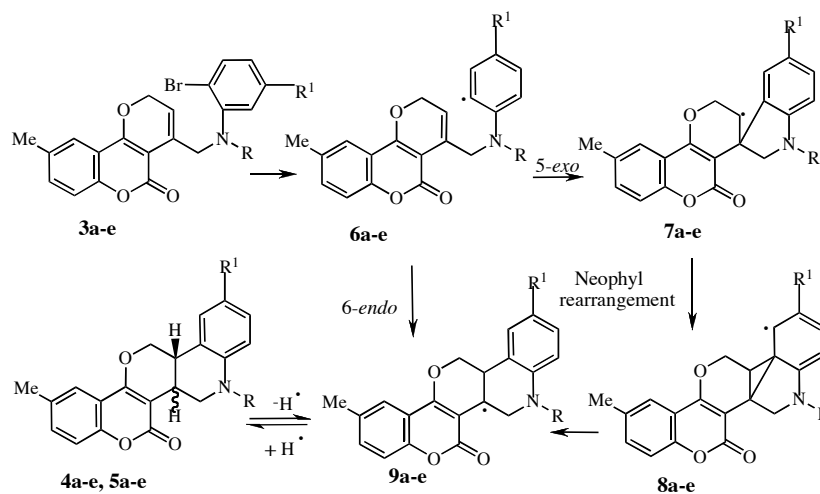
That the *cis*-isomer was also formed was confirmed on the basis of decoupling experiment. With irradiation at δ 4.54 ($-\text{OCH}_e$), the multiplicity of OCH_a resonance at δ 4.15 collapsed from a triplet to a doublet ($J = 11.5$ Hz) and the ring juncture proton resonance of $\text{CH}_{rj}\text{CH}_2\text{O}$ at δ 3.31 collapsed from ddd to a doublet of doublet ($J = 11.5, 5.3$ Hz). The remaining resonances remain unchanged. With irradiation at δ 4.15 ($-\text{OCH}_a$), the multiplicity of OCH_e resonance at δ 4.54 simplified from doublet of doublet to a doublet ($J = 4.5$ Hz) and the ring juncture proton resonance of $\text{CH}_{rj}\text{CH}_2\text{O}$ at δ 3.31 simplified from ddd to a doublet of doublet ($J = 5.3, 4.5$ Hz). The remaining resonances remain unchanged. The low coupling constant value ($J = 5.3$ Hz) due to the coupling of the two ring juncture protons clearly indicated that a *cis*-isomer was also formed *via* 6-*endo*-aryl radical cyclization.

The Homonuclear correlation or HOMCOR (COSY) spectrum of the compound **5a** showed that $-\text{OCH}_2$ protons at δ 4.15 and δ 4.54 correlate with each other and $-\text{NCH}_2$ protons at δ 3.08 and δ 3.74 correlate with each other. The

^{13}C chemical shift of the compound **5a** was assigned by DEPT experiment. DEPT showed 13 protonated carbons; two $-\text{CH}_3$, nine $>\text{CH}-$ and two $>\text{CH}_2$. Carbon resonances were established by direct correlation with proton resonance by Heteronuclear correlation (HETCOR) experiment (normal one bond C-H coupling). Methyl proton (ArCH_3 and NCH_3) resonance at δ 2.42 and δ 2.97 were related to carbon resonance at δ 20.95 and δ 39.01 respectively. Methylene proton (OCH_2) resonances at δ 4.15 and δ 4.54 were related to carbon resonance at δ 69.39 and methylene proton (NCH_2) resonances at δ 3.08 and δ 3.74 were related to carbon resonance at δ 51.05. Methine proton resonance ($\text{CH}_\eta\text{CH}_2\text{N}$ and $\text{CH}_\eta\text{CH}_2\text{O}$) at δ 3.42 and δ 3.31 were related to carbon resonance at δ 28.38 and δ 33.83 respectively. The mass spectrum of the compound showed molecular ion peak at m/z 333 (M^+). All these experiments confirmed the stereochemistry of the ring juncture to be *cis*. To test the generality of the reaction, compounds **3b-e** were similarly treated to afford a mixture of *trans*-fused **4b-e** and *cis*-fused **5b-e** cyclized products (Scheme 1).

5-ones was carried out. But in certain cases, reduced diastereoselectivity was observed and the diastereomeric mixture could not be separated [13]. In a recent publication [14] we have considered the reaction of different substituted *o*-bromo phenols with the same starting material 4-chloromethylpyrano[3,2-*c*][1]benzopyran-5(2*H*)-one. However, it has been reported [14] previously, that all efforts to separate the mixture of compounds formed after radical cyclization reaction failed miserably. In the present work, we were successful to separate the diastereomeric mixture, obtained after radical cyclization, by flash column chromatography.

It has already been established [15] that high levels of diastereoselectivity ($>50:1$) could be obtained when the concentration of the reactant is reduced from 0.1 to 0.01 *M*. These observations have been attributed to the reversibility of the cyclization and decreased availability of the $^t\text{Bu}_3\text{SnH}$. However, cyclization of **3a-e** even in very dilute condition always yielded a diastereomeric mixture having similar yields as obtained in using normal concentration. In conclusion, we have successfully extended the Bu_3SnH mediated



Scheme 2

The formation of six-membered heterocyclic ring **4a-e** and **5a-e** from the substrates **3a-e** may be explained by the initial formation of the aryl radical **6a-e** followed by a 6-*endo* ring closure to give a tertiary radical **9a-e** which may then accept a hydrogen radical to afford the final products **4a-e** and **5a-e**. In an alternative route, the aryl radical **6a-e** may undergo a 5-*exo* ring closure to generate a spiroheterocyclic radical [11] **7a-e** which may be converted to the tertiary radical **9a-e** via radical **8a-e** by a neophyl rearrangement [12] (Scheme 2).

In an earlier report [13], good to excellent diastereoselectivity was observed when radical cyclization of 4-(2'-bromophenoxymethyl)-7-methylthiopyrano-[3,2-*c*]pyran-

radical cyclizations. All the starting materials gave regioselectively a mixture of both *cis*-fused and *trans*-fused reduced six-membered heterocyclic ring by $^t\text{Bu}_3\text{SnH}$ mediated cyclization. The methodology described here is mild, regioselective but not stereoselective and is attractive because of its simplicity. The scope of the proposed method is that we could obtain in considerable yields both the *cis*-fused and *trans*-fused cyclized products in a single reaction step which could be successfully separated. However, the limitation of this methodology is that we could in no way obtain a single isomer even by varying the concentration of Bu_3SnH in the radical cyclization step.

EXPERIMENTAL

Melting points were determined in an open capillary and are uncorrected. IR spectra were recorded on a Perkin-Elmer L 120-000A spectrometer ($\nu_{\max}$ in cm^{-1}) using samples as neat liquids and solid samples were recorded on KBr disks. UV absorption spectra were recorded in EtOH on a Shimadzu UV-2401PC spectrophotometer ($\lambda_{\max}$ in nm). ^1H NMR (400 MHz, 500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a Bruker DPX-400 and Bruker DPX-500 spectrometer in CDCl_3 (chemical shift in δ) with TMS as internal standard. Silica gel [(60-120 mesh), Spectrochem, India] was used for chromatographic separation. Silica gel G [E-Merck (India)] was used for TLC. Petroleum ether refers to the fraction boiling between 60° and 80°C .

General procedure for the preparation of 3a-e. A mixture of **1** (5 mmol), 2-bromoanilines (**2a-e**, 5 mmol) and anhydrous potassium carbonate (5 g) was heated under reflux in dry acetone (125 mL) for 4 h. The reaction mixture was cooled, filtered and concentrated. The residual mass was extracted with CH_2Cl_2 (3×50 mL), washed with 10% Na_2CO_3 solution (2×25 mL), brine (3×50 mL) and dried (Na_2SO_4). The residual mass after the removal of solvent was subjected to column chromatography on silica gel using 5% ethylacetate-petroleum ether as eluant to give compounds **3a-e**, which were recrystallized from CHCl_3 -petroleum ether.

3a: Yield: 92%; White solid; mp $180\text{--}182^\circ\text{C}$; UV (EtOH): $\lambda_{\max} = 349, 284, 214$ nm; IR (KBr): $\nu_{\max} = 1715$ cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): $\delta_{\text{H}} = 2.39$ (s, 3H, ArCH_3), 2.75 (s, 3H, NCH_3), 4.24 (s, 2H, CH_2NCH_3), 4.97-4.99 (m, 2H, OCH_2), 5.94-5.96 (m, 1H, $=\text{CH}$), 6.85-6.89 (m, 1H, ArH), 7.15-7.18 (m, 2H, ArH), 7.20-7.22 (m, 1H, ArH), 7.30-7.33 (m, 1H, ArH), 7.51-7.54 (m, 2H, ArH); MS: $m/z = 411, 413$ (M^+). Anal. Calcd. for $\text{C}_{21}\text{H}_{18}\text{BrNO}_3$: C, 61.18; H, 4.40; N, 3.40 %. Found: C, 61.12; H, 4.61; N, 3.31 %.

3b: Yield: 95%; White solid; mp $157\text{--}159^\circ\text{C}$; UV (EtOH): $\lambda_{\max} = 316, 284, 214$ nm; IR (KBr): $\nu_{\max} = 1707$ cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): $\delta_{\text{H}} = 2.25$ (s, 3H, ArCH_3), 2.38 (s, 3H, ArCH_3 of coumarin ring), 2.72 (s, 3H, NCH_3), 4.02 (s, 2H, CH_2NCH_3), 4.96-4.98 (m, 2H, OCH_2), 5.92-5.93 (m, 1H, $=\text{CH}$), 7.01-7.02 (m, 1H, ArH), 7.04-7.06 (m, 1H, ArH), 7.15-7.17 (m, 1H, ArH), 7.30-7.32 (m, 1H, ArH), 7.35-7.36 (m, 1H, ArH), 7.54 (s, 1H, ArH); MS: $m/z = 425, 427$ (M^+). Anal. Calcd. for $\text{C}_{22}\text{H}_{20}\text{BrNO}_3$: C, 61.98; H, 4.73; N, 3.29 %. Found: C, 61.82; H, 4.59; N, 3.23 %.

3c: Yield: 90%; White solid; mp $130\text{--}132^\circ\text{C}$; UV (EtOH): $\lambda_{\max} = 329, 285, 213$ nm; IR (KBr): $\nu_{\max} = 1709$ cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): $\delta_{\text{H}} = 1.18$ (t, 3H, $J = 7.5$ Hz, ArCH_2CH_3), 2.38 (s, 3H, ArCH_3), 2.55 (q, 2H, $J = 7.5$ Hz, ArCH_2CH_3), 2.72 (s, 3H, NCH_3), 4.21 (s, 2H, CH_2NCH_3), 4.97-4.99 (m, 2H, OCH_2), 5.94-5.96 (m, 1H, $=\text{CH}$), 7.02-7.05 (m, 1H, ArH), 7.07-7.09 (m, 1H, ArH), 7.15-7.17 (m, 1H, ArH), 7.30-7.32 (m, 1H, ArH), 7.37-7.38 (m, 1H, ArH), 7.54 (s, 1H, ArH); MS: $m/z = 439, 441$ (M^+). Anal. Calcd. for $\text{C}_{23}\text{H}_{22}\text{BrNO}_3$: C, 62.74; H, 5.04; N, 3.18 %. Found: C, 62.90; H, 4.93; N, 3.11 %.

3d: Yield: 85%; White solid; mp $120\text{--}122^\circ\text{C}$; UV (EtOH): $\lambda_{\max} = 313, 305, 284, 211$ nm; IR (KBr): $\nu_{\max} = 1703$ cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): $\delta_{\text{H}} = 2.19$ (s, 3H, ArCH_3), 2.38 (s, 3H, ArCH_3 of coumarin ring), 4.41 (s, 2H, CH_2NH), 4.95-4.96 (m, 2H, OCH_2), 5.56-5.58 (m, 1H, $=\text{CH}$), 6.91-6.93 (m, 1H, ArH), 7.17-7.23 (m, 2H, ArH), 7.32-7.35 (m, 2H, ArH), 7.53 (s, 1H, ArH); MS: $m/z = 411, 413$ (M^+). Anal. Calcd. for $\text{C}_{21}\text{H}_{18}\text{BrNO}_3$: C, 61.18; H, 4.40; N, 3.40 %. Found: C, 60.94; H, 4.49; N, 3.45 %.

3e: Yield: 88%; White solid; mp $160\text{--}162^\circ\text{C}$; UV (EtOH): $\lambda_{\max} = 306, 285, 272, 212$ nm; IR (KBr): $\nu_{\max} = 1703$ cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): $\delta_{\text{H}} = 1.17$ (t, 3H, $J = 7.5$ Hz, ArCH_2CH_3), 2.39 (s, 3H, ArCH_3), 2.52 (q, 2H, $J = 7.5$ Hz, ArCH_2CH_3), 4.39 (s, 2H, CH_2NH), 4.96-4.97 (m, 2H, OCH_2), 5.61-5.62 (m, 1H, $=\text{CH}$), 6.85-6.86 (m, 1H, ArH), 7.03-7.05 (m, 1H, ArH), 7.19-7.21 (m, 1H, ArH), 7.27-7.28 (m, 1H, ArH), 7.34-7.37 (m, 1H, ArH), 7.54 (s, 1H, ArH); MS: $m/z = 425, 427$ (M^+). Anal. Calcd. for $\text{C}_{22}\text{H}_{20}\text{BrNO}_3$: C, 61.98; H, 4.73; N, 3.29 %. Found: C, 62.05; H, 4.56; N, 3.44 %.

General procedure for the preparation of 4a-e and 5a-e. Tributyltin hydride (1.1 mmol) was added to a stirred solution of (**3a-e**, 1 mmol) and azobisisobutyronitrile (0.5 mmol) in dry degassed toluene (5 mL) under nitrogen. The mixture was heated under reflux for 1 h and concentrated. The residue was dissolved in ether (10 mL) and stirred with a 10% aq. potassium fluoride solution (10 mL) for 45 min. The white precipitate was filtered and the aqueous phase extracted with ether (10 mL). The combined ether extract was washed with brine and dried over anhyd. Na_2SO_4 . The residual mass, after the removal of solvent, was subjected to column chromatography using 10% ethyl acetate-petroleum ether as eluant to give a mixture of cyclized products **4a-e** and **5a-e**. The mixture of compounds was then subjected to flash column chromatography using 10% ethyl acetate-petroleum ether as eluant whence we obtained the *trans*-fused isomers **4a-e** in 40-50% yields and *cis*-fused isomers **5a-e** in 30-37% yields.

4a: Yield: 45%; White solid; mp $248\text{--}250^\circ\text{C}$; UV (EtOH): $\lambda_{\max} = 310, 281, 265, 211$ nm; IR (KBr): $\nu_{\max} = 1706$ cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): $\delta_{\text{H}} = 2.43$ (s, 3H, ArCH_3), 2.90 (ddd, 1H, $J = 11.2, 11.1, 5.2$ Hz, $\text{CHCH}_2\text{NCH}_3$), 3.03 (s, 3H, NCH_3), 3.15 (ddd, 1H, $J = 11.2, 10.8, 3.7$ Hz, CHCH_2O), 3.27 (t, 1H, $J = 11.1$ Hz, NCH_a), 4.25 (t, 1H, $J = 10.8$ Hz, OCH_a), 4.52 (dd, 1H, $J = 11.1, 5.2$ Hz, NCH_b), 5.26 (dd, 1H, $J = 10.8, 3.7$ Hz, OCH_b), 6.73-6.76 (m, 2H, ArH), 6.93-6.94 (m, 1H, ArH), 7.21-7.23 (m, 2H, ArH), 7.34-7.35 (m, 1H, ArH), 7.63 (s, 1H, ArH); ^{13}C NMR (CDCl_3 , 125 MHz): $\delta_{\text{C}} = 20.95$ (ArCH_3), 32.99 ($\text{CHCH}_2\text{NCH}_3$), 36.63 (CHCH_2O), 38.98 (NCH_3), 54.06 (NCH_2), 69.01 (OCH_2), 101.01 (ArC), 115.09 (ArC), 116.24 (ArCH), 122.53 (ArCH), 122.72 (ArCH), 128.48 (ArCH), 129.95 (ArCH), 130.01 (ArC), 132.96 (ArC), 133.04 (ArCH), 133.92 (ArCH), 134.20 (ArC), 150.75 (ArC), 161.95 (ArC), 162.50 (CO); MS: $m/z = 333$ (M^+). Anal. Calcd. for $\text{C}_{21}\text{H}_{19}\text{NO}_3$: C, 75.66; H, 5.74; N, 4.20 %. Found: C, 75.68; H, 5.83; N, 4.13 %.

5a: Yield: 30%; White solid; mp $188\text{--}190^\circ\text{C}$; UV (EtOH): $\lambda_{\max} = 315, 280, 263, 220$ nm; IR (KBr): $\nu_{\max} = 1703$ cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): $\delta_{\text{H}} = 2.42$ (s, 3H, ArCH_3), 2.97 (s, 3H, NCH_3), 3.08 (t, 1H, $J = 11.5$ Hz, NCH_a), 3.31 (ddd, 1H, $J = 11.5, 5.3, 4.5$ Hz, CHCH_2O), 3.42 (ddd, 1H, $J = 11.5, 5.3, 4.0$ Hz, $\text{CHCH}_2\text{NCH}_3$), 3.74 (dd, 1H, $J = 11.5, 4.0$ Hz, NCH_b), 4.15 (t, 1H, $J = 11.5$ Hz, OCH_a), 4.54 (dd, 1H, $J = 11.5, 4.5$ Hz, OCH_b), 6.75-6.76 (m, 2H, ArH), 7.14-7.15 (m, 1H, ArH), 7.19-7.24 (m, 2H, ArH), 7.33-7.35 (m, 1H, ArH), 7.59 (s, 1H, ArH); ^{13}C NMR (CDCl_3 , 125 MHz): $\delta_{\text{C}} = 20.95$ (ArCH_3), 28.38 ($\text{CHCH}_2\text{NCH}_3$), 33.83 (CHCH_2O), 39.01 (NCH_3), 51.05 (NCH_2), 69.39 (OCH_2), 101.06 (ArC), 115.05 (ArC), 116.42 (ArCH), 122.36 (ArCH), 122.54 (ArCH), 128.76 (ArCH), 129.84 (ArCH), 130.01 (ArC), 132.96 (ArC), 133.04 (ArCH), 133.92 (ArCH), 134.20 (ArC), 150.75 (ArC), 161.95 (ArC), 162.50 (CO); MS: $m/z = 333$ (M^+). Anal. Calcd. for $\text{C}_{21}\text{H}_{19}\text{O}_3$: C, 75.66; H, 5.74; N, 4.20 %. Found: C, 75.89; H, 5.90; N, 4.07 %.

4b: Yield: 50%; White solid; mp 223-225°C; UV (EtOH): $\lambda_{\max}$ = 312, 285, 213 nm; IR (KBr): $\nu_{\max}$ = 1718 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ_{H} = 2.26 (s, 3H, ArCH_3), 2.42 (s, 3H, ArCH_3 of coumarin ring), 2.84 (ddd, 1H, J = 11.2, 11.1, 5.2 Hz, $\text{CHCH}_2\text{NCH}_3$), 2.96 (s, 3H, NCH_3), 3.06 (ddd, 1H, J = 11.2, 10.8, 3.7 Hz, CHCH_2O), 3.16 (t, 1H, J = 11.1 Hz, NCH_a), 4.22 (t, 1H, J = 10.8 Hz, OCH_a), 4.44 (dd, 1H, J = 11.1, 5.2 Hz, NCH_e), 5.23 (dd, 1H, J = 10.8, 3.7 Hz, OCH_e), 6.56 (d, 1H, J = 8.2 Hz, ArH), 6.70 (s, 1H, ArH), 7.00 (d, 1H, J = 8.2 Hz, ArH), 7.20 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.33 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.64 (s, 1H, ArH of coumarin); MS: m/z = 347 (M^+). Anal. Calcd. for $\text{C}_{22}\text{H}_{21}\text{NO}_3$: C, 76.06; H, 6.09; N, 4.03 %. Found: C, 76.31; H, 5.98; N, 3.94 %.

5b: Yield: 33%; White solid; mp 156-158°C; UV (EtOH): $\lambda_{\max}$ = 364, 244, 209 nm; IR (KBr): $\nu_{\max}$ = 1708 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ_{H} = 2.26 (s, 3H, ArCH_3), 2.42 (s, 3H, ArCH_3 of coumarin ring), 2.91 (s, 3H, NCH_3), 2.99 (t, 1H, J = 11.2 Hz, NCH_a), 3.25 (ddd, 1H, J = 11.5, 5.3, 3.3 Hz, CHCH_2O), 3.39 (ddd, 1H, J = 11.2, 5.3, 3.4 Hz, $\text{CHCH}_2\text{NCH}_3$), 3.69 (dd, 1H, J = 11.2, 3.4 Hz, NCH_e), 4.14 (t, 1H, J = 11.5 Hz, OCH_a), 4.53 (dd, 1H, J = 11.5, 3.3 Hz, OCH_e), 6.61 (d, 1H, J = 8.2 Hz, ArH), 6.93 (s, 1H, ArH), 7.00 (d, 1H, J = 8.2 Hz, ArH), 7.22 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.33 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.58 (s, 1H, ArH of coumarin); MS: m/z = 347 (M^+). Anal. Calcd. for $\text{C}_{22}\text{H}_{21}\text{NO}_3$: C, 76.06; H, 6.09; N, 4.03 %. Found: C, 75.97; H, 5.96; N, 4.23 %.

4c: Yield: 45%; White solid; mp 270-272°C; UV (EtOH): $\lambda_{\max}$ = 306, 283, 259, 208 nm; IR (KBr): $\nu_{\max}$ = 1708 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ_{H} = 1.22 (t, 3H, J = 7.5 Hz, ArCH_2CH_3), 2.43 (s, 3H, ArCH_3), 2.58 (q, 2H, J = 7.5 Hz, ArCH_2CH_3), 2.90 (ddd, 1H, J = 11.2, 11.1, 5.2 Hz, $\text{CHCH}_2\text{NCH}_3$), 3.00 (s, 3H, NCH_3), 3.11 (ddd, 1H, J = 11.2, 10.8, 3.7 Hz, CHCH_2O), 3.20 (t, 1H, J = 11.1 Hz, NCH_a), 4.25 (t, 1H, J = 10.8 Hz, OCH_a), 4.47 (dd, 1H, J = 11.1, 5.2 Hz, NCH_e), 5.24 (dd, 1H, J = 10.8, 3.7 Hz, OCH_e), 6.70 (d, 1H, J = 8.2 Hz, ArH), 6.76 (s, 1H, ArH), 7.07 (d, 1H, J = 8.2 Hz, ArH), 7.21 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.34 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.63 (s, 1H, ArH of coumarin); MS: m/z = 361 (M^+). Anal. Calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}_3$: C, 76.43; H, 6.41; N, 3.88 %. Found: C, 76.67; H, 6.35; N, 3.75 %.

5c: Yield: 35%; White solid; mp 165-167°C; UV (EtOH): $\lambda_{\max}$ = 312, 284, 260, 218 nm; IR (KBr): $\nu_{\max}$ = 1704 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ_{H} = 1.23 (t, 3H, J = 7.5 Hz, ArCH_2CH_3), 2.42 (s, 3H, ArCH_3), 2.58 (q, 2H, J = 7.5 Hz, ArCH_2CH_3), 2.95 (s, 3H, NCH_3), 3.05 (t, 1H, J = 11.2 Hz, NCH_a), 3.28 (m, 1H, CHCH_2O), 3.41 (m, 1H, $\text{CHCH}_2\text{NCH}_3$), 3.71 (dd, 1H, J = 11.2, 3.4 Hz, NCH_e), 4.15 (t, 1H, J = 11.5 Hz, OCH_a), 4.55 (dd, 1H, J = 11.5, 3.3 Hz, OCH_e), 6.73 (d, 1H, J = 8.2 Hz, ArH), 7.05 (s, 1H, ArH), 7.17 (d, 1H, J = 8.2 Hz, ArH), 7.22 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.34 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.58 (s, 1H, ArH of coumarin); MS: m/z = 361 (M^+). Anal. Calcd. for $\text{C}_{23}\text{H}_{23}\text{NO}_3$: C, 76.43; H, 6.41; N, 3.88 %. Found: C, 76.61; H, 6.48; N, 3.78 %.

4d: Yield: 40%; White solid; mp 208-210°C; UV (EtOH): $\lambda_{\max}$ = 371, 354, 284, 272, 212 nm; IR (KBr): $\nu_{\max}$ = 1705 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ_{H} = 2.22 (s, 3H, ArCH_3), 2.42 (s, 3H, ArCH_3 of coumarin ring), 2.97-2.99 (m, 1H, $\text{CHCH}_2\text{NCH}_3$), 3.20-3.26 (m, 2H, CHCH_2O and NCH_a), 4.24 (t, 1H, J = 10.8 Hz, OCH_a), 4.89 (dd, 1H, J = 11.1, 5.2 Hz, NCH_e), 5.23 (dd, 1H, J = 10.8, 3.7 Hz, OCH_e), 6.86-6.87 (m, 1H, ArH), 7.06-7.08 (m, 1H, ArH), 7.18-7.20 (m, 2H, ArH), 7.33-7.35 (m, 1H, ArH), 7.60 (s, 1H, ArH); MS: m/z = 333 (M^+). Anal. Calcd. for

$\text{C}_{21}\text{H}_{19}\text{NO}_3$: C, 75.66; H, 5.74; N, 4.20 %. Found: C, 75.41; H, 5.88; N, 4.25 %.

5d: Yield: 35%; White solid; mp 168-170°C; UV (EtOH): $\lambda_{\max}$ = 365, 353, 285, 272, 215 nm; IR (KBr): $\nu_{\max}$ = 1708 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ_{H} = 2.29 (s, 3H, ArCH_3), 2.41 (s, 3H, ArCH_3 of coumarin ring), 3.10 (t, 1H, J = 11.2 Hz, NCH_a), 3.28-3.31 (m, 1H, CHCH_2O), 3.44-3.47 (m, 1H, CHCH_2NH), 4.01 (dd, 1H, J = 11.2, 3.4 Hz, NCH_e), 4.14 (t, 1H, J = 11.5 Hz, OCH_a), 4.59 (dd, 1H, J = 11.5, 3.3 Hz, OCH_e), 6.92-6.93 (m, 1H, ArH), 7.00-7.03 (m, 2H, ArH), 7.20 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.33 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.57 (s, 1H, ArH of coumarin); ^{13}C NMR (CDCl_3 , 125 MHz): δ_{C} = 20.60 (ArCH_3), 20.96 (ArCH_3 of coumarin), 28.63 (CHCH_2NH), 33.14 (CHCH_2O), 42.42 (CH_2NH), 69.01 (OCH_2), 100.91 (ArC), 114.96 (ArC), 116.41 (ArCH), 117.65 (ArC), 117.85 (ArC), 122.38 (ArCH), 129.42 (ArCH), 130.46 (ArCH), 133.04 (ArCH), 133.25 (ArCH), 133.73 (ArC), 133.95 (ArC), 150.75 (ArC), 161.15 (ArC), 162.72 (CO); MS: m/z = 333 (M^+). Anal. Calcd. for $\text{C}_{21}\text{H}_{19}\text{NO}_3$: C, 75.66; H, 5.74; N, 4.20 %. Found: C, 75.40; H, 5.59; N, 4.32 %.

4e: Yield: 42%; White solid; mp 220-222°C; UV (EtOH): $\lambda_{\max}$ = 366, 354, 311, 285, 212 nm; IR (KBr): $\nu_{\max}$ = 1702 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ_{H} = 1.20 (t, 3H, J = 7.5 Hz, ArCH_2CH_3), 2.42 (s, 3H, ArCH_3), 2.54 (q, 2H, J = 7.5 Hz, ArCH_2CH_3), 2.86 (ddd, 1H, J = 11.2, 11.1, 5.2 Hz, CHCH_2NH), 3.06 (dt, 1H, J = 11.1, 1.5 Hz, NCH_a), 3.15 (ddd, 1H, J = 11.2, 10.8, 3.7 Hz, CHCH_2O), 4.01 (br s, 1H, NH), 4.21 (t, 1H, J = 10.8 Hz, OCH_a), 4.75 (ddd, 1H, J = 11.1, 5.2, 4.2 Hz, NCH_e), 5.25 (dd, 1H, J = 10.8, 3.7 Hz, OCH_e), 6.52 (d, 1H, J = 8.2 Hz, ArH), 6.77 (s, 1H, ArH), 6.92 (d, 1H, J = 8.2 Hz, ArH), 7.20 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.34 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.62 (s, 1H, ArH of coumarin); ^1H NMR (500 MHz, CDCl_3 , D_2O exchange): δ_{H} = 1.20 (t, 3H, J = 7.5 Hz, ArCH_2CH_3), 2.42 (s, 3H, ArCH_3), 2.54 (q, 2H, J = 7.5 Hz, ArCH_2CH_3), 2.86 (ddd, 1H, J = 11.2, 11.1, 5.2 Hz, CHCH_2NH), 3.06 (t, 1H, J = 11.1 Hz, NCH_a), 3.15 (ddd, 1H, J = 11.2, 10.8, 3.7 Hz, CHCH_2O), 4.21 (t, 1H, J = 10.8 Hz, OCH_a), 4.75 (dd, 1H, J = 11.1, 5.2 Hz, NCH_e), 5.25 (dd, 1H, J = 10.8, 3.7 Hz, OCH_e), 6.52 (d, 1H, J = 8.2 Hz, ArH), 6.77 (s, 1H, ArH), 6.92 (d, 1H, J = 8.2 Hz, ArH), 7.20 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.34 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.62 (s, 1H, ArH of coumarin); ^{13}C NMR (CDCl_3 , 125 MHz): δ_{C} = 16.14 (ArCH_2CH_3), 20.97 (ArCH_3), 28.14 (ArCH_2CH_3), 32.75 (CHCH_2NH), 37.25 (CHCH_2O), 44.96 (NCH_2), 69.53 (OCH_2), 101.87 (ArC), 113.82 (ArCH), 115.19 (ArC), 116.20 (ArCH), 118.32 (ArC), 122.54 (ArCH), 123.06 (ArCH), 127.55 (ArCH), 132.13 (ArC), 132.93 (ArCH), 133.57 (ArC), 141.96 (ArC), 150.84 (ArC), 161.49 (ArC), 162.01 (CO); MS: m/z = 347 (M^+). Anal. Calcd. for $\text{C}_{22}\text{H}_{21}\text{NO}_3$: C, 76.06; H, 6.09; N, 4.03 %. Found: C, 75.84; H, 6.15; N, 4.00 %.

5e: Yield: 37%; White solid; mp 130-132°C. UV (EtOH): $\lambda_{\max}$ = 360, 347, 310, 282, 202 nm; IR (KBr): $\nu_{\max}$ = 1709 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3): δ_{H} = 1.21 (t, 3H, J = 7.5 Hz, ArCH_2CH_3), 2.41 (s, 3H, ArCH_3), 2.55 (q, 2H, J = 7.5 Hz, ArCH_2CH_3), 3.05 (t, 1H, J = 11.2 Hz, NCH_a), 3.32-3.30 (m, 2H, CHCH_2O and CHCH_2NH), 3.84 (dd, 1H, J = 11.2, 3.4 Hz, NCH_e), 3.96 (br s, 1H, NH), 4.19 (t, 1H, J = 11.5 Hz, OCH_a), 4.58 (dd, 1H, J = 11.5, 3.3 Hz, OCH_e), 6.53-6.55 (m, 1H, ArH), 6.92-6.94 (m, 2H, ArH), 7.21 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.33 (d, 1H, J = 8.3 Hz, ArH of coumarin), 7.58 (s, 1H, ArH of coumarin); ^{13}C NMR (CDCl_3 , 125 MHz): δ_{C} = 15.90 (ArCH_2CH_3), 20.96 (ArCH_3), 27.94 (ArCH_2CH_3), 29.18

(CHCH₂NH), 33.48 (CHCH₂O), 42.50 (NCH₂), 69.44 (OCH₂), 101.49 (ArC), 115.16 (ArCH), 116.36 (ArCH), 117.03 (ArC), 117.24 (ArC), 122.32 (ArCH), 127.87 (ArCH), 129.21 (ArCH), 132.83 (ArCH), 133.40 (ArC), 133.62 (ArC), 143.11 (ArC), 150.72 (ArC), 160.95 (ArC), 162.88 (CO); MS: m/z = 347 (M⁺). Anal. Calcd. for C₂₂H₂₁NO₃: C, 76.06; H, 6.09; N, 4.03 %. Found: C, 76.14; H, 5.86; N, 4.11 %.

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REFERENCES

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- [1] Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon: New York, 1986.
- [2] Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237.
- [3] Motherwell, M. B.; Crich, D. *Best Synthetic Methods, Free Radical Chain Reactions in Organic Synthesis*; Academic Press: London, 1991.
- [4] Giese, B.; Kopping, B.; Gobel, T.; Dickhaut, L.; Thoma, G.; Kulicka, K. L.; Trach, F. *Org. React.* **1996**, *48*, 301.
- [5] Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions- Concepts, Guidelines and Synthetic Applications*; VCH: Weinheim, Germany, 1996.
- [6] Pattenden, G.; Sandeep, H. *Contemp. Org. Synth.* **1997**, 197.
- [7] Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073 and references therein.
- [8] (a) Della, E. W.; Graney, S. D. *Tetrahedron Lett.* **2000**, *41*, 7987. (b) Della, E. W.; Graney, S. D. *Org. Lett.* **2002**, *4*, 4065. (c) Cid, M. M.; Dominguez, D.; Castedo, L.; Va'zquez-Lopez, E. M. *Tetrahedron* **1999**, *55*, 5599. (d) Ishibashi, H.; Kato, I.; Takeda, Y.; Kogure, M.; Tamura, O. *Chem. Commun.* **2000**, 1527.
- [9] (a) Majumdar, K. C.; Basu, P. K.; Mukhopadhyay, P. P. *Tetrahedron Reports*, **2004**, *60*, 6239. (b) Majumdar, K. C.; Basu, P. K.; Mukhopadhyay, P. P. *Tetrahedron Reports*, **2005**, *61*, 10603. (c) Majumdar, K. C.; Basu, P. K.; Chattopadhyay, S. K. *Tetrahedron Reports*, **2007**, *63*, 793.
- [10] Majumdar, K. C.; Das, D. P.; Khan, A. T. *Synth. Commun.* **1988**, *18* (16 and 17), 2027.
- [11] Ishibashi, H.; Kawanami, H.; Nakagawa, H.; Ikeda, M. *J. Chem. Soc., Perkin Trans. I*, **1997**, 2291.
- [12] Abeywickrema, A. N.; Beckwith, A. L. J.; Gerba, S. J. *Org. Chem.* **1987**, *52*, 4072.
- [13] Majumdar, K. C.; Muhuri, S. *Synthesis*, **2006**, 2725.
- [14] Majumdar, K. C.; Jana, M. *Synth. Commun.* **2007**, *37*, 1735.
- [15] (a) Enholm, E. J.; Prasad, E. J.; Kinter, K. S. *J. Am. Chem. Soc.* **1991**, *113*, 7784. (b) Enholm, E. J.; Kinter, K. S. *J. Org. Chem.* **1995**, *60*, 4850.