Pergamon

Tetrahedron 58 (2002) 997–1003

TETRAHEDRON

High chemoselectivity in microwave accelerated intramolecular domino Knoevenagel hetero Diels–Alder reactions—an efficient synthesis of pyrano[3-2c]coumarin frameworks

M. Shanmugasundaram, S. Manikandan and R. Raghunathan*

Department of Organic Chemistry, University of Madras, Guindy Campus, Chennai 600 025, India

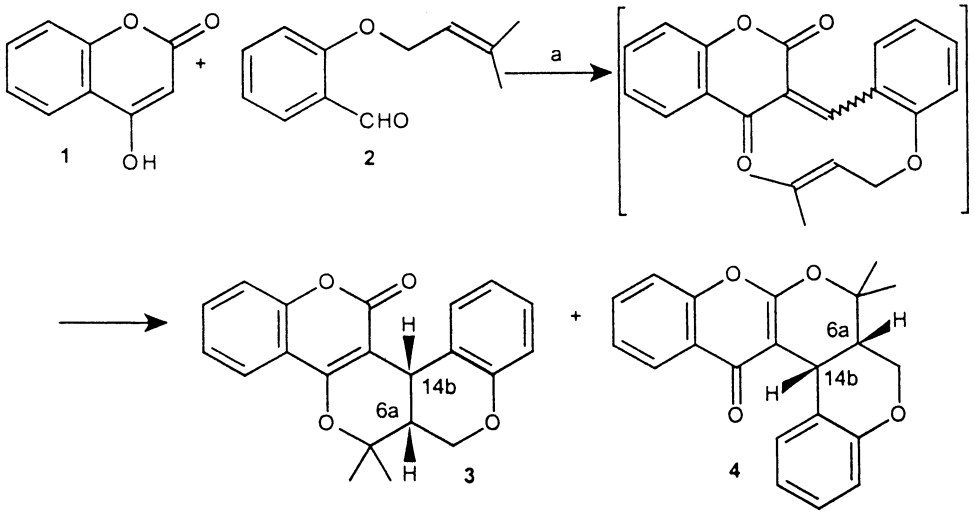
Received 4 June 2001; revised 10 October 2001; accepted 1 November 2001

Abstract—4-Hydroxy coumarin and its benzo-analogues undergo intramolecular domino Knoevenagel hetero Diels–Alder reactions with O-prenylated aromatic aldehydes and the aliphatic aldehyde, citronellal to afford pyrano fused polycyclic frameworks. A high degree of chemoselectivity was achieved by the application of microwave irradiation.

1. Introduction

The increasing number of heterodienes have made the domino Knoevenagel hetero Diels–Alder reaction a very attractive tool in organic synthesis, especially in the area of heterocycles and natural products.[1] The most widely used heterodienes are usually those where the olefinic bond is flanked between the symmetrical 1,3-dicarbonyl compounds.[1,2] In the present work, it was of interest to study the mode of cycloaddition of a heterodiene, wherein the olefinic segment is flanked by a keto carbonyl and a lactone carbonyl. In recent years, there has been a growing interest for the application of microwave irradiation in organic synthesis due to their shorter reaction time and operational simplicity, coupled with the higher conversions with high degree of selectivity.[3] To the best of our knowledge to date, the application of microwaves for the intramolecular domino Knoevenagel hetero Diels–Alder reaction has not yet been exploited.

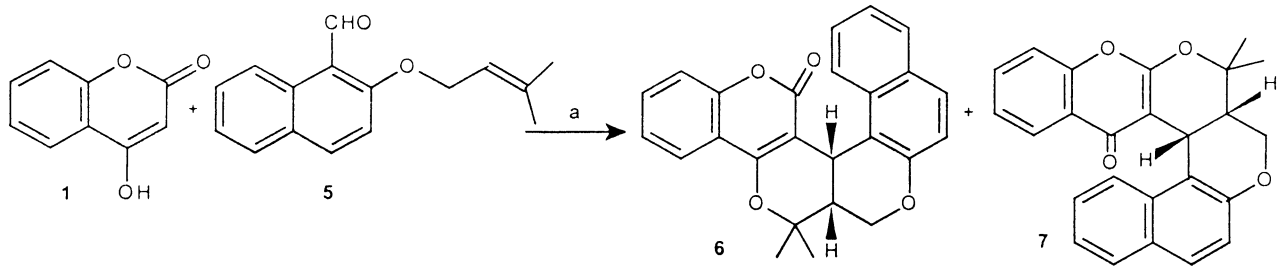
Coumarin derivatives are widely distributed in nature and are reported to have various biological activities such as anticoagulants, insecticidal, anthelminthincs, hypnotics, antifungals, phytoalexins and are known to be HIV protease



Scheme 1. a EtOH reflux, 4 h or Microwave irradiation, 15 s.

Keywords: Diels–Alder reactions; coumarins; chromones; microwave heating.
* Corresponding author. Tel.: +91-44-2351269; fax: +91-44-2352494; e-mail: ragharaghunathan@yahoo.com

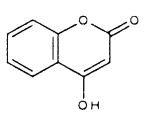
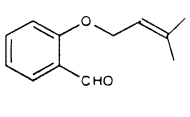
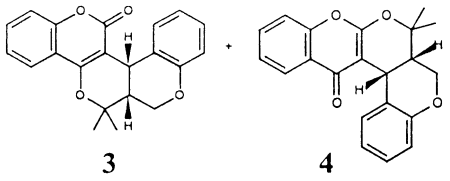
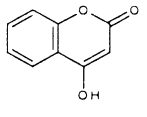
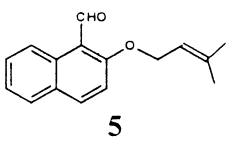
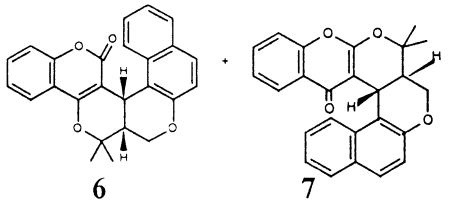
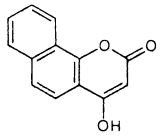
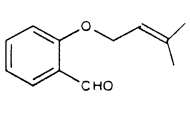
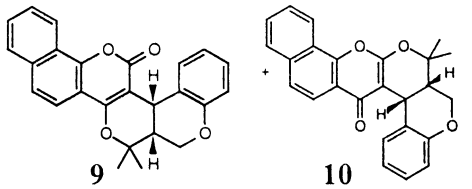
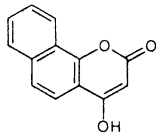
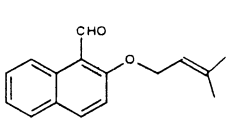
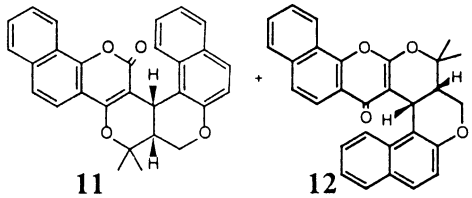
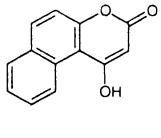
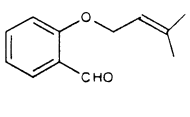
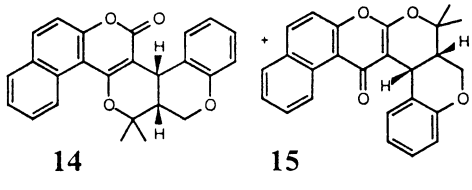
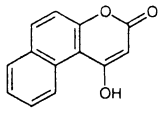
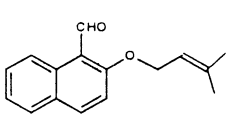
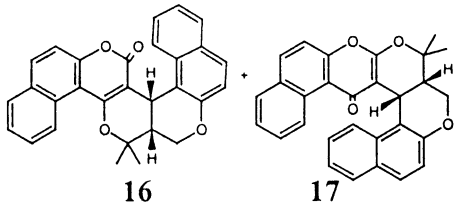
0040–4020/02/$ - see front matter
PII: S0040-4020(01)01076-6



Scheme 2. a EtOH reflux, 4 h or Microwave irradiation, 10 s.

inhibitors.[4] Many naturally occurring compounds having pyrano[3-2c]coumarin skeleton such as isoethuliacoumarin A, isoethuliacoumarin B, isoethuliacoumarin C, ethuliacoumarin A, ethuliacoumarin B and pterophyllin 3 have been isolated.[5] These wide range of biological applications have stimulated considerable interest in evolving newer synthetic methods for the construction of coumarin derivatives. In the continuation of our interest in the area

Table 1. Reaction of unsymmetrical 1,3-diones with aromatic aldehydes

S. no.	1,3-Dione	Aromatic aldehyde	Products	Time	Yield (%)	Coumarin/chromone
1	 1	 2	 3 + 4	4 h 15 s	57 82	68:32 93:7
2	 1	 5	 6 + 7	4 h 10 s	75 92	80:20 95:5
3	 8	 2	 9 + 10	8 h 1.5 min	66 83	57:43 79:21
4	 8	 5	 11 + 12	6 h 1.5 min	66 76	66:34 80:20
5	 13	 2	 14 + 15	8 h 2.5 min	40 77	55:45 81:19
6	 13	 5	 16 + 17	6.5 h 1.5 min	53 74	56:44 85:15

of cycloaddition reactions,[6–8] we herein report a simple and efficient synthesis of pyrano[3-2c]coumarin derivatives using a one pot procedure.

2. Results and discussion

The reaction of 4-hydroxy coumarin **1** with 2-(3-methyl-2-butenyloxy) benzaldehyde **2** in refluxing ethanol proceeded via the domino Knoevenagel hetero Diels–Alder reaction to afford pyrano[3-2c]coumarin and pyrano[2-3b]chromone derivatives **3** and **4** in the ratio of 68:32 amounting to the overall yield of 57% (Scheme 1). Examination of the spectral data revealed that both the keto carbonyl and lactone carbonyl could be involved in the cycloaddition reactions leading to **3** and **4**, respectively.

The structure of the cycloadducts was ascertained by the spectral data. The IR carbonyl absorption of **3** was observed at 1710 cm^{-1} whereas in the case of **4** it was observed at 1634 cm^{-1}. The most diagnostic signal to distinguish the coumarin and chromone derivatives is due to the carbonyl carbon in the ^{13}C NMR spectrum which appeared at δ 163.73 for coumarin derivative **3** and at δ 178.33 for chromone **4**. The *cis*-fusion of the two pyran rings in **3** and **4** was determined by the coupling constant $J_{6a,14b}$=4.5 and 4.1 Hz, respectively, as well as by the n.O.e experiment on the products **3** and **4**. Further, the polycyclic pyrano[3-2c]coumarin structure **3** was corroborated by X-ray single crystal analysis.[9]

When the same reaction was carried out under microwave irradiation in ethanol for 15 s furnished the polycyclic cycloadducts **3** and **4** in the ratio 93:7 with 82% overall yield. Thus, the pronounced chemoselectivity was achieved with the considerable reduction in reaction time.

Further, the reaction of 2-(3-methyl-2-butenyloxy)-1-naphthaldehyde **5** with **1** in refluxing ethanol for 4 h, afforded the polycyclic *cis*-fused cycloadducts **6** and **7**, in the ratio 80:20 in 75% overall yield. While applying the microwave irradiation for just 10 s, the ratio of the cycloadducts **6** and **7** was found to be 95:5 in 92% yield (Scheme 2). Confirmatory evidence for the structures **6** and **7** was available from IR, NMR, mass spectra and elemental analysis. Also the *cis*-fusion of the two pyran rings is confirmed by the difference n.O.e analysis.

We subsequently investigated the intramolecular domino Knoevenagel hetero Diels–Alder reaction of the benzo-analogues of 4-hydroxy coumarin, i.e. 4-hydroxy α-naphthocoumarin **8** and 4-hydroxy β-naphthocoumarin **13** with aromatic aldehydes **2** and **5**. In all the cases, the domino Knoevenagel hetero Diels–Alder reaction afforded novel polycyclic pyrano[3-2c]coumarin derivatives as major products in good yields. The results obtained under thermal as well as microwave irradiation conditions were included in Table 1. The structure and the stereochemistry of the pyrano[3-2c]coumarin and pyrano[2-3b]chromone derivatives were borne out from the NMR and mass spectral data. Fig. 1 shows the X-ray structure of [6a,16b]-*cis*-7,7-dimethyl-6,6a,7,16b-tetrahydrochromeno[4^1,3^1:3,4] pyrano-[3-2c]-α-naphthocoumarin.

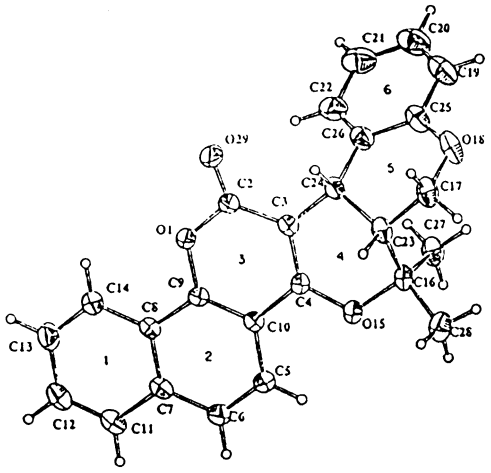


Figure 1. X-Ray structure of compound **9**.

From Table 1, it is obvious that pyrano[3-2c]coumarin adducts were predominant over the chromone derivatives under microwave irradiation condition. In all cases the stereochemistry of the major cycloadduct was proved to be *cis* by the observed ^1H n.O.e effect between the ring junction protons and also by the coupling constant value.

With these encouraging results, it was of further interest to study the reaction of unsymmetrical 1,3-diones with aliphatic aldehyde, citronellal. Thus, the reaction of **1** with citronellal **18** in refluxing ethanol for 4 h provided of *trans*-fused IMHDA adduct **19** and intramolecular domino Knoevenagel ene adduct **20** in the ratio 58:42 with the overall chemical yield being 55% (Scheme 2). The structure and *trans* annelation of the coumarin derivative was confirmed by X-ray structure determination of **19** (Fig. 2). The intramolecular ene adduct **20** exhibits keto–enol tautomerism in the ratio of 85:15 which was corroborated by the NMR data. The protons 5-H and 6-H involved in the ring closure of the intramolecular ene reaction are *trans* was assigned by coupling pattern for 5-H and 6-H protons. The 6-H proton resonated as a triplet of doublet at δ 3.13 with J=11.5, 3.0 Hz.

In order to improve the chemical yield and enhance the chemoselectivity, the same reaction was carried out under microwave irradiation. The reaction afforded

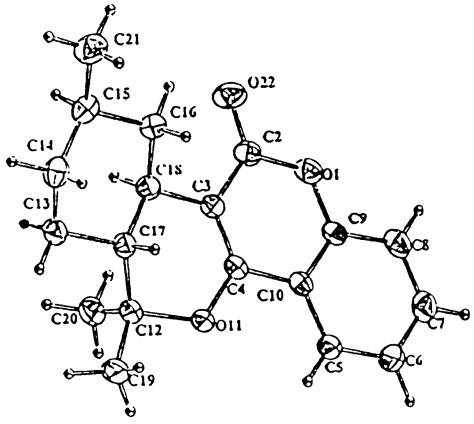
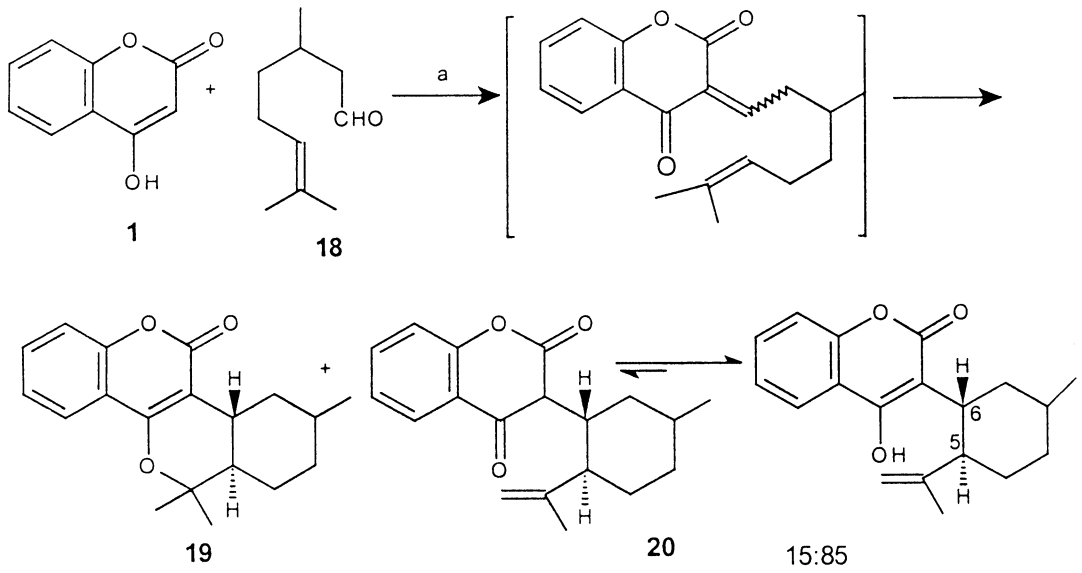


Figure 2. X-Ray structure of compound **19**.



Scheme 3. a EtOH reflux, 4 h or MW irradiation, 12 s.

pyrano[3-2c]coumarin **19** and intramolecular ene adduct **20** in the ratio 88:12 with chemical yield of 81% just 12 s (Scheme 3).

To test the generality of IMHDA reaction, the reaction of 4-hydroxy α-naphthocoumarin **8** and 4-hydroxy β-naphthocoumarin **13** with citronellal was studied. The reaction afforded the *trans* fused pyrano[3-2c]coumarin derivative as major product in both the cases with the formation of intramolecular ene product in minor amounts. As observed earlier, microwave irradiation enhanced the reaction rate and increased the chemical yield. The results obtained for the reaction of 1,3-diones with citronellal were depicted in Table 2.

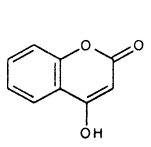
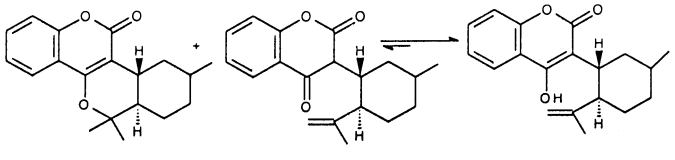
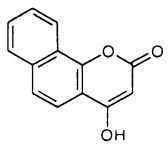
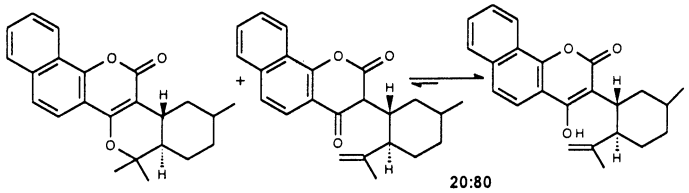
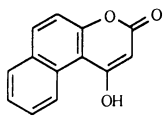
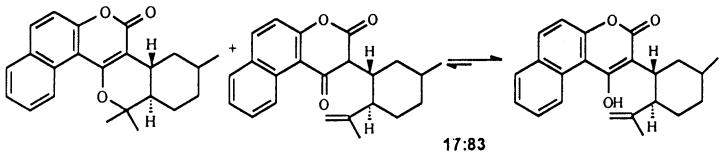
In conclusion, we have demonstrated a simple and flexible synthetic entry into novel polycyclic pyrano[3-2c]coumarin frameworks via domino Knoevenagel hetero Diels–Alder reaction from the readily available starting materials. High degree of chemoselectivity has been achieved in the competition between two different cycloaddition pathways for the unprecedented IMHDA reaction. The reaction protocol described is promising in the sense that they offer an easy access to pyrano[3-2c]coumarin skeleton which frequently occurs in many natural products.

3. Experimental

3.1. General

All melting points are uncorrected. IR spectra were recorded

Table 2. Reaction of 1,3-diones with citronellal

S. no.	1,3-Dione	Products	Time	Yield	IMHDA/IER[a]
1		 15:85	4 h 12 s	55 81	58:42 88:12
2		 20:80	6 h 3 min	69 75	63:27 84:16
3		 17:83	7 h 2.5 min	53 78	66:34 84:16

[a] IMHDA, intramolecular hetero Diels–Alder reaction; IER, intramolecular ene reaction.

on a SHIMADZU FT-IR 8300 instrument. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using TMS as an internal standard on a Bruker DPX200 at 200 and 50.3 MHz, respectively. Elemental analyses were carried out on a CEST 1106 instrument. MS spectra were recorded on a Finnigan MAT-8230 GC–Mass Spectrometer. Microwave irradiation experiments were carried out on a domestic microwave oven of power 800 W. Flash column chromatography was performed on silica gel (SISCO 230–400 mesh). The crystal structures of the compounds were solved by SHELXS97 method. Refinement on F^2 were carried our by full-matrix least squares technique using SHELXL97. The R value for compound **9** is 0.049 and for **19** is 0.033. Intensity date were collected using Siemens SMART CCD area detector diffractometer.

3.2. General procedure for the intramolecular domino Knoevenagel hetero Diels–Alder reaction

A solution of unsymmetrical 1,3-dione (1 mmol) and the corresponding aldehyde (1 mmol) in 10 mL of dry ethanol were refluxed (or) irradiated under microwaves until the TLC shows the disappearance of the starting material. After the completion of the reaction, the solvent was removed and the residue was subjected to flash column chromatography using hexane/ethylacetate (9:1) as eluent.

3.2.1. [6a,14b]-*cis*-7,7-Dimethyl-6,6a,7,14b-tetrahydrochromeno[4^1,3^1:3,4]pyrano[3-2c]coumarin (3). Colorless crystals, mp: 200–202°C; IR (KBr): 1712 cm^{-1}; ^{1}H NMR: δ 1.15 (s, 3H), 1.63 (s, 3H), 2.30 (m, 1H), 4.41 (d, J=4.5 Hz, 1H), 4.44 (dd, J=11.5, 10.5 Hz, 1H), 4.50 (dd, J=11.5, 6.1 Hz, 1H), 6.75 (d, J=8.1 Hz, 1H), 6.91–7.61 (m, 6H), 7.82 (d, J=8.0 Hz, 1H); ^{13}C NMR: δ 23.89, 27.96, 29.72, 38.43, 64.73, 80.84, 101.52, 115.64, 115.75, 115.92, 120.94, 121.58, 123.05, 123.75, 127.97, 129.72, 131.89, 152.67, 153.62, 159.16, 163.73; MS m/z: 334 (M$^+$); Anal. calcd for $C_{21}H_{18}O_4$: C, 75.52; H, 5.43. Found: C, 75.62; H, 5.39.

3.2.2. [6a,14b]-*cis*-7,7-Dimethyl-6,6a,7,14b-tetrahydrochromeno[4^1,3^1:3,4]pyrano[2-3b]chromone (4). Colorless crystals, mp: 196–197°C; IR (KBr): 1634 cm^{-1}; ^{1}H NMR: δ 1.18 (s, 3H), 1.52 (s, 3H), 2.32 (m, 1H), 4.30 (dd, J=11.5, 6.0 Hz, 1H), 4.46 (d, J=4.1 Hz, 1H), 4.61 (dd, J=12.0, 11.0 Hz, 1H), 6.81–7.62 (m, 7H), 8.21 (d, J=8.0 Hz, 1H); ^{13}C NMR: δ 23.75, 28.10, 28.91, 38.57, 64.83, 82.12, 96.87, 115.75, 116.57, 121.07, 122.16, 122.91, 125.03, 126.08, 127.79, 129.75, 132.86, 152.80, 153.75, 163.56, 178.33; MS m/z: 334 (M$^+$); Anal. calcd for $C_{21}H_{18}O_4$: C, 75.52; H, 5.43. Found: C, 75.49; H, 5.44.

3.2.3. [8a,16b]-*cis*-9,9-Dimethyl-8,8a,9,16b-tetrahydro-5,6-benzochromeno[4^1,3^1:3,4]pyrano[3-2c]coumarin (6). Colorless crystals, mp: 248–250°C; IR (KBr): 1716 cm^{-1}; ^{1}H NMR: δ 1.59 (s, 3H), 1.61 (s, 3H), 2.30 (m, 1H), 4.14 (t, J=11.2 Hz, 1H), 4.42 (ddd, J=11.1, 6.1, 1.5 Hz, 1H), 4.81 (d, J=4.1 Hz, 1H), 6.9 (d, J=8.8 Hz, 1H), 7.15–7.75 (m, 7H), 7.81 (dd, J=8.2, 1.5 Hz, 1H), 8.16 (d, J=8.8 Hz, 1H); ^{13}C NMR: δ 25.73, 26.38, 26.82, 38.26, 62.78, 78.50, 101.01, 114.55, 115.43, 116.18, 118.12, 122.92, 123.36, 124.09, 125.48, 128.15, 128.84, 129.29, 131.66, 132.69, 134.71, 151.16, 152.56, 158.47, 160.42; MS m/z: 384 (M$^+$); Anal. calcd for $C_{25}H_{20}O_4$: C, 78.10; H, 5.25. Found: C, 78.08; H, 5.33.

3.2.4. [8a,16b]-*cis*-9,9-Dimethyl-8,8a,9,16b-tetrahydro-5,6-benzochromeno[4^1,3^1:3,4]pyrano[2-3b]chromone (7). Colorless crystals, mp: 240–241°C; IR (KBr): 1635 cm^{-1}; ^{1}H NMR: δ 1.57 (s, 3H), 1.65 (s, 3H), 2.23 (m, 1H), 3.65 (dd, J=11.5, 6.0 Hz, 1H), 4.21 (t, J=11.2 Hz, 1H), 4.86 (d, J=4.0 Hz, 1H), 7.19–7.8 (m, 8H), 7.91 (dd, J=8.1, 1.5 Hz, 1H), 8.24 (d, J=8.8 Hz, 1H); ^{13}C NMR: δ 25.50, 25.97, 26.67, 38.75, 63.10, 81.14, 96.42, 115.43, 116.50, 118.21, 123.00, 124.12, 124.63, 125.52, 126.15, 128.29, 128.75, 129.22, 130.91, 131.59, 132.69, 151.01, 152.49, 162.11, 178.41; MS m/z: 384 (M$^+$); Anal. calcd for $C_{25}H_{20}O_4$: C, 78.10; H, 5.25. Found: C, 78.18; H, 5.19.

3.2.5. [6a,16b]-*cis*-7,7-Dimethyl-6,6a,7,16b-tetrahydrochromeno[4^1,3^1:3,4]pyrano[3-2c]-α-naphthocoumarin (9). Pale yellow crystals, mp: 222–224°C; IR (KBr): 1708 cm^{-1}; ^{1}H NMR: δ 1.16 (s, 3H), 1.67 (s, 3H), 2.46 (m, 1H), 4.16 (t, J=11.2 Hz, 1H), 4.52 (ddd, J=11.1, 6.1, 1.5 Hz, 1H), 4.61 (d, J=4.1 Hz, 1H), 6.80 (d, J=8.8 Hz, 1H), 6.97–7.75 (m, 8H), 7.91 (dd, J=8.0 Hz, 1H), 8.18 (d, J=8.8 Hz, 1H); ^{13}C NMR: δ 24.02, 28.00, 29.88, 38.57, 64.79, 80.96, 101.27, 110.90, 115.99, 116.87, 118.51, 122.51, 122.87, 123.70, 125.78, 127.71, 128.05, 128.55, 129.97, 134.96, 150.08, 153.73, 160.15, 163.79; MS m/z: 384 (M$^+$); Anal. calcd for $C_{25}H_{20}O_4$: C, 78.10; H, 5.25. Found: C, 78.06; H, 4.99.

3.2.6. [6a,16b]-*cis*-7,7-Dimethyl-6,6a,7,16b-tetrahydrochromeno[4^1,3^1:3,4]pyrano[2-3b]-α-naphthochromone (10). Colorless crystals, mp: 203–204°C; IR (KBr): 1639 cm^{-1}; ^{1}H NMR: δ 1.58 (s, 3H), 1.65 (s, 3H), 2.44 (m, 1H), 3.84 (dd, J=11.4, 6.0 Hz, 1H), 4.30 (t, J=11.2 Hz, 1H), 4.66 (d, J=4.0 Hz, 1H), 7.24–7.81 (m, 8H), 7.92 (dd, J=8.1, 1.4 Hz, 1H), 8.26 (d, J=8.8 Hz, 1H); ^{13}C NMR: δ 25.61, 25.84, 26.68, 38.66, 63.20, 81.14, 96.44, 115.62, 116.50, 118.21, 122.99, 124.16, 124.74, 125.61, 126.20, 128.21, 128.74, 129.12, 130.61, 131.66, 132.68, 151.44, 152.62, 162.11, 178.40; MS m/z: 384 (M$^+$); Anal. calcd for $C_{25}H_{20}O_4$: C, 78.10; H, 5.25. Found: C, 78.03; H, 5.19.

3.2.7. [8a,18b]-*cis*-9,9-Dimethyl-8,8a,9,18b-tetrahydro-5,6-benzochromeno[4^1,3^1:3,4]pyrano[3-2c]-α-naphthocoumarin (11). Yellow crystals, mp: 229–230°C; IR (KBr): 1708 cm^{-1}; ^{1}H NMR: δ 1.18 (s, 3H), 1.72 (s, 3H), 2.52 (m, 1H), 4.24 (t, J=11.2 Hz, 1H), 4.62 (ddd, J=11.1, 6.1, 1.5 Hz, 1H), 4.94 (d, J=4.1 Hz, 1H), 6.90 (d, J=8.8 Hz, 1H), 6.98–7.76 (m, 8H), 7.92 (dd, J=8.2, 1.2 Hz, 1H), 8.18 (d, J=9.0 Hz, 1H), 8.34 (d, J=8.8 Hz, 1H); ^{13}C NMR: δ 25.64, 26.32, 26.86, 38.32, 63.84, 78.51, 102.24, 114.60, 115.45, 116.32, 118.44, 122.84, 123.36, 124.43, 125.48, 126.12, 128.20, 128.91, 129.28, 130.99, 132.62, 132.94, 133.64, 134.71, 134.81, 151.46, 152.61, 158.46, 160.48; MS m/z: 434 (M$^+$); Anal. calcd for $C_{29}H_{22}O_4$: C, 80.16; H, 5.11. Found: C, 79.96; H, 5.17.

3.2.8. [8a,18b]-*cis*-9,9-Dimethyl-8,8a,9,18b-tetrahydro-5,6-benzochromeno[4^1,3^1:3,4]pyrano[2-3b]-α-naphthochromone (12). Colorless crystals, mp: 238–240°C; IR

(KBr): 1641 cm^{-1}; ^1H NMR: δ 1.46 (s, 3H), 1.65 (s, 3H), 2.42 (m, 1H), 3.82 (dd, J=11.6, 6.2 Hz, 1H), 4.26 (t, J=11.2 Hz, 1H), 4.79 (d, J=4.0 Hz, 1H), 7.16–7.84 (m, 8H), 7.94 (dd, J=8.1, 1.2 Hz, 1H), 8.26 (d, J=8.6 Hz, 1H), 8.36 (d, J=8.8 Hz, 1H), 9.24 (d, J=8.0 Hz, 1H); ^{13}C NMR: δ 25.61, 25.94, 26.42, 38.64, 63.20, 81.16, 96.42, 115.41, 116.42, 118.32, 122.82, 123.41, 124.32, 124.32, 124.66, 125.56, 126.25, 126.32, 128.29, 128.75, 129.32, 130.64, 131.64, 132.70, 132.81, 133.64, 151.44, 152.62, 163.12, 178.40; MS *m/z*: 434 (M^+); Anal. calcd for $C_{29}H_{22}O_4$: C, 80.16; H, 5.11. Found: C, 80.33; H, 4.98.

3.2.9. [6a,16b]-*cis*-7,7-Dimethyl-6,6a,7,16b-tetrahydrochromeno[4^1,3^1:3,4]pyrano[3-2c]-β-naphthocoumarin (14). Colorless crystals, mp: 240–242°C; IR (KBr): 1710 cm^{-1}; ^1H NMR: δ 1.21 (s, 3H), 1.52 (s, 3H), 2.32 (m, 1H), 4.12 (t, J=11.2 Hz, 1H), 4.62 (ddd, J=11.0, 6.2, 1.2 Hz, 1H), 4.86 (d, J=4.2 Hz, 1H), 6.80 (d, J=8.6 Hz, 1H), 6.89–7.62 (m, 8H), 8.32 (d, J=8.8 Hz, 1H), 9.32 (d, J=7.8 Hz, 1H); ^{13}C NMR: δ 25.62, 26.32, 26.94, 38.12, 62.62, 79.10, 100.99, 114.23, 115.61, 116.32, 118.32, 122.94, 123.35, 124.61, 125.38, 128.22, 128.91, 129.36, 131.64, 132.66, 134.64, 151.04, 152.91, 157.69, 161.44; MS *m/z*: 384 (M^+); Anal. calcd for $C_{25}H_{20}O_4$: C, 78.10; H, 5.25. Found: C, 78.03; H, 5.21.

3.2.10. [6a,16b]-*cis*-7,7-Dimethyl-6,6a,7,16b-tetrahydrochromeno[4^1,3^1:3,4]pyrano[2-3b]-β-naphthochromone (15). Colorless crystals, mp: 234–236°C; IR (KBr): 1639 cm^{-1}; ^1H NMR: δ 1.16 (s, 3H), 1.48 (s, 3H), 2.32 (m, 1H), 3.81 (dd, J=11.2, 6.0 Hz, 1H), 4.42 (t, J=11.3 Hz, 1H), 4.86 (d, J=4.0 Hz, 1H), 7.21–7.84 (m, 8H), 8.24 (d, J=8 Hz, 1H), 9.21 (d, J=7.8 Hz, 1H); ^{13}C NMR: δ 25.61, 25.91, 26.41, 38.62, 63.32, 80.64, 101.52, 115.63, 116.20, 118.32, 122.81, 124.20, 124.62, 125.62, 126.73, 128.12, 128.48, 129.04, 130.62, 131.71, 132.81, 151.44, 152.56, 162.04, 177.41; MS *m/z*: 384 (M^+); Anal. calcd for $C_{25}H_{20}O_4$: C, 78.10; H, 5.25. Found: C, 78.13; H, 5.19.

3.2.11. [8a,18b]-*cis*-9,9-Dimethyl-8,8a,9,18b-tetrahydro-5,6-benzochromeno[4^1,3^1:3,4]pyrano[3-2c]-β-naphthocoumarin (16). Colorless crystals, mp: 250–252°C; IR (KBr): 1712 cm^{-1}; ^1H NMR: δ 1.20 (s, 3H), 1.72 (s, 3H), 2.48 (m, 1H), 4.24 (t, J=11.2 Hz, 1H), 4.68 (ddd, J=11.1, 6.1, 1.5 Hz, 1H), 4.84 (d, J=4.2 Hz, 1H), 6.89 (d, J=8.8 Hz, 1H), 7.12–7.76 (m, 9H), 8.32 (d, J=7.8 Hz, 1H), 9.31 (d, J=8.8 Hz, 1H); ^{13}C NMR: δ 24.58, 26.12, 26.79, 37.80, 62.50, 78.43, 101.91, 113.59, 115.31, 116.23, 118.41, 121.91, 122.88, 124.32, 125.46, 126.13, 128.21, 128.81, 129.20, 130.81, 132.61, 132.81, 133.61, 134.64, 134.84, 151.45, 152.62, 158.46, 160.32; MS *m/z*: 434 (M^+); Anal. calcd for $C_{29}H_{22}O_4$: C, 80.16; H, 5.11. Found: C, 80.21; H, 4.92.

3.2.12. [8a,18b]-*cis*-9,9-Dimethyl-8,8a,9,18b-tetrahydro-5,6-benzochromeno[4^1,3^1:3,4]pyrano[2-3b]-β-naphthochromone (17). Colorless crystals, mp: 249–50°C; IR (KBr): 1642 cm^{-1}; ^1H NMR: δ 1.32 (s, 3H), 1.58 (s, 3H), 2.42 (m, 1H), 3.78 (dd, J=11.4, 6.1 Hz, 1H), 4.32 (t, J=11.0 Hz, 1H), 4.68 (d, J=4.0 Hz, 1H), 7.21–7.81 (m, 9H), 8.21 (d, J=8.0 Hz, 1H), 8.36 (d, J=7.8 Hz, 1H), 9.32 (d, J=8.0 Hz, 1H); ^{13}C NMR: δ 24.62, 25.61, 26.41, 38.14, 62.91, 81.20, 96.51, 114.32, 115.94, 118.12, 122.32, 123.41, 124.44, 124.84, 125.56, 126.23, 126.61, 128.31, 128.71, 129.41, 130.71, 131.32, 132.46, 132.81, 133.71, 151.64, 152.66, 163.08, 177.91; MS *m/z*: 434 (M^+); Anal. calcd for $C_{29}H_{22}O_4$: C, 80.16; H, 5.11. Found: C, 80.03; H, 5.17.

3.2.13. [4a,12b]-*trans*-2,5,5-Trimethyl-1,2,3,4,4a,12b-hexahydro-1*H*-[2]benzopyrano[3-2c]coumarin (19). Colorless crystals, mp: 129–130°C; IR (KBr): 1720 cm^{-1}; ^1H NMR: δ 0.6 (m, 1H), 0.96 (d, J=6.4 Hz, 3H), 1.19 (s, 3H), 1.0–1.22 (m, 2H), 1.45 (m, 1H), 1.52 (s, 3H), 1.62 (m, 1H), 1.85 (m, 2H), 2.36 (td, J=11.2, 3.0 Hz, 1H), 3.11 (m, 1H), 7.23 (m, 2H), 7.46 (m, 1H), 7.77 (dd, J=7.8, 1.5 Hz, 1H); ^{13}C NMR: δ 19.97, 22.61, 27.49, 27.85, 32.65, 34.59, 35.55, 37.66, 48.66, 81.67, 103.68, 116.48, 116.60, 123.02, 123.72, 131.48, 152.88, 159.30, 162.14; MS *m/z* 298 (M^+); Anal. calcd for $C_{19}H_{22}O_3$: C, 76.47; H, 7.4. Found: C, 76.49; H, 7.4.

3.2.14. Intramolecular ene product (20). Colorless crystals, mp: 136–137°C; IR (KBr): 1720 cm^{-1}; MS *m/z*: 298 (M^+); Anal. calcd for $C_{19}H_{22}O_3$: C, 76.47; H, 7.4. Found: C, 76.44; H, 7.38. *Keto-enol form*: ^1H NMR (DMSO-d_6): δ 0.95 (d, J=6.5 Hz, 3H), 0.90–1.90 (m, 7H), 1.61 (s, 3H), 2.95 (td, J=11.5, 3.0 Hz, 1H), 3.13 (td, J=11.5, 3.0 Hz, 1H), 4.45 (bs, 1H), 4.55 (bs, 1H), 7.31 (m, 2H), 7.55 (m, 1H), 7.91 (dd, J=8.0, 2.0 Hz, 1H), 11.10 (bs, 1H); ^{13}C NMR: δ 18.70, 21.12, 31.81, 32.28, 35.15, 38.11, 38.86, 48.15, 108.39, 116.26, 123.05, 123.56, 123.85, 131.02, 131.75, 148.77, 152.08, 159.50, 161.20. *Diketo form*: ^1H NMR (DMSO-d_6): δ 0.88 (d, J=6.4 Hz, 3H), 0.90–1.90 (m, 7H), 1.63 (s, 3H), 2.23 (m, 1H), 3.00 (td, J=11.5, 3.0 Hz, 1H), 3.85 (bs, 1H), 4.58 (bs, 1H), 4.70 (bs, 1H), 7.35 (m, 2H), 7.60 (m, 1H), 7.95 (dd, J=8.0, 1.9 Hz, 1H).

3.2.15. [4a,14b]-*trans*-2,5,5-Trimethyl-1,2,3,4,4a,14b-hexahydro-1*H*-[2]benzopyrano[3-2c]-α-naphthocoumarin (21). Colorless crystals, mp: 168–170°C; IR (KBr): 1712 cm^{-1}; ^1H NMR: δ 0.60 (m, 1H), 0.97 (d, J=7 Hz, 3H), 1.12 (s, 3H), 1.01–1.28 (m, 2H), 1.45 (m, 1H), 1.52 (s, 3H), 1.73 (m, 1H), 1.86 (m, 2H), 2.34 (td, J=11.1, 2.8 Hz, 1H), 3.04 (m, 1H), 7.24–7.61 (m, 4H), 7.86 (dd, J=7.8, 1.2 Hz, 1H), 8.13 (d, J=8 Hz, 1H); ^{13}C NMR: δ 18.62, 21.32, 26.58, 27.08, 33.14, 35.60, 35.78, 37.61, 47.60, 81.71, 106.31, 115.41, 116.78, 118.71, 122.41, 123.68, 130.52, 131.16, 152.60, 159.61, 163.88; MS *m/z*: 348 (M^+); Anal. calcd for $C_{23}H_{24}O_3$: C, 79.27; H, 6.95. Found: C, 79.24; H, 6.87.

3.2.16. Intramolecular ene product (22). Colorless crystals, mp: 189–190°C; IR (KBr): 3310, 1656 cm^{-1}; MS *m/z*: 348 (M^+). *Keto-enol form*: ^1H NMR (DMSO-d_6): δ 0.80 (d, J=6.0 Hz, 3H), 0.91–1.8 (m, 7H), 1.58 (s, 3H), 2.92 (td, J=11.0, 3.0 Hz, 1H), 3.06 (td, J=11.6, 3.0 Hz, 1H). 4.46 (bs, 1H), 4.61 (bs, 1H), 7.21–7.61 (m, 4H), 7.98 (dd, J=7.8, 1.2 Hz, 1H), 8.12 (d, J=8.0 Hz, 1H), 11.01 (bs, 1H); ^{13}C NMR: δ 18.62, 21.24, 30.88, 32.30, 34.49, 38.08, 48.32, 108.11, 116.32, 117.34, 120.81, 122.78, 123.44, 123.91, 130.61, 131.88, 148.81, 152.06, 158.61, 160.81. *Diketo form*: ^1H NMR: δ 0.6 (d, J=6.2 Hz, 3H), 0.91–1.8 (m, 7H), 1.63 (s, 3H), 2.23 (m, 1H), 3.12 (td, J=11.2, 3.0 Hz, 1H), 3.90 (bs, 1H), 4.61 (bs, 1H), 4.72

(bs, 1H), 7.20–7.66 (m, 4H), 7.97 (dd, *J*=8.0, 1.4 Hz, 1H), 8.12 (d, *J*=8.0 Hz, 1H).

3.2.17. [4a,14b]-*trans*-2,5,5-Trimethyl-1,2,3,4,4a,14b-hexahydro-1*H*-[2]-benzopyrano[3-2c]-β-naphthocoumarin (23). Colorless solid, mp: 172–174°C; IR (KBr): 1716 cm^{-1}; ^1H NMR: δ 0.61 (m, 1H), 0.92 (d, *J*=7.0 Hz, 3H), 1.16 (s, 3H), 1.01–1.26 (m, 2H), 1.42 (m, 1H), 1.61 (s, 3H), 1.81 (m, 1H), 1.94 (m, 2H), 2.36 (td, *J*=11.1, 2.8 Hz, 1H), 3.06 (m, 1H), 7.21–7.64 (m, 4H), 8.21 (d, *J*=8.0 Hz, 1H), 9.10 (d, *J*=7.2 Hz, 1H); ^{13}C NMR: δ 18.61, 22.41, 26.81, 27.60, 32.41, 35.51, 35.82, 37.61, 47.58, 80.59, 106.42, 115.41, 116.82, 118.61, 122.43, 123.77, 123.91, 130.91, 130.48, 131.08, 152.71, 158.68, 163.79; MS *m*/*z*: 348 (M^+); Anal. calcd for $C_{23}H_{24}O_3$: C, 79.27; H, 6.95. Found: C, 79.24; H, 6.87.

3.2.18. Intramolecular ene product (24). Colorless crystals, mp: 194–196°C; IR (KBr): 3309, 1657 cm^{-1}; MS *m*/*z*: 348 (M^+). *Keto-enol form*: ^1H NMR (DMSO-d_6): δ 0.74 (d, *J*=5.8 Hz, 3H), 0.9–1.90 (m, 7H), 1.58 (s, 3H), 3.01 (td, *J*=11.6, 3.0 Hz, 1H), 3.10 (td, *J*=11.6, 3.0 Hz, 1H), 4.31 (bs, 1H), 4.51 (bs, 1H), 7.21–7.61 (m, 4H), 8.13 (d, *J*=8.0 Hz, 1H), 9.10 (d, *J*=7.8 Hz, 1H), 11.06 (bs, 1H); ^{13}C NMR: δ 18.61, 21.11, 30.51, 32.14, 34.59, 38.11, 48.41, 108.13, 116.34, 117.41, 120.81, 122.56, 122.81, 123.51, 123.86, 130.58, 131.31, 131.91, 148.66, 151.64, 158.64, 160.80. *Diketo form*: ^1H NMR: δ 0.60 (d, *J*=6.2 Hz, 3H), 0.9–1.8 (m, 7H), 1.63 (s, 3H), 2.34 (m, 1H), 3.20 (td, *J*=11.6, 2.1 Hz, 1H), 4.61 (bs, 1H), 4.71 (bs, 1H), 7.20–7.66 (m, 4H), 8.12 (d, *J*=8.0 Hz, 1H), 9.1 (d, *J*=7.1 Hz, 1H).

Acknowledgements

S. M. thanks Council of Scientific and Industrial Research, New Delhi for the award of SRF. We acknowledge Professor D. Velmurugan, Department of Crystallography and Biophysics, University of Madras for providing X-ray single crystal analysis. Financial support from DST, New Delhi is gratefully acknowledged.

References

1. Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115.
2. (a) Tietze, L. F.; Kettschau, G.; Gewert, J. A.; Schuffenhauer, A. *Curr. Org. Chem.* **1998**, *2*, 19. (b) Tietze, L. F.; Zhou, Y. F. *Angew. Chem. Int. Ed.* **1999**, *38*, 2045.
3. (a) Bose, A. K.; Banik, B. K.; Lavlinskaia, N.; Jayaraman, M.; Manhas, M. C. *Chemtech* **1997**, *27*, 18. (b) Varma, R. S. *Green Chem.* **1999**, *2*, 43. (c) Loupy, A.; Petit, A.; Hamelin, J.; Boullet, F. T.; Jacquart, P.; Mathe, D. *Synthesis* **1998**, 1213.
4. (a) Feuer, G. In *Progress in Medicinal Chemistry*; Ellis, G. P., West, G. B., Eds.; North-Holland: New York, 1974. (b) Deana, A. A. *J. Med. Chem.* **1983**, *26*, 580. (c) Wenkert, E.; Buckwalter, B. L. *J. Am. Chem. Soc.* **1972**, *94*, 4367.
5. Rastogi, R. P.; Mehrotra, B. N. *Compendium of Indian Medicinal Plants*; Rastogi, R. P., Ed.; 1993; Vol. 3, p 273.
6. (a) Shanmugasundaram, M.; Raghunathan, R. *Tetrahedron Lett.* **1999**, *40*, 4869. (b) Shanmugasundaram, M.; Raghunathan, R. *Tetrahedron* **2000**, *56*, 5241.
7. (a) Manikandan, S.; Shanmugasundaram, M.; Raghunathan, R.; Padma Malar, E. J. *Heterocycles* **2000**, *53*, 579. (b) Manikandan, S.; Shanmugasundaram, M.; Raghunathan, R. *Heteroatom Chem.* **2001** in press. (c) Manikandan, S.; Shanmugasundaram, M.; Kumareshwaran, R.; Raghunathan, R. *Indian J. Chem., Sect. B.* **2001** in press.
8. (a) Manikandan, S.; Mohamed Ashraf, M.; Raghunathan, R. *Synth. Commun.* **2001** in press. (b) Subramaniyan, G.; Raghunathan, R. *Tetrahedron* **2001**, *57*, 2909.
9. Krishna, R.; Velmurugan, D.; Raj, S. S. S.; Fun, H. K.; Shanmugasundaram, M.; Raghunathan, R. *Cryst. Res. Technol.* **2001** in press.