Synthesis of Cyclopentacarbazolones via Palladium-Catalyzed Annulation of Internal Alkynes

Devanga K. Sreenivas, Jatoth Sandhyarani, Rajagopal Nagarajan*

School of Chemistry, University of Hyderabad, Hyderabad 500046, India
Fax +91(40)23012460; E-mail: rnsc@uohyd.ernet.in

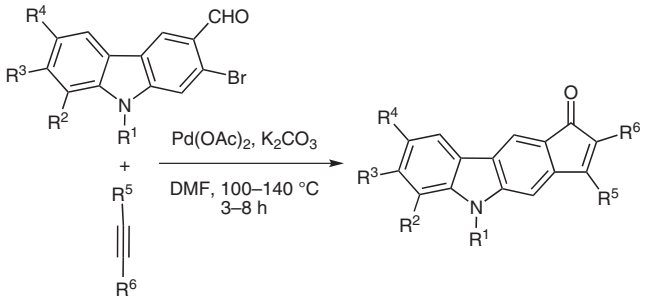
Received 8 December 2011; revised 28 January 2012

Abstract: A simple and efficient protocol for the synthesis of highly substituted cyclopentacarbazolones (50–82%) was developed by employing internal alkynes with 2-bromo-3-formylcarbazoles in the presence of palladium catalyst under ligand-free condition. High regioselectivity was observed for unsymmetrical (alkyl-, aryl-substituted) internal alkynes.

Key words: estrogen receptors, palladium catalyst, annulations, cyclopentacarbazolones, ligand-free synthesis

Cyclopentadienones[1] are members of a diverse class of attractive molecules with demonstrated value and even broader potential in synthesis, biology, materials science, and nanotechnology.[2] Fused and substituted cyclopentadienones[3] are also potentially useful building blocks in organic, organometallic, and medicinal chemistry and also possess a broad range of biological activities such as antiproliferative,[4] antitumor,[5] fungicidal,[6] and also act as estrogen binding receptors.[7] Moreover, carbazole motif[8] is a prominent structural unit discerned in various natural products and synthetic compounds with vital medicinal values.[9] Due to their significant pharmacological importance, the development of facile strategies to obtain such frameworks has become an attractive endeavor in synthetic organic and medicinal chemistry. Therefore, the synthesis of carbazole fused derivatives has become an important research field and several methods have been developed.[10]

In recent years, several methodologies have been reported for the synthesis of cyclopentadienone fused with heterocyclic based natural products.[11] Palladium-catalyzed annulation of internal alkynes by substituted *ortho*-halobenzaldehydes have been demonstrated to be a versatile method to construct a wide range of complicated hetero- and carbocycles. Significant work in this area was done by Larock and co-workers who introduced the first catalytic protocol for the efficient synthesis of indenones, even though this catalytic system has some limitations in the scope of the substrates.[12] To the best of our knowledge, no reports are available on the synthesis of carbazole fused with substituted cyclopentadienone. Considering the biological as well as material importance of carbazole and cyclopentadienone nuclei in various natural products and drugs, herein we wish to report a simple, and efficient protocol for the synthesis of various 2,3-disubstituted cyclopentacarbazolones by the reaction of 2-bromo-3-formylcarbazole with internal alkynes in the presence of palladium catalyst under ligand-free conditions as shown in Scheme 1.



Scheme 1 Schematic representation of the present work

2-Bromo-9-ethyl-6-methyl-9*H*-carbazole-3-carbaldehyde[13] and diphenylacetylene were used as model substrates for optimizing the reaction conditions. The influences of catalyst, ligand, additive, base, solvent, and temperature in the reaction outcome were examined as shown in Table 1. In the initial screenings in which various solvents were tested for the reaction, DMF was found to be an efficient media. Furthermore, different bases such as Cs_2CO_3, Na_2CO_3, DABCO, KOAc, and K_2CO_3 were tested in the reaction; it was found that K_2CO_3 was superior to other bases. Ligand and additive had no effect on the reaction; without ligand and additive the reaction proceeded well within three hours (Table 1, entry 14). No reaction occurred at or below 90 °C. By changing the catalyst loading below 5 mol%, the reaction took more time to reach completion whereas when the catalyst loading was increased (7.5–10 mol%), the reaction went to completion within three hours with increased yield of the product. Based on above findings, we concluded that the optimal conditions for this reaction involved 1.0 equivalent of **1a**, 1.0 equivalent of **2a** and 2.5 equivalents of K_2CO_3 in DMF with 7.5 mol% of $Pd(OAc)_2$ at 140 °C. By using the optimized condition the product **3a** was obtained in good yield (74%) within three hours. The product **3a** was confirmed by spectral data and single crystal X-ray analysis. The ORTEP diagram is shown in Figure 1.[14]

SYNTHESIS 2012, 44, 1268–1278
Advanced online publication: 27.03.2012
DOI: 10.1055/s-0031-1290807; Art ID: Z113711SS
© Georg Thieme Verlag Stuttgart · New York

Downloaded by: Universite Laval. Copyrighted material.

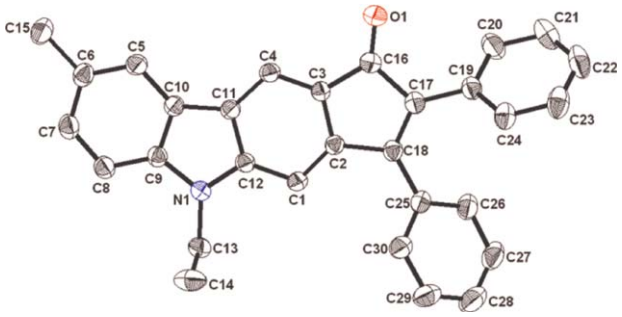


Figure 1 ORTEP diagram of **3a**

With the optimized condition in hand, various derivatives **1a**–**j** were treated with diphenylacetylene **2a**, the reaction proceeded well to afford the corresponding products **3a**–**j** in moderate to good yields as shown in Table 2. After the synthesis of 2,3-diphenylcyclopentacarbazolone derivatives **3a**–**j**, we noticed that the products with an electron-withdrawing group in 5-position were formed in good yields, for example, **3j** (82%) and **3d** (78%) (Table 2). In the case of higher alkyl chain substitution present at 5-position such as **3b**, **3c**, **3g**, and **3i** moderate yields were obtained. To check the versatility of this annulation, various types of internal alkynes such as symmetrically and unsymmetrically substituted alkyl- and arylalkynes were tested. Symmetrical alkylacetylenes **2b**,**c** afforded the products **3k**–**n** in moderate yields as shown in Table 3. In the case of symmetrically substituted arylalkynes, the products **3o** and **3p** were obtained in good yields (Table 4, see below).

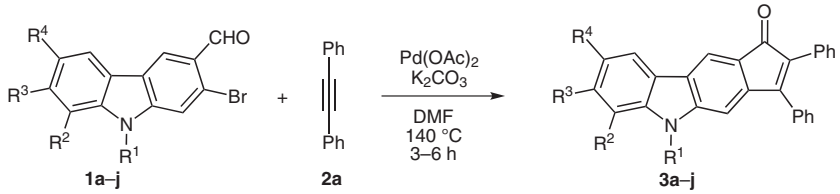
Table 1 The Screening of Reaction Conditions[a]

Entry	Catalyst	Ligand	Additive	Base	Solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	Pd/C[c]	–	–	Et_3N	DMF	120	24	NR[d]
2	$Pd(PPh_3)_2Cl_2$	–	TBAB	Cs_2CO_3	toulene	120	24	22
3	$Pd(OAc)_2$	–	–	DABCO	DMF	130	28	30
4	$Pd(PPh_3)_4$	–	–	Ag_2CO_3	DMF	140	24	NR[d]
5	$Pd(OAc)_2$	Ph_3P	TBAB	K_2CO_3	DMF	120	8	62
6	$Pd(OAc)_2$	Ph_3P	–	K_2CO_3	DMF	120	8	65
7	$Pd(OAc)_2$	–	TBAB	K_2CO_3	DMF	140	8	65
8	$Pd(OAc)_2$	Cy_3P	LiCl	K_2CO_3	DMF	140	10	70
9	$Pd(OAc)_2$	dppe	SDS	K_2CO_3	DMF	140	6	64
10	$Pd(OAc)_2$	–	SDS	KOAc	DMA	140	8	64
11	$Pd(OAc)_2$	–	LiCl	Cs_2CO_3	DMSO	140	10	70
12	$Pd(OAc)_2$	–	TBAB	KOAc	ODCB	130	18	42
13	$Pd(OAc)_2$	–	–	K_2CO_3	DMF	140	8	70
14	$Pd(OAc)_2$[e]	–	–	K_2CO_3	DMF	140	3	74
15	–	–	–	K_2CO_3	DMF	140	24	NR[d]
16	$Pd(OAc)_2$	–	–	KOAc	TEG	140	15	38
17	$PdCl_2$	–	–	$NaHCO_3$	DMF	140	15	48

[a] Unless otherwise stated, all the reactions were carried at in a Schlenk tube by employing 0.05 equiv of catalyst, 0.2 equiv of ligand, 1.0 equiv of additive, and 2.0 equiv of base. TBAB: Bu_4NBr; SDS: sodium lauryl sulfate; ODCB: 1,2-dichlorobenzene; TEG: tetraethylene glycol.
[b] Isolated yields.
[c] Pd/C used: 10 mol%.
[d] NR: no reaction.
[e] $Pd(OAc)_2$ used: 7.5 mol%.

Downloaded by: Universite Laval. Copyrighted material.

Table 2 Synthesis of 2,3-Diphenylcyclopentacarbazolones[a]

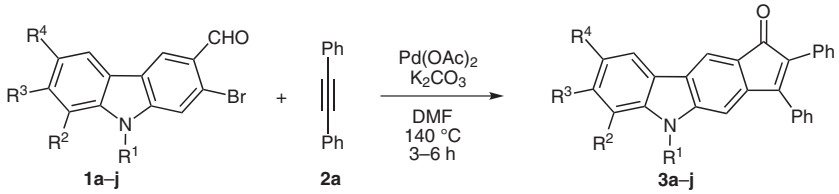


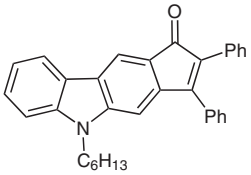
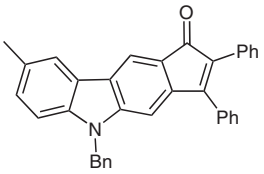
Entry	R^1	R^2	R^3	R^4	Time (h)	Product	Yield (%)
1	Et	H	H	Me	3	**3a**	74
2	*n*-Bu	H	H	H	5	**3b**	65
3	*n*-C_5H_{11}	H	H	Me		**3c**	63
4	Bn	H	H	H	4	**3d**	78
5	Et	H	H	*t*-Bu	4	**3e**	76
6	Et	H	H	H	4	**3f**	68
7	*n*-Bu	H	Br	H	6	**3g**	56
8	Et	Me	H	Me	3	**3h**	80

Downloaded by: Universite Laval. Copyrighted material.

 © Thieme Stuttgart · New York

Table 2 Synthesis of 2,3-Diphenylcyclopentacarbazolones[a] (continued)



Entry	R^1	R^2	R^3	R^4	Time (h)	Product	Yield (%)
9	*n*-C_6H_{13}	H	H	H	4	**3i** 	65
10	Bn	H	H	Me	4	**3j** 	82

[a] Alkyne **2a** used: 1.0 equiv.

When the unsymmetrical arylalkyne, chlorodiphenylacetylene **2e** was used, two regioisomers **3q** and **3q′** were obtained in a ratio of 1:1 as shown in Table 4. The substituents do not hinder sterically here, and as a result a mixture of isomers in a 1:1 ratio were obtained. However, in the case of alkynes with aryl and alkyl substituents such as **2f**–**g**, only one regioisomer was obtained in the range of 54–60% yield. This high regioselectivity is due to the more sterically hindered group (phenyl) in the 3-position of corresponding products **3r**–**u** as the major product as shown in Table 4. Further, from the 2D NOESY of the product **3r** it was confirmed that the ethyl group is adjacent to the carbonyl functional group. The structure of the product **3r** was also confirmed by single crystal X-ray analysis. The ORTEP diagram is shown in Figure 2.[14]

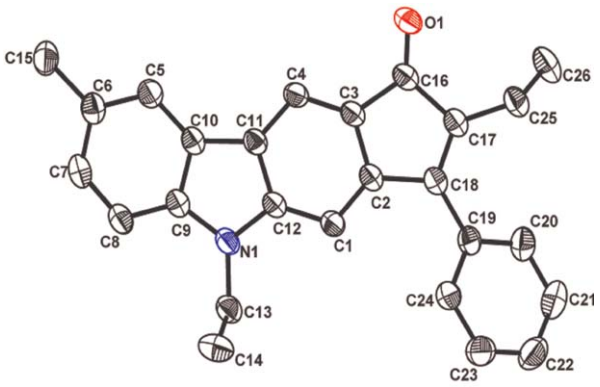


Figure 2 ORTEP diagram of **3r**

In the same manner, the products **3s**, **3t**, and **3u** were obtained as shown in Table 4. The product **3s** was also confirmed by single crystal X-ray analysis and the ORTEP diagram is shown in Figure 3.[14]

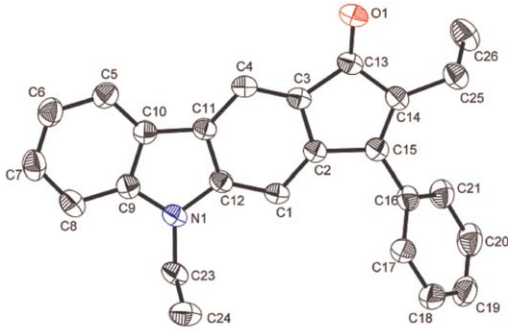
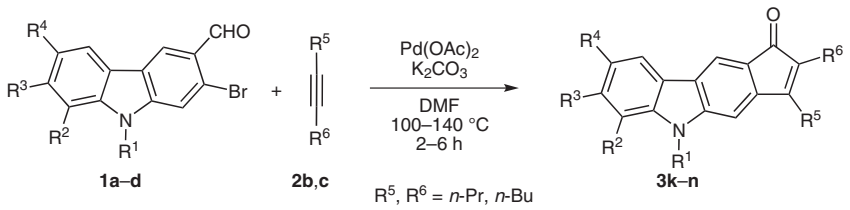


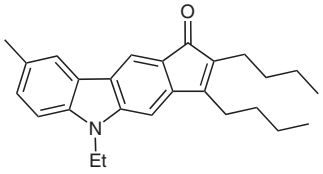
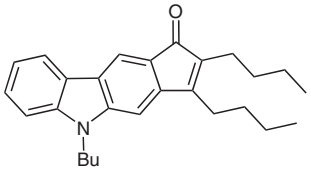
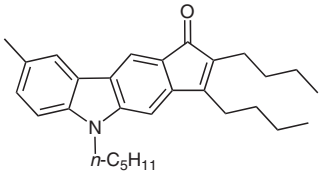
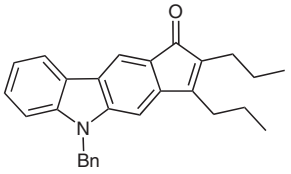
Figure 3 ORTEP diagram of **3s**

Based on the literature,[12] the possible mechanism of annulation is illustrated in Scheme 2 taking **3f** as an example. The oxidative addition of **1f** to the active species of Pd(0), which is formed by the reduction of $Pd(OAc)_2$, leads to the palladium(II) intermediate **1**. Then, the insertion of internal alkyne **2a** affords **3**, which has a newly formed C–Pd bond and it may undergo either an insertion or oxidative addition pathway resulting in **A** and **B**, respectively. The β-H elimination of **A** and the reductive elimination of **B** would give the same desired product **3f** and HPdBr species, which would be converted to the active Pd(0) species in the presence of base.

Downloaded by: Universite Laval. Copyrighted material.

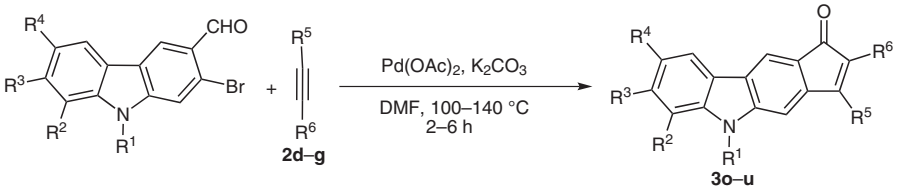
Table 3 Synthesis of 2,3-Dialkylcyclopentacarbazolones

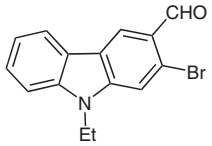
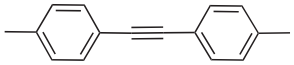
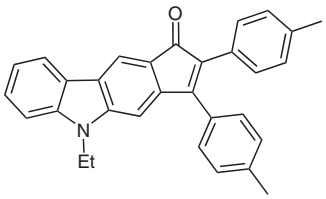


Entry	R^1	R^2	R^3	R^4	Alkyne[a]	Product	Yield (%)[b]
1	Et	H	H	Me	**2c**	**3k** 	60
2	*n*-Bu	H	H	H	**2c**	**3l** 	54
3	*n*-C_5H_{11}	H	H	Me	**2c**	**3m** 	50
4	Bn	H	H	H	**2b**	**3n** 	64

[a] Alkyne used: 2.5 equiv.
[b] Isolated yield.

Table 4 Synthesis of Various 2,3-Disubstituted Cyclopentacarbazolones

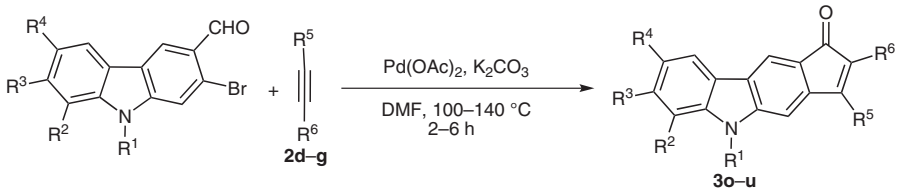


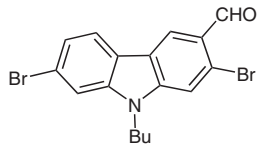
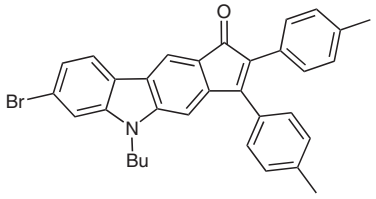
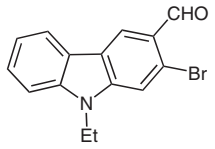
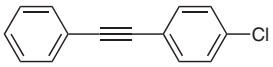
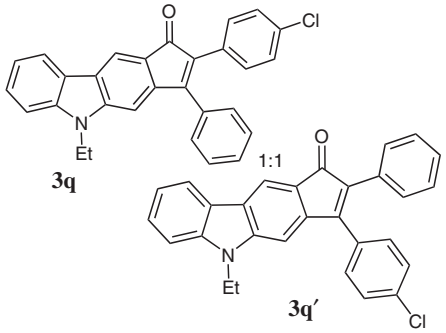
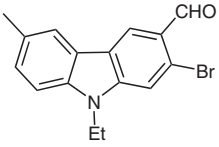
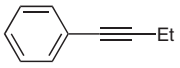
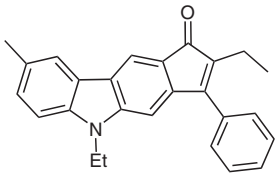
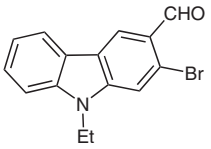
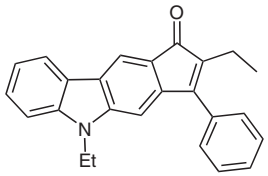
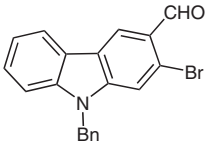
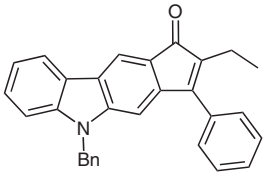
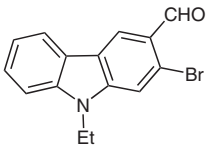
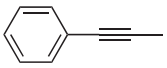
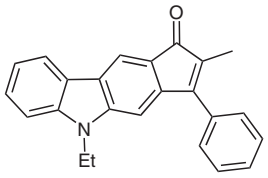
Entry	Aldehyde	Alkyne[a]	Time (h)	Temp (°C)	Product	Yield (%)[b]
1		 **2d**	3	140	 **3o**	80

© Thieme Stuttgart · New York

Downloaded by: Universite Laval. Copyrighted material.

Table 4 Synthesis of Various 2,3-Disubstituted Cyclopentacarbazolones (continued)

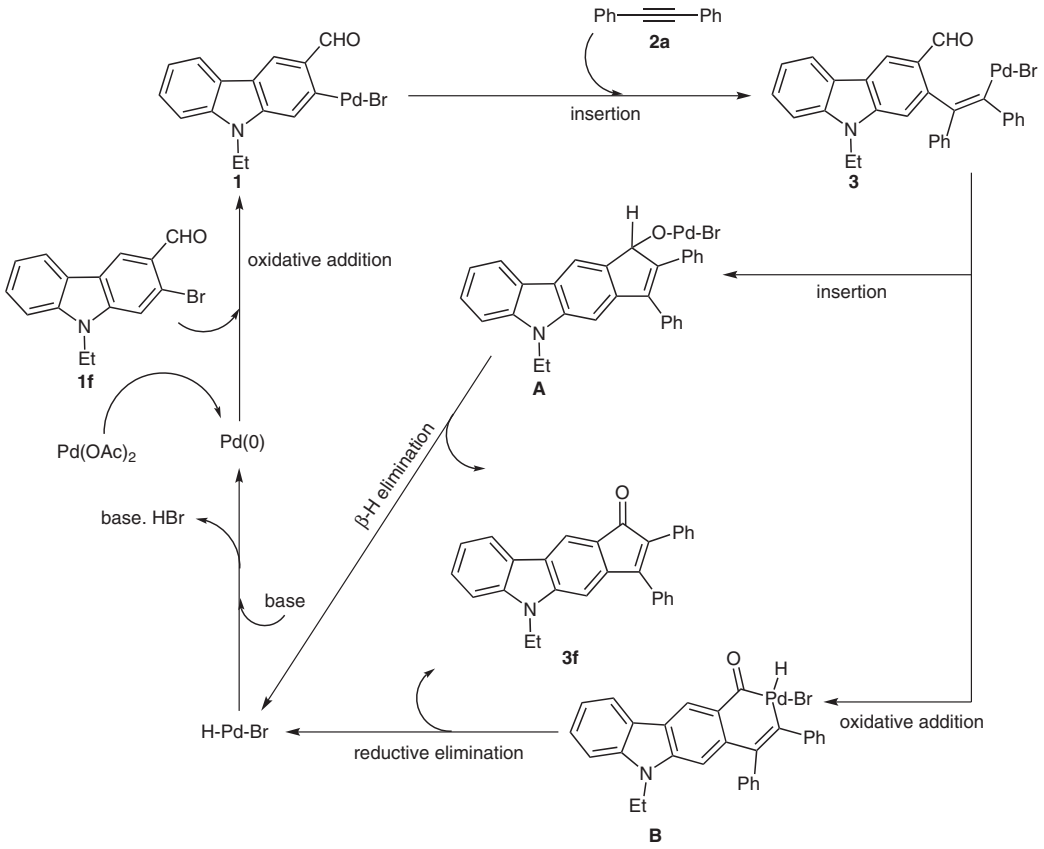


Entry	Aldehyde	Alkyne[a]	Time (h)	Temp (°C)	Product	Yield (%)[b]
2		**2d**	5	140	 **3p**	58
3		 **2e**	6	140	 **3q** 1:1 **3q′**	55
4		 **2f**	6	100	 **3r**	60
5		**2f**	6	100	 **3s**	54
6		**2f**	5	120	 **3t**	62
7		 **2g**	7	100	 **3u**	55

[a] Alkynes **2f**–**g** used: 2.5 equiv.
[b] Isolated yield.

© Thieme Stuttgart · New York

Downloaded by: Universite Laval. Copyrighted material.



Scheme 2 Proposed mechanism for the annulation reaction

In conclusion, an efficient synthesis of 2,3-disubstituted cyclopentacarbazolones has been developed by using palladium-catalyzed annulation of internal alkynes with various 2-bromo-3- formylcarbazoles. The reaction proceeds well under relatively mild conditions with shorter reaction times. For unsymmetrical (alkyl-, aryl-substituted) alkynes, the one-pot annulation approach affords selectively a single regioisomer.

The procedure does not require inert atmosphere. All the products obtained were purified by column chromatography using silica gel (100–200 mesh). Hexane was used as a co-eluent. The ^{1}H NMR and ^{13}C NMR spectra were recorded at 500, 400 MHz and 125, 100 MHz, respectively. The chemical shifts are reported in ppm downfield to TMS (δ = 0.00 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0 ppm) and DMSO-d_6 (δ = 39.51 ppm) for ^{13}C NMR spectroscopy. The coupling constants *J* are given in Hz. IR spectra were recorded on FT/IR-5300 spectrophotometer. The X-ray diffraction measurements were carried out at 298 K on an automated diffractometer using graphite monochromated Mo-Kα (λ = 0.71073 Å) radiation with CAD4 software or the X-ray intensity data were measured at 298 K equipped with a graphite monochromator and a Mo-Kα fine-focus sealed tube (λ = 0.71073 Å). Elemental analyses were recorded on a Thermo Finnigan Flash EA 1112 analyzer at the School of Chemistry, University of Hyderabad. Mass spectra were recorded on either VG7070H mass spectrometer using EI technique or Shimadzu-LCMS 2010A mass spectrometer. Melting points were measured in open capillary tubes and are uncorrected.

5-Ethyl-8-methyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (3a); Typical Procedure

A Schlenk tube was charged with **1a** (0.10 g, 0.315 mmol) and diphenylacetylene (**2a**; 0.056 g, 0.315 mmol) in DMF, and then K_2CO_3 (0.10 g, 0.78 mmol) and $Pd(OAc)_2$ (5.0 mg, 0.023 mmol) were added. The mixture was heated in an oil bath till the completion of the reaction as indicated by TLC (eluent: EtOAc–hexanes, 7:93). The reaction mixture was cooled to r.t., poured into H_2O (20 mL), and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with H_2O (3 × 10 mL) followed by brine (20 mL) and dried (Na_2SO_4). The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography over silica gel (100–200 mesh) using 7% EtOAc in hexanes as an eluent to afford **3a**; yield: 0.096 g (74%); orange solid; R_f = 0.53; mp 170–172 °C (50% EtOAc in hexanes).

IR (KBr): 2922, 1682, 1589, 1481, 1327, 1244, 788, 509 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$/TMS): δ = 8.24 (s, 1 H), 7.82 (s, 1 H), 7.44 (d, *J* = 3.5 Hz, 5 H), 7.30–7.23 (m, 7 H), 6.97 (s, 1 H), 4.26 (q, *J* = 7.5 Hz, 2 H), 2.52 (s, 3 H), 1.37 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 195.3, 154.6, 143.7, 142.9, 138.5, 134.6, 133.4, 131.2, 130.0, 129.9, 128.9, 127.9, 127.4, 127.2, 124.2, 122.9, 121.5, 120.2, 117.1, 108.9, 103.3, 37.8, 21.4, 14.0.

LC-MS (positive mode): *m*/*z* = 414 $(M + H)^+$.

Anal. Calcd for $C_{30}H_{23}NO$: C, 87.14; H, 5.61; N, 3.39. Found: C, 87.21; H, 5.58; N, 3.32.

5-Butyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (3b)

Yield: 0.083 g (65%); orange solid; mp 120–121 °C.

IR (KBr): 2926, 1691, 1585, 1365, 727 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$/TMS): δ = 8.28 (s, 1 H), 8.03 (d, *J* = 10.0 Hz, 1 H), 7.46–7.37 (m, 7 H), 7.31–7.23 (m, 6 H), 7.01 (s,

 © Thieme Stuttgart · New York

Downloaded by: Universite Laval. Copyrighted material.

1 H), 4.23 (t, *J* = 6.5 Hz, 2 H), 1.83–1.77 (m, 2 H), 1.38–1.32 (m, 2 H), 0.92 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 195.3, 154.6, 143.8, 143.3, 140.7, 134.6, 133.3, 130.0, 129.0, 128.8, 128.6, 127.9, 127.5, 125.7, 124.0, 123.1, 121.6, 120.4, 120.3, 117.0, 109.5, 103.6, 42.9, 31.2, 20.3, 13.7.

LC-MS (negative mode): *m*/*z* = 426 (M – H).

Anal. Calcd for $C_{31}H_{25}NO$: C, 87.09; H, 5.89; N, 3.28. Found: C, 87.22; H, 5.81; N, 3.19.

8-Methyl-5-pentyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (3c)
Yield: 0.080 g (63%); red solid; mp 168 °C.

IR (KBr): 2957, 1693, 1481, 1304, 1122, 794 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$/TMS): δ = 8.24 (s, 1 H), 7.82 (s, 1 H), 7.45–7.43 (m, 5 H), 7.31–7.22 (m, 7 H), 6.98 (s, 1 H), 4.19 (t, *J* = 7.2 Hz, 2 H), 2.52 (s, 3 H), 1.84–1.77 (m, 2 H), 1.33–1.27 (m, 4 H), 0.85 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 195.4, 154.6, 143.6, 139.0, 134.5, 133.3, 131.2, 130.0, 128.8, 128.6, 127.9, 127.1, 124.1, 122.9, 121.3, 120.1, 117.1, 109.2, 103.6, 43.2, 29.2, 28.8, 22.3, 21.4, 13.9.

LC-MS (positive mode): *m*/*z* = 456 (M + H)$^+$.

Anal. Calcd for $C_{33}H_{29}NO$: C, 87.00; H, 6.42; N, 3.07. Found: C, 86.75; H, 6.35; N, 3.15.

5-Benzyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (3d)
Yield: 0.098 g (78%); red solid; mp 192 °C.

IR (KBr): 1691, 1589, 1385, 1263, 1163, 1030, 787 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$/TMS): δ = 8.30 (s, 1 H), 8.05 (d, *J* = 7.5 Hz, 1 H), 7.39 (d, *J* = 5.0 Hz, 4 H), 7.32 (d, *J* = 3.5 Hz, 3 H), 7.27–7.22 (m, 9 H), 7.08 (d, *J* = 6.0 Hz, 2 H), 6.99 (s, 1 H), 5.44 (s, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 195.3, 154.6, 144.0, 143.5, 140.9, 136.3, 134.5, 133.1, 131.1, 130.0, 129.0, 128.9, 128.8, 127.9, 127.7, 126.4, 126.0, 124.1, 123.6, 121.9, 120.8, 120.3, 117.0, 109.7, 103.9, 46.9.

LC-MS (positive mode): *m*/*z* = 462 (M + H)$^+$.

Anal. Calcd for $C_{34}H_{23}NO$: C, 88.48; H, 5.02; N, 3.07. Found: C, 88.32; H, 4.96; N, 3.12.

8-*tert*-Butyl-5-ethyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (3e)
Yield: 0.096 g (76%); red solid; mp 185–187 °C.

IR (KBr): 2957, 1693, 1591, 1477, 1302, 1059, 1026, 744 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$/TMS): δ = 8.31 (s, 1 H), 8.05 (s, 1 H), 7.53–7.22 (m, 6 H), 7.33–7.22 (m, 6 H), 6.99 (s, 1 H), 4.27 (q, *J* = 5.0 Hz, 2 H), 1.56 (s, 9 H), 1.39 (t, *J* = 10.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 195.4, 154.6, 143.6, 143.1, 138.4, 134.5, 133.4, 131.2, 130.0, 128.9, 128.8, 128.6, 127.9, 127.4, 123.9, 123.8, 123.0, 121.9, 117.1, 116.4, 108.8, 103.3, 37.9, 31.8, 14.1.

LC-MS (positive mode): *m*/*z* = 456 (M + H)$^+$.

Anal. Calcd for $C_{33}H_{29}NO$: C, 87.00; H, 6.42; N, 3.07. Found: C, 86.91; H, 6.38; N, 3.15.

5-Ethyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (3f)
Yield: 0.089 g (68%); red solid; mp 220 °C.

IR (KBr): 2974, 2930, 1684, 1587, 1469, 1325, 1168, 841, 750, 694, 513 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$/TMS): δ = 8.31 (s, 1 H), 8.07 (d, *J* = 8.0 Hz, 1 H), 7.51–7.45 (m, 6 H), 7.41 (d, *J* = 8.0 Hz, 1 H), 7.34–7.27 (m, 6 H), 7.04 (s, 1 H), 4.33 (q, *J* = 7.5 Hz, 2 H), 1.43 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 195.3, 154.6, 143.9, 142.8, 140.2, 134.6, 133.3, 131.2, 130.0, 129.0, 128.9, 128.6, 127.9, 127.5, 125.7, 124.1, 123.2, 121.7, 120.4, 117.1, 109.2, 103.3, 37.8, 14.0.

LC-MS (positive mode): *m*/*z* = 400 (M + H)$^+$.

Anal. Calcd for $C_{29}H_{21}NO$: C, 87.19; H, 5.30; N, 3.51. Found: C, 87.09; H, 5.36; N, 3.48.

7-Bromo-5-butyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (3g)
Yield: 0.068 g (56%); red solid; mp 180 °C.

IR (KBr): 2961, 2858, 1684, 1585, 1481, 1386, 1244, 1116, 1055, 896, 794, 698 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$/TMS): δ = 8.22 (s, 1 H), 7.87 (d, *J* = 8.0 Hz, 1 H), 7.52 (s, 1 H), 7.47–7.42 (m, 5 H), 7.37–7.35 (dd, *J* = 1.5, 1.5 Hz, 1 H), 7.30–7.23 (m, 5 H), 7.01 (s, 1 H), 4.19 (t, *J* = 7.5 Hz, 2 H), 1.82–1.76 (m, 2 H), 1.38–1.32 (m, 2 H), 0.93 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 195.1, 154.5, 144.2, 143.5, 141.4, 134.7, 133.1, 133.0, 129.9, 129.1, 128.9, 128.5, 128.0, 127.6, 123.7, 123.6, 122.8, 121.4, 121.2, 119.3, 116.8, 112.6, 103.7, 43.1, 31.1, 20.3, 13.7.

LC-MS (positive mode): *m*/*z* = 507 (M + H)$^+$, 509 (M + 2).

Anal. Calcd for $C_{31}H_{24}BrNO$: C, 73.52; H, 4.78; N, 2.77. Found: C, 73.45; H, 4.86; N, 2.71.

5-Ethyl-6,8-dimethyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (3h)
Yield: 0.103 g (80%); red solid; mp 187 °C.

IR (KBr): 2914, 1685, 1593, 1469, 1313, 1232, 846, 744, 582, 511 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$/TMS): δ = 8.19 (s, 1 H), 7.65 (s, 1 H), 7.47–7.41 (m, 5 H), 7.29–7.20 (m, 5 H), 6.97 (s, 1 H), 6.93 (s, 1 H), 4.43 (q, *J* = 7.0 Hz, 2 H), 2.71 (s, 3 H), 2.45 (s, 3 H), 1.35 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 195.3, 154.7, 143.6, 143.5, 137.2, 134.5, 133.4, 1131.3, 130.7, 130.0, 128.9, 128.8, 127.9, 127.4, 125.2, 123.1, 121.8, 120.3, 118.0, 116.8, 103.4, 39.6, 21.0, 19.7, 15.8.

LC-MS (positive mode): *m*/*z* = 428 (M + H)$^+$.

Anal. Calcd for $C_{31}H_{25}NO$: C, 87.09; H, 5.89; N, 3.28. Found: C, 87.22; H, 5.81; N, 3.36.

5-Hexyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (3i)
Yield: 0.082 g (65%); red solid; mp 130 °C.

IR (KBr): 2924, 1687, 1589, 1468, 1251, 1161, 790 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$/TMS): δ = 8.27 (s, 1 H), 8.02 (d, *J* = 8.0 Hz, 1 H), 7.45–7.41 (m, 6 H), 7.37 (d, *J* = 8.0 Hz, 1 H), 7.30 (d, *J* = 6.5 Hz, 2 H), 7.26 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 8.5 Hz, 2 H), 7.00 (s, 1 H), 4.21 (t, *J* = 7.5 Hz, 2 H), 1.84–1.78 (m, 2 H), 1.33–1.25 (m, 6 H), 0.84 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 195.3, 154.6, 143.8, 143.3, 140.7, 134.6, 133.3, 131.2, 130.0, 129.0, 128.8, 127.9, 125.7, 124.0, 123.1, 121.6, 120.4, 117.0, 109.5, 103.6, 43.2, 31.4, 29.0, 26.7, 22.4, 13.9.

LC-MS (positive mode): *m*/*z* = 456 (M + H)$^+$.

Anal. Calcd for $C_{33}H_{29}NO$: C, 87.00; H, 6.42; N, 3.07. Found: C, 87.19; H, 6.37; N, 3.15.

Downloaded by: Universite Laval. Copyrighted material.

© Thieme Stuttgart · New York

5-Benzyl-8-methyl-2,3-diphenylcyclopenta[*b*]carbazol-1(5*H*)-one (3j)
Yield: 0.102 g (82%); orange solid; mp 156–157 °C.

IR (KBr): 2922, 1685, 1481, 1302, 1149, 1026, 696 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 8.28 (s, 1 H), 7.85 (s, 1 H), 7.40–7.38 (m, 3 H), 7.33–7.31 (m, 2 H), 7.28–7.24 (m, 7 H), 7.23 (d, *J* = 2.0 Hz, 1 H), 7.20 (d, *J* = 0.8 Hz, 2 H), 7.08–7.06 (dd, *J* = 2.0, 1.2 Hz, 2 H), 6.97 (s, 1 H), 5.42 (s, 2 H), 2.52 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 195.3, 154.5, 143.8, 143.7, 139.2, 136.4, 134.5, 131.2, 130.3, 129.9, 128.8, 128.7, 128.5, 127.9, 127.7, 127.5, 127.4, 126.4, 124.3, 123.4, 121.7, 120.2, 117.0, 109.4, 103.9, 46.9, 21.4.

LC-MS (positive mode): *m*/*z* = 476 $(M + H)^+$.

Anal. Calcd for $C_{35}H_{25}NO$: C, 88.39; H, 5.30; N, 2.95. Found: C, 88.25; H, 5.36; N, 2.87.

2,3-Dibutyl-5-ethyl-8-methylcyclopenta[*b*]carbazol-1(5*H*)-one (3k)
Yield: 0.070 g (60%); viscous orange liquid.

IR (KBr): 2926, 1693, 1599, 1483, 1304, 1022, 794 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 8.06 (s, 1 H), 7.79 (s, 1 H), 7.32 (d, *J* = 2.8 Hz, 1 H), 7.28 (d, *J* = 2.0 Hz, 1 H), 6.95 (s, 1 H), 4.36 (q, *J* = 5.6 Hz, 2 H), 2.26 (t, *J* = 6.4 Hz, 2 H), 2.53 (s, 3 H), 2.31 (t, *J* = 6.0 Hz, 2 H), 1.72–1.67 (m, 4 H), 1.55–1.49 (m, 4 H), 1.46 (t, *J* = 5.6 Hz, 6 H), 1.03 (t, *J* = 6.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 197.5, 156.4, 144.4, 143.0, 138.2, 137.1, 129.6, 126.6, 123.4, 120.8, 120.0, 115.7, 108.7, 103.6, 100.8, 37.8, 31.5, 30.6, 25.8, 23.0, 22.9, 22.8, 21.3, 14.1, 14.0, 13.9.

LC-MS (positive mode): *m*/*z* = 374 $(M + H)^+$.

Anal. Calcd for $C_{26}H_{31}NO$: C, 83.60; H, 8.37; N, 3.75. Found: C, 83.45; H, 8.31; N, 3.82.

2,3,5-Tributylcyclopenta[*b*]carbazol-1(5*H*)-one (3l)
Yield: 0.063 g (54%); viscous orange liqid.

IR (KBr): 2957, 1693, 1467, 1331, 1209, 1016, 742 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$/TMS): δ = 8.04 (s, 1 H), 7.96 (d, *J* = 7.5 Hz, 1 H), 7.39–7.33 (m, 2 H), 7.23–7.19 (m, 1 H), 6.93 (s, 1 H), 4.26 (t, *J* = 7.0 Hz, 2 H), 2.58 (t, *J* = 8.0 Hz, 2 H), 2.28 (t, *J* = 7.5 Hz, 2 H), 1.86–1.80 (m, 2 H), 1.70–1.62 (m, 2 H), 1.52–1.47 (m, 4 H), 1.41–1.37 (m, 4 H), 1.00 (t, *J* = 7.0 Hz, 3 H), 0.94 (t, *J* = 7.5 Hz, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 197.5, 156.4, 144.5, 143.4, 140.3, 137.2, 125.2, 124.7, 124.1, 123.6, 121.0, 120.6, 120.1, 115.6, 109.3, 101.2, 31.5, 30.6, 25.8, 23.1, 23.0, 22.9, 20.4, 14.0, 13.9, 13.8.

LC-MS (positive mode): *m*/*z* = 388 $(M + H)^+$.

Anal. Calcd for $C_{27}H_{33}NO$: C, 83.68; H, 8.58; N, 3.61. Found: C, 83.55; H, 8.51; N, 3.68.

2,3-Dibutyl-8-methyl-5-pentylcyclopenta[*b*]carbazol-1(5*H*)-one (3m)
Yield: 0.057 g (50%); viscous liquid.

IR (KBr): 2957, 1693, 1601, 1466, 1259, 1022, 794 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 8.02 (s, 1 H), 7.76 (s, 1 H), 7.40 (d, *J* = 2.0 Hz, 1 H), 7.24 (d, *J* = 0.8 Hz, 1 H), 6.91 (s, 1 H), 4.25 (t, *J* = 7.2 Hz, 2 H), 2.58 (t, *J* = 8.0 Hz, 2 H), 2.50 (s, 3 H), 2.28 (t, *J* = 7.6 Hz, 2 H), 1.87–1.83 (m, 2 H), 1.67–1.62 (m, 2 H), 1.52–1.45 (m, 6 H), 1.36–1.32 (m, 4 H), 0.99 (t, *J* = 7.6 Hz, 3 H), 0.93 (t, *J* = 7.2 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 197.9, 156.4, 144.3, 143.5, 138.7, 137.1, 135.3, 133.2, 128.8, 127.7, 126.6, 119.9, 115.6, 108.9, 101.1, 43.2, 31.5, 30.6, 28.9, 25.8, 23.1, 23.0, 22.9, 22.7, 22.4, 21.4, 14.0, 13.9, 13.8.

LC-MS (positive mode): *m*/*z* = 416 $(M + H)^+$.

Anal. Calcd for $C_{29}H_{37}NO$: C, 83.81; H, 8.97; N, 3.37. Found: C, 83.95; H, 8.91; N, 3.45.

5-Benzyl-2,3-dipropylcyclopenta[*b*]carbazol-1(5*H*)-one (3n)
Yield: 0.068 g (64%); red solid; mp 72 °C.

IR (KBr): 2926, 1693, 1467, 1390, 1331 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$/TMS): δ = 8.09 (s, 1 H), 8.00 (d, *J* = 8.0 Hz, 1 H), 7.35 (t, *J* = 7.5 Hz, 1 H), 7.30–7.22 (m, 5 H), 7.12 (d, *J* = 7.0 Hz, 2 H), 6.9 (s, 1 H), 5.40 (s, 2 H), 2.49 (t, *J* = 10.0 Hz, 2 H), 2.25 (t, *J* = 10.0 Hz, 2 H), 1.64–1.58 (m, 2 H), 1.54–1.50 (m, 2 H), 1.00 (t, *J* = 7.5 Hz, 3 H), 0.95 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 197.5, 156.5, 144.7, 143.6, 140.6, 137.2, 136.5, 128.9, 127.7, 126.3, 125.5, 124.2, 120.9, 120.5, 120.0, 115.6, 109.5, 101.5, 46.8, 29.6, 25.2, 22.6, 21.7, 14.4, 14.2.

LC-MS (positive mode): *m*/*z* = 394 $(M + H)^+$.

Anal. Calcd for $C_{28}H_{27}NO$: C, 85.46; H, 6.92; N, 3.56. Found: C, 85.32; H, 7.06; N, 3.45.

5-Ethyl-2,3-(di-*p*-tolyl)cyclopenta[*b*]carbazol-1(5*H*)-one (3o)
Yield: 0.112 g (80%); red solid; mp 195 °C.

IR (KBr): 2924, 2852, 1682, 1589, 1467, 1392, 1242, 1168, 1105, 817, 736 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$/TMS): δ = 8.29 (s, 1 H), 8.06 (d, *J* = 8.0 Hz, 1 H), 7.46 (t, *J* = 7.5 Hz, 1 H), 7.38 (q, *J* = 8.0 Hz, 3 H), 7.29 (t, *J* = 7.5 Hz, 3 H), 7.24 (d, *J* = 8.0 Hz, 2 H), 7.11 (d, *J* = 7.5 Hz, 2 H), 7.05 (s, 1 H), 4.33 (q, *J* = 7.5 Hz, 2 H), 2.47 (s, 3 H), 2.35 (s, 3 H), 1.43 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 195.6, 154.1, 144.2, 142.8, 140.1, 138.9, 137.2, 134.3, 130.5, 129.8, 129.5, 128.7, 128.5, 128.4, 125.6, 124.1, 123.4, 121.6, 120.4, 120.3, 116.9, 109.2, 103.2, 37.8, 21.5, 14.0.

LC-MS (positive mode): *m*/*z* = 428 $(M + H)^+$.

Anal. Calcd for $C_{31}H_{25}NO$: C, 87.09; H, 5.89; N, 3.28. Found: C, 87.12; H, 6.36; N, 3.12.

7-Bromo-5-butyl-2,3-di(*p*-tolyl)cyclopenta[*b*]carbazol-1(5*H*)-one (3p)
Yield: 0.075 g (58%); red solid; mp 167–167 °C.

IR (KBr): 2924, 1693, 1595, 1464, 1388, 1016, 819 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 8.23 (s, 1 H), 7.88 (d, *J* = 8.5 Hz, 1 H), 7.54 (s, 1 H), 7.37 (t, *J* = 7.5 Hz, 3 H), 7.28 (d, *J* = 4.0 Hz, 3 H), 7.23 (d, *J* = 8.0 Hz, 1 H), 7.11 (d, *J* = 8.0 Hz, 2 H), 7.05 (s, 1 H), 4.21 (t, *J* = 7.0 Hz, 2 H), 2.47 (s, 3 H), 2.35 (s, 3 H), 1.87–1.89 (m, 2 H), 1.39–1.33 (m, 2 H), 0.96 (t, *J* = 6.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 195.4, 154.0, 144.4, 143.5, 141.4, 139.1, 137.4, 134.4, 130.2, 129.8, 129.5, 128.7, 128.5, 125.6, 123.5, 121.3, 119.2, 116.6, 112.5, 103.5, 43.1, 31.1, 21.4, 21.3, 20.3, 13.7.

LC-MS (positive mode): *m*/*z* = 535 $(M + H)^+$, 537 (M + 2).

Anal. Calcd for $C_{33}H_{28}BrNO$: C, 74.16; H, 5.28; N, 2.62. Found: C, 74.31; H, 5.32; N, 2.58.

2-(4-Chlorophenyl)-5-ethyl-3-phenylcyclopenta[*b*]carbazol-1(5*H*)-one (3q)
Yield: 0.039 g (50%); red solid; mp 206–208 °C.

Downloaded by: Universite Laval. Copyrighted material.

 © Thieme Stuttgart · New York

IR (KBr): 2908, 1676, 1450, 1014 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 8.30 (s, 1 H), 8.06 (d, *J* = 8.0 Hz, 1 H), 7.52–7.48 (m, 3 H), 7.45 (d, *J* = 8.0 Hz, 3 H), 7.41 (d, *J* = 8.0 Hz, 1 H), 7.31–7.24 (m, 5 H), 7.02 (s, 1 H), 4.33 (q, *J* = 8.0 Hz, 2 H), 1.42 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 195.6, 155.3, 143.6, 140.2, 133.5, 133.0, 131.2, 129.6, 129.0, 128.5, 128.2, 125.9, 124.0, 123.0, 121.9, 120.5, 117.3, 109.3, 103.5, 39.7, 14.1.

LC-MS (positive mode): *m*/*z* = 433 $(M + H)^+$, 434 (M + 1).

Anal. Calcd for $C_{29}H_{20}ClNO$: C, 80.27; H, 4.65; N, 3.23. Found: C, 80.36; H, 4.98; N, 3.07.

3-(4-Chlorophenyl)-5-ethyl-2-phenylcyclopenta[*b*]carbazol-1(5*H*)-one (3q′)
Yield: 0.039 g (50%); red solid; mp >280 °C.

IR (KBr): 2922, 1682, 1464, 1323, 1086, 750 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 8.31 (s, 1 H), 8.06 (d, *J* = 7.6 Hz, 1 H), 7.48–7.45 (m, 3 H), 7.42–7.49 (m, 3 H), 7.30–7.26 (m, 6 H), 6.98 (s, 1 H), 4.34 (q, *J* = 7.32 Hz, 2 H), 1.43 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 195.1, 153.2, 143.5, 142.8, 140.2, 134.9, 131.7, 130.8, 129.9, 129.3, 128.1, 127.7, 125.9, 124.0, 122.9, 121.8, 120.5, 120.4, 117.3, 109.3, 103.1, 37.9, 14.1.

LC-MS (positive mode): *m*/*z* = 433 $(M + H)^+$, 434 (M + 1).

Anal. Calcd for $C_{29}H_{20}ClNO$: C, 80.27; H, 4.65; N, 3.23. Found: C, 80.52; H, 4.85; N, 3.18.

2,5-Diethyl-8-methyl-3-phenylcyclopenta[*b*]carbazol-1(5*H*)-one (3r)
Yield: 0.069 g (60%); orange solid; mp 106–108 °C.

IR (KBr): 2966, 2920, 1689, 1597, 1375, 1238, 1022, 704 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 8.17 (s, 1 H), 7.82 (s, 1 H), 7.68–7.50 (m, 5 H), 7.27 (dd, *J* = 2.0, 1.2 Hz, 2 H), 6.89 (s, 1 H), 4.26 (q, *J* = 7.2 Hz, 2 H), 2.54 (s, 3 H), 2.40 (q, *J* = 7.2 Hz, 2 H), 1.38 (t, *J* = 7.2 Hz, 3 H), 1.16 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 197.1, 153.8, 144.4, 142.8, 139.1, 138.3, 133.3, 129.8, 128.8, 127.9, 126.0, 123.1, 120.7, 120.0, 116.6, 108.9, 102.7, 37.8, 21.4, 16.9, 14.1, 14.0.

LC-MS (positive mode): *m*/*z* = 367 $(M + H)^+$.

Anal. Calcd for $C_{26}H_{23}NO$: C, 85.45; H, 6.34; N, 3.83. Found: C, 85.32; H, 6.41; N, 3.79.

2,5-Diethyl-3-phenylcyclopenta[*b*]carbazol-1(5*H*)-one (3s)
Yield: 0.066 g (54%); orange solid; mp 178–180 °C ($CDCl_3$).

IR (KBr): 2976, 1687, 1593, 1392, 1331, 1016, 785 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 8.20 (s, 1 H), 8.03 (d, *J* = 8.0 Hz, 1 H), 7.62–7.52 (m, 5 H), 7.46–7.38 (m, 2 H), 7.29–7.25 (m, 1 H), 6.91 (s, 1 H), 4.30 (q, *J* = 7.2 Hz, 2 H), 2.40 (q, *J* = 7.2 Hz, 2 H), 1.40 (t, *J* = 7.2 Hz, 3 H), 1.16 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 197.1, 153.9, 144.6, 142.7, 140.0, 139.2, 133.3, 128.8, 127.9, 125.4, 124.1, 123.4, 121.0, 120.3, 120.2, 116.6, 109.1, 102.7, 37.8, 16.9, 14.1.

LC-MS (positive mode): *m*/*z* = 351 $(M + H)^+$.

Anal. Calcd for $C_{25}H_{21}NO$: C, 85.44; H, 6.02; N, 3.99. Found: C, 85.36; H, 6.08; N, 3.86.

5-Benzyl-2-ethyl-3-phenylcyclopenta[*b*]carbazol-1(5*H*)-one (3t)
Yield: 0.070 g (62%); orange solid; mp 98–99 °C.

IR (KBr): 2962, 1685, 1470, 1229, 792 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 8.23 (s, 1 H), 8.06 (d, *J* = 7.6 Hz, 1 H), 7.55–7.48 (m, 3 H), 7.45–7.43 (m, 2 H), 7.39–7.37 (dd, *J* = 1.2, 1.0 Hz, 1 H), 7.34–7.27 (m, 5 H), 7.10–7.08 (dd, *J* = 2.8, 1.6 Hz, 2 H), 6.91 (s, 1 H), 5.45 (s, 2 H), 2.39 (q, *J* = 7.6 Hz, 2 H), 1.15 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 197.1, 153.8, 144.7, 143.5, 140.6, 139.1, 136.3, 133.1, 128.9, 128.8, 127.9, 127.7, 126.4, 125.7, 124.1, 123.8, 121.2, 120.6, 120.1, 116.5, 109.7, 103.3, 46.7, 16.9, 14.0.

LC-MS (positive mode): *m*/*z* = 414 $(M + H)^+$.

Anal. Calcd for $C_{30}H_{23}NO$: C, 85.43; H, 5.68; N, 4.15. Found: C, 85.32; H, 5.62; N, 4.21.

5-Ethyl-2-methyl-3-phenyl-2,3-dihydrocyclopenta[*b*]carbazol-1(5*H*)-one (3u)
Yield: 0.061 g (55%); orange solid; mp 189–190 °C.

IR (KBr): 1687, 1469, 1339, 785 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$/TMS): δ = 8.21 (s, 1 H), 8.02 (d, *J* = 7.6 Hz, 1 H), 7.62–7.50 (m, 5 H), 7.44–7.38 (m, 2 H), 7.28 (t, *J* = 8.0 Hz, 1 H), 6.97 (s, 1 H), 4.31 (q, *J* = 7.2 Hz, 2 H), 1.97 (s, 3 H), 1.41 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$/TMS): δ = 197.2, 153.9, 144.5, 142.7, 140.0, 133.6, 133.2, 128.9, 128.8, 128.1, 125.4, 124.1, 123.4, 120.9, 120.3, 120.2, 116.7, 109.1, 102.6, 37.8, 14.1, 8.89.

LC-MS (positive mode): *m*/*z* = 338 $(M + H)^+$.

Anal. Calcd for $C_{24}H_{19}NO$: C, 85.43; H, 5.68; N, 4.15. Found: C, 85.32; H, 5.62; N, 4.21.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis. Included are spectroscopic data of all synthesized compounds **3a**–**u**: ^1H NMR, ^{13}C NMR, DEPT, LC-MS, and elemental analysis, and 2D NOESY of **3r**.

Acknowledgment

We gratefully acknowledge DST for financial assistance (project number SR/S1/OC-70/2008) and providing a single-crystal X-ray diffractometer facility in our school. D.K.S. thanks CSIR for a Senior Research Fellowship. D.K.S. also thanks Rambabu for helping with crystal studies.

References

(1) (a) Wu, Y.-T.; Hayama, T.; Baldridge, K. K.; Linden, A.; Siegel, J. S. *J. Am. Chem. Soc.* **2006**, *128*, 6870. (b) Ogliaruso, M. A.; Romanelli, M. G.; Becker, E. I. *Chem. Rev.* **1965**, *65*, 261. (c) Tius, M. A. *Eur. J. Org. Chem.* **2005**, 2193. (d) Alcaide, B.; Almendros, P. *Eur. J. Org. Chem.* **2004**, 3377. (e) Vaidya, T.; Eisenberg, R.; Frontier, A. J. *ChemCatChem* **2011**, *3*, 1531. (f) Leboeuf, D.; Huang, J.; Gandon, V.; Fronteir, A. L. *Angew. Chem. Int. Ed.* **2011**, *50*, 10981.

(2) (a) Tyagi, P.; Venkateswararao, A.; Thomas, K. R. J. *J. Org. Chem.* **2011**, *76*, 4571. (b) Cai, Z.; Harmata, M. *Org. Lett.* **2010**, *12*, 5668. (c) Andrew, T. L.; Cox, J. R.; Swager, T. M. *Org. Lett.* **2010**, *12*, 5302. (d) Oesterling, I.; Mullen, K. *J. Am. Chem. Soc.* **2007**, *129*, 4595. (e) Lor, M.; Thielemans, J.; Viaene, L.; Cotlet, M.; Hofkens, J.; Weil, T.;

Downloaded by: Universite Laval. Copyrighted material.

Hampel, C.; Mullen, K.; Verhoeven, J. W.; Auweraer, M. V.; De Schryver, F. C. *J. Am. Chem. Soc.* **2002**, *124*, 9918. (f) Godschalx, J. P.; Romer, D. R.; So, Y. H.; Lysenko, Z.; Mills, M. E.; Buske, G. R.; Townsend, P. H.; Smith, D. W.; Martin, S. J.; Devries, R. A. US Patent 5965679, **1999**. (g) Dorta, E.; Diaz-Marrero, A. R.; Cueto, M.; D'Croz, L.; Mate, J. L.; Darias, J. *Org. Lett.* **2004**, *6*, 2229.

(3) (a) Shibata, T.; Yamashita, K.; Ishida, H.; Takagi, K. *Org. Lett.* **2001**, *3*, 1217. (b) Gamba, A.; Gandolfi, R.; Oberti, R.; Sardone, N. *Tetrahedron* **1993**, *49*, 6331. (c) Jikyo, T.; Eto, M.; Harano, K. *Tetrahedron* **1999**, *55*, 6051. (d) Rainier, J. D.; Imbriglio, J. E. *Org. Lett.* **1999**, *1*, 2037. (e) Ding, L.; Ying, H.-Z.; Zhou, Y.; Lei, T.; Pei, J. *Org. Lett.* **2010**, *12*, 5522. (f) Gagnier, S. V.; Larock, R. C. *J. Am. Chem. Soc.* **2003**, *125*, 4804. (g) Talaz, O.; Gülçin, I.; Göksu, S.; Saracoglu, N. *Bioorg. Med. Chem.* **2009**, *17*, 6583. (h) Larock, R. C.; Emrich, D. E. *J. Organomet. Chem.* **2004**, *689*, 3756. (i) Vasilyev, A. V.; Walspurger, S.; Paleb, P.; Sommer, J. *Tetrahedron Lett.* **2004**, *45*, 3379. (j) Coyanis, E. M.; Panayides, J.-E.; Fernandes, M. A.; DeKoning, C. B.; Van Otterlo, W. A. L. *J. Organomet. Chem.* **2006**, *691*, 5222. (k) Larock, R. C.; Yian, Q.; Pletnev, A. A. *J. Am. Chem. Soc.* **1999**, *121*, 3238.

(4) Leoni, L. M.; Hamel, E.; Genini, D.; Hsiencheng, S.; Carrera, C. J.; Cottam, H. B.; Carson, D. A. *J. Natl. Cancer Inst.* **2000**, *92*, 217.

(5) Kerr, D. J.; Hamel, E.; Jung, M. K.; Flynn, B. L. *Bioorg. Med. Chem.* **2007**, *15*, 3290.

(6) Jourdan, G. P.; Dreikom, B. A.; Hackler, R. E.; Hall, H. R.; Arnold, W. R. In *Synthesis and Chemistry of Agrochemicals II*, ACS Symposium Series 566; American Chemical Society: Washington DC, **1991**.

(7) (a) Ahn, J. H.; Shin, M. S.; Jung, S. H.; Kang, S. K.; Kim, K. R.; Rhee, S. D.; Jung, W. H.; Yang, S. D.; Kim, S. J.; Woo, J. R.; Lee, J. H.; Cheon, H. G.; Kim, S. S. *J. Med. Chem.* **2006**, *49*, 4781. (b) Ahn, J. H.; Shin, M. S.; Jung, S. H.; Kim, J. A.; Kim, H. M.; Kim, S. H.; Kang, S. K.; Kim, K. R.; Rhee, S. D.; Park, S. D.; Lee, J. H.; Cheon, H. G.; Kim, S. S. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5239. (c) Anstead, G. M.; Altenbach, R. J.; Wilson, S. R.; Katzenellenbogen, J. A. *J. Med. Chem.* **1998**, *31*, 1316.

(8) (a) Goodwin, S.; Smith, A. F.; Horning, E. C. *J. Am. Chem. Soc.* **1959**, *81*, 1903. (b) Cho, S. H.; Yoon, J.; Chang, S. *J. Am. Chem. Soc.* **2011**, *133*, 5996. (c) Alcaide, B.; Almendros, P.; Alonso, J. M.; Quiros, T.; Gadzinski, P. *Adv. Synth. Catal.* **2011**, *353*, 1871. (d) Knölker, H.-J. *Chem. Lett.* **2009**, *38*, 8. (e) Knölker, H.-J.; Reddy, K. R. In *The Alkaloids*, Vol. 65; Cordell, G. A., Ed.; Elsevier Science: Amsterdam, **2008**, 1–430. (f) Knölker, H.-J.; Reddy, K. R. *Chem. Rev.* **2002**, *102*, 4303. (g) Chakraborty, D. P.; Das, K. C.; Chowdhury, B. K. *J. Org. Chem.* **1971**, *36*, 725.

(9) (a) Archer, S.; Ross, B. S.; Pica-Mattoccia, L.; Cioli, D. *J. Med. Chem.* **1987**, *30*, 1204. (b) Ayats, C.; Soley, R.; Albericio, F.; Alvarez, M. *Org. Biomol. Chem.* **2009**, *5*, 860. (c) Laronze, M.; Boisbrun, M.; Léonce, S.; Pfeiffer, B.; Renard, P.; Lozach, O.; Meijer, L.; Lansiuax, A.; Bailly, M.; Sapi, J.; Laronze, J.-Y. *Bioorg. Med. Chem.* **2005**, *6*, 2263.

(10) (a) Gruner, K. K.; Knölker, H.-J. *Org. Biomol. Chem.* **2008**, *6*, 3902. (b) Molina, P.; Fresneda, P. M.; Almendros, P. *Tetrahedron* **1993**, *49*, 1223. (c) Lebold, T. P.; Kerr, M. A. *Org. Lett.* **2007**, *9*, 1883.

(11) (a) Basavaiah, D.; Lenin, V. *Eur. J. Org. Chem.* **2010**, 5650. (b) Kuninobu, Y.; Matsuki, T.; Takai, K. *Org. Lett.* **2010**, *12*, 2948. (c) Morimoto, T.; Yamasaki, K.; Hirano, A.; Tsutsumi, K.; Kagawa, N.; Kakiuchi, K.; Harada, Y.; Fukumoto, Y.; Chatani, N.; Nishioka, T. *Org. Lett.* **2009**, *11*, 1777. (d) Hatjiarapoglou, L.; Varvoglis, A.; Alcock, N. W.; Pike, G. A. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2839. (e) Vicente, J.; Abad, J.-A.; Lopez-Pelaez, B.; Martinez-Viviente, E. *Organometallics* **2002**, *21*, 58. (f) Pletnev, A. A.; Tian, Q.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 9276. (g) Bo, C.; Xingang, X.; Jiangping, L.; Qiaoling, W.; Jiyong, Z.; Shouchu, T.; Xuegong, S.; Xinfu, P. *Synlett* **2006**, 259. (h) Alonso, D. A.; Najera, C.; Pacheco, M. C. *Adv. Synth. Catal.* **2002**, *344*, 172. (i) Zhang, H.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 9318. (j) Zhang, H.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 5132. (k) Vasilyev, A. V.; Walspurger, S.; Paleb, P.; Sommera, J. *Tetrahedron Lett.* **2004**, *45*, 3379. (l) Chang, K.-J.; Rayabarapu, D. K.; Cheng, C.-H. *Org. Lett.* **2003**, *5*, 3963.

(12) (a) Larock, R. C.; Doty, M. J.; Cacchi, S. *J. Org. Chem.* **1993**, *58*, 4579. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2006**, *106*, 4644. (c) Gevorgyan, V.; Quan, L. G.; Yamamoto, Y. *Tetrahedron Lett.* **1999**, *40*, 4089. (d) Wang, S.; Zhu, Y.; Wang, Y.; Lu, P. *Org. Lett.* **2009**, *11*, 2615. (e) Waldo, J. P.; Zhang, X.; Shi, F.; Larock, R. C. *J. Org. Chem.* **2008**, *73*, 6679. (f) Zang, J.; Yang, F.; Wu, Y. *Appl. Organomet. Chem.* **2011**, *25*, 675. (g) Leng, Y.; Yang, F.; Wei, K.; Wu, Y. *Tetrahedron* **2011**, *66*, 1244.

(13) (a) Chaitanya, T. K.; Nagarajan, R. *Org. Biomol. Chem.* **2011**, *9*, 4662. (b) Chaitanya, T. K.; Prakash, K. S.; Nagarajan, R. *Tetrahedron* **2011**, *67*, 6934.

(14) X-ray crystallographic data for **3a**: Formula: $C_{30}H_{23}N_1O_1$. Unit cell parameters: a = 9.0690(13), b = 10.359(2), c = 13.357(2), α = 85.794(15), β = 72.369(13), γ = 70.831(16), space group $P\bar{1}$. X-ray crystallographic data for **3r**: Formula: $C_{26}H_{23}N_1O_1$. Unit cell parameters: a = 8.3997(16), b = 10.227(2), c = 12.402(2), α = 76.514(3), β = 78.141(3), γ = 75.769(3), space group $P\bar{1}$. X-ray crystallographic data for **3s**: Formula: $C_{25}H_{21}N_1O_1$. Unit cell parameters: a = 7.9184(6), b = 10.4371(7), c = 12.1136(10), α = 76.338(6), β = 83.212(7), γ = 77.905(6), space group $P\bar{1}$. The CCDC deposition numbers of compounds **3a**,**r**,**s** are 840023, 840025, and 840024, respectively. Further data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(1223)336033, E-mail: deposit@ccdc.cam.ac.uk].

Downloaded by: Universite Laval. Copyrighted material.

 © Thieme Stuttgart · New York