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Novel domino products from the reaction of phenyl vinyl ketone and its derivatives with cyclic ketones

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Dedicated to Professor J. Subramanian on the occasion of his 60th birthday

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Abstract—Reaction of phenyl vinyl ketone with cyclopentanone under thermal conditions resulted in novel domino products, 1,5,9-triketones along with the expected 1,5-diketones. The 1,5,9-triketones were formed via a Michael–Michael-rearrangement pathway. On the other hand, reaction under basic conditions furnished a spiro[4.5]decanone, formed by domino pathways involving Michael–Michael-aldol condensation reactions. Microwave mediated reductive amination–cyclization of the 1,5,9-triketone furnished the perhydrocyclopenta[*ij*]quinolizine derivative.

1. Introduction

The generation of complex molecular architectures by multi-bond formation in a one-pot operation is of ongoing interest in synthetic organic chemistry.[1] A multitude of designations and classifications have been used to describe these multi-step reactions, viz. consecutive, serial, sequential, domino, cascade, tandem, coupled process, multi-step package, tactical combination, and merging processes.[2–6] The increasing interest in domino processes over the past decade is spurred by the simplicity of building up complex molecules through a sequence of same-pot reactions taking place under identical reaction conditions. In the domino process, subsequent reaction result as a consequence of the functionality formed in the previous step.[2]

Successive carbon–carbon bond forming reactions initiated by an inter- or intramolecular Michael reaction (conjugate addition) are a powerful weapon for the synthesis of a plethora of complex carbocyclic compounds.[1] In this regard, phenyl vinyl ketone has been employed extensively as a Michael acceptor for the generation of a wide range of useful products, including amino acids,[7] nucleic acid derivatives,[8,9] and 1,5- and 1,6-diketones.[10–13] Phenyl vinyl ketone and its derivatives have also been utilized to form several interesting heterocyclic,[14–16] carbocyclic[17–21] and spiro compounds.[22] We planned to utilize the 1,5-diketones generated from the conjugate addition of cyclic ketones to phenyl vinyl ketone in syntheses of aza-steroidal systems. In the course of generating the necessary 1,5-diketones, we discovered several interesting complex products formed in a one-pot reaction through domino pathways.

2. Results and discussion

It has been reported in the literature that heating the Mannich base, dimethylaminopropiophenone **1** with cyclopentanone **2** without solvent at elevated temperatures furnished the corresponding 1,5-diketone **3** (Scheme 1).[23] Phenyl vinyl ketone was the reacting species in the medium, generated on the pyrolysis of the Mannich base **1**. When we repeated this reaction at 155°C we observed the formation of the 1,5-diketone **3** along with the 1,5,9-triketone **4** in 7% yield as a mixture of diasteromers (Scheme 1). When the reaction was conducted in polyethylene glycol medium under microwave irradiation for 2 min in a domestic microwave oven (230 V, 50 Hz, microwave frequency: 2450 MHz at 370 W) the yield of **4** marginally increased to 17%.

During the column purification of the diasteromeric mixture of triketones **4**, single isomer **4a**, crystallized out of column fractions as colorless needles (mp 94°C). The EI mass spectrum and elemental analysis data of **4a** were consistent with the molecular formula $C_{23}H_{24}O_3$. The IR spectrum of **4a** revealed characteristic absorption at 1710 and 1660 cm^{-1} assignable to cyclopentanone and aromatic ketone moieties, respectively. Analysis of the ^1H NMR spectrum of **4a** clearly showed that it was formed by the condensation of two molecules of phenyl vinyl ketone and one molecule of cyclopentanone. The proton-decoupled ^{13}C NMR spectrum revealed the presence of four aliphatic carbons, two carbonyl carbons and four aromatic carbons. On the basis of this spectral analysis and on comparison of the ^{13}C NMR

Keywords: Domino reaction; phenyl vinyl ketone; cyclopentanone; quinolizine; quinolizine.

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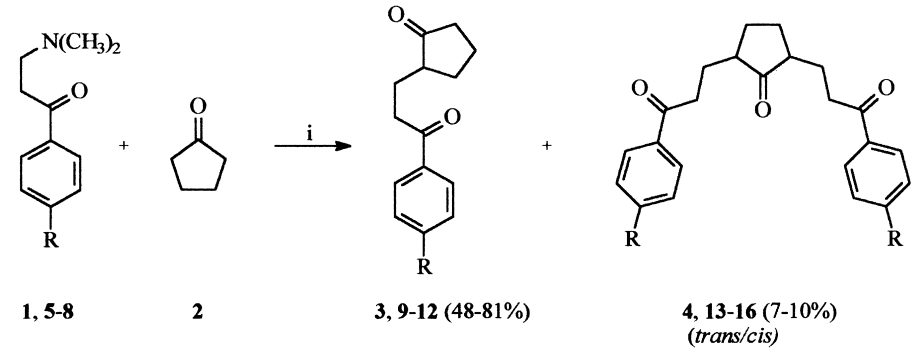


Scheme 1. **1**,**3**,**4**: R=H; **5**,**9**,**13**: R=Cl; **6**,**10**,**14**: R=Br; **7**,**11**,**15**: R=Me; **8**,**12**,**16**: R=OMe. *Reagents and conditions*: (i) 155°C, neat, 30 min.

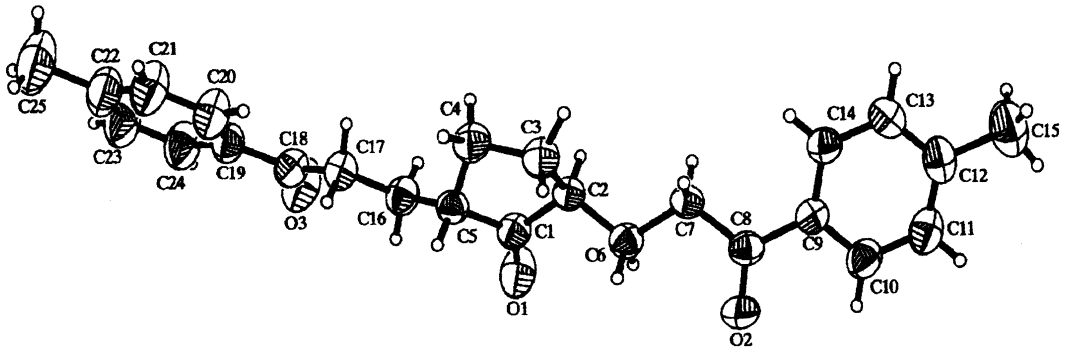


Figure 1. ORTEP diagram of *trans*-2,5-di[3-(4-methylphenyl)-3-oxopropyl] cyclopentan-1-one (**15a**) with crystallographic numbering.

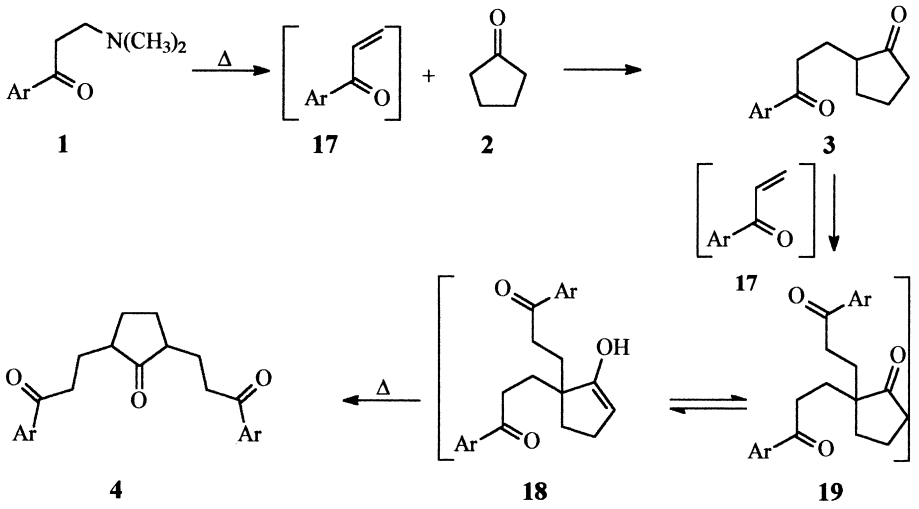
spectral correlation with literature data for similar compounds[24,25] the structure of triketone **4a** was assigned as *trans*-2,5-di-(3-oxo-3-phenylpropyl)-1-cyclopentanone. The assigned structure was confirmed on the basis of the analysis of single crystal X-ray data gathered on *trans*-2,5-di-(3-oxo-3-(4-methylphenyl)propyl)-1-cyclopentanone **15a** (Fig. 1).[26] The *trans*-triketone **15a** was obtained in pure form, from fractional crystallization of the column fractions during purification of the mixture. The NMR spectral characteristics of the *trans*-triketone **15a** were similar to the parent *trans*-triketone **4a**. However, the ^{13}C NMR spectrum of the crude product from the reaction of phenyl vinyl ketone and cyclopentanone clearly revealed the presence of both *trans* (**4a**) and *cis* (**4b**) triketones in the ratio of 70:30. Previously, Buchanan and coworkers isolated the diasteromeric mixture of triketones **4** along with the diketone **3** from the thermal reaction of Mannich base **1** and cyclopentanone.[27] However, they did not study the scope of this interesting thermal reaction for the generation of differently substituted triketones of the type **4** and the mechanism for its formation. Recently, Borioni and coworkers reported the isolation of diasteromeric mixture of 2,5-di[3-(3-methoxyphenyl)-3-oxopropyl]-1-cyclopentanone a *meta*-methoxy analogue of the triketone **4** as a byproduct in the reaction of enamine of cyclopentanone and 3-dimethylamino-1-(3-methoxyphenyl)propan-1-one.[28] The ^{1}H NMR spectral data reported by Borioni and coworkers matched well with that of triketone **4**.

The reaction of several 4-substituted Mannich bases such as 4-chloro-, 4-bromo-, 4-methyl- and 4-methoxy-dimethylaminopropiophenone (**5**–**8**) with cyclopentanone **2** under thermal conditions (155°C) furnished corresponding 1,5-diketones **9**–**12** as well as diastereomeric mixtures of the triketones **13**–**16** in about 8–10% yield (Scheme 1). Yields of the triketones in the reaction increased to 15–20% when they were conducted under microwave irradiation. In all the cases the *trans*-triketones were obtained as major products. The ratio of the *trans*/*cis* isomers formed in the condensation reaction, derived from the analysis of the ^{13}C NMR spectra of the mixture, is given in Table 1. When reactions were conducted above 155°C, decomposition of the products was noticed and the yield was lower. At temperatures less than 150°C, pyrolysis of the Mannich base was slow.

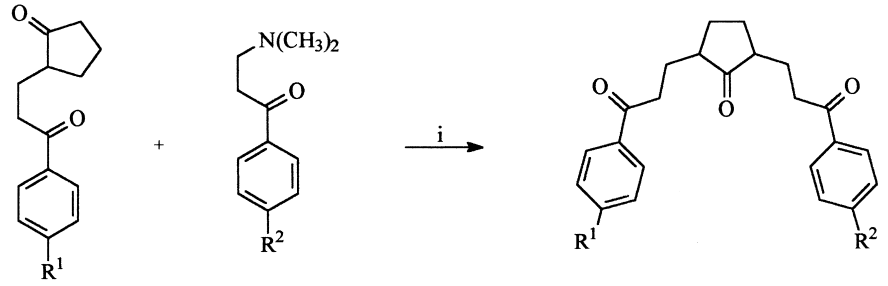
Table 1. Ratio of *trans*- and *cis*-isomers formed in the reaction of Mannich bases with cyclopentanone

Substituent R	Compound No.	*trans*-Isomer (%)	*cis*-Isomer (%)
H	**4**	**4a**: 70	**4b**: 30
Cl	**13**	**13a**: 67	**13b**: 33
Br	**14**	**14a**: 79	**14b**: 21
Me	**15**	**15a**: 64	**15b**: 36
OMe	**16**	**16a**: 86	**16b**: 14

The proposed mechanism for the formation of triketone **4** from the reaction of Mannich base **1** with cyclopentanone **2** is given in Scheme 2. Initial reaction of in situ generated phenyl vinyl ketone **17** with 1 mol of cyclopentanone **2** in a Michael fashion results in 1,5-diketone **3**. Michael addition of the diketone **3** to a second molecule of phenyl vinyl ketone **17** furnished the thermodynamic product 2,2-bisalkylated cyclopentanone **19**. The intermediate **19** then



Scheme 2.



Scheme 3. **1** R^2=H; **3**: R^1=H; **5**: R^2=Cl; **9**: R^1=Cl; **10**: R^1=Br; **11**: Me; **12**: OMe; **20**: R^1=Cl, R^2=H; **21**: R^1=Br, R^2=H; **22**: R^1=Me, R^2=H; **23**: R^1=OMe, R^2=H. *Reagents and conditions*: (i) 155°C, neat, 30 min.

undergoes rearrangement to 2,5-bisalkylated product **4**, to relieve steric crowding through a symmetry-allowed 1,3-sigmatropic-carbon shift (via enol form **18**). Molecular mechanics calculations reveal that the *trans* isomer of **4** is marginally more stable than the *cis*-isomer (MM2 minimum energy for *trans*-isomer=19.76 kcal; MM2 minimum energy for *cis*-isomer=20.39 kcal).[29]

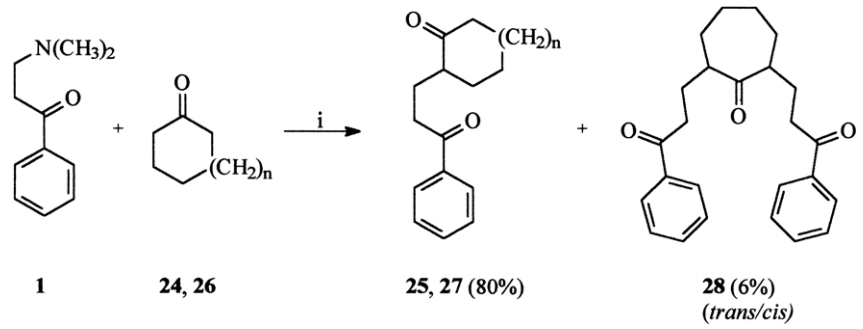
To confirm the proposed mechanism, intermediate 4-chlorophenyl 1,5-diketone **9** was heated with *N*,*N*-dimethylaminopropiophenone **1** at 155°C (Scheme 3). From this reaction the unsymmetrical 1,5,9-triketone **20** was isolated in 47% yield as a mixture of *trans*- and *cis*-isomers (73:27). The reverse addition of 4-chlorophenyl substituted Mannich base **5** with 1,5-diketone **3** furnished a mixture of *trans*- and *cis*-triketones **20** in 67% yield (Scheme 3). The increased yield of the triketone **20** from this reaction is evidently due to higher reactivity of 4-chlorophenyl vinyl ketone as a Michael acceptor. Absence of symmetrical ketones such as **13** and **4** from the above reaction indicated that the triketone does not undergo equilibration with its precursors. Synthesis of unsymmetrical triketones was extended to other cases using 1,5-diketones having different 4-substituted phenyl rings. The 1,5-diketones **10**–**12** were subjected to Michael addition with in situ-generated phenyl vinyl ketone (Scheme 3). In each case, the *trans*-isomer was the major product in the reaction (Table 2). Interestingly, the reaction of diketone **9** and Mannich base **1** under microwave irradiation did not improve the yield of triketone **20**.

Table 2. Ratio of *trans*- and *cis*-isomers formed in the reaction of 1,5-diketones with Mannich bases

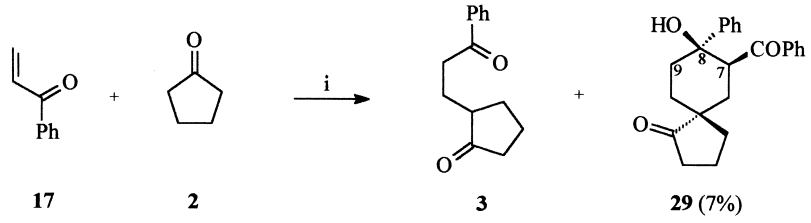
Substituent R	Compound No.	*trans*-Isomer (%)	*cis*-Isomer (%)
Cl	**20**	73	27
Br	**21**	69	31
Me	**22**	64	36
OMe	**23**	67	33

Reaction of Mannich base **1** with cyclohexanone **24** under thermal conditions or under microwave irradiation resulted in the isolation of known[23] 1,5-diketone **25**; no triketone was observed (Scheme 4). On the other hand, reaction of Mannich base **1** with cycloheptanone **26** furnished known[30] 1,5-diketone **27** along with a diastereomeric mixture of triketones **28** (6%) yield. The *trans*-triketone was once again the major product (Scheme 4).

We have also studied the Michael reaction of phenyl vinyl ketone and cyclic ketones in the presence of barium hydroxide following the experimental conditions reported



Scheme 4. **24**,**25**: n=1; **26**,**27**: n=2. *Reagents and conditions*: (i) 155°C, neat, 30 min.



Scheme 5. *Reagents and conditions*: (i) $Ba(OH)_2$, EtOH, rt, 12 h.

in the literature for conjugate addition of cyclopentanone to chalcones (Scheme 5).[31–33] Thus, when phenyl vinyl ketone **17** was reacted with cyclopentanone **2** in ethanol using barium hydroxide as base, the reaction furnished known[23] diketone **3** (80%) along with a new product **29** in 7% yield. The mass spectrum and elemental analysis data of **29** were consistent with the molecular formula $C_{23}H_{24}O_3$. The IR spectrum revealed the presence of a hydrogen-bonded hydroxyl group (3460 cm^{-1}) and two carbonyl groups (1720 and 1660 cm^{-1}), assignable to a cyclopentanone and an aromatic ketone. The ^1H NMR spectrum revealed the presence of aromatic protons and aliphatic protons in the ratio of 1:1.4, in agreement with the formation of the product from two units of phenyl vinyl ketone and one unit of cyclopentanone. A double doublet (1H) at δ 5.13 ppm (J=9, 3.5 Hz) indicated an axially oriented hydrogen having axial–axial and axial–equatorial coupling with adjacent diasterotopic hydrogens. A double multiplet (2H) at δ 7.86 ppm revealed the presence of only one benzoyl group in the molecule. The proton-decoupled ^{13}C NMR spectrum revealed the presence of nine aliphatic carbons, eight aromatic carbons and two carbonyl carbons. On the basis of the spectral data and mechanistic considerations, the structure of **29** was assigned as (±) (8*S*,5*R*,7*R*)-7-benzoyl-

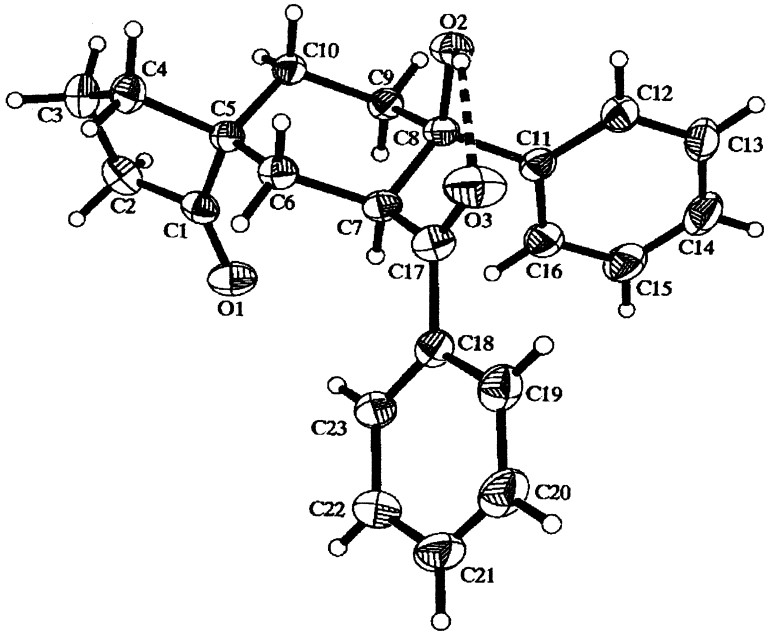
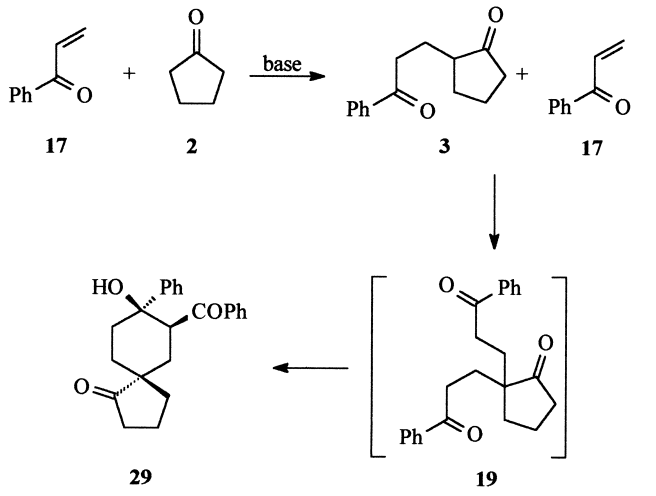


Figure 2. ORTEP diagram of 7-benzoyl-8-hydroxy-8-phenylspiro[4.5]decan-1-one (**29**) with crystallographic numbering.

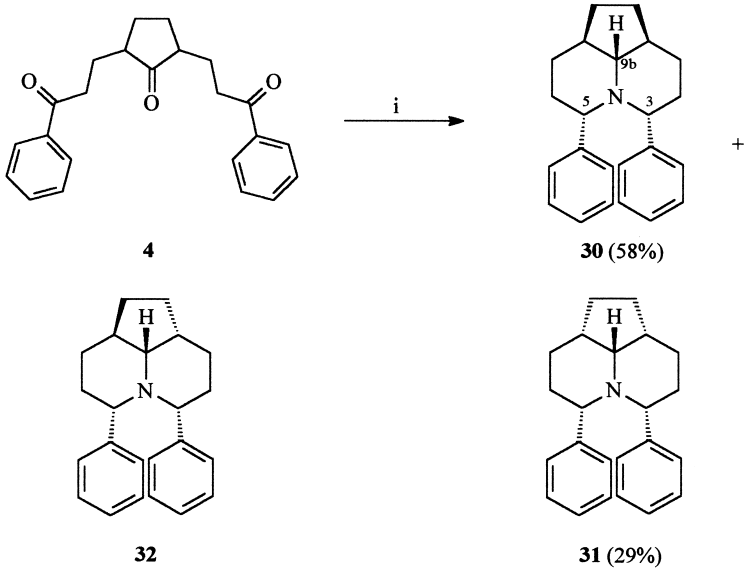


Scheme 6.

8-hydroxy-8-phenylspiro[4.5]decan-1-one. The configuration of the spiro carbon was fixed on the basis of the unusually high downfield shift of the C_7 axial hydrogen (δ 5.13 ppm). Molecular models revealed that this hydrogen is under the anisotropic environment of the carbonyl group. Confirmation of the structure of **29** came from single crystal X-ray crystallographic data (Fig. 2).[34]

A possible mechanism for the formation of spiroketoalcohol **29** is given in Scheme 6. Base-mediated Michael addition of cyclopentanone **2** to phenyl vinyl ketone **17** results in 1,5-diketone **3**, which on further reaction with another molecule of phenyl vinyl ketone **17** furnishes the bis-alkylated product **19**. Cyclization of **19** through intramolecular aldol condensation results in the spiroketoalcohol **29**. Bis-alkylation at the α position of cyclopentanone is expected to take place under equilibrium conditions (thermodynamic control). It is interesting to note that only a single diastereomer in which the cyclopentanone carbonyl is oriented α was isolated from the reaction. Intramolecular hydrogen bonding interactions may be the driving force for the formation of this diastereomer. Attempts to isolate spiroketoalcohols derived from substituted phenyl vinyl ketones using similar experimental conditions proved to be surprisingly futile. This base mediated three component condensation also did not take place when other bases (potassium hydroxide, sodium hydroxide, sodium methoxide and sodium hydride) were used.

Having established a simple procedure for the generation of 1,5,9-triketones in a one-pot operation from phenyl vinyl ketone and cyclopentanone, we next attempted molecular stitching of carbonyl carbons through a reductive amination–cyclization procedure. Borioni and coworkers reported reductive amination of 1,5-diktones of the type **3** with methylamine and ammonium acetate to generate bicyclic azacompounds for testing acetylcholinesterase inhibitor activity.[28] When the diasteromeric mixture of triketones **4** was subjected to reductive amination–cyclization with ammonium formate in polyethyleneglycol-200 under microwave irradiation at 370 W power they were smoothly transformed within 1 min into a diasteromeric mixture of 3,5-diphenylperhydrocyclopenta[*ij*]quinolizines **30** and **31** in 87% yield in the ratio of 2:1 (Scheme 7). The quinolizine skeleton is well distributed as the nucleus of a number of alkaloids. Particularly, perhydrocyclopenta[*ij*]quinolizine is found as a structural motif in the alkaloids such as vallesamidine,[35] callichiline[36] and norvallesamidine.[37] The diasteromeric mixture of amines **30** and **31** were separated by column chromatography and were characterized separately. The ^{1}H NMR spectrum of the major product **30** showed two characteristic triplets at δ 3.28 (2H, J=5.1 Hz) and δ 2.90 (1H, J=4.2 Hz) for C_3–H, C_5–H and C_{9b}–H, respectively, indicating pseudo-equatorial orientation of phenyl groups and *cis*,*cis*-ring junction at perhydrocyclopentaquinolizine moiety. The triplet nature of the C_3–H, C_5–H and C_{9b}–H signals indicate pseudo-symmetry in the molecule, which can arise from the dynamic equilibrium due to conformational changes in the cyclohexane rings and inversion at the nitrogen atom.



Scheme 7. *Reagents and conditions*: (i) $H_3N^+HCOO^-$, PEG-200, microwave, 370 W, 1 min.

Interestingly the ^{1}H NMR spectrum of **30** revealed the aromatic protons as a broad singlet at δ 6.78 ppm indicating a shielding environment around them. The ^{13}C NMR spectrum of **30** showed only six signals for aliphatic carbons and four signals for aromatic carbons indicating pseudo-mirror plane symmetry arising from chemical equivalence due to dynamic equilibrium. The ^{1}H NMR spectrum of the minor product **31** revealed two characteristic triplets at δ 3.92 (J=6.2 Hz) and δ 3.40 (J=8.1 Hz) indicating pseudo-equatorial orientation of phenyl groups and *trans*,*trans*-ring junction in cyclopentaquinalizine portion. Similar to that of 30 ^{1}H NMR spectrum of 31 indicated symmetric nature of the molecule due to chemical equivalence arising from dynamic equilibrium. However, the aromatic protons in 31 showed discrete signals for *ortho*, *meta* and *para* hydrogens in the expected region (7.07–7.36 ppm). The ^{13}C NMR spectrum of **31** revealed six signals for aliphatic carbons and four signals for aromatic carbons, which also point to existence of pseudo-mirror plane symmetry in the molecule. The symmetric nature of ^{13}C NMR spectra for cyclopentaquinalizines **30** and **31** clearly rule out the possibility of *cis*,*trans*-isomer **32** as the product in the reaction.

Previously, the stereochemistry of perhydroquinolizine and perhydro methylquinolizines have been studied extensively by the application of IR, ^{1}H NMR, ^{13}C NMR and dynamic NMR spectroscopy.[38–41] It was shown that the nitrogen inversion barrier in perhydroquinolizine is about 11.5 kcal mol^{-1} and the inversion is faster than NMR time scale at rt. The NMR spectra of *cis*,*cis*-(**30**) and *trans*,*trans*-perhydroquinolizine **31** also indicate dynamic inversion at nitrogen center along with a conformational equilibrium in the cyclohexyl rings. The phenyl rings occupy average environment to avoid steric and dipole–dipole repulsion. However, further studies are required to clearly discern the conformation equilibration due to the nitrogen inversion and flipping in the cyclohexyl rings. Interestingly, energy minimization in MM2[27] mode indicated that structure **31** is energetically more stable (MM2 energy=20.80 kcal) compared to **30** (MM2 energy=24.29 kcal) indicating kinetic control in the reduction cyclization reaction. Furthermore, energy minimization of *cis*, *trans*-perhydroquinolizine **32** was found to be about 7 kcal mol^{-1} less stable than the *cis*,*cis*-isomer **30** (MM2 minimum energy=31.29 kcal mol^{-1}).[27]

The reductive amination–cyclization reaction was conducted on the *trans*-triketone **4a** separately. This reaction furnished the same diasteromeric mixture of cyclopentaquinolizidines **30**, **31** in the ratio of 2:1. This result indicated that in the multi-step reductive amination–cyclization sequence enamine intermediates were being reduced to amine moiety from the same face leading to *cis*-orientation of the substituents on the cyclopentane ring.

3. Conclusions

In conclusion we have studied the condensation of phenyl vinyl ketone and cyclopentanone under both thermal and basic conditions. For each set of conditions, we have identified novel and interesting products generated by multi-component condensation via domino pathways. Reductive amination–cyclization reaction on 1,5,9-triketones obtained in the study resulted in perhydrocyclopenta[*ij*]quinolizine derivatives.

4. Experimental

4.1. General

Progress of all the reactions was monitored by TLC (TLC silica gel: Qualigens or TLC alumina: SRL, India) using hexane/ethyl acetate as eluent. After completion of the reaction, the reaction mixture was diluted with dichloromethane and washed with water and brine. The organic extract was dried with anhydrous sodium sulfate and the solvent was distilled under reduced pressure. Column chromatography was accomplished on silica gel (100–200 mesh, Acme synthetic chemicals) using hexane/ethyl acetate as eluent. Melting points were determined using a Gallenkamp melting point apparatus. IR spectra were recorded neat, as KBr pellets, or Nujol mulls using a JASCO FT IR or Perkin–Elmer spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with Bruker 500 MHz, JEOL 400 MHz, Varian 300 MHz and Bruker 200 MHz spectrophotometers. 2D NMR spectra were recorded on a Bruker 500 MHz instrument. Mass spectra were recorded on Finnigan MAT 8230 Mass spectrometer. The elemental analysis was carried out on a Elementar vario EL (Germany) apparatus. The X-ray diffraction data was generated on a Enraf–Nonius CAD4 and SMART (Siemens) diffractometer. The microwave reactions were carried out using BPL-Sanyo, India; mono-made, multi-power; power source: 230 V, 50 Hz, Microwave Frequency: 2450 MHz microwave oven.

4.2. General procedure for the synthesis of symmetrical 1,5,9-triketones (4, 13–16) from the reaction of Mannich base under thermal conditions

β-Dimethylaminopropiophenone hydrochloride (10 g, 46.9 mmol) was taken in a beaker and the minimum amount of water (15 mL) was added to dissolve the salt. The beaker was kept in an ice bath and 20% aqueous sodium hydroxide was added drop wise while periodically checking pH using pH paper. As neutralization proceeded the solution became turbid. The addition of sodium hydroxide was continued until the pH reached 10, at which point an oily layer of base was visible. This oily layer was extracted with dichloromethane and concentrated to give β-dimethylaminopropiophenone **1** (Yield 97%). To this Mannich base **1** (8.06 g, 45.5 mmol), cyclopentanone **2** (11.47 g, 136.5 mmol) was added and heated for 30 min at 155°C (internal temperature). The cooled reaction mixture was then directly subjected to column chromatography (hexane/ethyl acetate 98:2 to 85:15) to give two products **3** and **4**. The 1,5,9-triketone **4** crystallized out of the column fractions on standing overnight.

4.2.1. 2-(3-Oxo-3-phenylpropyl)-1-cyclopentanone (3). Yield 7.87 g (80%); mp 39°C; R_f (90:10 hexane/ethyl acetate) 0.38; ν_{max} (KBr) 3065, 2953, 2868, 1730, 1680, 1597, 1450, 1402, 1261, 1217, 1157, 1105, 1001, 833,

742, 690, 655 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.89–7.94 (2H, m), 7.35–7.55 (3H, m), 3.03–3.11 (2H, m), 1.90–2.33 (6H, m), 1.68–1.89 (2H, m), 1.56–1.65 (1H, m); δ_C (50 MHz, $CDCl_3$) 220.63, 199.75, 136.88, 132.95, 128.54, 128.01, 48.13, 38.01, 36.13, 29.84, 24.27, 20.60.

4.2.2. *trans*-2,5-Di-(3-oxo-3-phenylpropyl)-1-cyclopentanone (4a). Yield 555 mg (7%); R_f (90:10 hexane/ethyl acetate) 0.18; ν_{max} (KBr) 2900, 2820, 1710, 1660, 1430, 1350, 1240, 1140, 980, 730, 670 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.96 (4H, d, J=8.3 Hz), 7.42–7.56 (6H, m), 3.09–3.13 (4H, m), 2.10–2.22 (4H, m), 1.82–1.85 (4H, m), 1.45–1.46 (2H, m); δ_C (100 MHz, $CDCl_3$) 221.76, 200.05, 137.04, 133.31, 128.85, 128.30, 48.70, 36.31, 28.07, 24.93; LRMS: 348 (M^+, 0.6), 331 (5), 229 (11), 228 (54), 210 (10), 133 (9), 121 (6), 109 (12), 105 (100), 95 (12), 77 (75), 76 (26), 55 (16), 51 (18%); elemental analysis calcd for $C_{23}H_{24}O_3$: C, 79.28; H, 6.94. Found: C, 79.11; H, 6.91.

4.3. Reaction of *N*,*N*-dimethylamino-4-chloropropiophenone (5) with cyclopentanone (2)

Following the general procedure described above, the reaction of Mannich base **5** (1.62 g, 7.7 mmol) and cyclopentanone **2** (1.94 g, 23 mmol) furnished a mixture of diketone **9** and triketone **13** which were purified by column chromatography.

4.3.1. 1-(4-Chlorophenyl)-3-(2-oxocyclopentyl)-1-propanone (9). Yield 1.38 g (72%); mp 115°C; R_f (90:10 hexane/ethyl acetate) 0.46; ν_{max} (Nujol) 2962, 1734, 1676, 1587, 1452, 1406, 1371, 1255, 1217, 1153, 1093, 1014, 979, 827, 769, 569, 491 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.90 (2H, dd, J=4.3, 1.9 Hz), 7.36 (2H, dd, J=7.3, 1.9 Hz), 3.09 (2H, ddd, J=10.8, 6.9, 1.9 Hz), 2.00–2.31 (6H, m), 1.77–1.87 (2H, m), 1.61–1.64 (1H, m); δ_C (50 MHz, $CDCl_3$): δ 220.45, 198.51, 139.42, 135.30, 129.48, 128.87, 48.05, 38.03, 36.10, 29.93, 24.33, 20.58.

4.3.2. Mixture of *cis*- and *trans*-2,5-di[3-(4-chlorophenyl)-3-oxopropyl]cyclopentan-1-one (13). Yield 144 mg (9%); R_f (90:10 hexane/ethyl acetate) 0.21; ν_{max} (Nujol) 2961, 1724, 1684, 1589, 1487, 1452, 1400, 1367, 1309, 1255, 1203, 1155, 1093, 987, 831, 769, 565, 518 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.90 (4H, d, J=8.3 Hz), 7.43 (4H, d, J=8.0 Hz), 3.10 (4H, t, J=8.3 Hz), 2.05–2.22 (4H, m), 1.70–1.95 (4H, m), 1.47–1.60 (2H, m); δ_C (50 MHz, $CDCl_3$) 221.49 (2CO), 198.50 (2CO), 139.46 (2C), 135.07 (2C), 129.46 (4C), 128.88 (4C), 48.29, 47.20, 36.10, 35.97, 27.81, 27.28, 24.76, 24.58; LRMS: 415 (M^+, 4), 417 (2.5), 262 (46), 264 (15), 154 (38), 156 (12), 139 (100), 141 (34), 111 (44), 113 (14), 56 (40%); elemental analysis calcd for $C_{23}H_{22}Cl_2O_3$: C, 66.19; H, 5.31. Found: C, 65.75; H, 5.31.

4.4. Reaction of *N*,*N*-dimethylamino-4-bromopropiophenone (6) with cyclopentanone (2)

Following the general procedure described above, the reaction of Mannich base **6** (955 mg, 3.8 mmol) and cyclopentanone **2** (941 mg, 11.2 mmol) furnished a mixture of diketone **10** and triketone **14** which were purified by column chromatography.

4.4.1. 1-(4-Bromophenyl)-3-(2-oxocyclopentyl)-1-propanone (10). Yield 529 mg (48%); mp 67°C; R_f (90:10 hexane/ethyl acetate) 0.44; ν_{max} (Nujol) 3079, 2958, 2878, 1944, 1736, 1676, 1488, 1454, 1407, 1266, 1158, 984, 829, 776, 574, 500 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.83 (2H, dd, J=4.9, 2.0 Hz), 7.59 (2H, dd, J=4.9, 2.0 Hz), 3.02–3.16 (2H, dm, J=6.8 Hz), 1.98–2.35 (6H, m), 1.77–1.86 (2H, m), 1.57 (1H, ddd, J=17.0, 10.0, 7.0 Hz); δ_C (100 MHz, $CDCl_3$) 220.62, 198.53, 135.30, 131.66, 129.39, 127.91, 47.84, 37.88, 35.88, 29.68, 23.93, 20.42.

4.4.2. Mixture of *cis*- and *trans*-2,5-di[3-(4-bromophenyl)-3-oxopropyl]cyclopentan-1-one (14). Yield 76 mg (8%); R_f (90:10 hexane/ethyl acetate) 0.23; ν_{max} (Nujol) 2960, 1726, 1680, 1587, 1480, 1462, 1378, 1250, 1210, 1158, 1093, 823, 769, 565 cm^{-1}; δ_H (400 MHz, $CDCl_3$): δ 7.83 (4H, dd, J=6.8, 2.0 Hz), 7.59 (4H, dd, J=6.3, 2.0 Hz), 3.03–3.15 (4H, m), 1.98–2.30 (4H, m), 1.70–1.88 (4H, m), 1.45–1.49 (2H, m); δ_C (100 MHz, $CDCl_3$) 221.82 (2CO), 199.00, 198.95, 135.74 (2C), 132.17 (4C), 129.87 (4C), 128.50 (2C), 48.58, 47.49, 36.37, 36.26, 28.11, 27.58, 25.03, 24.84; LRMS: M^+ peak did not appear, 306 (70), 308 (72), 198 (31), 200 (29), 183 (100), 185 (99), 182 (47), 184 (53), 155 (50), 157 (51), 154 (25), 156 (39), 131 (13), 76 (63), 55 (66%); elemental analysis calcd for $C_{23}H_{22}Br_2O_3$: C, 54.57; H, 4.38. Found: C, 54.39; H, 4.39.

4.5. Reaction of *N*,*N*-dimethylamino-4-methylpropiophenone (7) with cyclopentanone (2)

Following the general procedure described above, the reaction of Mannich base **7** (1.67 g, 8.8 mmol) and cyclopentanone **2** (2.21 g, 26.3 mmol) furnished a mixture of diketone **11** and triketone **15** which were purified by column chromatography.

4.5.1. 1-(4-Methylphenyl)-3-(2-oxocyclopentyl)-1-propanone (11). Yield 1.31 g (65%); mp 71°C; R_f (90:10 hexane/ethyl acetate) 0.41; ν_{max} (Nujol) 2958, 2878, 1729, 1676, 1608, 1454, 1373, 1259, 1219, 1158, 984, 829, 769, 567, 494, 467, 420 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.86 (2H, d, J=9.5 Hz), 7.25 (2H, d, J=10.9 Hz), 3.08 (2H, ddd, J=9.0, 6.3, 3.0 Hz), 2.4 (3H, s, CH_3), 2.00–2.30 (6H, m), 1.75–1.83 (2H, m), 1.54–1.59 (1H, m); δ_C (75 MHz, $CDCl_3$) 220.91, 199.54, 143.79, 134.40, 129.70, 128.20, 48.24, 38.10, 36.07, 29.90, 24.39, 21.61, 20.66.

4.5.2. Mixture of *cis*- and *trans*-2,5-di[3-(4-methylphenyl)-3-oxopropyl]cyclopentan-1-one (15). Yield 164 mg (10%); R_f (90:10 hexane/ethyl acetate) 0.19; ν_{max} (Nujol) 2958, 2911, 2871, 1729, 1682, 1608, 1373, 1306, 1232, 1185, 984, 823, 782, 567, 460 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.86 (4H, d, J=5.2 Hz), 7.25 (4H, d, J=4.7 Hz), 3.08 (4H, ddd, J=5.0, 3.0, 1.8 Hz), 2.40 (6H, s, CH_3), 2.00–2.33 (4H, m), 1.81–1.86 (4H, m), 1.69–1.76 (2H, m); δ_C (75 MHz, $CDCl_3$) 221.54 (2CO), 199.49, 199.42, 143.77 (2C), 134.32 (2C), 129.24 (4C), 128.17 (4C), 48.48, 47.37, 36.07, 35.93, 27.79, 27.22, 24.96, 24.76, 21.61 (2C); LRMS: 376 (M^+, 0.8), 358 (6), 243 (11), 242 (48), 147 (12), 135 (11), 134 (59), 119 (100), 96 (11), 91 (68), 65 (23), 55 (17%); elemental analysis calcd for $C_{23}H_{28}O_3$: C, 79.75; H, 7.50. Found: C, 79.66; H, 7.47.

4.6. Reaction of *N*,*N*-dimethylamino-4-methoxypropiophenone (8) with cyclopentanone (2)

Following the general procedure described above, the reaction of Mannich base **8** (331 mg, 1.6 mmol) and cyclopentanone **2** (403 mg, 4.8 mmol) furnished a mixture of diketone **12** and triketone **16** which were purified by column chromatography.

4.6.1. 1-(4-Methoxyphenyl)-3-(2-oxocyclopentyl)-1-propanone (12). Yield 319 mg (81%); R_f (80:20 hexane/ethyl acetate) 0.39; mp 67°C; ν_{max} (Nujol) 2880, 1710, 1650, 1580, 1550, 1480, 1440, 1360, 1290, 1240, 1220, 1160, 1140, 1080, 1000, 820, 780, 700 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.95 (2H, dd, J=7.3, 2.4 Hz), 6.93 (2H, dd, J=6.8, 1.9 Hz), 3.86 (3H, s, OCH_3), 3.07 (2H, ddd, J=9.8, 6.3, 2.9 Hz), 1.98–2.34 (6H, m), 1.76–1.84 (2H, m), 1.54–1.62 (1H, m); δ_C (100 MHz, $CDCl_3$) 221.03, 198.46, 163.38, 130.30, 129.86, 113.67, 55.41, 48.23, 38.08, 35.78, 29.85, 24.45, 20.61.

4.6.2. Mixture of *cis*- and *trans*-2,5-di[3-(4-methoxyphenyl)-3-oxopropyl]cyclopentan-1-one (16). Yield 26 mg (8%); R_f (80:20 hexane/ethyl acetate) 0.23; ν_{max} (Nujol) 1724, 1678, 1602, 1510, 1255, 1178, 1028, 837 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.95 (4H, dd, J=6.9, 2.2 Hz), 6.93 (4H, dd, J=8.8, 1.9 Hz), 3.86 (6H, s, OCH_3), 3.02–3.09 (4H, m), 2.05–2.21 (4H, m), 1.70–1.90 (4H, m), 1.44–1.47 (2H, m); δ_C (50 MHz, $CDCl_3$) 221.38 (2CO), 198.12, 198.05, 163.08 (2C), 130.00 (2C), 129.55 (4C), 113.38 (4C), 55.13, 55.08, 48.21, 47.08, 35.38 (2C), 27.44 (2C), 24.57 (2C); LRMS: 408 (M^+, 8), 258 (18), 192 (12), 150 (60), 135 (100), 122 (20), 105 (38), 77 (60), 56 (25%); elemental analysis calcd for $C_{25}H_{28}O_5$: C, 73.51; H, 6.91. Found: C, 73.24; H, 6.90.

4.7. General procedure for the synthesis of symmetrical triketones (4, 13–16) under microwave irradiation

The reaction of Mannich base (1 mmol) with cyclopentanone (1 mmol) in PEG-200 under microwave oven (BPL-Sanyo, India; mono-made, multi-power; power source: 230 V, 50 Hz, microwave frequency: 2450 MHz) at 370 W for 2 min resulted in a mixture of di- and triketones. The mixture was cooled to room temperature, diluted with 20 mL dichloromethane and poured over ice-cooled water, the organic layer was separated and washed again with water (2×30 mL), saturated aqueous sodium chloride (40 mL) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the crude reaction mixture was separated by column chromatography (silica gel 100–200 mesh, hexane/ethyl acetate 98:2 to 85:15) to yield expected diketone as well as 1,5,9-triketone.

4.8. Reaction of *N*,*N*-dimethylaminopropiophenone (1) with cyclopentanone (2)

Following the general procedure described above, the reaction of *N*,*N*-dimethylaminopropiophenone **1** (326 mg, 1.9 mmol) and cyclopentanone **2** (160 mg, 1.9 mmol) furnished a mixture of diketone **3** (286 mg, 72%) and triketone **4** (55 mg, 17%) which were purified by column chromatography.

4.9. Reaction of *N*,*N*-dimethylamino-4-chloropropiophenone (5) with cyclopentanone (2)

Following the general procedure described above, the reaction of *N*,*N*-dimethylamino-4-chloropropiophenone **5** (274 mg, 1.3 mmol) and cyclopentanone **2** (109 mg, 1.3 mmol) furnished a mixture of diketone **9** (198 mg, 61%) and triketone **13** (54 mg, 20%) which were purified by column chromatography.

4.10. Reaction of *N*,*N*-dimethylamino-4-bromopropiophenone (6) with cyclopentanone (2)

Following the general procedure described above, the reaction of *N*,*N*-dimethylamino-4-bromopropiophenone **6** (433 mg, 1.7 mmol) and cyclopentanone **2** (143 mg, 1.7 mmol) furnished a mixture of diketone **10** (210 mg, 42%) and triketone **14** (77 mg, 18%) which were purified by column chromatography.

4.11. Reaction of *N*,*N*-dimethylamino-4-methylpropiophenone (7) with cyclopentanone (2)

Following the general procedure described above, the reaction of *N*,*N*-dimethylamino-4-methylpropiophenone **7** (744 mg, 4.2 mmol) and cyclopentanone **2** (353 mg, 4.2 mmol) furnished a mixture of diketone **11** (564 mg, 63%) and triketone **15** (125 mg, 17%) which were purified by column chromatography.

4.12. Reaction of *N*,*N*-dimethylamino-4-methoxypropiophenone (8) with cyclopentanone (2)

Following the general procedure described above, the reaction of *N*,*N*-dimethylamino-4-methoxypropiophenone **8** (738 mg, 3 mmol) and cyclopentanone **2** (252 mg, 3 mmol) furnished a mixture of diketone **12** (605 mg, 69%) and triketone **16** (109 mg, 15%) which were purified by column chromatography.

4.13. General procedure for the synthesis of unsymmetrical 1,5,9-triketones (20–23)

The substituted 1,5-diketone (1 mmol) was added to the Mannich base (1.1 mmol) and the mixture was heated at 155°C for 30 min. The reaction mixture was then cooled to room temperature and the product was purified by column chromatography (silica 100–200 mesh) using hexane/ethyl acetate (85:15) as eluent to yield the corresponding triketone.

4.14. Reaction of *N*,*N*-dimethylaminopropiophenone (1) with 1-(4-chlorophenyl)-3-(2-oxocyclopentyl)-1-propanone (9)

Following the general procedure described above, the reaction of Mannich base **1** (933 mg, 3.7 mmol) and 1,5-diketone **9** (848 mg, 3.4 mmol) yielded triketone **20** which was purified by column chromatography.

4.14.1. Mixture of *cis*- and *trans*-2-[3-(4-chlorophenyl)-3-oxopropyl]-5-(3-oxo-3-phenylpropyl)cyclopentan-1-one (20). Yield 583 mg (45%); R_f (90:10 hexane/ethyl acetate) 0.24; ν_{max} (Nujol) 2900, 2840, 1720, 1670, 1580, 1445, 1365, 1250, 1200, 1080, 980, 825, 730, 680 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.94 (4H, dd, J=15.0, 8.0 Hz), 7.54–7.57 (4H, m), 7.44–7.47 (4H, m), 7.20–7.44 (6H, m), 3.07–3.14 (8H, m), 2.06–2.22 (8H, m), 1.83–1.87 (8H, m), 1.47 (4H, m); δ_C (100 MHz, $CDCl_3$) 221.57 (2CO), 199.80 (2CO), 198.58 (2CO), 139.48 (2C), 136.78 (2C), 135.08 (2C), 133.06 (2C), 129.50 (4C), 128.90 (4C), 128.59 (4C), 128.06 (4C), 48.44 (2C), 48.31 (2C), 36.00 (4C), 27.84 (4C), 24.59 (4C); LRMS: 382 (M^+, 10), 384 (3), 262 (26), 264 (9), 228 (72), 154 (18), 156 (6), 139 (34), 141 (12), 120 (32), 105 (100), 77 (55), 56 (25%); elemental analysis calcd for $C_{23}H_{23}ClO_3$: C, 72.15; H, 6.05. Found: C, 72.91; H, 6.13.

4.15. Reaction of *N*,*N*-dimethylaminopropiophenone (1) with 1-(4-bromophenyl)-3-(2-oxocyclopentyl)-1-propanone (10)

Following the general procedure described above, the reaction of Mannich base **1** (265 mg, 1.5 mmol) and 1,5-diketone **10** (400 mg, 1.4 mmol) yielded triketone **21** which was purified by column chromatography.

4.15.1. Mixture of *cis*- and *trans*-2-[3-(4-bromophenyl)-3-oxopropyl]-5-(3-oxo-3-phenylpropyl)cyclopentan-1-one (21). Yield 244 mg (42%); R_f (90:10 hexane/ethyl acetate) 0.19; ν_{max} (Nujol) 2900, 2840, 1715, 1670, 1580, 1445, 1370, 1310, 1250, 1200, 1150, 1065, 980, 830, 730, 680 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.96 (4H, d, J=7.8 Hz), 7.82 (4H, d, J=8.3 Hz), 7.54–7.60 (6H, m), 7.43–7.47 (4H, m), 3.04–3.18 (8H, m), 2.03–2.29 (8H, m), 1.78–1.88 (8H, m), 1.45–1.47 (4H, m); δ_C (100 MHz, $CDCl_3$) 221.52 (2CO), 199.75 (2CO), 198.74 (2CO), 136.73 (2C), 135.44 (2C), 133.01 (2C), 131.86 (2C), 129.57 (4C), 128.55 (4C), 128.15 (4C), 128.02 (4C), 48.41 (2C), 48.27 (2C), 35.98 (2C), 35.96 (2C), 27.77 (2C), 27.21 (2C), 24.62 (2C), 24.53 (2C); LRMS: 426 (M^+, 2), 428 (2), 407 (2), 409 (2), 347 (10), 329 (12), 305 (8), 307 (8), 228 (100), 183 (12), 185 (12), 120 (35), 105 (52), 77 (28), 56 (16%); elemental analysis calcd for $C_{23}H_{23}BrO_3$: C, 64.64; H, 5.42. Found: C, 64.37; H, 5.39.

4.16. Reaction of *N*,*N*-dimethylaminopropiophenone (1) with 1-(4-methylphenyl)-3-(2-oxocyclopentyl)-1-propanone (11)

Following the general procedure described above, the reaction of Mannich base **1** (351 mg, 2.0 mmol) and 1,5-diketone **11** (454 mg, 1.8 mmol) yielded triketone **22** which was purified by column chromatography.

4.16.1. Mixture of *cis*- and *trans*-2-[3-(4-methylphenyl)-3-oxopropyl]-5-(3-oxo-3-phenylpropyl)cyclopentan-1-one (22). Yield 257 mg (36%); R_f (90:10 hexane/ethyl acetate) 0.22; ν_{max} (Nujol) 2900, 2840, 1720, 1690, 1670, 1600, 1450, 1370, 1250, 1200, 1180, 1000, 980, 830, 740, 680 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.93 (4H, d, J=10.3 Hz), 7.84 (4H, d, J=10.3 Hz), 7.50 (6H, dt, J=19.8, 9.2 Hz), 7.22 (4H, d, J=10.3 Hz), 3.07 (8H, dd, J=11.5, 3.4 Hz), 2.37 (6H, s, CH_3), 2.07–2.23 (8H, m), 1.71–1.82 (8H, m), 1.41–1.46 (4H, m); δ_C (75 MHz, $CDCl_3$) 221.54 (2CO), 199.80 (2CO), 199.47 (2CO), 143.77 (2C), 136.75 (2C), 134.28 (2C), 133.01 (2C), 129.23 (4C), 128.55 (4C), 128.15 (4C), 128.02 (4C), 48.47 (2C), 47.36 (2C), 36.03 (2C), 35.92 (2C), 27.78 (2C), 27.22 (2C), 24.83 (2C), 24.73 (2C), 21.58 (2C); LRMS: 362 (M^+, 12), 343 (18), 241 (46), 227 (84), 134 (58), 119 (100), 105 (92), 77 (52), 55 (26%); elemental analysis calcd for $C_{24}H_{26}O_3$: C, 79.53; H, 7.23. Found: C, 79.82; H, 7.13.

4.17. Reaction of *N*,*N*-dimethylaminopropiophenone (1) with 1-(4-methoxyphenyl)-3-(2-oxocyclopentyl)-1-propanone (12)

Following the general procedure described above, the reaction of Mannich base **1** (239 mg, 1.4 mmol) and 1,5-diketone **12** (303 mg, 1.2 mmol) yielded triketone **23** which was purified by column chromatography.

4.17.1. Mixture of *cis*- and *trans*-2-[3-(4-methoxyphenyl)-3-oxopropyl]-5-(3-oxo-3-phenylpropyl)cyclopentan-1-one (23). Yield 149 mg (32%); R_f (90:10 hexane/ethyl acetate) 0.21; ν_{max} (Nujol) 2900, 2820, 1700, 1660, 1585, 1440, 1360, 1290, 1240, 1160, 1020, 980, 825, 730, 680 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.96 (4H, d, J=9.3 Hz), 7.93 (4H, d, J=6.8 Hz), 7.55 (2H, t, J=6.8 Hz), 7.45 (4H, t, J=7.8 Hz), 6.92 (4H, d, J=9.3 Hz), 3.85 (6H, s, OCH_3), 3.04–3.14 (8H, m), 2.01–2.30 (8H, m), 1.71–1.87 (8H, m), 1.44–1.47 (4H, m); δ_C (100 MHz, $CDCl_3$) 221.55 (2CO), 199.75 (2CO), 198.37 (2CO), 163.35 (2C), 136.70 (2C), 132.98 (2C), 130.26 (4C), 129.79 (4C), 128.52 (4C), 127.97 (2C), 113.63 (4C), 55.37 (2C), 48.46 (2C), 48.39 (2C), 35.99 (2C), 35.75 (2C), 27.73 (2C), 27.17 (2C), 24.83 (2C), 24.59 (2C); LRMS: 377 (M^+, 12), 359 (10), 257 (24), 227 (90), 150 (58), 135 (100), 120 (42), 105 (90), 77 (60), 55 (24%); elemental analysis calcd for $C_{24}H_{26}O_4$: C, 76.17; H, 6.92. Found: C, 75.94; H, 6.89.

4.18. Reaction of *N*,*N*-dimethylamino-4-chloropropiophenone (5) with 2-(3-oxo-3-phenylpropyl)-1-cyclopentanone (3)

Following the general procedure described above, the reaction of Mannich base **5** (776 mg, 3.7 mmol) and 1,5-diketone **3** (724 mg, 3.4 mmol) yielded triketone **20** (858 mg, 67%).

4.19. Reaction of *N*,*N*-dimethylaminopropiophenone (1) with cycloheptanone (26)

Cycloheptanone **26** (1.53 g, 13.7 mmol) was added to **1** (808 mg, 4.5 mmol) and the mixture was heated at 155°C for 30 min. The cooled reaction mixture was subjected to column chromatography (silica gel 100–200 mesh, hexane/ethyl acetate 98:2 to 85:15) to give two products **27** and **28**.

4.19.1. 2-(3-Oxo-3-phenylpropyl)-1-cycloheptanone (27). Yield 891 mg (80%); R_f (90:10 hexane/ethyl acetate) 0.44; ν_{max} (Neat) 2928, 2857, 1694, 1596, 1450, 1369, 1266, 1212, 1125, 1073, 999, 934, 749, 694 cm^{-1}; δ_H

(300 MHz, $CDCl_3/CCl_4$) 7.94 (2H, d, J=8.1 Hz), 7.41–7.55 (3H, m), 2.85–3.06 (2H, m), 2.54–2.60 (1H, m), 2.40–2.54 (2H, m), 2.00–2.09 (1H, m), 1.59–1.62 (1H, m), 1.20–1.85 (8H, m); δ_C (75 MHz, $CDCl_3/CCl_4$) δ 215.23, 199.49, 136.82, 134.85, 128.46, 128.05, 51.28, 42.76, 36.11, 32.01, 29.40, 28.60, 26.84, 24.31.

4.19.2. Mixture of *cis*- and *trans*-2,7-di-(3-oxo-3-phenylpropyl)-1-cycloheptanone (28). Yield 54 mg (6%); R_f (90:10 hexane/ethyl acetate) 0.23; ν_{max} (Neat) 2928, 2859, 1694, 1593, 1451, 1371, 1268, 1211, 1177, 1073, 934, 749, 693 cm^{-1}; δ_H (300 MHz, $CDCl_3/CCl_4$) 7.85–7.92 (4H, d, J=8.1 Hz), 7.20–7.50 (6H, m), 2.80–2.86 (4H, t, J=9.0 Hz), 2.60–2.73 (2H, m), 1.71–1.98 (8H, m), 1.25–1.31 (4H, m); δ_C (75 MHz, $CDCl_3/CCl_4$) 217.33 (2CO), 199.70 (2CO), 198.97 (2CO), 136.85, 136.79, 132.90 (2C), 128.55, 128.51, 128.12, 128.01, 50.98, 50.62, 36.53, 36.07, 32.44, 31.51, 28.55 (2C), 26.79, 26.52; LRMS: 376 (M^+, 6), 358 (22), 257 (24), 133 (14), 120 (26), 105 (100), 77 (42), 56 (18%); elemental analysis calcd for $C_{25}H_{28}O_3$: C, 79.75; H, 7.50. Found: C, 79.69; H, 7.42.

4.20. Reaction of phenyl vinyl ketone 17 with cyclopentanone 2 under basic conditions

To a stirred suspension of freshly activated $Ba(OH)_2$ (heated to 100°C for 2 h and cooled in a desiccator, 343 mg, 2 mmol) in 7 mL of absolute alcohol, cyclopentanone **2** (924 mg, 11 mmol) was added drop wise at room temperature. After 10 min, phenyl vinyl ketone[42] **17** (1.32 g, 10 mmol) was added drop wise to the reaction mixture, which was then stirred for an additional 12 h at room temperature. TLC of the reaction mixture revealed the presence of two products. The reaction mixture was diluted with 40 mL dichloromethane and poured over ice-cooled water, the organic layer was separated and washed again with water (2×20 mL), saturated aqueous sodium chloride (2×20 mL) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure. The crude reaction mixture was separated by column chromatography (silica gel 100–200 mesh, hexane/ethyl acetate 99:1 to 90:10) to give **3** and **29**.

4.20.1. 7-Benzoyl-8-hydroxy-8-phenylspiro[4.5]decan-1-one (29). Yield 122 mg (7%); mp 113–114°C; R_f (90:10 hexane/ethyl acetate) 0.42; ν_{max} (KBr) 3460, 2800, 2600, 1720, 1660, 1580, 1450, 1390, 1270, 1230, 1050, 1000 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.86 (2H, dt, J=8.5, 2.0 Hz), 7.52 (1H, m), 7.49 (2H, m), 7.39 (2H, tt, J=8.5, 1.5 Hz), 7.20 (2H, tt, J=7.0, 2.0 Hz), 7.08 (1H, tt, J=7.0, 1.5 Hz), 5.13 (1H, dd, J=9.0, 3.5 Hz), 5.06 (1H, s), 2.43–2.50 (1H, m), 2.30 (1H, dt, J=8.5, 19.0 Hz), 2.07 (1H, dd, J=13.5, 4.5 Hz), 2.03 (1H, t, J=13.5 Hz), 2.00–2.01 (1H, m), 1.88–1.99 (2H, m), 1.86–1.88 (1H, m), 1.79–1.82 (1H, m), 1.75–1.78 (1H, m), 1.74–1.75 (1H, m), 1.69 (1H, dd, J=13.5, 5.0 Hz); δ_C (125 MHz, $CDCl_3$) 223.12, 206.43, 147.84, 135.76, 133.62, 128.69, 128.40, 128.05, 126.45, 124.53, 74.12, 46.23, 45.48, 39.33, 38.14, 36.04, 32.97, 28.16, 18.33; CIMS 349 (M+H, 100), 332 (15), 331 (61%); elemental analysis calcd for $C_{23}H_{24}O_3$: C, 79.28; H, 6.94. Found: C, 79.51; H, 6.83.

4.21. Reductive amination–cyclization of mixture of *cis*- and *trans*-2,5-di-(3-oxo-3-phenylpropyl)-1-cyclopentanone (4)

A mixture of *cis*- and *trans*-2,5-di-(3-oxo-3-phenylpropyl)-1-cyclopentanone **4** (301 mg, 0.9 mmol), ammonium formate (542 mg, 8.6 mmol) and PEG-200 were taken in a 10 mL conical flask and the resulting mixture was irradiated in a domestic microwave oven (BPL-Sanyo, India; monomade, multi-power; power source: 230 V, 50 Hz, microwave frequency: 2450 MHz) at 370 W for 1 min. The mixture was cooled to room temperature, diluted with 30 mL dichloromethane and poured over ice-cooled water, the organic layer was separated and washed again with water (2×50 mL), saturated aqueous sodium chloride (50 mL) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the crude reaction mixture was separated by column chromatography (silica gel 100–200 mesh, hexane/dichloromethane 95:5 to 90:10) to give **30** and **31**.

4.21.1. *cis*,*cis*-3,5-Diphenylperhydrocyclopenta[*ij*]quinolizine (30). Yield 160 mg (58%); mp 147°C; R_f (95:5 hexane/dichloromethane) 0.41; ν_{max} (KBr) 2939, 2804, 1488, 1451, 1119, 1068, 757, 699 cm^{-1}; δ_H (300 MHz, $CDCl_3/CCl_4$) 6.78 (10H, br s, C_6H_5), 3.28 (2H, t, J=5.1 Hz), 2.90 (1H, t, J=4.2 Hz), 1.93–2.25 (2H, m), 1.87–1.91 (3H, m), 1.50–1.85 (9H, m); δ_C (75 MHz, $CDCl_3/CCl_4$) 145.22, 128.69, 126.74, 125.58, 67.69, 64.00, 40.91, 30.71, 30.10, 24.03; LRMS: 317 (M^+, 38), 315 (28), 240 (100), 117 (12), 105 (14), 91 (12), 77 (14%); HRMS m/z (M^+) for $C_{23}H_{27}N$ calcd 317.2143 obsd. 317.2148.

4.21.2. *trans*,*trans*-3,5-Diphenylperhydrocyclopenta[*ij*]-quinolizine (31). Yield 79 mg (29%); R_f (95:5 hexane/dichloromethane) 0.11; ν_{max} (Neat) 2932, 2864, 1491, 1451, 1126, 759, 699 cm^{-1}; δ_H (300 MHz, $CDCl_3/CCl_4$) 7.35 (2H, d, J=7.8 Hz), 7.18 (4H, t, J=7.8 Hz), 7.09 (4H, t, J=7.8 Hz), 3.92 (2H, t, J=6.2 Hz), 3.40 (1H, t, J=8.1 Hz), 1.94–2.09 (4H, m), 1.31–1.91 (10H, m); δ_C (75 MHz, $CDCl_3/CCl_4$) 145.96, 127.94, 127.65, 126.27, 60.83, 55.50, 38.44, 30.60, 29.20, 26.68; LRMS: 317 (12), 240 (100), 117 (27), 105 (12), 91 (15), 77 (21%); HRMS m/z (M^+) for $C_{23}H_{27}N$ calcd 317.2143 obsd. 317.2141.

4.22. Reductive amination–cyclization of *trans*-2,5-di-(3-oxo-3-phenylpropyl)-1-cyclopentanone (4a)

Following the general procedure described above, *trans*-2,5-di-(3-oxo-3-phenylpropyl)-1-cyclopentanone **4a** (210 mg, 0.6 mmol) and ammonium formate (378 mg, 6 mmol) furnished a mixture of *cis*,*cis*-**30** and *trans*,*trans*-perhydroquinolizine **31** in the ratio of 2:1, which were separated and purified by column chromatography (silica gel 100–200 mesh, hexane/dichloromethane 95:5 to 90:10).

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