

A direct, efficient synthesis of unsymmetrically substituted bis(arylidene)alkanones†

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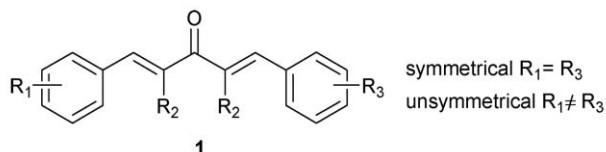
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A direct method to unsymmetrically substituted bis(arylidene)alkanones by sequential, selective condensation reactions is reported. Analytically pure compounds were obtained in high yield using atom-economical reactions and without the need for purification of the final products. Although a two-step process could be conducted in one pot by three different methods, recrystallisation was required.

Introduction

Bis(arylidene)alkanones **1** are useful chemical building blocks for the synthesis of biologically important heterocycles such as dihydropyrazoles,¹ substituted pyridines or pyran derivatives,² as well as for mixed systems containing pyrroles in combination with pyrazolines and isoxazolines.³ We have employed this motif in the construction of dienone macrocycles that may find uses themselves or that can be readily converted to new families such as Horning-crowns by simple chemical transformations.⁴



In addition, some examples of **1** have activity as enzyme inhibitors,⁵ cytotoxic agents,⁶ blood coagulators,⁷ antitumour⁸ and anticancer agents.⁹ Remarkably, most of the compounds tested in this regard have been symmetrical bis(arylidene)alkanones **1**. Few unsymmetrically substituted ($R_1 \neq R_3$) compounds have been described, presumably owing to difficulties with preparation. A direct, energy efficient, high yielding route to unsymmetrical bis(arylidene)alkanones, amenable to applications in combinatorial library synthesis, would provide ready access to libraries of such compounds.

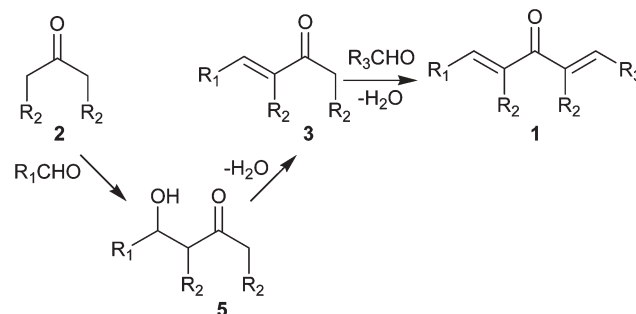
As α,β -unsaturated ketones are readily prepared by Claisen-Schmidt condensation of aldehydes and ketones, it is tempting to suggest that careful control of stoichiometry might allow preparation of unsymmetrical examples of **1**, using sequential

aldol condensation reactions with different aldehydes, Scheme 1. Unfortunately, even with a large molar excess of the ketone **2**, the intermediate α,β -unsaturated ketone **3**, preferentially reacts with a second mole of aldehyde providing symmetrical **1**.¹⁰

The α,β -unsaturated ketone **3** may be prepared by dehydration of the aldol addition product **5**,¹¹ which can be synthesised by a number of routes including a Mukaiyama type reaction utilising a silyl enol ether of the ketone,¹² with organocatalysts such as proline or 5,5-dimethyl thiazolidinium-4-carboxylate¹³ as well as with aqueous base.¹⁴ The first of these routes yields a stoichiometric quantity of waste, significantly lowering atom economy and the last is not always predictable or high yielding. Preformed enamines of ketones with cyclic amines have been used to form α,β -unsaturated ketones **3** in preference to symmetrical **1**, yielding a stoichiometric quantity of amine as waste.¹⁵

We have recently demonstrated that α,β -unsaturated ketones **3** are readily accessible by using the 'distillable ionic medium' DIMCARB.¹⁶ We chose this as the starting point for a simple, direct, low-waste route to a range of unsymmetrically substituted examples of **1**.

DIMCARB is the product of reaction between the gases carbon dioxide and dimethylamine, which react rapidly (and exothermically) yielding a free-flowing liquid: a mixture of *N,N*-dimethylcarbamic acid and the salt, *N,N*-dimethylammonium *N',N'*-dimethylcarbamate, Scheme 2.¹⁷ DIMCARB may be used as both solvent and catalyst, and is comparably similar to store and handle as organic solvents such as acetone. Herein



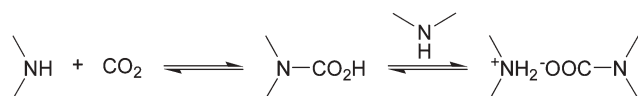
Scheme 1

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† Electronic supplementary information (ESI) available: NMR spectra for selected compounds **1a–d**. Crystal structure data for compounds **1n**, **1o**, **1p** (CCDC 605464–605466), **8a**, **8b** and **9** (CCDC 605784–605786). See DOI: 10.1039/b606042k



Scheme 2

is reported a simple synthesis of unsymmetrically substituted bis(arylidene)alkanones **1** by condensation of **3** (prepared in DIMCARB) with a range of aryl aldehydes. Analytically pure products are provided directly in good to excellent yields, and DIMCARB may be readily recovered and recycled in a process analogous to distillation.¹⁸ Examination of reaction by-products obtained under certain conditions sheds light on the mechanism of action of DIMCARB.

Results and discussion

Pure samples of α,β -unsaturated ketones **3a–d** (Scheme 4) were prepared by DIMCARB-mediated reactions of *p*-anisaldehyde or *p*-diethylaminobenzaldehyde with cyclohexanone, cyclopentanone or acetone as previously described.¹⁶ These were, in turn, reacted with a second arylaldehyde in a classical Claisen-Schmidt type reaction to provide analytically pure **1a–w** directly in good to excellent yields (see Table 1). Claisen-Schmidt condensation is particularly favoured as it is predictable, generally proceeds to completion at ambient temperature, is simple to execute and yields only water as a

by-product. Thus the overall reaction is atom economical, energy efficient and low in hazard, with little attendant waste.

To develop convenient means for condensation and product isolation, Amberlite[®] IRA-400(OH) resin and (*n*-Bu)₄NOH (as well as more common NaOH and KOH) were explored as catalytic bases. Use of the resin allows for separation of soluble products by filtration and the converse applies with the soluble base and poorly soluble **1**. The latter approach proved to be more effective for recovering pure products directly as crystallisation of poorly soluble **1** (compared with **2**) from solution is a purification step. Occasionally, the use of less than stoichiometric quantities of base at room temperature afforded minor amounts of aldol adducts among products **1**. Microwave heating was useful in shortening reaction times and lowered the requirements of base to catalytic quantities.¹⁹ A diverse range of non-enolisable, mostly aromatic aldehydes were condensed with **3** in this manner, yielding arylidenes containing carbocycles, furfural and pyridyl groups. Cinnamaldehydes were similarly employed to afford 2-arylidene-5-(3-phenylallylidene)cyclopentanones.

Previously, in the DIMCARB-mediated reaction of aldehyde and ketone to yield **3**, the intervention of an enamine, formed by reaction of the ketone with *N,N*-dimethylamine, was postulated, but not demonstrated.¹⁶ Here also, no enamine formation was detected spectroscopically. Nonetheless, in some cases the formation of by-products indicated that enamines were involved. In the reaction between benzaldehyde

Table 1 Summary of reaction conditions and isolated yields of unsymmetrical bis(arylidene)alkanones **1**, Scheme 4

Ketone	Aldehyde		Catalyst	Mol. eq. cat.	<i>T</i> /°C	<i>t</i> /h	Product	Yield (%)
	R ₃	R ₄						
3a	H	H	NaOH	1.0	22	3	1a	82
3a	furfural		(<i>n</i> -Bu) ₄ NOH	0.1	78 ^a	25 min	1a	87
			NaOH	1.0	22	2	1b	90
			Amberlite	1.7	78	1	1b	92
			(<i>n</i> -Bu) ₄ NOH	0.1	78 ^a	10 min	1b	92
3a	1-naphthaldehyde		NaOH	1.0	22	2	1c	87
			NaOH	0.2	78 ^a	30 min	1c	80
3a	3-NO ₂	H	NaOH	1.0	22	6	1d	91
			(<i>n</i> -Bu) ₄ NOH	0.1	78 ^a	10 min	1d	91
3a	4-Br	H	NaOH	1.0	22	4	1e	88
			(<i>n</i> -Bu) ₄ NOH	0.1	78 ^a	10 min	1e	88
3a	pyridine-3-carbaldehyde		NaOH	1.0	22	2	1f	77
			(<i>n</i> -Bu) ₄ NOH	0.2	22	30 min	1f	82
3a	2-MeO	5-Br	NaOH	1.0	22	24	1g	81
			(<i>n</i> -Bu) ₄ NOH	0.2	22 (78) ^b	30 (+10) min ^b	1g	90
3a	2-MeO	H	NaOH	1.0	22	3	1h	86
			(<i>n</i> -Bu) ₄ NOH	0.1	78 ^a	10 min	1h	80
3a	3-MeO	4-MeO	Amberlite	1.14	78	3	1i	97
3a	4-Me	H	Amberlite	0.7	78	3	1j	97
3a	cinnamaldehyde		Amberlite	0.6	78	1.5	1k	73
3a	2-nitrocinnamaldehyde		(<i>n</i> -Bu) ₄ NOH	1.0	22	3	1l	74
3b	4-Br	H	(<i>n</i> -Bu) ₄ NOH	0.16	22	13	1m	87
3b	3-MeO	4-EtO	(<i>n</i> -Bu) ₄ NOH	0.16	22	10	1n	78
3b	4-NO ₂	H	(<i>n</i> -Bu) ₄ NOH	0.16	22	10 min	1o	97
3b	6-bromopyridine-2-carbaldehyde		(<i>n</i> -Bu) ₄ NOH	0.16	22	1	1p	78
3b	3-NO ₂	H	(<i>n</i> -Bu) ₄ NOH	0.16	22	15	1q	85
3b	furfural		(<i>n</i> -Bu) ₄ NOH	0.16	22	10 min	1r	76
3b	pyridine-3-carbaldehyde		(<i>n</i> -Bu) ₄ NOH	0.16	22	10 min	1s	79
3c	4-NO ₂	H	NaOH	0.2	22 (78) ^b	1 (+10 min) ^b	1t	90
3c	furfural		NaOH	0.2	22 (78) ^b	1.25 (+10 min) ^b	1u	92
3d	4-Br	H	KOH	0.2	22 (78) ^b	10 (+10 min) ^b	1v	83
3d	4-NO ₂	H	KOH	0.2	22 (78) ^b	10 (+10 min) ^b	1w	75

^a microwave heating ^b +10 min at reflux.

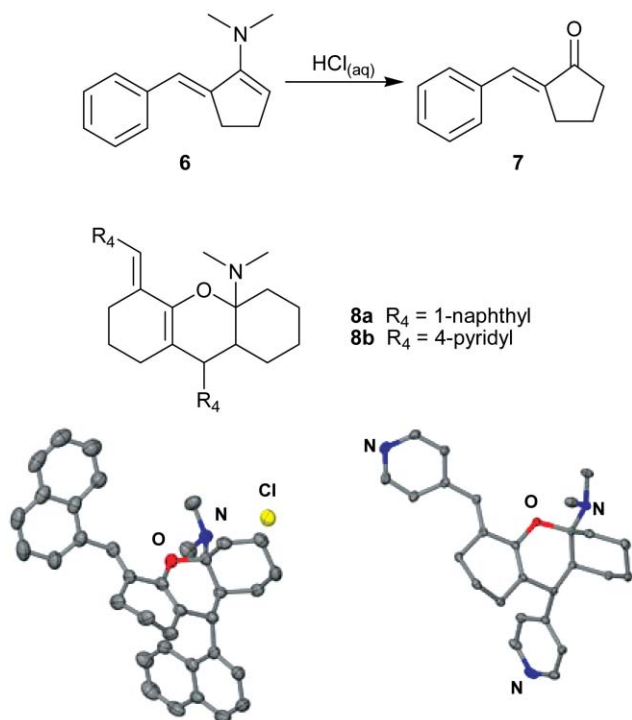
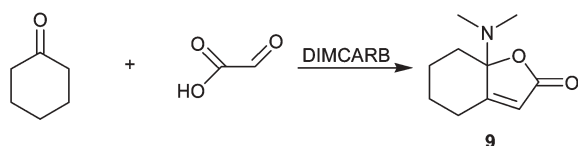


Fig. 1 Molecular diagrams from single crystal structures of **8a** (as the HCl salt) (top) and **8b**. Ellipsoids are at the 50% probability level and data were collected at 293 K and 123 K for **8a**·HCl and **8b** respectively.



Scheme 3

and cyclopentanone in DIMCARB–diethyl ether (1 : 1), 5-benzylidene-1-(*N,N*-dimethylamino)cyclopent-1-ene **6** was detected. This product could be hydrolysed to the α,β -unsaturated ketone **7** by treatment with dilute aqueous acid (the method of choice for clean workup of reaction mixtures from DIMCARB). Conversely, treatment of **7** with DIMCARB did not yield appreciable quantities of **6**, indicating participation of the enamine of cyclopentanone in the reaction rather than through attack on **7**.

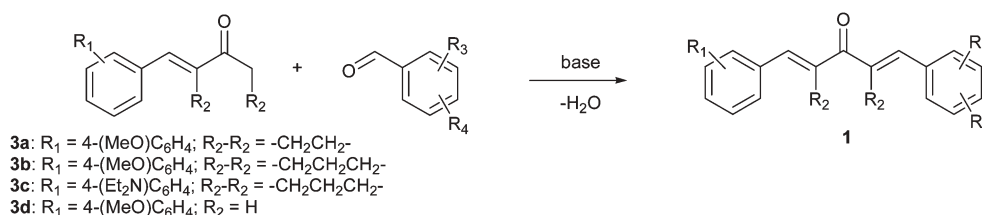
Myers *et al.* have previously discussed the importance of the rate of hydrolysis of analogues of **7** in controlling further reaction.²⁰ In two instances here, products analogous to these xanthenyl derivatives were isolated as the major components

of DIMCARB-mediated reactions. They involved 1-naphthaldehyde and cyclohexanone to afford **8a**, and isonicotinaldehyde and cyclohexanone to give **8b**. Single crystal structures of these products were obtained (see Fig. 1). Further evidence for the presence of enamine intermediates formed between the ketone and dimethylamine was obtained through the isolation of the stable lactone **9** in the DIMCARB mediated reaction of cyclohexanone and glyoxylic acid, Scheme 3 (again verified by single crystal structure analysis).

The work described above established a convenient, direct and high-yielding method to unsymmetrically substituted bis(arylidene)alkanones in two steps. Attention was next directed toward obtaining the products in one pot, without isolation of crude intermediates **3**. Three different approaches were pursued. *p*-Anisaldehyde and cyclopentanone were allowed to react in DIMCARB at ambient temperature for 4.75 h in each case, this was followed by the introduction of *m*-nitrobenzaldehyde under the conditions outlined below. In the first case, the second aldehyde was added in DIMCARB and the temperature elevated to 50 °C and held for 12 h. This process afforded a crude mixture of **1d**, accompanied by symmetrical **1** [(*R*₁ = *R*₃ = *p*-MeO) and (*R*₁ = *R*₃ = *m*-NO₂)]. Recrystallisation from toluene afforded the desired pure product **1d** in 61% yield. In the second case, in a procedure that was repeated once, EtOH was added to the crude reaction mixture, which was heated to 60 °C *in vacuo*. These manipulations concentrated the crude intermediate **3a** in EtOH and were followed by addition of NaOH and *m*-nitrobenzaldehyde. During the course of reaction at room temperature for 3 h, the crude product **1d** (in greater than 90% purity) crystallised out and was purified by recrystallisation to afford an 80% yield. In the final variant, the DIMCARB was removed by heating *in vacuo* at 60 °C, before the addition of EtOH, NaOH and *m*-nitrobenzaldehyde. The outcome was comparable with that of the second procedure outlined immediately above. These experiments confirmed that the sequential process could be conducted in one pot and in good yields, but necessitated recrystallisation of the product **1**.

Conclusions

A direct, two-step route to unsymmetrically substituted bis(arylidene)alkanones by DIMCARB-mediated condensation of aldehyde and ketone to form a mono(arylidene)alkanone (by *in situ* formation and reaction of an enamine) followed by a Claisen-Schmidt condensation is reported. Thus, eighteen new products were prepared using three simple symmetrical ketones, illustrating the scope of this procedure. Pure crystalline products were isolated directly



Scheme 4

from the reaction mixture. An example of the two step process was conducted successfully in one pot, by three different methods.

Experimental

Most reagents were used as obtained from suppliers (97% purity or better). Benzaldehyde, cinnamaldehyde and *p*-tolualdehyde were dissolved in ether, washed with aqueous NaOH solution to remove any carboxylic acid formed during storage, dried with MgSO₄, filtered and distilled at reduced pressure.

Elemental analyses were performed by Chemical & Micro Analytical Services Pty. Ltd., Victoria, Australia or by the University of Otago, Dunedin, New Zealand. ¹H and ¹³C NMR spectra were recorded on a Bruker AC-200 spectrometer, DPX-300 spectrometer or Bruker Avance DRX 400 spectrometer in CDCl₃ using TMS as the internal standard. Infrared (IR) spectra were recorded on a Perkin-Elmer 1600 Series Fourier Transform spectrophotometer (cm⁻¹ scale) and refer to KBr pellets (KBr) or nujol mulls (nujol). High-resolution mass spectra (HRMS) were recorded on a Bruker BioApex 47e FTMS fitted with an Analytical electrospray source, using NaI for accurate mass calibration (accuracy ±3 ppm). Low-resolution mass spectra were recorded on a Micromass Platform II (now Waters) QMS quadrupole fitted with Waters Alliance autosampler. Melting points were recorded on a Stuart Scientific melting point apparatus, SMP3. UV-vis spectra were recorded using a Varian Cary 100 UV-visible spectrophotometer as solutions in ethanol (96%). Microwave heating was performed in a Milestone HPR3600 reactor equipped with a thermocouple.

Crystals suitable for single crystal X-ray diffraction experiments were grown by slow evaporation of solutions in suitable solvents (usually hexane or hexane/MeOH) and data were collected on an Enraf-Nonius Kappa CCD or Bruker Kappa Apex CCD diffractometer at 123 K (or 293 K for **8a**) using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å, φ and ω scans in 1° or 0.5° steps as appropriate). Structures were solved by direct methods using the program SHELXS-97²¹ and refined by full matrix least squares refinement on *F*² using the programs SHELXL-97²² and XSeed.²³ Non-hydrogen atoms were refined anisotropically and hydrogen atoms inserted in geometrically determined positions with temperature factors fixed at 1.2 that of the parent atom.

Synthesis of 3b and 3c

3b; 1-(4-Methoxybenzylidene)acetone. *p*-Anisaldehyde (1.36 g, 10 mmol) and acetone (0.70 g, 12.0 mmol) were added to DIMCARB (5 mL) at ambient temperature with stirring. After reaction at room temperature (22 °C) for 22 h, the solvent was removed *in vacuo* providing an oil, which yielded, post flash chromatography on silica with Et₂O/hexane (70 : 30) eluent, 1-(4-methoxybenzylidene)acetone (1.20 g, 70%) as a yellow solid; mp 70.7–73.6 °C (lit.²⁴ mp 72–72.5 °C). δ_H(300 MHz, CDCl₃, Me₄Si) 2.36 (3H, s, Me), 3.85 (3H, s, OMe), 6.60 (1H, d, *J* 16.2, CH=C), 6.92 (2H, d, *J* 8.9, Ar), 7.48 (1H, d, *J* 16.5, CH=C), 7.50 (2H, d, *J* 8.5, Ar).

3c; 2-(4-Diethylaminobenzylidene)cyclohexanone. 4-Diethylaminobenzaldehyde (1.77 g, 10.0 mmol) and cyclohexanone (0.98 g, 10.0 mmol) were added to DIMCARB (5 mL) at ambient temperature with stirring. No gas was evolved. After reaction at room temperature (22 °C) for 22 h, the solvent was removed *in vacuo* providing a dark orange oil, which yielded, post flash chromatography on silica with hexane eluent, 2-(4-diethylaminobenzylidene)cyclohexanone (1.74 g, 68%) as a yellow solid; mp 89.0–90.5 °C (Found: C, 79.50; H, 8.99; N, 5.44. C₁₇H₂₃NO requires C, 79.33; H, 9.01; N, 5.44%); λ_{max}(EtOH)/nm 389, 259 (ε/dm³ mol⁻¹ cm⁻¹ 13262, 7347); ν_{max}(KBr)/cm⁻¹ 2967 w, 2937 w, 2902 w, 2806 w, 1662 m, 1612 m, 1570 s, 1556 s, 1518 s, 1410 m, 1312 m, 1275 m, 1192 s, 1143 m, 1068 w; δ_H(200 MHz, CDCl₃, Me₄Si) 1.19 (6H, t, *J* 7.1, CH₃), 1.72–1.96 (4H, m, CH₂CH₂CH₂CH₂), 2.50 (2H, t, *J* 6.6, C=OCH₂), 2.87 (2H, td, *J* 6.3, 1.7, C=CCH₂), 3.39 (4H, q, *J* 7.1, NCH₂), 6.65 (2H, d, *J* 9.0, Ar), 7.39 (2H, d, *J* 8.9, Ar), 7.53 (1H, t, *J* 1.9, CH=C); δ_C(50 MHz, CDCl₃, Me₄Si) 12.8 (2C), 23.5, 24.1, 29.3, 40.2, 44.6 (2C), 111.2 (2C), 122.9, 131.3, 133.2 (2C), 137.6, 148.3, 201.3; *m/z* (ESI) 258.2 ([M + H]⁺ C₁₇H₂₄NO⁺ requires 258.2).

Representative procedure for NaOH method at 22 °C

1t; 2-(4-Diethylaminobenzylidene)-6-(4-nitrobenzylidene)cyclohexanone. To a solution of 2-(4-diethylaminobenzylidene)cyclohexanone (0.321 g, 1.25 mmol) and 4-nitrobenzaldehyde (0.189 g, 1.25 mmol) in 7.5 mL ethanol (96%) was added 2.5% (w/v) aqueous NaOH solution (0.400 mL, 0.25 mmol). The mixture was stirred at room temperature for 1 h, during which time a precipitate formed. If required, the reaction mixture was heated to reflux for 10 min, cooled and the crystalline product recovered by filtration, yielding 2-(4-diethylamino-benzylidene)-6-(4-nitrobenzaldehyde)cyclohexanone (0.424 g, 90%) as a deep red solid, mp 184.0–186.5 °C (Found: C, 73.73; H, 6.77; N, 7.05. C₂₄H₂₆N₂O₃ requires C, 73.82; H, 6.71; N, 7.17%); λ_{max}(EtOH)/nm 219, 323, 460 (ε/dm³ mol⁻¹ cm⁻¹ 15521, 19914, 23526); ν_{max}(KBr)/cm⁻¹ 2974 w, 2927 w, 2862 w, 1654 m, 1601 m, 1589 m, 1546 m, 1520 s, 1509 s, 1340 s, 1275 m, 1197 w, 1167 m, 1154 s, 1133 m, 1078 w, 1012 w, 966 w; δ_H(200 MHz, CDCl₃, Me₄Si) 1.20 (6H, t, *J* 7.1, CH₂CH₃), 1.83 (2H, app p, *J* 6.2, CH₂CH₂CH₂), 2.87 (2H, t, *J* 5.8, CH₂CH₂CH₂), 2.97 (2H, t, *J* 6.0, CH₂CH₂CH₂), 3.41 (4H, q, *J* 7.1, NCH₂), 6.68 (2H, d, *J* 8.8, Ar), 7.45 (2H, d, *J* 8.7, Ar), 7.56 (2H, d, *J* 8.9, Ar), 7.76 (1H, s, CH=C), 7.80 (1H, s, CH=C), 8.29 (2H, d, *J* 8.8, Ar); δ_C(50 MHz, CDCl₃, Me₄Si) 12.8 (2C), 23.1, 28.6, 29.0, 44.7 (2C), 111.3 (2C), 123.0, 123.8 (2C), 130.6, 130.8 (2C), 132.7, 133.6 (2C), 140.0, 140.2, 143.3, 147.2, 148.7, 189.4; *m/z* (ESI) 391.2 ([M + H]⁺ C₂₄H₂₇N₂O₃⁺ requires 391.2).

Representative procedure for Amberlite resin method

1i; 2-(3,4-Dimethoxybenzylidene)-5-(4-methoxybenzylidene)cyclopentanone. To a solution of 2-(4-methoxybenzylidene)cyclopentanone (0.505 g, 2.50 mmol) and 3,4-dimethoxybenzaldehyde (0.415 g, 2.50 mmol) in 20 mL absolute ethanol was added Amberlite-400(OH) resin (1.0 g, 2.85 mmol). The mixture was stirred and refluxed for 3 h. During this period a yellow precipitate formed and post cooling the product and resin were collected by filtration.

Product was recovered from the Amberlite resin by dissolution in hot toluene and solvent was removed *in vacuo* to afford pure 2-(3,4-dimethoxybenzylidene)-5-(4-methoxybenzylidene)cyclopentanone (0.85 g, 97%) as a yellow solid, mp 180–182 °C (lit.²⁵ mp 182–183 °C) (Found: C, 75.30; H, 6.30. C₂₂H₂₂O₄ requires C, 75.41; H, 6.33%); $\lambda_{\max}(\text{EtOH})/\text{nm}$ 245, 397 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 8661, 18197); $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 2913 w, 1686 w, 1619 m, 1600 s, 1560 m, 1509 s, 1421 w, 1310 w, 1256 s, 1171 s, 1117 w, 1032 w, 985 w, 816 w; $\delta_{\text{H}}(300 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 3.10 (4H, m, CH₂CH₂), 3.86 (3H, s, OMe), 3.93 (6H, m, OMe), 6.94 (2H, d, *J* 8.3, Ar), 6.98 (1H, s, Ar), 7.13 (1H, d, *J* 2.0, Ar), 7.23 (1H, d, *J* 8.4, Ar), 7.54–7.58 (4H, m, CH=C, Ar); $\delta_{\text{C}}(75 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 26.7 (2 \times), 55.6, 56.2, 56.2, 111.5, 113.8, 114.6 (2C), 124.7, 129.0, 129.3, 132.7 (2C), 133.5, 133.8, 135.4, 135.8, 149.2, 150.3, 160.6; 196.1; *m/z* (ESI) 351.4 ([M + H]⁺ C₂₂H₂₃O₄⁺ requires 351.2).

Representative procedure for (n-Bu)₄NOH at 22 °C

1f; 2-(4-Methoxybenzylidene)-5-(pyridin-3-ylmethylidene)cyclopentanone. To a solution of 2-(4-methoxybenzylidene)cyclopentanone (0.253 g, 1.25 mmol) and 3-pyridylcarboxaldehyde (0.134 g, 1.25 mmol) in 10.0 mL ethanol (96%) was added 20% (w/v) (n-Bu)₄NOH in water (0.162 mL, 0.125 mmol). The mixture was stirred at room temperature (22 °C) for 30 min, during which time a precipitate formed.

Filtration of the precipitate afforded pure (*E,E*)-2-(4-methoxybenzylidene)-5-(pyridin-3-ylmethylidene)cyclopentanone (0.424 g, 90%) as a yellow solid; mp 162.0–163.5 °C (Found: C, 78.40; H, 5.91; N, 4.84. C₁₉H₁₇NO₂ requires C, 78.33; H, 5.88; N, 4.81%); $\lambda_{\max}(\text{EtOH})/\text{nm}$ 235, 380 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 15746, 30442); $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 3054 w, 3023 w, 2970 w, 2840 w, 1684 s, 1628 m, 1610 s, 1591 s, 1566 s, 1560 s, 1546 w, 1512 s, 1466 w, 1418 m, 1313 w, 1418 m, 1313 w, 1265 s, 1202 s, 1182 s, 1116 w, 1027 m; $\delta_{\text{H}}(400 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 3.09 (4H, s, CH₂CH₂), 3.85 (3H, s, OMe), 6.96 (2H, d, *J* 8.8, Ar), 7.35 (1H, ddd, *J* 7.9, 4.8, 0.4, Ar), 7.50 (1H, s, CH=C), 7.56 (2H, d, *J* 8.8, Ar), 7.58 (1H, s, CH=C), 7.85 (1H, td, *J* 8.0, 1.8, Ar), 8.57 (1H, dd, *J* 4.8, 1.6, Ar), 8.83 (1H, d, *J* 2.0, Ar); $\delta_{\text{C}}(100 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 26.6, 26.7, 55.6, 114.6 (2C), 123.7, 128.6, 129.4, 132.0, 132.9 (2C), 134.5, 134.8, 137.0, 140.0, 149.7, 151.8, 161.1, 195.8; *m/z* (ESI) 292.2 ([M + H]⁺ C₁₉H₁₈NO₂⁺ requires 292.1).

Representative procedure for reaction under MW heating

1d; 2-(4-Methoxybenzylidene)-5-(3-nitrobenzylidene)cyclopentanone. To a solution of 2-(4-methoxybenzylidene)cyclopentanone (0.253 g, 1.25 mmol) and 3-nitrobenzaldehyde (0.189 g, 1.25 mmol) in 10 mL ethanol (96%) was added 20% (w/v) (n-Bu)₄NOH in water (0.162 mL, 0.125 mmol). The mixture was heated steadily for 3 min from 22 to 78 °C, using MW energy, and maintained at 78 °C for 10 min. Upon cooling, a precipitate formed, which was recovered by filtration to afford pure 2-(4-methoxybenzylidene)-5-(3-nitrobenzylidene)cyclopentanone (0.382 g, 91%) as a yellow solid, mp 215.5–216.5 °C (Found: C, 71.37; H, 5.00; N, 4.17. C₂₀H₁₇NO₄ requires C, 71.63; H, 5.11; 4.18%); $\lambda_{\max}(\text{EtOH})/\text{nm}$ 380 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 28840); $\nu_{\max}(\text{nujol})/\text{cm}^{-1}$ 1672 w, 1589 s, 1517 s, 1344 m, 1244 s, 1178 s, 1028 w; $\delta_{\text{H}}(200 \text{ MHz},$

$\text{CDCl}_3, \text{Me}_4\text{Si})$ 3.15 (4H, m, CH₂CH₂), 3.87 (3H, s, OMe), 6.98 (2H, d, *J* 8.8, Ar), 7.57–7.63 (5H, m, CH=C, Ar), 7.86 (1H, d, *J* 7.8, CH=C), 8.21 (1H, dd, *J* 8.04, 1.23, Ar), 8.45 (1H, s, Ar); $\delta_{\text{C}}(50 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 26.6, 26.7, 55.6, 114.7 (2C), 123.7, 124.5, 128.5, 130.0, 130.3, 133.1 (2C), 134.4, 135.3, 136.6, 137.8, 140.7, 148.7, 161.2, 195.9; *m/z* (ESI) 336.1240 ([M + H]⁺ C₂₀H₁₈NO₄⁺ requires 336.1236).

Characterisation of compounds 1a–c, 1e, 1g–h, 1j–s & 1u–w.

1a; 2-(4-Methoxybenzylidene)-5-benzylidenecyclopentanone.

Yellow solid (0.440 g, 87%); mp 170–171 °C (lit.²⁵ 171–172 °C) (Found: C, 82.49; H, 6.37. C₂₀H₁₈O₂ requires C, 82.73; H, 6.25%); $\lambda_{\max}(\text{EtOH})/\text{nm}$ 377 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 24498); $\nu_{\max}(\text{nujol})/\text{cm}^{-1}$ 1689 w, 1626 w, 1589 s, 1510 m, 1377 s, 1317 w, 1256 m, 1172 m, 1127 w, 1035 w; $\delta_{\text{H}}(200 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 3.08 (4H, m, CH₂CH₂), 3.85 (3H, s, OMe), 6.95 (2H, d, *J* 8.8, Ar), 7.35–7.47 (3H, m, Ar), 7.53–7.58 (6H, m, CH=C, Ar). $\delta_{\text{C}}(50 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 26.7 (2 \times), 55.6, 114.5 (2C), 128.9, 128.9 (2C), 129.4, 130.9 (2C), 132.8 (2C), 133.5, 134.0, 135.2, 136.2, 137.9, 160.9, 196.5; *m/z* (ESI) 291.1385 ([M + H]⁺ C₂₀H₁₉O₂⁺ requires 291.1380).

1b; 2-Furfurylidene-5-(4-methoxybenzylidene)cyclopentanone.

Yellow solid (0.322 g, 92%); mp 181–183 °C (lit.²⁵ mp 178–179 °C) (Found: C, 77.23; H, 5.61. C₁₈H₁₆O₃ requires C, 77.12; H, 5.75%); $\lambda_{\max}(\text{EtOH})/\text{nm}$ 397 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 14875); $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 1681 w, 1623 s, 1606 s, 1588 s, 1568 m, 1512 m, 1474 w, 1425 w, 1252 s, 1180 m, 1024 w; $\delta_{\text{H}}(200 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 3.05–3.15 (4H, m, CH₂CH₂), 3.83 (3H, s, OMe), 6.52 (1H, t, *J* 3.4, Ar), 6.66 (1H, d, *J* 3.4, Ar), 6.94 (2H, dd, *J* 6.8, 1.9, Ar), 7.36–7.40 (1H, m, CH=C), 7.52–7.60 (4H, m, CH=C, Ar); $\delta_{\text{C}}(50 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 26.1 (2 \times), 55.3, 112.5, 114.3 (2C), 115.7, 119.7, 128.7, 132.5 (2C), 133.4, 135.4, 135.6, 144.8, 152.8, 160.6, 195.6; *m/z* (ESI) 281.1168 ([M + H]⁺ C₁₈H₁₇O₃⁺ requires 281.1172).

1c; 2-(4-Methoxybenzylidene)-5-(naphth-1-ylmethylidene)cyclopentanone.

Yellow solid (0.340 g, 80%); mp 157.5–159 °C (Found: C, 84.85; H, 5.84. C₂₄H₂₀O₂ requires C, 84.68; H, 5.92%); $\lambda_{\max}(\text{EtOH})/\text{nm}$ 378 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 17689); $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 1680 m, 1610 s, 1587 s, 1513 s, 1309 w, 1258 s, 1198 m, 1170 s, 1035 m; $\delta_{\text{H}}(200 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 3.06 (4H, s, CH₂CH₂), 3.86 (3H, s, OMe), 6.97 (2H, d, *J* 8.8, Ar), 7.49–7.55 (5H, m, Ar), 7.63 (1H, s, Ar), 7.67 (1H, d, *J* 7.1, Ar), 7.68–7.89 (2H, m, Ar), 8.05 (1H, d, *J* 8.0, Ar), 8.31 (1H, s, CH=C); $\delta_{\text{C}}(50 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 26.8, 26.9, 55.6, 114.5 (2C), 124.3, 125.3, 126.4, 126.9, 127.3, 128.8, 128.9, 129.8, 129.9, 132.5, 132.8 (2C), 132.8, 133.8, 134.2, 135.4, 140.1, 160.9, 196.2; *m/z* (ESI) 341.1526 ([M + H]⁺ C₂₄H₂₁O₂⁺ requires 341.1536).

1e; 2-(4-Bromobenzylidene)-5-(4-methoxybenzylidene)cyclopentanone.

Green/yellow solid (0.407 g, 88%); mp 235.5–236.5 °C (Found: C, 65.14; H, 4.68. C₂₀H₁₇BrO₂ requires C, 65.05; H, 4.64%); $\lambda_{\max}(\text{EtOH})/\text{nm}$ 240, 380 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 12185, 20235); $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$ 1696 m, 1594 s, 1510 s, 1486 m, 1460 w, 1401 w, 1308 w, 1257 s, 1172 s; $\delta_{\text{H}}(200 \text{ MHz}, \text{CDCl}_3, \text{Me}_4\text{Si})$ 3.07 (4H, m, CH₂CH₂), 3.85 (3H, s, OMe), 6.96 (2H, d,

J 8.9, Ar), 7.44 (2H, d, *J* 8.5, Ar), 7.48 (1H, s, CH=C), 7.53–7.58 (5H, m, 4 × Ar, 1 × CH=C); δ_{C} (75 MHz, CDCl₃, Me₄Si) 26.7 (2 ×), 55.6, 114.6 (2C), 123.7, 128.8, 132.1, 132.2 (2C), 132.2 (2C), 132.9 (2C), 134.4, 134.9, 135.1, 138.6, 161.0, 196.2; *m/z* (ESI) 369.0492 ([M + H]⁺ + C₂₀H₁₈⁷⁹BrO₂⁺ requires 369.0485) and 371.0470 ([M + H]⁺ + C₂₀H₁₈⁸¹BrO₂⁺ requires 371.0464).

1g; 2-(5-Bromo-2-methoxybenzylidene)-5-(4-methoxybenzylidene)cyclopentanone. Yellow solid (0.451 g, 90%); mp 200–202 °C (Found: C, 63.47; H, 4.71. C₂₁H₁₉BrO₃ requires C, 63.17; H, 4.80%); λ_{max} (EtOH)/nm 386 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 47337); ν_{max} (KBr)/cm^{−1} 1697 m, 1612 s, 1595 s, 1510 m, 1258 s, 1173 s, 1119 w, 1076 m; δ_{H} (200 MHz, CDCl₃, Me₄Si) 3.02 (4H, m, CH₂CH₂), 3.84 (3H, s, OMe); 3.85 (3H, s, OMe), 6.79 (1H, d, *J* 8.8, Ar), 6.95 (2H, d, *J* 8.8, Ar), 7.40 (1H, dd, *J* 8.8, 2.4, Ar), 7.52–7.60 (4H, m, CH=C, Ar), 7.84 (1H, s, CH=C); δ_{C} (50 MHz, CDCl₃, Me₄Si) 26.4, 26.6, 55.4, 55.9, 112.6, 112.7, 114.4 (2C), 126.2, 127.2, 128.7, 132.1, 132.6 (2C), 132.9, 133.9, 135.0, 138.8, 158.0, 160.7, 195.9; *m/z* (ESI) 399.0603 ([M + H]⁺ + C₂₀H₂₀⁷⁹BrO₃⁺ requires 399.0590) and 401.0571 ([M + H]⁺ + C₂₀H₂₀⁸¹BrO₃⁺ requires 401.0570).

1h; 2-(2-Methoxybenzylidene)-5-(4-methoxybenzylidene)cyclopentanone. Yellow solid (0.322 g, 80%); mp 147–148 °C (Found: C, 78.59, H, 6.11. C₂₁H₂₀O₃ requires C, 78.73; H, 6.29%); λ_{max} (EtOH)/nm 383 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 23776); ν_{max} (nujol)/cm^{−1} 1698 m, 1626 s, 1595 s, 1569 m, 1511 s, 1485 m, 1422 m, 1305 w, 1246 s, 1204 w, 1174 s, 1163 s, 1121 w, 1032 w; δ_{H} (300 MHz, CDCl₃, Me₄Si) 3.05 (4H, m, CH₂CH₂), 3.86 (3H, s, OMe), 3.89 (3H, s, OMe), 6.92–7.02 (4H, m, Ar), 7.32–7.37 (1H, m, Ar), 7.53–7.58 (4H, m, CH=C, Ar), 7.99 (1H, s, CH=C); δ_{C} (50 MHz, CDCl₃, Me₄Si) 26.8, 26.9, 55.6, 55.7, 105.2, 111.0 (2C), 114.5, 120.5, 125.2, 128.1, 129.0, 130.9, 132.7 (2C), 133.6, 135.5, 137.8, 159.1, 160.7, 196.5; *m/z* (ESI) 321.1477 ([M + H]⁺ + C₂₁H₂₁O₃⁺ requires 321.1485).

1j; 2-(4-Methoxybenzylidene)-5-(4-methylbenzylidene)cyclopentanone. Yellow solid (0.740 g, 97%); mp 196–197 °C (lit.²⁵ 197–198 °C) (Found: C, 82.66; H, 6.62. C₂₁H₂₀O₂ requires C, 82.86; H, 6.62%); λ_{max} (EtOH)/nm 239, 379 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 19088, 34877); ν_{max} (KBr)/cm^{−1} 2913 w, 1686 w, 1619 m, 1600 s, 1560 m, 1509 s, 1421 w, 1310 w, 1256 s, 1171 s, 1117 w, 1032 w, 985 w, 816 w; δ_{H} (400 MHz, CDCl₃, Me₄Si) 2.39 (3H, s, ArMe), 3.08 (4H, m, CH₂CH₂), 3.85 (3H, s, OMe), 6.96 (2H, d, *J* 8.5, Ar), 7.24 (2H, d, *J* 8.5, Ar), 7.50 (2H, d, *J* 8.1, Ar), 7.56 (2H, d, *J* 8.5, Ar), 7.55–7.57 (2H, m, CH=C); δ_{C} (100 MHz, CDCl₃, Me₄Si) 21.7, 26.7, 26.8, 55.6, 114.6 (2C), 129.7 (2C), 131.0 (2C), 132.8 (2C), 133.6, 133.8, 129.1, 133.5, 135.4, 136.9, 139.9, 160.8, 196.5; *m/z* (ESI) 305.3 ([M + H]⁺ + C₂₁H₂₁O₂⁺ requires 305.2).

1k; 2-(4-Methoxybenzylidene)-5-cinnamylidenecyclopentanone. Yellow solid (0.290 g, 73%); mp 179–180 °C (lit.²⁵ 180–181 °C) (Found: C, 83.49; H, 6.40. C₂₂H₂₀O₂ requires C, 83.52; H, 6.37%); ν_{max} (KBr)/cm^{−1} 1682 m, 1628 m, 1598 s, 1509 m, 1442 w, 1304 w, 1281 m, 1034 m, 970 m, 828 m, 756 m, 696 w; δ_{H} (400 MHz, CDCl₃, Me₄Si) 2.89–2.94 (2H, m, CH₂CH₂),

3.00–3.05 (2H, m, CH₂CH₂), 3.84 (3H, s, OMe), 6.91–6.99 (4H, m, Ar, CH=C), 7.28–7.40 (4H, m, Ar, CH=C), 7.47–7.50 (3H, m, Ar), 7.53 (2H, d, *J* 8.8, Ar); δ_{C} (100 MHz, CDCl₃, Me₄Si) 24.5, 26.2, 55.5, 114.5 (2C), 125.0, 127.4 (2C), 128.9, 129.0 (2C), 129.1, 132.7 (2C), 132.9, 133.5, 136.5, 136.8, 139.0, 141.4, 160.8, 195.8; *m/z* (EI) 316 (M⁺, 100%), 239 (29), 207 (26), 165 (11), 141 (36), 115 (35), 103 (22), 91 (32), 77 (35), 55 (34).

1l; 2-(4-Methoxybenzylidene)-5-(2-nitrocinnamylidene)cyclopentanone. Yellow solid (0.335 g, 74%); mp 171–173 °C (Found: C, 73.20; H, 5.31; N, 3.74. C₂₂H₁₉NO₄ requires C, 73.12; H, 5.30; N, 3.88%); λ_{max} (EtOH)/nm 244, 396 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 18955, 39549); ν_{max} (KBr)/cm^{−1} 2913 w, 1677 s, 1621 s, 1600 s, 1580 m, 1523 s, 1426 m, 1364 m, 1262 s, 1195 m, 1164 m, 1026 m; δ_{H} (300 MHz, CDCl₃, Me₄Si) 2.92–2.97 (2H, m, CH₂CH₂), 3.04–3.09 (2H, m, CH₂CH₂), 3.86 (3H, s, OMe), 6.96 (2H, d, *J* 8.9, Ar), 6.90–6.99 (1H, m, CH=CH), 7.30 (1H, dt, *J* 11.7, 2.4, CH=CH), 7.4–7.49 (2H, m, Ar, CH=C), 7.52–7.59 (2H, m, CH=C), 7.55 (2H, d, *J* 8.8, Ar), 7.61 (1H, td, *J* 7.7, 1.1, Ar), 7.73 (1H, dd, *J* 7.9, 1.4, Ar), 7.97 (1H, dd, *J* 8.2, 1.2, Ar); δ_{C} (75 MHz, CDCl₃, Me₄Si) 24.6, 26.3, 55.6, 114.6 (2C), 125.1, 128.6, 128.8, 129.2, 129.8, 131.6, 132.4, 132.9 (2C), 133.3, 134.2, 135.1, 136.0, 141.3, 148.2, 161.0, 195.6; *m/z* (EI) 361 (M⁺, 100%), 344 (68), 316 (18), 226 (22), 199 (43), 183 (36), 145 (34), 128 (33), 115 (62), 103 (48), 91 (27), 77 (50), 63 (17).

1m; 2-(4-Bromobenzylidene)-6-(4-methoxybenzylidene)cyclohexanone. Yellow solid (0.417 g, 87%); mp 154–158 °C (Found: C, 65.97; H, 5.11. C₂₁H₁₉BrO₂ requires C, 65.81; H, 5.00%); λ_{max} (EtOH)/nm 238, 347 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 20737, 18678); ν_{max} /cm^{−1} 1658 w, 1600 s, 1599 m, 1560 m, 1509 m, 1399 m, 1312 m, 1253 s, 1162 s, 1141 s; δ_{H} (200 MHz, CDCl₃, Me₄Si) 1.74–1.86 (2H, m, CH₂CH₂CH₂), 2.83–2.97 (4H, m, CH₂CH₂CH₂), 3.85 (3H, s, OMe), 6.94 (2H, d, *J* 8.9, Ar), 7.31 (2H, d, *J* 8.5, Ar), 7.46 (2H, d, *J* 8.8, Ar), 7.53 (2H, d, *J* 8.6, Ar), 7.69 (1H, t, *J* 2.0, CH=C), 7.76 (1H, t, *J* 2.0, CH=C); δ_{C} (75 MHz, CDCl₃, Me₄Si) 23.2, 28.6, 28.8, 55.6, 114.2 (2C), 122.9, 128.8, 131.8 (2C), 132.0 (2C), 132.6 (2C), 134.2, 135.2, 135.3, 137.2, 137.6, 160.4, 190.2; *m/z* (ESI) 383.2 (100%) ([M + H]⁺ + C₂₁H₂₀⁷⁹BrO₂⁺ requires 383.1) and 385.2 (98) ([M + H]⁺ + C₂₁H₂₀⁸¹BrO₂⁺ requires 385.1).

1n; 2-(4-Ethoxy-3-methoxybenzylidene)-6-(4-methoxybenzylidene)cyclohexanone. Yellow solid (0.368 g, 78%); mp 131–133 °C (Found: C, 76.35; H, 7.01. C₂₄H₂₆O₄ requires C, 76.17; H, 6.92%); λ_{max} (EtOH)/nm 246, 368 ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ 23464, 35070); ν_{max} /cm^{−1} 1660 w, 1597 m, 1510 m, 1256 s, 1159 m, 1136 m, 1027 m, 811 w; δ_{H} (200 MHz, CDCl₃, Me₄Si) 1.48 (3H, t, *J* 7.0, CH₂CH₃) 1.75–1.88 (2H, m, CH₂CH₂CH₂), 2.90–2.97 (4H, m, CH₂CH₂CH₂), 3.85 (3H, s, OMe), 3.90 (3H, s, OMe), 4.14 (2H, q, *J* 7.0, CH₂CH₃), 6.88–6.97 (3H, m, Ar), 7.02 (1H, d, *J* 1.9, 1H), 7.09 (1H, dd, *J* 8.3, 1.9, Ar), 7.45 (2H, d, *J* 8.8, Ar), 7.74–7.78 (2H, m, CH=C); δ_{C} (75 MHz, CDCl₃, Me₄Si) 15.0, 23.3, 28.7, 28.8, 55.6, 56.3, 64.6, 112.4, 114.2 (2C), 114.4, 124.2, 129.0, 129.2, 132.5 (2C), 134.6, 134.7, 136.8, 137.0, 149.2 (2 ×), 160.2, 190.4; *m/z* (ESI) 379.2 ([M + H]⁺ + C₂₄H₂₇O₄⁺ requires 379.2).

Crystal data for 1n. $C_{24}H_{26}O_4$, $M_r = 378.45$, triclinic, space group $P\bar{1}$, $a = 11.2190(3)$, $b = 12.8515(3)$, $c = 14.1651(4)$ Å, $\alpha = 82.272(1)^\circ$, $\beta = 88.467(1)^\circ$, $\gamma = 75.715(1)^\circ$, $V = 1961.17(9)$ Å³, $Z = 4$ (2 molecules with distinctly different conformations in the ASU), $D_{\text{calc}} = 1.282$ g cm⁻³, $\mu(\text{MoK}\alpha) = 0.086$ mm⁻¹. Of 112188 reflections measured, 11417 were unique ($R_{\text{int}} = 0.0381$), with 8758 $I > 2\sigma(I)$, R indices [$I > 2\sigma(I)$] $R_1 = 0.0450$, $wR_2 = 0.1069$, GoF on $F^2 = 1.024$ for 511 refined parameters and 0 restraints.

CCDC reference number 605464. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b606042k

1o; 2-(4-Methoxybenzylidene)-6-(4-nitrobenzylidene)cyclohexanone. Yellow solid (0.425 g, 97%); mp 197–198 °C, (Found: C, 72.29; H, 5.58; N, 3.95. $C_{21}H_{19}NO_4$ requires C, 72.19; H, 5.48; N, 4.01%); $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 348 ($\epsilon/\text{dm}^3 \text{ mol}^{-1}$ 19448); $\nu_{\text{max}}/\text{cm}^{-1}$ 1658 w, 1600 s, 1557 m, 1164 m, 1149 m, 1024 m; $\delta_{\text{H}}(300 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})$ 1.79–1.87 (2H, m, $\text{CH}_2\text{CH}_2\text{CH}_2$), 2.87–2.98 (4H, m, $\text{CH}_2\text{CH}_2\text{CH}_2$), 3.85 (3H, s, OMe), 6.95 (2H, d, J 8.9, Ar), 7.47 (2H, d, J 8.6, Ar), 7.57 (2H, d, J 8.4, Ar), 7.77 (1H, t, J 2.0, CH=C), 7.79 (1H, t, J 2.1, CH=C), 8.25 (2H, d, J 8.7, Ar); $\delta_{\text{C}}(100 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})$ 23.0, 28.6, 28.7, 55.6, 114.3 (2C), 123.8 (2C), 128.6, 130.9 (2C), 132.7 (2C), 133.6, 133.7, 138.4, 139.8, 143.0, 147.4, 160.6, 189.8; m/z (ESI) 350.2 ($[\text{M} + \text{H}]^+$ $C_{21}H_{20}NO_4^+$ requires 350.1).

Crystal data for 1o. $C_{21}H_{19}NO_4$, $M_r = 349.37$, triclinic, space group $P\bar{1}$, $a = 7.8646(3)$, $b = 9.6830(3)$, $c = 11.3746(5)$ Å, $\alpha = 95.587(1)^\circ$, $\beta = 102.801(1)^\circ$, $\gamma = 91.992(2)^\circ$, $V = 839.25(6)$ Å³, $Z = 2$, $D_{\text{calc}} = 1.383$ g cm⁻³, $\mu(\text{MoK}\alpha) = 0.096$ mm⁻¹. Of 6955 reflections measured, 3102 were unique ($R_{\text{int}} = 0.0390$), with 2280 $I > 2\sigma(I)$, R indices [$I > 2\sigma(I)$] $R_1 = 0.0400$, $wR_2 = 0.0904$, GoF on $F^2 = 1.044$ for 236 refined parameters and 0 restraints.

CCDC reference number 605465. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b606042k

1p; 2-(6-Bromopyridin-2-ylmethylidene)-6-(4-methoxybenzylidene)cyclohexanone. Yellow solid (0.344 g, 78%); mp 119 °C, (Found: C, 62.49; H, 4.87; N, 3.64. $C_{20}H_{18}BrNO_2$ requires C, 62.51; H, 4.72; N, 3.65%); $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 341 ($\epsilon/\text{dm}^3 \text{ mol}^{-1}$ 14026); $\nu_{\text{max}}/\text{cm}^{-1}$ 1662 m, 1600 m, 1572 m, 1546 m, 1508 m, 1434 m, 1310 m, 1298 m, 1248 m, 1161 m, 1144 m, 411 s; $\delta_{\text{H}}(400 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})$ 1.80–1.87 (2H, m, $\text{CH}_2\text{CH}_2\text{CH}_2$), 2.93 (2H, td, J 7.2, 2.0, $\text{CH}_2\text{CH}_2\text{CH}_2$), 3.29 (2H, td, J 7.4, 2.2, $\text{CH}_2\text{CH}_2\text{CH}_2$), 3.85 (3H, s, OMe), 6.94 (2H, d, J 8.9, Ar), 7.36–7.38 (2H, m, Ar), 7.46 (2H, d, J 8.7, Ar), 7.52–7.75 (2H, m, CH=C, Ar), 7.76 (1H, s, CH=C); $\delta_{\text{C}}(100 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})$ 22.7, 28.5, 28.7, 55.6, 114.3 (2C), 126.0, 126.9, 128.8, 131.5, 132.7 (2C), 134.4, 137.7, 138.7, 141.8, 142.0, 156.8, 160.4, 190.8; m/z (ESI) 384.2 (100%) ($[\text{M} + \text{H}]^+$ $C_{20}H_{19}^{79}\text{BrNO}_2^+$ requires 384.1) and 386.2 (98%) ($[\text{M} + \text{H}]^+$ $C_{20}H_{19}^{81}\text{BrNO}_2^+$ requires 386.1).

Crystal data for 1p. $C_{20}H_{18}BrNO_2$, $M_r = 384.26$, monoclinic, space group $P2_1/c$, $a = 18.5748(1)$, $b = 6.2641(1)$, $c = 15.9337(1)$ Å, $\beta = 115.194(1)^\circ$, $V = 1677.59(3)$ Å³, $Z = 4$, $D_{\text{calc}} = 1.521$ g cm⁻³, $\mu(\text{MoK}\alpha) = 2.462$ mm⁻¹. Of 6923 reflections measured, 3878 were unique ($R_{\text{int}} = 0.0409$), with

2825 $I > 2\sigma(I)$, R indices [$I > 2\sigma(I)$] $R_1 = 0.0371$, $wR_2 = 0.0697$, GoF on $F^2 = 1.027$ for 218 refined parameters and 0 restraints.

CCDC reference number 605466. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b606042k

1q; 2-(4-Methoxybenzylidene)-6-(3-nitrobenzylidene)cyclohexanone. Yellow solid (0.370 g, 85%); mp 118–119 °C, (Found: C, 72.38; H, 5.54; N, 4.11. $C_{21}H_{19}NO_4$ requires C, 72.19; H, 5.48; N, 4.01%); $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 348 ($\epsilon/\text{dm}^3 \text{ mol}^{-1}$ 18430); $\nu_{\text{max}}/\text{cm}^{-1}$ 1716 w, 1660 w, 1634 w, 1600 m, 1559 m, 1522 m, 1377 m, 1347 m, 1301 m, 1275 m, 1258 m, 1165 m, 1144 s, 1033 m; $\delta_{\text{H}}(300 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})$ 1.81–2.16 (2H, m, $\text{CH}_2\text{CH}_2\text{CH}_2$), 2.17–2.99 (4H, m, $\text{CH}_2\text{CH}_2\text{CH}_2$), 3.86 (3H, s, OMe), 6.95 (2H, d, J 8.8, Ar), 7.47 (2H, d, J 8.6, Ar), 7.55–7.61 (1H, m, Ar), 7.73 (1H, d, J 7.7, Ar), 7.77 (1H, t, J 2.1, CH=C), 7.80 (1H, J 2.1, CH=C), 8.16–8.20 (1H, m, Ar), 8.30 (1H, t, J 2.0, Ar); $\delta_{\text{C}}(75 \text{ Hz, CDCl}_3, \text{Me}_4\text{Si})$ 23.1, 28.5, 28.7, 55.6, 114.3 (2C), 123.2, 124.6, 128.7, 129.6, 132.7 (2C), 133.5, 133.8, 136.3, 138.0, 138.2, 138.0, 148.6, 160.5, 189.8; m/z (ESI) 350.2 ($[\text{M} + \text{H}]^+$ $C_{21}H_{20}NO_4^+$ requires 350.1).

1r; 2-(Furfurylidene)-6-(4-methoxybenzylidene)cyclohexanone. Yellow solid (0.280 g, 76%); mp 105–106 °C (lit.²⁶ mp 99–100 °C) (Found: C, 77.51; H, 6.28. $C_{19}H_{18}O_3$ requires C, 77.53; H, 6.16%); $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 243, 368 ($\epsilon/\text{dm}^3 \text{ mol}^{-1}$ 14558, 25368); $\nu_{\text{max}}/\text{cm}^{-1}$ 1656 w, 1596 w, 1508 w, 1301 w, 1259 w, 1182 w, 1162 w, 1140 w, 1029 w, 981 w; $\delta_{\text{H}}(200 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})$ 1.78–1.90 (2H, m, $\text{CH}_2\text{CH}_2\text{CH}_2$), 2.87–3.04 (4H, m, $\text{CH}_2\text{CH}_2\text{CH}_2$), 3.84 (3H, s, OMe), 6.49–6.53 (1H, m, Ar), 6.65–6.67 (1H, m, Ar), 6.93 (2H, d, J 8.8, Ar), 7.44 (2H, d, J 8.7, Ar), 7.55–7.58 (2H, m, CH=C), 7.75–7.76 (1H, m, Ar); $\delta_{\text{C}}(50 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})$ 22.6, 28.4, 28.6, 55.6, 112.5, 114.2 (2C), 116.1, 123.7, 129.0, 132.5 (2C), 133.5, 134.5, 136.8, 144.7, 153.2, 160.2, 189.8; m/z (ESI) 295.2 ($[\text{M} + \text{H}]^+$ $C_{19}H_{19}O_3^+$ requires 295.1).

1s; 2-(4-Methoxybenzylidene)-6-(pyrid-3-ylmethylidene)cyclohexanone. Yellow solid (0.301 g, 79%); mp 146–148 °C, (Found: C, 78.78; H, 6.34; N, 4.66. $C_{20}H_{19}NO_2$ requires C, 78.66; H, 6.27; N, 4.59%); $\nu_{\text{max}}/\text{cm}^{-1}$ 1663 m, 1607 m, 1562 m, 1507 m, 1416 m, 1308 w, 1276 m, 1248 s, 1155 s, 1022 m, 837 m, 710 m; $\delta_{\text{H}}(200 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})$ 1.82 (2H, app p, J 6.2, $\text{CH}_2\text{CH}_2\text{CH}_2$), 2.88–2.98 (4H, m, $\text{CH}_2\text{CH}_2\text{CH}_2$), 3.85 (3H, s, OMe), 6.94 (2H, d, J 8.8, Ar), 7.40–7.49 (3H, m, Ar), 7.70–7.87 (3H, m, 2 × CH=C, Ar), 8.58 (1H, d, J 3.89, Ar), 8.72 (1H, s, Ar); $\delta_{\text{C}}(100 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})$ 23.1, 28.6, 28.7, 55.6, 114.2 (2C), 123.5, 128.7, 132.2, 132.6 (2C), 132.7, 134.0, 137.2, 137.9, 138.6, 149.3, 151.3, 160.4, 189.9; m/z (ESI) 306.2 ($[\text{M} + \text{H}]^+$ $C_{20}H_{20}NO_2^+$ requires 306.2).

1u; 2-(4-Diethylaminobenzylidene)-6-(furfurylidene)cyclohexanone. Orange solid (0.386 g, 92%); mp 107.5–109.5 °C (Found: C, 78.77; H, 7.54; N, 4.20. $C_{22}H_{25}NO_2$ requires C, 78.77; H, 7.51; N, 4.18%); $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 269, 348, 449 ($\epsilon/\text{dm}^3 \text{ mol}^{-1}$ 14599, 16204, 34672); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 2967 w, 2932 w, 2898 w, 2872 w, 1637 m, 1599 s, 1586 s, 1570 w, 1560 s, 1540 m, 1518 s, 1466 w, 1405 w, 1358 m, 1308 w, 1282 m, 1272 m, 1196 m, 1168 s, 1132 s, 1074 m, 1030 w; $\delta_{\text{H}}(300 \text{ MHz, CDCl}_3, \text{Me}_4\text{Si})$ 1.19 (6H, t, J 7.1, Me), 1.84 (2H, app p, J 6.3,

CH₂CH₂CH₂), 2.93 (2H, td, *J* 6.2, 1.9, CH₂CH₂CH₂), 2.99 (2H, td, *J* 6.3, 2.0, CH₂CH₂CH₂), 3.40 (4H, q, *J* 7.1, NCH₂), 6.50 (1H, dd, *J* 3.3, 1.7, Ar); 6.63 (1H, d, *J* 3.5, Ar), 6.67 (2H, d, *J* 9.0, Ar), 7.42 (2H, d, *J* 8.9, Ar); 7.53–7.56 (2H, m, CH=C, Ar), 7.76 (1H, s, CH=C); δ_{C} (75 MHz, CDCl₃, Me₄Si) 12.9 (2C), 22.7, 28.4, 28.8, 44.6 (2C), 111.3 (2C), 112.4, 115.5, 122.8, 123.3, 131.5, 133.2 (2C), 134.0, 138.3, 144.3, 148.3, 153.3, 189.6; *m/z* (ESI) 336.3 ([M + H]⁺ C₂₂H₂₆NO₂⁺ requires 336.2).

1v; 1-(4-Bromobenzylidene)-3-(4-methoxybenzylidene)acetone. Pale green solid (0.295 g, 90%); mp 182–183 °C (Found: C, 62.86; H, 4.41. C₁₈H₁₅BrO₂ requires C, 62.99; H, 4.41, %); λ_{max} (EtOH)/nm 237, 348 (ϵ /dm³ mol⁻¹ cm⁻¹ 23089, 30031); ν_{max} /cm⁻¹ 1647 m, 1591 m, 1560 m, 1511 m, 1460 s, 1420 w, 1400 w, 1340 w, 1300 w, 1265 w, 1249 m, 1194 w, 1174 m, 1111 w, 1070 w, 1032 m, 1008 w, 980 m, 886 w, 864 w, 829 m, 809 w; δ_{H} (300 MHz, CDCl₃, Me₄Si) 3.86 (3H, s, OMe), 6.94 (1H, d, *J* 15.9, CH=C), 6.94 (2H, d, *J* 8.8, Ar), 7.06 (1H, d, *J* 15.9, CH=C), 7.65 (1H, d, *J* 15.9, CH=C), 7.71 (1H, d, *J* 15.9, CH=C), 7.47 (2H, d, *J* 8.5, Ar), 7.55 (2H, d, *J* 8.3, Ar), 7.57 (2H, d, *J* 8.4, Ar); δ_{C} (75 Hz, CDCl₃, Me₄Si) 55.7, 114.8 (2C), 123.6, 124.8, 126.3, 127.7, 129.9 (2C), 130.5 (2C), 132.5 (2C), 134.2, 141.6, 143.7, 162.1, 188.8, *m/z* (ESI) 365.1 ([M + Na]⁺ C₁₈H₁₅⁷⁹BrO₂Na⁺ requires 365.0) and 367.1 ([M + Na]⁺ C₁₈H₁₅⁸¹BrO₂Na⁺ requires 367.0).

1w; 1-(4-Methoxybenzylidene)-3-(4-nitrobenzylidene)acetone. Yellow solid (0.355 g, 83%); mp 181–183 °C, (Found: C, 69.76; H, 5.10; N, 4.55. C₁₈H₁₅NO₄ requires C, 69.89; H, 4.89; N, 4.53%); λ_{max} (EtOH)/nm 347 (ϵ /dm³ mol⁻¹ cm⁻¹ 21420); ν_{max} /cm⁻¹ 1651 s, 1600 s, 1588 s, 1519 s, 1463 s, 1410 w, 1377 m, 1340 s, 1309 w, 1258 m, 1198 m, 1173 m, 1105 w, 1024 w, 988 w; δ_{H} (200 MHz, CDCl₃, Me₄Si) 3.87 (3H, s, OMe), 6.94 (1H, d, *J* 15.9, CH=C), 6.95 (2H, d, *J* 6.8, Ar), 7.18 (1H, d, *J* 15.9, CH=C), 7.59 (2H, d, *J* 6.7, Ar), 7.70–7.77 (4H, m, Ar, CH=C), 8.27 (2H, d, *J* 6.9, Ar); δ_{C} (75 Hz, CDCl₃, Me₄Si); 55.7, 114.8 (2C), 123.4, 124.4 (2C), 127.5, 129.1 (2C), 129.3, 130.6 (2C), 139.8, 141.5, 144.5, 148.7, 162.3, 188.3; *m/z* (ESI) 332.09 ([M + Na]⁺ C₁₈H₁₅NO₄Na⁺ requires 332.09).

8a. Crystal data for **8a**. C₃₆H₃₈NOCl, *M_r* = 536.12, triclinic, space group *P1*(bar), *a* = 11.5683(4), *b* = 12.3023(4), *c* = 13.6088(5) Å, α = 98.825(1), β = 110.125(2), γ = 111.483(2)°, *V* = 1603.3(1) Å³, *Z* = 2, *D*_{calc} = 1.111 g cm⁻³, μ (MoK α) = 0.146 mm⁻¹. Of 27554 reflections measured, 7612 were unique (*R*_{int} = 0.087), with 3336 *I* > 2 σ (*I*), *R* indices [*I* > 2 σ (*I*)] *R*₁ = 0.0644, *wR*₂ = 0.1623, GoF on *F*² = 0.988 for 355 refined parameters and 0 restraints

CCDC reference number 605784. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b606042k

8b. Crystal data for **8b**. C₂₆H₃₁N₃O, *M_r* = 401.54, monoclinic, space group *P2₁/n*, *a* = 10.0896(1), *b* = 13.2900(2), *c* = 16.6649(3) Å, β = 103.981(1)°, *V* = 2168.41(6) Å³, *Z* = 4, *D*_{calc} = 1.230 g cm⁻³, μ (MoK α) = 0.076 mm⁻¹. Of 30375 reflections measured, 5297 were unique (*R*_{int} = 0.050), with 3772 *I* > 2 σ (*I*), *R* indices [*I* > 2 σ (*I*)] *R*₁ = 0.0498, *wR*₂ = 0.0985, GoF on *F*² = 1.059 for 273 refined parameters and 0 restraints.

CCDC reference number 605785. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b606042k

9; 7a-Dimethylamino-5,6,7a-tetrahydro-4H-benzofuran-2-one. Glyoxylic acid monohydrate (0.98 g, 10 mmol) was added to DIMCARB (5 mL) at ambient temperature while stirring, resulting in the evolution of gas. The solution was heated to 50 °C, followed by addition of cyclohexanone (1.035 mL, 10.0 mmol) and stirring for a further 3 h at 50 °C.

DIMCARB was removed *in vacuo* and the residual mixture washed with water (10 mL) and extracted with dichloromethane (3 × 20 mL). The combined organic fractions were collected, dried with anhydrous MgSO₄, filtered and the solvent removed *in vacuo* to afford an orange oil, which post silica gel chromatography (eluent 1 : 1 hexane–ethyl acetate) yielded 7a-dimethylamino-5,6,7a-tetrahydro-4H-benzofuran-2-one (1.09 g, 60%) which was crystallised as clear crystals from ethyl acetate, mp 62–64 °C (Found: C, 66.27; H, 8.31; N, 7.76. C₁₀H₁₅NO₂ requires C, 66.27; H, 8.34; N, 7.73%); δ_{H} (200 MHz, CDCl₃, Me₄Si) 1.26–1.42 (2H, m, –CH₂–), 1.58–1.70 (2H, m, –CH₂–), 1.94–2.08 (1H, m, –CH₂–), 2.15–2.29 (1H, m, –CH₂–), 2.32 (6H, s, N(CH₃)₂), 2.70–2.75 (2H, m, –CH₂CO(N)), 5.71 (1H, t, *J* 1.8, CH=C); δ_{C} (50 MHz, CDCl₃, Me₄Si) 21.9, 27.6, 27.9, 37.0, 37.4 (2C), 103.0, 114.2, 172.0, 172.1; *m/z* (ESI) 181.8 ([M + H]⁺ C₁₀H₁₆NO₂⁺ requires 182.1).

Crystal data for **9**. C₁₀H₁₅NO₂, *M_r* = 181.23, orthorhombic, space group *Pbca*, *a* = 8.7630(2), *b* = 10.9240(2), *c* = 20.1019(5) Å, *V* = 1924.29(7) Å³, *Z* = 8, *D*_{calc} = 1.251 g cm⁻³, μ (MoK α) = 0.087 mm⁻¹. Of 2322 unique reflections measured with 1545 *I* > 2 σ (*I*), *R* indices [*I* > 2 σ (*I*)] *R*₁ = 0.0496, *wR*₂ = 0.1182, GoF on *F*² = 1.083 for 120 refined parameters and 0 restraints.

CCDC reference number 605786. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b606042k.

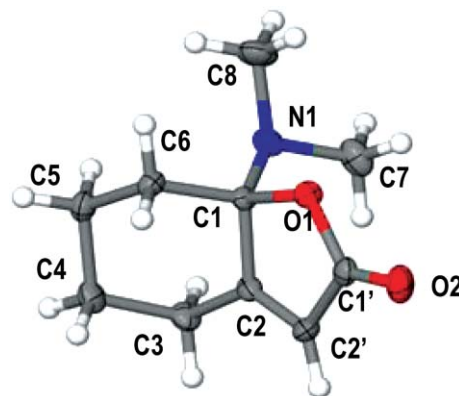


Fig. 2 Molecular diagram of **9** derived from single crystal structure analysis.

6; (E)-5-Benzylidene-1-(*N,N*-dimethylamino)cyclopent-1-ene. To an RBF containing a 1 : 1 DIMCARB/ether mixture (10 mL) was added benzaldehyde (1.06 g, 10.0 mmol) and cyclopentanone (1.01 g, 12.0 mmol) and stirred at room

temperature. After 24 h the volatile components, including cyclopentanone, were removed under high vacuum without heating. NMR analysis indicated two products present: 2-Benzylidenecyclopentanone; partial δ_{H} (200 MHz, CDCl_3 , Me_4Si) indicative peaks; 2.01 (2H, app p, J 7.4, $\text{CH}_2\text{CH}_2\text{CH}_2$), 2.96 (2H, td, J 7.2, 2.8, $\text{C}=\text{CCH}_2$); δ_{C} (50 MHz, CDCl_3 , Me_4Si) 20.4, 29.5, 38.0, 128.9 (2C), 129.5, 130.7 (2C), 132.5, 135.7, 136.3, 208.20 and 5-benzylidene-1-(N,N -dimethylamino)cyclopent-1-ene; δ_{H} (200 MHz, CDCl_3 , Me_4Si) indicative peaks; 2.86 (2H, td, J 5.3, 2.6, $\text{C}=\text{CCH}_2$), 5.29 (1H, t, J 2.8, $\text{NC}=\text{CH}$), 6.44 (1H, t, J 2.6, $\text{ArCH}=\text{C}$); δ_{C} (50 MHz, CDCl_3) 29.5, 32.1, 43.3 (2C), 115.1, 118.3, 125.9, 128.4 (2C), 128.5 (2C), 138.8, 144.2, 155.9.

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