Tetrahedron 66 (2010) 9512–9518

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

CAN-promoted, diastereoselective synthesis of fused 2,3-dihydrofurans and their transformation into tetrahydroindoles

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ARTICLE INFO

Article history:
Received 10 September 2010
Received in revised form 6 October 2010
Accepted 8 October 2010
Available online 14 October 2010

ABSTRACT

The reaction between 1,3-cyclohexanediones and chalcones (or their vinilogs) in the presence of 2.5 equiv of cerium(IV) ammonium nitrate afforded *trans*-2-arylcarbonyl-3-aryl (or styryl)-2,3,6,7-tetrahydrobenzofuran-4(5*H*)-ones in good to excellent yields and in high diastereoselectivities. The method was also extended to the preparation of derivatives of the 5,6-dihydro-2*H*-cyclopenta[*b*]furan-4(3*H*)-one system. The fused 2,3-dihydrofuran derivatives were transformed into 1-alkyl-2-acyl-3-aryl-6,7-dihydroindole-4(5*H*)-ones by 2,3-dehydrogenation followed by reaction with primary amines. The direct reaction of the tetrahydrobenzofuran-4(5*H*)-one compounds derived from dimedone with amines gave 1-alkyl-2-alkylimino-3-aryl-6,7-dihydroindole-4(5*H*)-ones, while starting materials derived from 1,3-cyclohexanedione underwent an unprecedented 2-deacylation reaction and gave 1-alkyl-3-aryl-6,7-dihydroindole-4(5*H*)-ones.

1. Introduction

Oxahydrindanes (hydrobenzo[*b*]furans) are central structural cores of a broad range of natural products, such as 3,6-dimethyl-2,3,3a,4,5,7a-hexahydrobenzofuran, one of the major aroma compounds in the dill herb, paniculide A, evodone, pongamol, isoeupatin, the aurones and the tubipofurans, among others, and are also structural fragments of complex bioactive macrocyclic natural products like the milbemycins and the avermerctins. While there is a plethora of methods for the synthesis of fully aromatic benzo[*b*]furan derivatives,[1] not many general routes are known for the preparation of the various types of oxhydrindanes.[2] Regarding the particular case of 2,3,4,5,6,7-hexahydrobenzofurans, an efficient entry has been recently established, based on a pyridine-catalyzed, three-component reaction between cyclic 1,3-diketones, aromatic aldehydes and benzyl or phenacyl bromides.[3] Following the discovery of the oxidative addition of 1,3-dicarbonyl compounds to alkenes promoted by one-electron oxidants,[4] the oxidative cycloaddition of 1,3-dicarbonyl compounds and 2-substituted acrylates has been identified as a reliable method for the synthesis of 2,2-disubstituted 2,3,4,5,6,7-hexahydrobenzofurans[5] and a similar reaction starting from nitrostyrenes has been applied to the preparation of 2-hydroxyimino-3-substituted compounds.[6] However, with the exception of a few examples related to the construction of 2-spiro compounds,[7] the stereochemical outcome of the radical-mediated synthesis of hexahydrobenzofurans has not been studied. We describe here our results in this area, together with our work on the modification of the reaction to allow the functionalization of the C-3 position and the preparation of other fused 2,3-dihydrofuran systems. Finally, we also report our studies on the transformation of oxhydrindanes into several types of tetrahydroindoles.

2. Results and discussion

Cerium(IV) ammonium nitrate (CAN) is a stable, easily handled and inexpensive reagent that has found widespread application in synthesis[8,9] mainly because of its ability to generate carbon-centered radicals, which is associated to its strong one-electron oxidative properties. Due to our interest in the synthetic applications of Ce(IV) salts,[10] we undertook the study of the CAN-promoted reaction between cyclic β-diketones and chalcones as α,β-unsaturated carbonyl substrates able to generate 2,3-disubstituted 2,3,4,5,6,7-hexahydrobenzofurans and hence useful for the study of the diastereoselectivity of the radical cyclization leading to the benzofuran skeleton. The conditions found in the literature for related examples[4] failed to give any recognizable products; however, after some optimization work, we found that slow addition of CAN in acetonitrile at −20 °C to a solution of the reactants in the same solvent, followed by stirring at room temperature for 24 h, afforded the expected products in good to excellent yields (Scheme 1 and Table 1). The overall transformation involves the generation of

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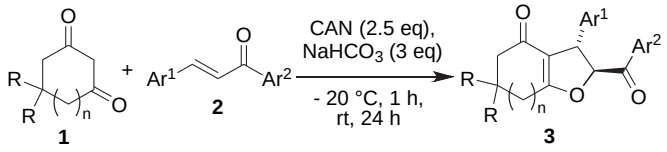
doi:10.1016/j.tet.2010.10.017

a C–C and a C–O bond and affords 2,3-disubstituted hexahydrobenzofuran derivatives bearing functional groups at the C-2 and C-4 positions. The diastereoselectivities were also normally very good, with most of the reactions giving *trans*/*cis* ratios higher than 10:1 and half of them giving exclusively the *trans* isomer. In an effort to extend the synthetic scope of the method, we also investigated the CAN-promoted reaction between 1,3-cyclopentanedione **7** and chalcones **2**, which afforded compounds **3n** and **3o** in good yields and with diastereoselectivities comparable to those found for the six-membered substrates (entries 14 and 15). This result is interesting in view of the limited availability of methods for the preparation of cyclopenta[*b*]furan derivatives. In fact, the 2,3-disubstituted 2,3,5,6-tetrahydrocyclopenta[*b*]furan framework found in **3n** and **3o** is unknown in the literature.[11]



Scheme 1. CAN-promoted, *trans*-diastereoselective synthesis of 2,3-disubstituted 2,3,6,7-tetrahydrobenzofuran-4(5*H*)-one derivatives.

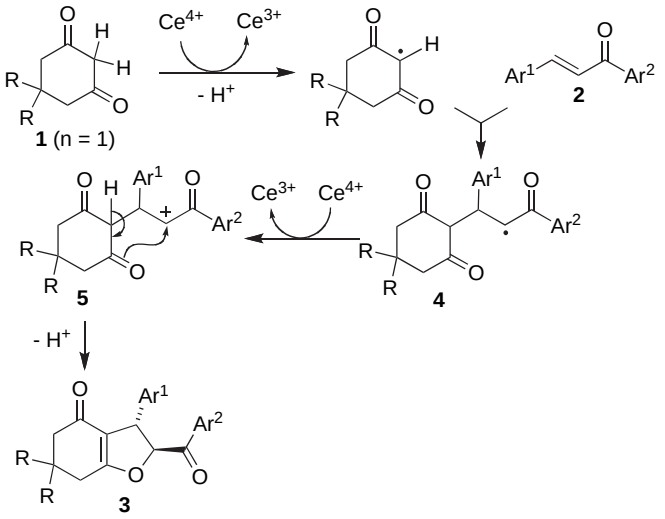
Table 1
Scope and yields of the synthesis of compounds **3**

Entry	Product	*n*	Ar^1	Ar^2	R	Yield (%)	dr (*trans*/*cis*)
1	**3a**	1	Ph	Ph	Me	82	8:1
2	**3b**	1	Ph	Ph	H	81	7:1
3	**3c**	1	Ph	4-MeC_6H_4	Me	80	1:0
4	**3d**	1	Ph	4-MeC_6H_4	H	85	1:0
5	**3e**	1	4-MeC_6H_4	Ph	Me	80	1:0
6	**3f**	1	4-MeC_6H_4	Ph	H	85	1:0
7	**3g**	1	4-MeC_6H_4	4-MeC_6H_4	Me	85	20:1
8	**3h**	1	4-MeC_6H_4	4-MeC_6H_4	H	83	11:1
9	**3i**	1	Ph	4-ClC_6H_4	Me	70	17:1
10	**3j**	1	Ph	4-ClC_6H_4	H	72	18:1
11	**3k**	1	4-BrC_6H_4	4-MeC_6H_4	H	65	6:1
12	**3l**	1		Ph	H	81	1:0
13	**3m**	1		4-MeC_6H_4	H	82	1:0
14	**3n**	0	Ph	Ph	H	85	6:1
15	**3O**	0	Ph	4-MeC_6H_4	H	80	1:0

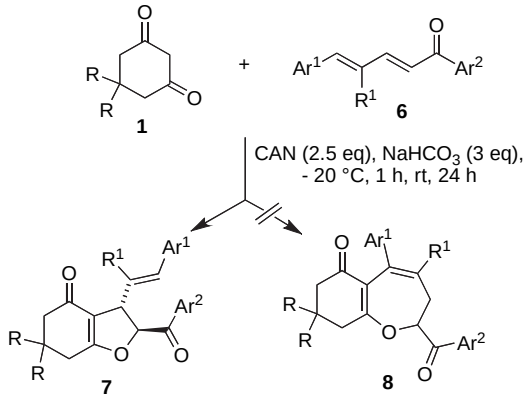
A mechanistic proposal to explain the isolation of compounds **3** is summarized in Scheme 2 and involves an initial one-electron oxidation of the starting dicarbonyl compound **1** to generate a C-centered radical **4**, followed by its addition to chalcone **2**, a second oxidation step to generate carbocation **5** and a final cyclization.

In order to achieve functionalization also at C-3, we studied the reaction starting from compounds with extended conjugation **6**,[12] which can be regarded as chalcone vinilogues. As shown in Scheme 3 and Table 2, these reactions afforded the expected 3-vinylated products **7** in good yields, and also with good *trans*-diastereoselectivities same for the case where R^1=Me. Interestingly, the radical reactions starting from compounds **4** proceeded with full regioselectivity and afforded exclusively compounds **7**, with no trace of the other potential products according to the proposed mechanism, namely the fused oxepines **8**.

With a reliable method for the synthesis of fused 2,3-dihydrofuran derivatives in hand, we set out to study their application to the synthesis of nitrogen heterocycles, which we considered of interest in view of the biological importance of 4-hydroxyindoles[13] and the difficulties often found in their preparation by traditional methods.[14]



Scheme 2. Mechanistic proposal to account for the CAN-promoted synthesis of 2,3,6,7-tetrahydrobenzofuran-4(5*H*)-ones.

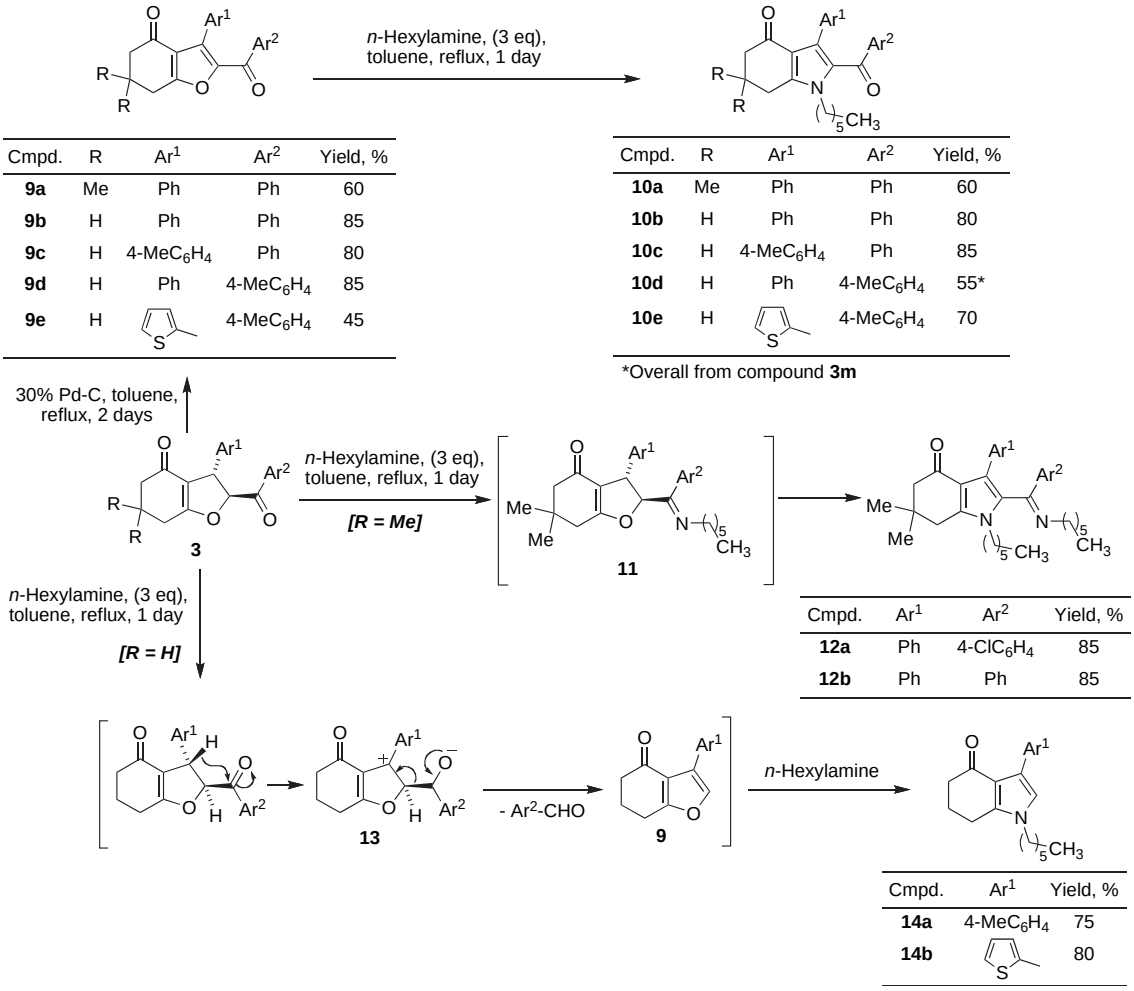


Scheme 3. CAN-promoted synthesis of C_3-functionalized 2,3,6,7-tetrahydrobenzofuran-4(5*H*)-ones **7**.

Table 2
Scope and yields of the synthesis of C_3-functionalized compounds **7**

Entry	Product	Ar^1	Ar^2	R	R^1	Yield (%)	dr (*trans*/*cis*)
1	**7a**	Ph	Ph	Me	H	80	10:1
2	**7b**	Ph	Ph	H	H	82	8:1
3	**7c**	Ph	4-MeC_6H_4	Me	H	85	11:1
4	**7d**	Ph	4-ClC_6H_4	Me	H	80	6:1
5	**7e**	Ph	Ph	Me	Me	70	2:1

While the transformation of fused furans bearing a 2-methyl substituent into the corresponding pyrroles by reaction with primary amines is known in the literature,[15] we desired to investigate the generalization of this result to 2-acyl derivatives, and also were intrigued by the possibility of carrying out a similar transformation starting directly from our fused 2,3-dihydro systems **3**. For the initial study (Scheme 4), we first dehydrogenated compounds **3** to tetrahydrobenzofuran derivatives **9** by refluxing them in toluene containing suspended palladium on charcoal. Subsequent treatment of compounds **9** with hexylamine, used as a model primary amine, again in refluxing toluene, afforded, as expected, the 1-hexyl-2-arylcarbonyl-3-aryl-4-oxo-4,5,6,7-tetrahydroindoles **10**, presumably by an ANRORC (Addition of Nucleophile, Ring-Opening and Ring-Closure) mechanism. These compounds are of interest in themselves and also as potential precursor to 4-hydroxyindoles through oxygen-promoted dehydrogenation.[12] Since we had purposefully designed the conditions to be similar for both reactions, we attempted the one-pot



Cmpd.	R	Ar^1	Ar^2	Yield, %
9a	Me	Ph	Ph	60
9b	H	Ph	Ph	85
9c	H	4-MeC_6H_4	Ph	80
9d	H	Ph	4-MeC_6H_4	85
9e	H		4-MeC_6H_4	45

Cmpd.	R	Ar^1	Ar^2	Yield, %
10a	Me	Ph	Ph	60
10b	H	Ph	Ph	80
10c	H	4-MeC_6H_4	Ph	85
10d	H	Ph	4-MeC_6H_4	55*
10e	H		4-MeC_6H_4	70

*Overall from compound **3m**

Cmpd.	Ar^1	Ar^2	Yield, %
12a	Ph	4-ClC_6H_4	85
12b	Ph	Ph	85

Cmpd.	Ar^1	Yield, %
14a	4-MeC_6H_4	75
14b		80

Scheme 4. Transformation of compounds **3** into fused pyrroles **10**–**12**.

transformation of compounds **3** into **10**, but obtained only complex mixtures.

We next attempted the direct reaction of 2,3-dihydrofuran derivatives **3** with hexylamine, and obtained the results shown in the lower half of Scheme 4. For the case R=Me, the observed products were imines **12**. These compounds were not observed in the reactions leading to **10**, which shows that the reaction of the amine with the carbonyl group in **10**, which is conjugated with the electron-releasing pyrrole nitrogen atom, is not possible under the reaction conditions. Therefore, the imine formation step can be assumed to take place on **3** leading to intermediate **11**, which would then undergo the same reaction sequence as above, finally furnishing **12**. On the other hand, for starting materials where R=H, the final products were 3-aryltetrahydroindoles **14**, lacking the 2-acyl group, which is a relevant result due to the importance of 3-arylindole frameworks.[16] Loss of the 2-acyl substituent can be rationalized as a consequence of an intramolecular hydride transfer furnishing the highly stabilized carbocation **13**, which would then evolve to intermediates with structure **9** and a molecule of aldehyde Ar^2CHO. Compounds **9** would then afford the observed final products **14** by ANRORC-type reaction with the primary amine, as described above. The difference in behaviour between the cases R=Me and R=H is probably due to the fact that in the latter case hydride shift takes place before imine formation, for reasons that are not clearly understood at present.

In summary and conclusion, we have shown that the CAN-promoted reaction between cyclic 1,3-diketones and chalcones, affords oxygen heterocycles containing a 2,3-dihydrofuran fragment fused to a five-or six-membered carbocycle. These reactions, which involve the use of very simple and inexpensive reagents, are highly diastereoselective in favour of the *trans* diastereoisomers, and could be designed to yield products functionalized at the C-2 and C-4 or C-2,3,4 positions. The fused 2,3-dihydrofuran derivatives were shown to be useful precursors for 6,7-dihydroindole-4(5*H*)-ones. Thus, 2-acyl-3-aryl-6,7-dihydrobenzofuran-4(5*H*)-ones were transformed into 1-alkyl-2-acyl-3-aryl-6,7-dihydroindole-4(5*H*)-ones by 2,3-dehydrogenation followed by reaction with primary amines. The direct reaction of the tetrahydrobenzofuran-4(5*H*)-one compounds derived from dimedone with amines was also possible and gave 1-alkyl-2-alkylimino-3-aryl-6,7-dihydroindole-4(5*H*)-ones, while analogous starting materials derived from 1,3-cyclohexanedione underwent an unprecedented 2-deacylation reaction and gave 1-alkyl-3-aryl-6,7-dihydroindole-4(5*H*)-ones. These processes significantly extend the synthetic scope of the reaction between 1,3-dicarbonyl compounds and alkenes under free-radical conditions and the subsequent transformation of the initial benzofuran products into indole derivatives.

3. Experimental

3.1. General

All reagents were of commercial quality (Aldrich, Fluka, SDS, Probus) and were used as received. Solvents (from SDS) were dried and purified using standard techniques. Reactions were monitored by thin layer chromatography, on aluminium plates coated with

silica gel with fluorescent indicator (SDS CCM221254). Separations by flash chromatography were performed on silica gel (SDS 60 ACC, 230–40 mesh). Melting points were measured with a Reichert 723 hot stage microscope, and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer Paragon 1000 FT-IR spectrophotometer, with all compounds examined as films on a NaCl disk. NMR spectra were obtained on a Bruker Avance instrument (250 MHz for ^{1}H, 62.9 MHz for ^{13}C), maintained by the Servicio de RMN, Universidad Complutense, with $CDCl_3$ as solvent. Combustion elemental analyses were determined by the Servicio de Microanálisis Elemental, Universidad Complutense, using a Leco 932 CHNS microanalyzer.

3.2. General procedure for the CAN-promoted synthesis of fused 2,3-dihydrobenzofurans: preparation of compounds (3) and (7)

A mixture of the suitable 1,3-dicarbonyl compound **1** (1 mmol), chalcone **2** (1 mmol) for the synthesis of **3** or vinylogous chalcone **4** for the synthesis of **5** and $NaHCO_3$ (3 mmol) in acetonitrile (5 mL) was cooled to −20 °C. To this stirred solution was dropwise added a solution of CAN (2.5 equiv) in acetonitrile (10 mL), over 30 min. The reaction mixture was stirred at −20 °C for 1 h and then at room temperature for 24 h. After completion of the reaction as monitored by TLC, the mixture was diluted with CH_2Cl_2 (60 mL) and washed with water. The organic layer was dried (anhydrous Na_2SO_4) and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel, eluting with a petroleum ether–ethyl acetate mixture (80:20, v/v).

*3.2.1. (±)-trans-2-Benzoyl-6,6-dimethyl-3-phenyl-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**3a**).* Colourless solid, mp 98 °C. IR (neat) 2959.1, 1684.0, 1636.3, 1395.9, 1216.3, 1069.9, 963.5, 758.5, 696.4 cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.19 (s, 3H), 1.22 (s, 3H), 2.29–2.30 (m, 2H), 2.51–2.53 (m, 2H), 5.05 (d, J=5.8 Hz, 1H), 5.89 (d, J=5.8 Hz, 1H), 7.26–7.32 (m, 2H), 7.38–7.48 (m, 5H), 7.55–7.62 (m, 1H), 8.02 (dd, J=1.1 and 8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 28.9, 29.1, 34.9, 38.3, 44.1, 54.9, 90.5, 113.2, 126.2 (2C), 128.9 (2C), 129.5 (2C), 129.6 (3C), 134.1, 136.6, 139.9, 177.9, 194.1, 199.5. Anal. Calcd for $C_{23}H_{22}O_3$: C, 79.74; H, 6.40. Found: C, 79.53; H, 6.59.

*3.2.2. (±)-trans-2-Benzoyl-3-phenyl-2,3,6,7-tetrahydrobenzo-furan-4(5H)-one (**3b**).* Colourless solid, mp 104 °C. IR (neat) 2948.2, 1682.7, 1637.8, 1448.4, 1394.4, 1215.3, 1176.1, 759.4, 692.1 cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.09–2.21 (m, 2H), 2.33–2.46 (m, 2H), 2.62–2.74 (m, 2H), 5.07 (dd, J=1.4 and 6.1 Hz, 1H), 5.93 (d, J=6.2 Hz, 1H), 7.28–7.32 (m, 2H), 7.36–7.49 (m, 5H), 7.56–7.63 (m, 1H), 8.03 (dd, J=1.1 and 8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.9, 24.5, 36.9, 55.1, 90.4, 114.8, 126.2 (2C), 128.9 (2C), 129.5 (2C), 129.6 (3C), 134.1, 136.8, 139.8, 178.7, 194.5, 199.6. Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 79.02; H, 6.18.

*3.2.3. (±)-trans-6,6-Dimethyl-2-(4-methylbenzoyl)-3-phenyl-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**3c**).* Colourless viscous liquid. IR (neat) 2960.2, 1678.3, 1641.5, 1606.1, 1396.4, 1227.2, 1183.9, 1070.1, 963.7, 759.0, 699.8 cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.18 (s, 3H), 1.20 (s, 3H), 2.27 (d, J=2.6 Hz, 2H), 2.39 (s, 3H), 2.50 (br s, 2H), 5.01 (d, J=5.7 Hz, 1H), 5.86 (d, J=5.7 Hz, 1H), 7.24–7.32 (m, 4H), 7.36–7.43 (m, 3H), 7.90 (d, J=8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 22.1, 28.9, 29.1, 34.8, 38.3, 44.0, 54.8, 90.5, 113.2, 126.2 (2C), 129.4, 129.5 (2C), 129.7 (2C), 129.7 (2C), 134.1, 139.9, 145.1, 166.8, 194.1, 198.9. Anal. Calcd for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71. Found: C, 79.62; H, 6.43.

*3.2.4. (±)-trans-2-(4-Methylbenzoyl)-3-phenyl-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**3d**).* Colourless solid, mp 202–204 °C. IR (neat) 2947.4, 1674.9, 1639.9, 1605.6, 1394.1, 1230.7, 1177.4, 1063.9, 759.4, 699.8 cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.07–2.24 (m, 2H), 2.30–2.50 (m, 2H), 2.42 (s, 3H), 2.57–2.74 (m, 2H), 5.06 (dd, J=1.0 and 6.1 Hz, 1H), 5.93 (dd, J=1.4 and 6.1 Hz, 1H), 7.24–7.34 (m, 4H), 7.40–7.46 (m, 3H), 7.96 (dd, J=1.6 and 8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.9, 22.2, 24.5, 36.9, 54.9, 90.4, 114.7, 126.2 (2C), 129.4, 129.5 (2C), 129.6 (2C), 129.8 (2C), 134.2, 139.9, 145.1, 178.6, 194.5, 199.0. Anal. Calcd for $C_{22}H_{20}O_3$: C, 79.50; H, 6.06. Found: C, 79.27; H, 5.94.

*3.2.5. (±)-trans-2-Benzoyl-6,6-dimethyl-3-(4-methylphenyl)-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**3e**).* Light yellow viscous liquid. IR (neat) 2958.0, 1683.1, 1640.6, 1395.6, 1216.2, 1068.5, 963.3, 692.5 cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.20 (s, 3H), 1.23 (s, 3H), 2.21–2.32 (m, 2H), 2.40 (s, 3H), 2.50–2.52 (m, 2H), 5.05 (d, J=5.7 Hz, 1H), 5.84 (d, J=5.7 Hz, 1H), 7.17–7.25 (m, 2H), 7.21 (d, J=3.8 Hz, 2H), 7.42–7.52 (m, 2H), 7.56–7.63 (m, 1H), 8.02 (d, J=7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.7, 29.0, 29.1, 34.9, 38.4, 44.2, 54.9, 90.6, 113.2, 126.3 (2C), 128.9 (2C), 129.6 (2C), 130.2 (2C), 134.1, 136.7, 136.9, 139.6, 177.8, 194.1, 199.5. Anal. Calcd for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71. Found: C, 79.65; H, 6.52.

*3.2.6. (±)-trans-2-Benzoyl-3-(4-methylpheny)-2,3,6,7-tetra-hydrobenzofuran-4(5H)-one (**3f**).* Light yellow viscous liquid. IR (neat) 2924.3, 1682.1, 1634.2, 1393.7, 1215.7, 1176.3, 1064.1, 813.4 cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.07–2.26 (m, 2H), 2.31–2.46 (m, 2H), 2.39 (s, 3H), 2.61–2.75 (m, 2H), 5.07 (d, J=6.1 Hz, 1H), 5.88 (d, J=6.1 Hz, 1H), 7.18–7.29 (m, 4H), 7.42–7.48 (m, 2H), 7.56–7.62 (m, 1H), 8.03 (d, J=8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.7, 22.0, 24.6, 36.9, 55.0, 90.5, 114.8, 126.3 (2C), 128.9 (2C), 129.6 (2C), 130.1 (2C), 134.0, 136.8, 136.9, 139.5, 178.7, 194.6, 199.6. Anal. Calcd for $C_{22}H_{20}O_3$: C, 79.50; H, 6.06. Found: C, 79.23; H, 6.19.

*3.2.7. (±)-trans-6,6-Dimethyl-2-(4-methylbenzoyl)-3-(4-methylphenyl)-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**3g**).* Colourless viscous liquid. IR (neat) 2959.4, 1678.8, 1641.4, 1606.5, 1395.7, 1226.5, 1182.3, 1067.7, 963.1 cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.19 (s, 3H), 1.22 (s, 3H), 2.22–2.37 (m, 2H), 2.39 (s, 3H), 2.41 (s, 3H), 2.49–2.51 (m, 2H), 5.02 (d, J=5.6 Hz, 1H), 5.84 (d, J=5.7 Hz, 1H), 7.17–7.29 (m, 6H), 7.92 (d, J=8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.7, 22.1, 29.0, 29.1, 34.9, 38.3, 44.1, 54.7, 90.5, 113.2, 126.3 (2C), 129.7 (2C), 129.8 (2C), 130.1 (2C), 134.1, 137.0, 139.4, 144.9, 177.6, 194.0, 198.9. Anal. Calcd for $C_{25}H_{26}O_3$: C, 80.18; H, 7.00. Found: C, 80.11; H, 7.07.

*3.2.8. (±)-trans-2-(4-Methylbenzoyl)-3-(4-methylphenyl)-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**3h**).* Colourless viscous liquid. IR (neat) 2945.7, 1678.0, 1636.0, 1606.2, 1393.8, 1230.7, 1177.0, 811.7 cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 2.09–2.20 (m, 2H), 2.30–2.44 (m, 2H), 2.39 (s, 3H), 2.41 (s, 3H), 2.55–2.72 (m, 2H), 5.04 (d, J=6.1 Hz, 1H), 5.87 (d, J=6.1 Hz, 1H), 7.17–7.21 (m, 4H), 7.28 (d, J=6.3 Hz, 2H), 7.93 (d, J=8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.7, 22.0, 22.1, 24.6, 36.9, 54.9, 90.5, 114.7, 126.3 (2C), 129.6 (2C), 129.8 (2C), 130.1 (2C), 134.3, 136.9, 139.4, 144.9, 178.6, 194.6, 199.0. Anal. Calcd for $C_{23}H_{22}O_3$: C, 79.74; H, 6.40. Found: C, 79.45; H, 6.22.

*3.2.9. (±)-trans-2-Benzoyl-3-(4-chlorophenyl)-6,6-dimethyl-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**3i**).* Colourless viscous liquid. IR (neat) 2958.7, 1683.8, 1652.1, 1588.9, 1397.4, 1213.2, 1091.2, 1003.1, 760.5, 698.2 cm^{-1}. ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.20 (s, 3H), 1.21 (s, 3H), 2.28–2.29 (m, 2H), 2.51–2.53 (m, 2H), 4.99 (d, J=5.7 Hz, 1H), 5.94 (d, J=5.7 Hz, 1H), 7.26–7.29 (m, 2H), 7.41–7.45 (m, 5H), 7.98 (dd, J=1.9 and 8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 29.0, 29.1, 34.9, 38.3, 51.4, 55.0, 90.4, 113.0, 126.1 (2C), 129.3 (2C), 129.6 (3C),

130.1 (2C), 135.0, 139.8, 140.7, 177.9, 193.9, 198.4. Anal. Calcd for $C_{23}H_{21}ClO_3$: C, 72.53; H, 5.56. Found: C, 72.31; H, 5.31.

*3.2.10. (±)-trans-2-Benzoyl-3-(4-chlorophenyl)-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**3j**).* Colourless viscous liquid. IR (neat) 2947.4, 1679.5, 1636.7, 1588.0, 1394.9, 1213.2, 1174.6, 1090.8, 760.4, 699.6 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.07–2.23 (m, 2H), 2.36–2.43 (m, 2H), 2.57–2.69 (m, 2H), 5.01 (dd, J=1.3 and 6.1 Hz, 1H), 5.96 (d, J=6.1 Hz, 1H), 7.25–7.30 (m, 2H), 7.37–7.45 (m, 5H), 8.01 (dd, J=1.9 and 6.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.9, 24.5, 36.9, 55.2, 90.4, 114.6, 126.1 (2C), 129.2 (2C), 129.5 (3C), 130.1 (2C), 135.1, 139.7, 140.7, 178.9, 194.5, 198.6. Anal. Calcd for $C_{21}H_{17}ClO_3$: C, 71.49; H, 4.86. Found: C, 71.27; H, 4.71.

*3.2.11. (±)-trans-3-(4-Bromophenyl)-2-(4-chlorobenzoyl)-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**3k**).* Colourless viscous liquid. IR (neat) 2946.6, 1677.9, 1640.7, 1606.2, 1488.0, 1391.3, 1230.4, 1177.2, 1070.9, 1010.5 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.07–2.18 (m, 2H), 2.29–2.47 (m, 2H), 2.43 (s, 3H), 2.54–2.76 (m, 2H), 4.98 (d, J=6.1 Hz, 1H), 5.89 (d, J=6.2 Hz, 1H), 7.15 (d, J=8.5 Hz, 2H), 7.27 (d, J=8.4 Hz, 2H), 7.53 (d, J=8.9 Hz, 2H), 7.93 (d, J=8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.9, 22.2, 24.5, 36.9, 54.9, 89.6, 114.7, 123.4, 127.8 (2C), 129.7 (2C), 129.8 (2C), 132.6 (2C), 134.1, 138.9, 145.2, 178.4, 194.5, 198.8. Anal. Calcd for $C_{22}H_{19}BrO_3$: C, 64.25; H, 4.66. Found: C, 63.98; H, 4.42.

*3.2.12. (±)-trans-2-Benzoyl-3-(2-thienyl)-2,3,6,7-tetrahydro-benzofuran-4(5H)-one (**3l**).* Pale brown crystals, mp 132 °C (EtOAc–hexane). IR (neat) 2948.7, 1683.7, 1635.5, 1448.1, 1394.4, 1229.2, 1181.3, 912.5 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.04–2.23 (m, 2H), 2.29–2.44 (m, 2H), 2.47–2.70 (m, 2H), 5.19 (dd, J=1.3 and 5.7 Hz, 1H), 6.16 (d, J=5.8 Hz, 1H), 7.00–7.04 (m, 1H), 7.09–7.11 (m, 1H), 7.37–7.39 (m, 1H), 7.44–7.50 (m, 2H), 7.56–7.63 (m, 1H), 8.07 (dd, J=1.5 and 8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.9, 24.6, 36.9, 55.1, 85.9, 114.6, 127.0, 127.3, 127.5, 128.9 (2C), 129.6 (2C), 134.2, 136.6, 142.0, 177.9, 194.5, 198.9. Anal. Calcd for $C_{19}H_{16}SO_3$: C, 70.35; H, 4.97; S, 9.88. Found: C, 70.05; H, 4.94; S, 9.79.

*3.2.13. (±)-trans-2-(4-Methylbenzoyl)-3-(2-thienyl)-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**3m**).* Light yellow viscous liquid. IR (neat) 2949.3, 1677.1, 1634.3, 1606.1, 1394.0, 1229.0, 1182.2, 1064.3, 709.8 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.99–2.21 (m, 2H), 2.36–2.49 (m, 2H), 2.41 (s, 3H), 2.52–2.69 (m, 2H), 5.17 (d, J=5.7 Hz, 1H), 6.16 (d, J=5.7 Hz, 1H), 7.00–7.03 (m, 1H), 7.09–7.11 (m, 1H), 7.26 (d, J=8.0 Hz, 2H), 7.37 (d, J=5.0 Hz, 1H), 8.00 (d, J=8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.9, 22.2, 24.6, 36.9, 54.9, 85.5, 114.5, 126.9, 127.2, 127.5, 129.7 (2C), 129.8 (2C), 134.0, 142.2, 145.2, 177.9, 194.5, 198.3. Anal. Calcd for $C_{20}H_{18}SO_3$: C, 70.98; H, 5.36; S, 9.47. Found: C, 70.73; H, 5.12; S, 9.21.

*3.2.14. 2-Benzoyl-3-phenyl-5,6-dihydro-2H-cyclopenta[b]furan-4(3H)-one (**3n**).* Colourless viscous liquid. IR (neat) 2924.8, 1684.5, 1626.0, 1448.2, 1400.5, 1242.7, 755.7, 690.7 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.72–2.76 (m, 2H), 2.85–2.89 (m, 2H), 4.83–4.87 (m, 1H), 6.86 (d, J=5.5 Hz, 1H), 7.29–7.66 (m, 8H), 8.17 (dd, J=1.4 and 6.9 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 22.7, 41.2, 54.5, 98.2, 119.8, 126.1 (2C), 128.9 (2C), 129.5 (2C), 129.7, 129.9 (2C), 134.5, 135.8, 139.5, 195.1, 196.1, 196.3. Anal. Calcd for $C_{20}H_{16}O_3$: C, 78.93; H, 5.30. Found: C, 78.64; H, 5.17.

*3.2.15. 2-(4-Methylbenzoyl)-3-phenyl-5,6-dihydro-2H-cyclopenta[b]-furan-4(3H)-one (**3o**).* Colourless viscous liquid. IR (neat) 2925.4, 1681.5, 1626.2, 1606.3, 1400.6, 1243.3, 1180.2, 847.8, 754.9, 699.1 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.44 (s, 3H), 2.73–2.75 (m, 2H), 2.85–2.87 (m, 2H), 4.82 (d, J=5.3 Hz, 1H), 6.85 (d, J=5.4 Hz, 1H), 7.29–7.42 (m, 7H), 8.07 (d, J=8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 22.3, 22.7, 41.3, 54.4, 89.1, 119.9, 126.2 (2C), 129.6 (3C), 129.7 (2C), 130.1 (2C), 133.3, 139.6, 145.5, 195.2, 195.8, 196.1. Anal. Calcd for $C_{21}H_{18}O_3$: C, 79.22; H, 5.70. Found: C, 78.92; H, 5.61.

*3.2.16. (±)-trans-2-Benzoyl-6,6-dimethyl-3-styryl-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**7a**).* Colourless viscous liquid. IR (neat) 2958.9, 1684.0, 1652.8, 1635.9, 1558.5, 1540.3, 1506.8, 1396.5, 1223.6 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.19 (s, 3H), 1.22 (s, 3H), 2.29 (br s, 2H), 2.48 (br s, 2H), 4.90 (d, J=5.1 Hz, 1H), 5.51 (dd, J=5.3 and 7.9 Hz, 1H), 6.35 (dd, J=7.9 and 15.8 Hz, 1H), 6.67 (d, J=15.8 Hz, 1H), 7.29–7.65(m, 8H), 8.11 (d, J=8.3 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 28.8, 29.3, 34.8, 38.4, 51.3, 52.9, 89.9, 113.1, 125.8, 127.3 (2C), 129.0 (2C), 129.1, 129.2 (2C), 129.6 (2C), 134.1, 134.6, 135.8, 136.6, 177.5, 194.1, 198.9. Anal. Calcd for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49. Found: C, 80.32; H, 6.28.

*3.2.17. (±)-trans-2-Benzoyl-3-styryl-2,3,6,7-tetrahydro-benzofuran-4(5H)-one (**7b**).* Colourless viscous liquid. IR (neat) 2947.3, 1678.9, 1640.9, 1596.7, 1448.9, 1396.1, 1231.6, 1178.4, 914.4, 691.7 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.07–2.18 (m, 2H), 2.36–2.43 (m, 2H), 2.57–2.64 (m, 2H), 4.92 (d, J=5.5 Hz, 1H), 5.54 (dd, J=5.6 and 7.9 Hz, 1H), 6.35 (dd, J=7.9 and 15.8 Hz, 1H), 6.67 (d, J=15.8 Hz, 1H), 7.29–7.64 (m, 8H), 8.12 (dd, J=1.5 and 8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.9, 24.6, 36.9, 53.0, 89.9, 114.6, 125.8, 127.3 (2C), 129.0 (2C), 129.1, 129.2 (2C), 129.6 (2C), 134.1, 134.7, 135.8, 136.7, 178.6, 194.7, 199.1. Anal. Calcd for $C_{23}H_{20}O_3$: C, 80.21; H, 5.85. Found: C, 79.96; H, 6.04.

*3.2.18. (±)-trans-6,6-Dimethyl-2-(4-methylbenzoyl)-3-styryl-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**7c**).* Colourless viscous liquid. IR (neat) 2957.9, 1678.6, 1640.4, 1606.2, 1397.1, 1224.5, 1182.6, 968.2, 693.3 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.18 (s, 3H), 1.22 (s, 3H), 2.29 (br s, 2H), 2.44 (s, 3H), 2.47 (br s, 2H), 4.88 (d, J=5.1 Hz, 1H), 5.51 (dd, J=5.2 and 7.9 Hz, 1H), 6.35 (dd, J=7.9 and 15.8 Hz, 1H), 6.67 (d, J=15.8 Hz, 1H), 7.28–7.46 (m, 7H), 8.01 (d, J=8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 22.2, 28.8, 29.3, 34.8, 38.4, 51.3, 52.7, 89.9, 113.0, 125.9, 127.3 (3C), 129.1, 129.2 (2C), 129.7 (3C), 134.0, 134.5, 135.8, 145.1, 177.4, 194.1, 198.4. Anal. Calcd for $C_{26}H_{26}O_3$: C, 80.80; H, 6.78. Found: C, 80.65; H, 6.38.

*3.2.19. (±)-trans-2-(4-Chlorobenzoyl)-6,6-dimethyl-3-styryl-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**7d**).* White crystals, mp 120 °C (EtOAc–hexane). IR (neat) 2959.3, 1682.0, 1636.4, 1588.5, 1399.5, 1225.6, 1091.8, 965.0 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.17 (s, 3H), 1.18 (s, 3H), 2.26 (br s, 2H), 2.46 (s, 2H), 4.85 (d, J=5.2 Hz, 1H), 5.55 (dd, J=5.3 and 7.9 Hz, 1H), 6.32 (dd, J=7.9 and 15.8 Hz, 1H), 6.67 (d, J=15.8 Hz, 1H), 7.29–7.47 (m, 7H), 8.07 (d, J=8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 28.8, 29.3, 34.8, 38.4, 44.1, 52.9, 89.9, 112.9, 125.7, 127.3 (2C), 129.2 (3C), 129.3 (2C), 131.0 (2C), 134.7, 134.9, 135.7, 140.6, 177.7, 194.1, 197.9. Anal. Calcd for $C_{25}H_{23}ClO_3$: C, 73.79; H, 5.70. Found: C, 69.56; H, 5.90.

*3.2.20. (±)-trans-2-Benzoyl-6,6-dimethyl-3-(1-methyl-2-phenyl-vinyl)-2,3,6,7-tetrahydrobenzofuran-4(5H)-one (**7e**).* Colourless viscous liquid. IR (neat) 2960.4, 1643.4, 1394.8, 1287.8, 1221.8, 1028.8, 700.3 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.22 (s, 3H), 1.26 (s, 3H), 1.67 (s, 3H), 2.32 (s, 2H), 2.52–2.57 (m, 2H), 4.24 (s, 1H), 6.24 (d, J=15.9 Hz, 1H), 6.67 (d, J=15.9 Hz, 1H), 7.06–7.09 (m, 2H), 7.27–7.54 (m, 8H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 28.2, 29.1, 29.5, 34.6, 38.5, 51.6, 56.3, 94.3, 115.1, 125.7, 127.9, 128.7 (2C), 128.8 (2C), 129.1 (2C), 129.2 (2C), 132.9, 137.5, 138.6, 147.9, 175.4, 192.8, 194.6. Anal. Calcd for $C_{26}H_{26}O_3$: C, 80.80; H, 6.78. Found: C, 80.54; H, 6.56.

3.3. General procedure for the dehydrogenation of (3): synthesis of compounds (9)

The suitable compound **3** (1 mmol) was dissolved in dry toluene (20 mL) and Pd–C (30%, 1 mmol) was added. The suspension was

refluxed for 2 days. After completion of the reaction, the mixture was filtered through Celite, which was washed with CH_2Cl_2 (20 mL), and the solvent was evaporated under reduced pressure. Pure compounds **11** were obtained by column chromatography on silica gel, eluting with a petroleum ether–ethyl acetate mixture (85:15, v/v).

*3.3.1. 2-Benzoyl-6,6-dimethyl-3-phenyl-6,7-dihydro-benzofuran-4(5H)-one (**9a**).* Colourless solid, mp 145 °C. IR (neat) 2960.0, 1681.7, 1448.9, 1332.8, 1227.0, 1053.3, 894.3, 767.7 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.24 (s, 6H), 2.39 (s, 2H), 2.92 (s, 2H), 7.29–7.36 (m, 3H), 7.41–7.47 (m, 2H), 7.54–7.63 (m, 3H), 7.92–7.95 (m, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 29.0 (2C), 35.8, 37.8, 52.4, 117.7, 121.7, 126.2 (2C), 129.1 (2C), 129.1 (2C), 129.2, 129.3, 129.8 (2C), 134.1, 137.7, 152.3, 165.3, 192.5, 192.9. Anal. Calcd for $C_{23}H_{20}O_3$: C, 80.21; H, 5.85. Found: C, 79.93; H, 5.76.

*3.3.2. 2-Benzoyl-3-phenyl-6,7-dihydrobenzofuran-4(5H)-one (**9b**).* Colourless solid, mp 175 °C. IR (neat) 3061.5, 2952.9, 1681.7, 1493.0, 1448.9, 1331.9, 1227.8, 1011.5, 692.1 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.24–2.32 (m, 2H), 2.51 (d, J=6.0 Hz, 2H), 3.05 (d, J=6.3 Hz, 2H), 7.29–7.36 (m, 3H), 7.40–7.49 (m, 3H), 7.53–7.62 (m, 3H), 7.93–7.97 (m, 1H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 22.8, 23.8, 38.1, 117.8, 122.9, 126.2 (2C), 129.0 (2C), 129.2 (2C), 129.3, 129.5, 129.6, 129.9 (2C), 134.1, 137.6, 151.8, 166.2, 193.1. Anal. Calcd for $C_{21}H_{16}O_3$: C, 79.73; H, 5.10. Found: C, 79.45; H, 4.97.

*3.3.3. 2-Benzoyl-3-(4-methylphenyl)-6,7-dihydrobenzofuran-4(5H)-one (**9c**).* Colourless viscous liquid. IR (neat) 2954.0, 1681.6, 1506.0, 1450.1, 1332.4, 1227.9, 1011.9, 893.3 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.20–2.30 (m, 2H), 2.32 (s, 3H), 2.50 (t, J=6.1 Hz, 2H), 3.05 (t, J=6.2 Hz, 2H), 7.12 (d, J=8.1 Hz, 2H), 7.39–7.63 (m, 5H), 7.95 (d, J=8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 21.7, 22.8, 23.8, 38.1, 122.8, 126.2 (2C), 126.4, 128.9, 128.9 (2C), 129.8 (2C), 129.9 (2C), 130.6, 134.1, 139.5, 152.1, 166.1, 193.1, 193.3. Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 79.78; H, 5.32.

*3.3.4. 2-(4-Methylbenzoyl)-3-phenyl-6,7-dihydrobenzofuran-4(5H)-one (**9d**).* White solid, mp 195 °C. IR (neat) 2950.6, 1682.1, 1604.4, 1491.6, 1430.4, 1331.3, 1230.1, 1175.9, 1011.2, 896.2, 768.6 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.25 (t, J=6.3 Hz, 2H), 2.41 (s, 3H), 2.49–2.54 (m, 2H), 3.05 (t, J=6.3 Hz, 2H), 7.22–7.37 (m, 5H), 7.56–7.61 (m, 2H), 7.85 (d, J=8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 19.9, 20.5, 21.5, 35.7, 115.6, 120.5, 123.8 (2C), 126.7 (2C), 126.8, 126.9, 127.4 (2C), 127.7 (2C), 132.8, 142.7, 149.2, 163.7, 190.3, 190.7. Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 79.69; H, 5.30.

*3.3.5. 2-(4-Methylbenzoyl)-3-(2-thienyl)-6,7-dihydro-benzofuran-4(5H)-one (**9e**).* Off-white solid, mp 197 °C. IR (neat) 2952.3, 1681.8, 1605.5, 1410.1, 1233.5, 1177.9, 1011.9, 835.4, 709.0 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.20–2.33 (m, 2H), 2.42 (s, 3H), 2.51 (t, J=6.0 Hz, 2H), 3.03 (t, J=6.3 Hz, 2H), 6.98–7.01 (m, 1H), 7.26 (d, J=7.9 Hz, 2H), 7.29–7.35 (m, 2H), 7.82 (d, J=8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 22.2, 22.7, 23.8, 38.1, 116.9, 122.6, 126.8, 127.3, 128.1, 129.7 (2C), 129.9 (2C), 130.9, 135.3, 144.9, 148.5, 165.8, 191.5, 192.9. Anal. Calcd for $C_{20}H_{16}O_3S$: C, 71.41; H, 4.79. Found: C, 71.28; H, 4.65.

3.4. General procedure for the reaction between benzofuran derivatives and primary amines. Synthesis of compounds (10), (12) and (14)

The suitable compound **3** or **9** (1 mmol) was dissolved in dry toluene (20 mL) and hexylamine (3 mmol) was added. The reaction mixture was refluxed for 24 h. After completion of the reaction, the solvent was evaporated under reduced pressure. Pure reaction products were obtained by a column chromatography on silica gel, eluting with a petroleum ether–ethyl acetate mixture (85:15, v/v).

*3.4.1. 2-Benzoyl-1-(n-hexyl)-6,6-dimethyl-3-phenyl-6,7-dihydroindol-4(5H)-one (**10a**).* Colourless viscous liquid. IR (neat) 2929.3, 1682.3, 1489.8, 1434.9, 1334.7, 1054.2, 767.5, 691.1 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.84–0.88 (m, 3H), 1.22 (s, 3H), 1.23 (s, 3H), 1.13–1.31 (m, 6H), 1.66–1.71 (m, 2H), 2.39 (d, J=2.0 Hz, 2H), 2.93 (d, J=1.5 Hz, 2H), 3.41 (dt, J=1.2 and 7.1 Hz, 2H), 7.28–7.37 (m, 6H), 7.60–7.64 (m, 2H), 7.77–7.82 (m, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.5, 23.0, 27.8, 28.8, 29.3, 30.9, 32.1, 35.7, 38.0, 52.6, 54.9, 113.4, 121.1, 124.8 (2C), 127.9 (2C), 128.7 (2C), 129.3 (2C), 129.8, 130.3, 131.5, 139.2, 149.6, 160.9, 165.8, 192.6. Anal. Calcd for $C_{29}H_{33}NO_2$: C, 81.46; H, 7.78; N, 3.28. Found: C, 81.23; H, 7.67; N, 3.12.

*3.4.2. 2-Benzoyl-1-(n-hexyl)-3-phenyl-6,7-dihydroindol-4(5H)-one (**10b**).* Colourless viscous liquid. IR (neat) 2956.9, 2929.8, 1674.5, 1651.9, 1488.9, 1470.3, 1367.1, 1122.2, 701.2 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.85 (t, J=6.4 Hz, 3H), 1.19–1.32 (m, 6H), 1.61–1.69 (m, 2H), 2.23–2.29 (m, 2H), 2.49 (t, J=6.0 Hz, 2H), 3.07 (t, J=6.2 Hz, 2H), 3.37 (dt, J=2.1 and 6.9 Hz, 2H), 7.29–7.36 (m, 6H), 7.60–7.64 (m, 2H), 7.76–7.79 (m, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.5, 22.8, 22.9, 24.0, 27.7, 30.9, 32.1, 38.3, 54.8, 113.5, 122.2, 124.9 (2C), 127.9 (2C), 128.6 (2C), 128.7, 129.3 (2C), 129.8, 130.3, 139.2, 149.2, 161.0, 166.8, 193.3. Anal. Calcd for $C_{27}H_{29}NO_2$: C, 81.17; H, 7.32; N, 3.51. Found: C, 79.98; H, 7.19; N, 3.32.

*3.4.3. 2-Benzoyl-1-(n-hexyl)-3-(4-methylphenyl)-6,7-dihydro-indol-4(5H)-one (**10c**).* Colourless viscous liquid. IR (neat) 2926.9, 2855.7, 1683.2, 1506.1, 1428.8, 1332.2, 1061.6, 1010.4, 819.6 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.86 (t, J=6.5 Hz, 3H), 1.16–1.37 (m, 6H), 1.63–1.74 (m, 2H), 2.19–2.29 (m, 2H), 2.33 (s, 3H), 2.48 (t, J=5.9 Hz, 2H), 3.05 (t, J=6.2 Hz, 2H), 3.37–3.43 (m, 2H), 7.12 (d, J=8.1 Hz, 2H), 7.31–7.36 (m, 3H), 7.52 (d, J=8.2 Hz, 2H), 7.76–7.80 (m, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.5, 21.7, 22.9, 23.0, 24.0, 27.7, 30.9, 32.1, 38.3, 54.8, 122.1, 124.8 (2C), 127.1, 127.9 (2C), 128.7 (2C), 129.9 (2C), 130.2, 138.8, 139.3, 149.1, 149.4, 161.2, 166.5, 193.4. Anal. Calcd for $C_{28}H_{31}NO_2$: C, 81.32; H, 7.56; N, 3.39. Found: C, 81.13; H, 7.32; N, 3.19.

*3.4.4. 1-(n-Hexyl)-6,6-dimethyl-2-(4-methylbenzoyl)-3-phenyl-6,7-dihydro-indol-4(5H)-one (**10d**).* Colourless viscous liquid. IR (neat) 2957.4, 2928.9, 1682.4, 1606.3, 1435.4, 1333.1, 1054.5, 766.9, 692.0 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.84 (t, J=7.1 Hz, 3H), 1.21 (s, 3H), 1.22 (s, 3H), 1.24–1.34 (m, 6H), 1.61–1.69 (m, 2H), 2.35 (s, 3H), 2.37 (s, 2H), 2.93 (m, 2H), 3.39 (t, J=7.1 Hz, 2H), 7.15 (d, J=8.0 Hz, 2H), 7.26–7.35 (m, 3H), 7.61–7.64 (m, 2H), 7.68 (d, J=7.9 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.5, 21.8, 23.0, 27.8, 28.7, 29.3, 30.9, 32.1, 35.6, 38.0, 52.6, 54.7, 113.5, 121.1, 124.8 (2C), 127.8 (2C), 128.6, 129.2 (2C), 129.5 (2C), 129.9, 136.5, 140.3, 149.5, 160.8, 165.8, 192.6. Anal. Calcd for $C_{30}H_{35}NO_2$: C, 81.59; H, 7.99; N, 3.17. Found: C, 81.31; H, 7.84; N, 2.98.

*3.4.5. 1-(n-Hexyl)-2-(4-methylbenzoyl)-3-phenyl-6,7-dihydro-indol-4(5H)-one (**10e**).* Colourless viscous liquid. IR (neat) 2929.4, 2857.0, 1681.7, 1606.4, 1492.4, 1453.7, 1428.4, 1412.0, 1332.5, 1177.8, 1062.2, 1011.0 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.86 (t, J=6.4 Hz, 3H), 1.18–1.31 (m, 6H), 1.67 (t, J=6.4 Hz, 2H), 2.25 (t, J=6.2 Hz, 2H), 2.35 (s, 3H), 2.48 (t, J=5.6 Hz, 2H), 3.06 (t, J=5.7 Hz, 2H), 3.36–3.42 (m, 2H), 7.15 (d, J=7.9 Hz, 2H), 7.23–7.35 (m, 3H), 7.62–7.65 (m, 2H), 7.69 (d, J=8.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.5, 21.8, 22.9, 23.0, 24.1, 27.7, 30.9, 32.1, 38.3, 54.7, 113.7, 122.2, 124.9 (2C), 127.9 (2C), 128.7, 129.3 (2C), 129.5 (2C), 129.9, 136.5, 140.3, 149.1, 160.9, 166.7, 193.3. Anal. Calcd for

$C_{28}H_{31}NO_2$: C, 81.32; H, 7.56; N, 3.39. Found: C, 81.19; H, 7.31; N, 3.21.

*3.4.6. 2-[(4-Chlorophenyl)(n-hexylimino)]methyl-1-(n-hexyl)-3-phenyl-6,7-dihydro-indol-4(5H)-one (**12a**).* Colourless viscous liquid. IR (neat) 2927.3, 2855.9, 1661.1, 1486.1, 1455.5, 1373.7, 1089.3, 1014.0, 700.7 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.88 (br s, 6H), 1.18–1.58 (m, 20H), 2.21–2.26 (m, 2H), 2.44–2.46 (m, 2H), 2.81–2.91 (m, 2H), 3.00–3.11 (m, 1H), 3.25–3.35 (m, 1H), 3.79–4.02 (m, 2H), 7.13–7.29 (m, 5H), 7.23 (d, J=8.4 Hz, 2H), 7.58 (d, J=8.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.4, 14.6, 22.9, 23.0, 23.1, 24.1, 26.8, 28.0, 29.0, 29.7, 30.9, 31.0, 31.9, 32.3, 38.7, 45.1, 54.9, 115.8, 119.3, 128.4 (2C), 128.7, 129.0 (2C), 129.3 (2C), 129.8 (2C), 131.3, 133.0, 135.2, 140.1, 144.1, 162.0, 193.0. Anal. Calcd for $C_{35}H_{45}ClN_2O$: C, 77.10; H, 8.32; N, 5.14. Found: C, 76.89; H, 8.15; N, 4.98.

*3.4.7. 1-(n-Hexyl)-2-[(n-hexylimino)(phenyl)]methyl-3-phenyl-6,7-dihydro-indol-4(5H)-one (**12b**).* Colourless viscous liquid. IR (neat) 2956.2, 2928.8, 2857.1, 1660.8, 1487.7, 1446.2, 1367.9, 768.2, 694.7 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.81–0.89 (m, 6H), 1.17–1.54 (m, 22H), 2.34 (s, 2H), 2.76 (s, 2H), 3.05–3.16 (m, 1H), 3.29–3.39 (m, 1H), 3.82–4.0 (m, 2H), 7.12–7.26 (m, 8H), 7.62–7.66 (m, 2H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.3, 14.6, 22.8, 23.1, 26.4, 27.8, 29.1, 29.2, 30.9, 31.0, 31.5, 32.2, 35.8, 37.0, 44.8, 52.6, 54.8, 116.1, 118.3, 127.9 (2C), 128.1 (2C), 128.4, 128.9 (2C), 129.3, 129.8 (2C), 131.6, 133.0, 141.7, 142.9, 163.1, 192.2. Anal. Calcd for $C_{35}H_{46}N_2O$: C, 82.30; H, 9.08; N, 5.48. Found: C, 82.01; H, 9.22; N, 5.31.

*3.4.8. 1-(n-Hexyl)-3-(4-methylphenyl)-6,7-dihydro-indol-4(5H)-one (**14a**).* Colourless viscous liquid. IR (neat) 2928.0, 2857.8, 1659.5, 1475.6, 1414.0, 1171.5, 825.2, 806.8 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.85 (t, J=6.6 Hz, 3H), 1.18–1.28 (m, 6H), 1.56 (br s, 2H), 2.20–2.28 (m, 2H), 2.42 (s, 3H), 2.54 (t, J=5.8 Hz, 2H), 2.85 (t, J=6.0 Hz, 2H), 3.87 (t, J=7.5 Hz, 2H), 6.54 (s, 1H), 7.26–7.29 (m, 4H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.3, 21.7, 22.8, 22.9, 24.2, 26.6, 31.0, 31.5, 38.3, 44.9, 105.6, 120.8, 129.6 (2C), 129.7 (2C), 130.1, 136.4, 138.1, 144.6, 194.7. Anal. Calcd for $C_{21}H_{27}NO$: C, 81.51; H, 8.79; N, 4.53. Found: C, 81.37; H, 8.54; N, 4.31.

*3.4.9. 1-(n-Hexyl)-3-(2-thienyl)-6,7-dihydro-indol-4(5H)-one (**14b**).* Light brown viscous liquid. IR (neat) 2930.1, 2857.9, 1652.7, 1474.9, 1417.6, 1373.8, 1172.1, 762.5, 701.4 cm^{-1}. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.81–0.95 (m, 3H), 1.17–1.31 (m, 6H), 1.52–1.58 (m, 2H), 2.18–2.28 (m, 2H), 2.54 (t, J=5.9 Hz, 2H), 2.85 (t, J=5.8 Hz, 2H), 3.88 (t, J=7.6 Hz, 2H), 6.57(s, 1H), 7.29–7.44 (m, 3H). ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 14.3, 22.8, 22.9, 24.2, 26.5, 30.9, 31.5, 38.3, 44.9, 105.9, 120.8, 128.2, 128.9, 129.7, 133.1, 136.3, 144.8, 194.7. Anal. Calcd for $C_{18}H_{23}NOS$: C, 71.72; H, 7.69; N, 4.65; S, 10.64. Found: C, 71.43; H, 7.52; N, 4.42.

Acknowledgements

We thank MICINN (grants CTQ2009-12320-BQU and ACI2009-0956) and UCM (Grupos de Investigación, grant 920234) for financial support. A three-month stay of PTP in Madrid that made this work possible was funded by a fellowship from the Santander-UCM Program for Distinguished Academic Visitors, which is also gratefully acknowledged.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.10.017. These data include MOL files and InChiKeys of the most important compounds described in this article.

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