6-(α-Hydroxy-α-aryl/naphthyl)methyl-3,4-dihydro-2,5-benzodiazocin-1(2*H*)-ones and diphenylmethanes from C-2 arylated 1,3-indanediones

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Stirring 2-hydroxy-2-aryl-1,3-indanediones in ethylenediamine at room temperature for 1-2 h produces 6-(α-hydroxy-α-aryl/naphthyl)methyl-3,4-dihydro-2,5-benzodiazocin-1(2*H*)-ones in high yields. Under similar reaction conditions 2,2-diaryl-1,3-indanediones furnish diphenylmethanes.

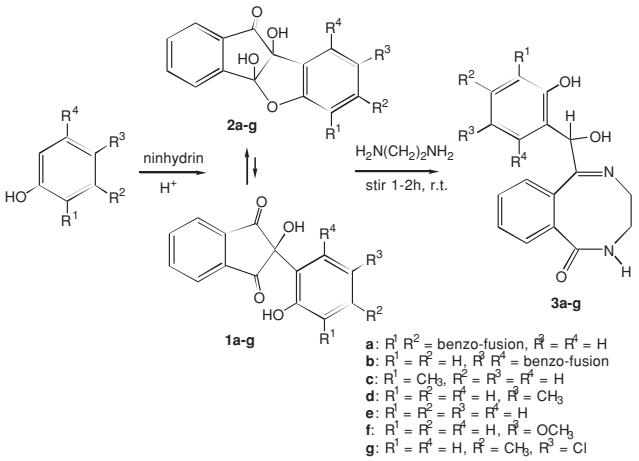
Keywords: 1,3-indanediones, 2,5-benzodiazocines, diphenylmethanes, microwave heating

The nitrogenous heterocycles of the benzodiazocine type are generally biologically active and are widely used as day-time sedatives, tranquilisers, anticonvulsants and bactericides, *etc*.[1] There are therefore numerous reports of the synthesis of various substituted benzodiazocines.[1c, 2, 3] Generally, 6-aryl-3,4-dihydro-2,5-benzodiazocin-1(2*H*)-ones are synthesised by condensation of 2-acylbenzoic acids with ethylenediamine.[2a] However, this method is not suitable for synthesis of compounds such as 6-(α-hydroxy-α-aryl/naphthyl)methyl-3,4-dihydro-2,5-benzodiazocin-1(2*H*)-ones, since the required starting materials, *viz*. the corresponding 2-acylbenzoic acids, are not easily obtained by conventional synthesis. Therefore, it becomes pertinent to develop suitable and efficient routes to prepare these potentially bioactive benzodiazocines from readily available materials.

Starting from the easily accessible ninhydrin, we have developed a general and efficient synthetic route toward 6-(α-hydroxy-α-aryl/naphthyl)methyl-3,4-dihydro-2,5-benzodiazocin-1(2*H*)-ones. It was thought that the chemical reaction of 2-hydroxy-2-aryl-1,3-indanediones with ethylenediamine might be similar to that of 2-acylbenzoic acids. Accordingly, a series of 2-hydroxy-2-aryl-1,3-indanediones (**1a–g**, Scheme 1) were prepared by condensation of ninhydrin with α-naphthol, β–naphthol, *o*-cresol, *p*-cresol, phenol, 4-methoxyphenol, *p*-chloro-*m*-cresol, *etc*., in acetic acid.[4] It is known that ninhydrin adducts of phenols exist predominantly in the cyclic hemiketal form (**2a–g**).[5]

In accordance with our expectation, the adducts **1a–g** underwent condensation with ethylenediamine (99%) by stirring at room temperature for 1-2 hr to furnish the eight-membered nitrogenous heterocycles 6-(α-hydroxy-α-aryl/naphthyl)methyl-3,4-dihydro-2,5-benzodiazocin-1(2*H*)-ones **3a–g** in high yields (Table 1). The solid products were isolated by filtration of the acidified reaction mixtures and thorough washing with cold water. Due to the presence of a chiral substituent at position 6, the 2,5-benzodiazocin-1(2*H*)-ones **3a–g** are formed as racemic mixtures. The formation of products **3a–g** allows the ready incorporation of a side chain containing an α-aryl group at position 6 of 2,5-benzodiazocin-1(2*H*)-ones.

Products **3a–g** were thoroughly characterised by IR, ^{1}H and ^{13}C NMR studies and confirmed for **3e** by two dimensional ^{13}C–^{1}H correlation studies optimized for one-bond and long range couplings. The ^{1}H NMR (in DMSO-d_6) spectrum of **3a** shows signals at δ 3.61–3.49 (4H, m) for CH_2–CH_2 of the ethylenediamine moiety. In ^{13}C NMR, the appearance of two methylene peaks at δ 38.5 and 38.0 further confirms the presence of a CH_2–CH_2 moiety in **3a**. Two characteristic proton signals at δ 9.02 (1H, t, J = 7.1 Hz) and δ 5.91 (1H, d, J = 8.7 Hz) correspond to the amide N-H and α-H respectively. A further two sets of proton signals, at δ 8.24 (1H, m) and δ 7.78 (3H, m) from the benzene moiety of **3a**, indicate an unsymmetrical molecular structure. Other 2,5-benzodiazocin-1(2*H*)-ones **3b–g** possess spectral (^{1}H and ^{13}C) characteristics similar to those of **3a**, except for the changes expected on account of the substituents.



Scheme 1

Table 1 Preparation of 6-(α-hydroxy-α-aryl/naphthyl)methyl-3,4-dihydro-2,5-benzodiazocin-1(2*H*)-ones **3a–g** from 2-hydroxy-2-aryl-1,3-indanediones **2a–g**

Entry	Substrate	Product	Reaction time/h	Yield/%[a]	M.p./°C
a	**2a**	**3a**	1.5	85	180–181
b	**2b**	**3b**	2.0	82	204–205
c	**2c**	**3c**	1.7	85	142–143
d	**2d**	**3d**	2.0	87	98–99
e	**2e**	**3e**	1.7	90	110–111
f	**2f**	**3f**	2.0	85	175–176
g	**2g**	**3g**	2.0	80	202–203

[a]Yields refer to pure isolated products.

In an attempt to extend the scope of the reactions, a series of 2,2-diaryl-1,3-indanediones (**1h–o**) (Scheme 2) were derived by acid catalyzed condensation of benzene, halobenzenes, methoxy-benzenes, *etc*., with ninhydrin, following the reported procedure.[6] The substrate 2-(2,3,4-trimethoxyphenyl)-2-(4-methoxyphenyl)-1,3-indanedione **1o,** where the two aryl groups are different**,** was prepared following a slightly modified technique:[6b] initial arylation of ninhydrin with 1,2,3-trimethoxybenzene in acid medium produces the stable monoarylated adduct 2-(2,3,4-trimethoxyphenyl)-2-hydroxy-1,3-indanedione which on further arylation with anisole affords **1o**.

Unexpectedly, it was found that the 2,2-diaryl-1,3-indanediones **1h–m** on stirring with ethylenediamine (99%) all furnished the elimination products 4,4'-disubstituted diphenylmethanes **4h–m** corresponding to the diaryl groups at the C-2 position of the indanediones, in high yields (Table 2).

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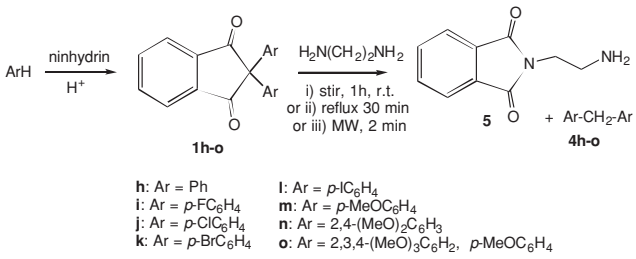


Scheme 2

Table 2 Preparation of diphenylmethanes (**4h-o**) from 2,2-diaryl-1,3-indanediones (**1h-o**)

Entry	Substrate	Product	Yield/%[a] C.M.[b]	Yield/%[a] M.W.[c]	M.p./°C observed	M.p./°C lit.[8]
h	**1h**	**4h**	83	85	liquid	25–26
i	**1i**	**4i**	87	88	liquid	29–30
j	**1j**	**4j**	87	90	52–53	54–56
k	**1k**	**4k**	90	88	63–64	63–64
l	**1l**	**4l**	86	88	92–93	91–94
m	**1m**	**4m**	89	91	45–46	–
n	**1n**	**4n**	81	83	54–55	–
o	**1o**	**4o**	80	85	60–61	–

[a]Yields refer to pure isolated products; [b] conventional method; [c]microwave heating.

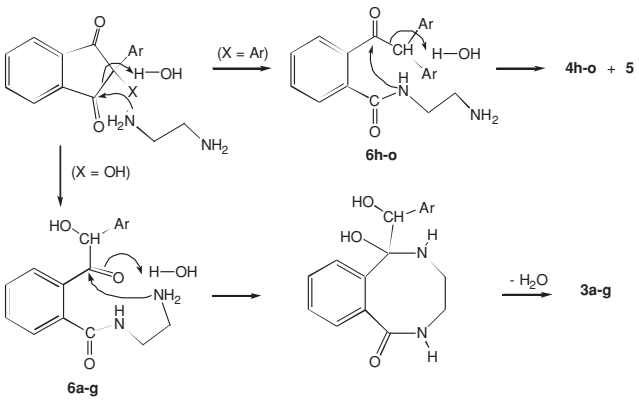
By heating under reflux the same reaction takes about 30 min for completion. It was also observed that the reaction also takes place under microwave irradiation[7] of the reaction mixture of 2,2-diaryl-1,3-indanediones **1h–m** in ethylenediamine to produce diphenylmethanes **4h–m** within 2 min in yields comparable to those from the above reaction conditions. The substrates **1n** and **1o** (Scheme 2) react with ethylenediamine in a similar way, to produce 2,2',4,4'-tetramethoxy- and 2,3,4,4'-tetramethoxy-diphenylmethanes **4n** and **4o** respectively (Table 2). The solid products **4j–o** were isolated by filtration of the acidified reaction mixtures and thorough washing with cold water. The diphenylmethanes **4h–o** were characterised by ^{1}H and ^{13}C NMR studies in $CDCl_3$. Compounds **4j–l** prepared by the present methodology have similar melting points to those reported in the literature.[8]

Scheme 3 presents a possible mechanism for the reactions. Nucleophilic attack by ethylenediamine at one of the cabonyl groups of the 2,2-diaryl-1,3-indanediones (**1h–o**) produces the open-chain amides **6h–o**, which undergo a subsequent intramolecular nucleophilic attack on the other carbonyl group to eliminate diphenylmethanes **4h–o** and form the side product 2-(2-aminoethyl)-1*H*-isoindole-1,3(2*H*)-dione (*N*-(2-aminoethyl)phthalimide, **5**). On the other hand, because of the lesser leaving aptitude of an α-hydroxy-α-(aryl/naphthyl)methyl group, the amides **6a–g** (Scheme 3) undergo intramolecular nuleophilic attack by the free NH_2 on the other carbonyl group, followed by dehydration to produce the eight membered ring products **3a–g**.

In conclusion, we have developed an efficient method for converting the readily available 2-hydroxy-2-aryl/naphthyl-1,3-indanediones into the potentially bioactive 6-(α-hydroxy-α-aryl/naphthyl)methyl-3,4-dihydro-2,5-benzodiazocin-1 (2*H*)-ones simply by stirring in ethylenediamine. Under similar reaction conditions 2,2-diaryl-1,3-indanediones furnish diphenylmethanes.

Experimental

IR spectra were examined in KBr disc on a Perkin Elmer-782 spectrophotometer. NMR (^{1}H and ^{13}C) spectra were recorded on a Bruker AM 300L supercon spectrometer.



Scheme 3

2-Hydroxy-2-(1-hydroxy-2-naphthyl)-1,3-indanedione (**1a**; exists as the hemiketal **2a**)

Ninhydrin (0.25 g, 1.4 mmol) and α-naphthol (0.60 g, 4.2 mmol) were stirred in acetic acid (10 ml) for 30 min. The solid product which separated was filtered off and washed thoroughly with acetic acid and then with water. The product was purified by silica-gel column chromatography using acetone as the eluent. Further purification by crystallisation from acetone-petroleum ether afforded **1a** (0.32 g, 75%); m. p. 216-217 °C. IR (KBr) ν_{max} 3370, 1709, 1600, 1467, 1383 cm^{-1}. ^{1}H NMR (acetone-d_6): δ_H 8.09 (1H, d, J = 6.6 Hz), 7.95 (1H, apparent d, J = 5.4 Hz), 7.84-7.79 (2H, m), 7.72 (1H, d, J = 6.6 Hz), 7.55 (2H, m), 7.44 (3H, m). ^{13}C NMR (acetone-d_6): δ_C 200.1, 155.2, 150.9, 138.3 (d), 137.6, 136.6, 132.9 (d), 130.0 (d), 129.1 (d), 127.7 (d), 127.0 (d), 124.9 (d), 123.8 (d), 123.4 (d), 123.3 (d), 122.4, 120.4, 85.5. Anal. Calcd for $C_{19}H_{12}O_4$: C, 74.99; H, 3.97. Found: C, 75.12; H, 3.85 %.

2-Hydroxy-2-(2-hydroxy-1-naphthyl)-1,3-indanedione (**1b**; exists as the hemi-ketal **2b**)

Ninhydrin (0.25 g, 1.4 mmol) and β-naphthol (0.60 g, 4.2 mmol) were stirred in acetic acid (10 ml) for 30 min. Usual work-up and purification furnished **1b** (0.33 g, 78%), m.p. 225–226 °C. IR (KBr) ν_{max} 3489, 1712, 1629, 1519, 1460 cm^{-1}. ^{1}H NMR (acetone-d_6): δ_H 8.60 (1H, d, J = 8.4 Hz), 8.03 (1H, d, J = 8.2 Hz), 7.84 (1H, t, J = 7.3 Hz), 7.80 (1H, d, J = 9.0 Hz), 7.77 (1H, d, J = 9.0 Hz), 7.71 (1H, d, J = 9.0 Hz), 7.56 (1H, t, J = 7.3 Hz), 7.53 (1H, t, J = 7.5 Hz), 7.31 (1H, t, J = 7.5 Hz), 7.04 (1H, d, J = 8.9 Hz), 7.04 (1H, d, J = 8.9 Hz), 3.30 (br.s, 2 × OH). ^{13}C NMR (acetone-d_6): δ_C 199.9, 157.4, 150.5, 138.4 (d), 136.7, 134.8 (d), 132.9 (d), 131.8 (d), 130.4, 129.1 (d), 127.0 (d), 126.1 (d). 125.5 (d), 125.0 (d), 117.8, 114.2 (d), 112.0, 87.1. Anal. Calcd for $C_{19}H_{12}O_4$: C, 74.99; H, 3.97. Found: C, 74.90; H, 4.09 %.

Ninhydrin adducts **1c–g** were prepared following the reported procedure.[4]

General procedure for preparation of 6-(α-hydroxy-α-aryl/naphthyl)methyl-3,4-dihydro-2,5-benzodiazocin-1(2H)-ones (**3a–g**)

The appropriate substrate **1**/**2a–g** (1.4 mmol) was added to ethylenediamine (10ml, 99%) and the mixture was stirred at room temperature for *ca* 1–2 h. Then the reaction mixture was acidified with 6 N HCl to pH 6. The solid products **3a–g** were isolated by filtration and thorough washing with cold water. Then column chromatography with hexane-EtOAc afforded pure **3a–g** as solid (Table 1). The pure solid products were crystallised from acetone–petroleum ether.

6-[α-Hydroxy-α-(1-hydroxy-2-naphthyl)]methyl-3,4-dihydro-2,5-benzodiazocin-1(2H)-one (**3a**): IR (KBr) ν_{max} 3432, 3184, 1656, 1624, 1432 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ_H 9.02 (N-H, t, J = 7.1 Hz), 8.24 (1H, m), 7.78 (3H, m), 7.62–7.46 (6H, m), 6.61 (1H, d, J = 8.7 Hz), 5.91 (1H, d, J = 8.7 Hz), 3.61–3.49 (4H, m); ^{13}C NMR (DMSO-d_6): δ_C 170.8, 166.6, 159.7, 145.3, 135.9, 132.0 (d), 131.7, 129.3 (d), 128.9 (d), 127.5 (d), 125.8 (d), 124.8, 123.6 (d), 123.1 (d), 122.6 (d), 122.4 (d), 117.7 (d), 107.2, 81.2 (d), 38.5 (t), 38.0 (t); Anal. Calcd for $C_{21}H_{18}N_2O_3$: C 72.82; H 5.24; N 8.09. Found: C, 72.73; H, 5.16; N, 8.15 %.

6-[α-Hydroxy-α-(2-hydroxy-1-naphthyl)]methyl-3,4-dihydro-2,5-benzodiazocin-1(2H)-one (**3b**): IR (KBr) ν_{max} 3432, 3184, 1656, 1609, 1551 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ_H 8.93 (N-H, t, J = 7.5 Hz), 8.01-7.33 (10H, m), 6.03 (1H, d, J = 9.0 Hz), 5.60 (1H, d, J = 9.0 Hz), 3.93-3.75 (4H, m); Anal. Calcd for $C_{21}H_{18}N_2O_3$: C, 72.82; H, 5.24; N, 8.09. Found: C, 72.76; H, 5.14; N, 8.12 %.

6-[α-Hydroxy-α-(2-hydroxy-3-methylphenyl)]methyl-3,4-dihydro-2,5-benzodiazocin-1(2H)-one (**3c**): IR (KBr): ν_{max} 3313, 1696, 1630,

1590, 1548 cm^{-1}; ^{1}H NMR (acetone-d_6): δ_H 13.02 (1H, s), 8.48 (1H, s, N-H), 7.68-7.51 (4H, m), 7.25 (1H, d, *J* = 7.2Hz), 6.72 (1H, t, *J* = 7.7Hz), 6.03 (1H, d, *J* = 6.0 Hz), 5.86 (1H, br. s), 3.95-3.68 (4H, m), 2.38 (3H, s); ^{13}C NMR (acetone-d_6): δ_C 171.8, 168.5, 161.0, 146.1, 135.4 (d), 132.9 (d), 132.8, 130.2 (d), 127.5, 124.9 (d), 124.3 (d), 123.5 (d), 118.6 (d), 114.7, 83.2 (d), 40.3 (t), 40.1 (t), 15.6 (q); Anal. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.65; H, 5.85; N, 9.02. Found: C, 69.57; H, 5.91; N, 8.95 %.

6-[α-Hydroxy-α-(2-hydroxy-5-methylphenyl)]methyl-3,4-dihydro-2,5-benzodiazocin-1(2H)-one (**3d**): IR (KBr) ν_{max} 3325, 1690, 1620, 1547 cm^{-1}; ^{1}H NMR (acetone-d_6): δ_H 12.38 (1H, s), 8.44 (1H, s, N-H), 7.66-7.60 (4H, m), 7.50 (1H, m), 7.18 (1H, dd, *J* = 8.5 Hz), 6.75 (1H, d, *J* = 8.5 Hz), 6.02 (1H, d, *J* = 9.2 Hz), 5.83 (1H, d, *J* = 9.2 Hz), 3.87-3.68 (4H, m), 2.30 (3H, s); ^{13}C NMR (acetone-d_6): δ_C 171.4, 168.4, 160.4, 146.1, 135.4 (d), 132.9 (d), 132.8, 130.2 (d), 128.3, 127.5 (d), 124.3 (d), 123.5 (d), 118.5 (d), 115.2, 83.1 (d), 40.2 (t), 39.9 (t), 20.5 (q); Anal. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.01. Found: C, 69.72; H, 5.79; N, 9.13 %.

6-[α-Hydroxy-α-(2-hydroxyphenyl)]methyl-3,4-dihydro-2,5-benzodiazocin-1(2H)-one (**3e**): IR (KBr) ν_{max} 3345, 1687, 1635, 1590, 1430 cm.$^{-1}$; ^{1}H NMR (acetone-d_6): δ_H 12.66 (1H, br. s, N-H), 7.72-7.60 (4H, m), 7.52-7.50 (1H, m), 7.39-7.34 (1H, m), 6.87-6.82 (2H, m), 6.02 (1H, d, *J* = 9.0 Hz), 5.86 (1H, d, *J* = 9.0 Hz), 3.87-3.69 (4H, m); ^{13}C NMR (acetone-d_6): δ_C 171.3, 168.5, 162.6, 146.0, 134.7 (d), 132.9 (d), 132.8 (d), 130.2 (d), 127.5 (d), 124.3 (d), 123.4 (d), 119.3 (d), 118.7 (d), 115.6, 83.2 (d), 40.3 (t), 40.1 (t); Anal. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.90; H, 5.44; N, 9.46. Found: C, 68.97; H, 5.53; N, 9.54 %.

6-[α-Hydroxy-α-(2-hydroxy-5-methoxyphenyl)]methyl-3,4-dihydro-2,5-benzodiazocin-1(2H)-one (**3f**): IR (KBr) ν_{max} 3355, 1686, 1565 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ_H 11.89 (1H, s), 8.87 (1H, s, N–H), 7.62-7.49 (4H, m), 7.29 (1H, br. s), 6.98 (1H, d, *J* = 9.6 Hz), 6.78 (1H, d, *J* = 8.8 Hz), 6.61 (1H, d, *J* = 8.8 Hz), 5.88 (1H, d, *J* = 7.8 Hz), 3.79–3.74 (2H, m), 3.71 (3H, s), 3.59-3.48 (2H, m); Anal. Calcd for $C_{18}H_{18}N_2O_4$: C, 66.24; H, 5.56; N, 8.59. Found: C, 66.30; H, 5.65; N, 8.68 %.

6-[α-Hydroxy-α-(2-hydroxy-5-chloro-4-methylphenyl)]methyl-3,4-dihydro-2,5-benzodiazocin-1(2H)-one (**3g**): IR (KBr) ν_{max} 3357, 1686, 1614, 1562 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ_H 12.41 (1H, s), 8.88 (1H, s, N-H), 7.79 (1H, s), 7.62–7.49 (4H, m), 6.86 (1H, s), 6.59 (1H, d, *J* = 9.1 Hz), 5.87 (1H, d, *J* = 9.1 Hz), 6.61 (1H, d, *J* = 8.8 Hz), 3.81–3.74 (2H, m), 3.60–3.45 (2H, m), 2.23 (3H, s); Anal. Calcd for $C_{18}H_{17}ClN_2O_3$: C, 62.69; H, 4.97; N, 8.13; Cl, 10.29. Found: C, 62.75; H, 5.08; N, 8.21; Cl, 10.37 %.

The ninhydrin adducts 2,2-diaryl-1,3-indanediones **1h–o** were prepared following the reported procedure.[6]

General procedures for preparation of diphenylmethanes **4h–o**: *Conventional Method:* The appropriate substrate **1h–o** (1.4 mol) was added to ethylenediamine (10 ml, 99%) and the mixture was stirred for *ca* 1 h at room temperature (the reaction takes *ca* 30 min for completion by reflux). Then the reaction mixture was acidified with 6N HCl to pH 6. The solid product **4h-o** separated was extracted with $CHCl_3$ and worked up as usual. The residue from the $CHCl_3$ layer was purified by column chromatography over silica gel and $CHCl_3$ eluate fractions afforded pure solid products **4h-o**, which were crystallised from $CHCl_3$–petroleum ether (Table 2).

Under microwave irradiation: The reaction mixture containing appropriate substrate **1h–o** (1.4 mmol) and ethylenediamine (10 ml, 99%) in a 25 ml Erlenmeyer flask was placed in side of a BPL-SANYO domestic microwave oven (2454 MHz) which was operated at full power (1200 W) for 2 min. Then the cooled reaction mixture was acidified with 6N HCl to pH 6. The solid product **4h–o** separated was extracted with $CHCl_3$ and worked up as usual. The residue from the $CHCl_3$ layer was purified by column chromatography over silica gel and $CHCl_3$ eluate fractions afforded pure solid products **4h–o** (Table 2), which were crystallised from $CHCl_3$-petroleum ether.

4,4′-Dimethoxydiphenylmethane (**4m**): IR (KBr) ν_{max} 1609, 1509, 1458, 1244, 1028, 809, 751 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ_H 7.11 (4H, d, *J* = 8.4 Hz), 6.84 (4H, d, *J* = 8.4 Hz), 3.90 (2H, s), 3.80 (6H, s); ^{13}C NMR ($CDCl_3$): δ_C 158.1 (2C), 133.8 (2C), 129.7 (d, 4C), 114.0 (d, 4C), 55.3 (q, 2C), 40.2 (t); Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.99; H, 7.18 %.

2,2′,4,4′-Tetramethoxydiphenylmethane (**4n**): IR (KBr) ν_{max} 1605, 1503, 1450, 1020, 859, 780 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ_H 7.24 (2H, d, *J* = 8.7 Hz), 6.25 (2H, dd, *J* = 8.7 Hz), 6.01 (2H, d, *J* = 2.1 Hz), 3.89 (2H, s), 3.27 (6H, s), 3.25 (6H, s); Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.93; H, 7.09 %.

2,3,4,4′-Tetramethoxydiphenylmethane (**4o**): IR (KBr) ν_{max} 1614, 1507, 1448, 1233, 862, 783 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ_H 7.49 (1H, d, *J* = 8.7 Hz), 7.32 (1H, d, *J* = 8.7 Hz), 7.01 (2H, d, *J* = 8.4 Hz), 6.84 (2H, d, *J* = 8.4 Hz), 3.90 (2H, s), 3.80 (12H, s); ^{13}C NMR ($CDCl_3$): δ_C 160.0, 158.6, 152.9, 149.2, 133.3, 131.0, 130.2 (d, 2C), 125.1 (d), 114.0 (d, 2C), 107.2 (d), 60.7 (q), 56.9 (q), 55.7 (q), 55.1 (q), 39.9 (t); Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.90; H, 7.11 %.

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References

1 (a) W.O. Foye, T.L. Iemke and D.A. Williams, *Principles of Medicinal Chemistry*, 4th ed. 1995, 174; (b) J. D. Sara and R. A. Stephani, *Med. Chem. Res*. 2000, 10, 81; (c) P. Herold, J. W. Herzig, P. Wenk, T. Leutert, P. Zbinden, W. Fuhrer, S. Stutz, K. Schenker, M. Meier and G. Rihs, *J. Med. Chem*. 1995, 38, 2946; (d) I.A. Nicholls, P.F. Alewood, R.I. Brinkworth, S.F. Morrison and P.R. Andrews, *J. Chem. Res. (S)*, 1993, 408.

2 (a) Y. Pei, M.J. Lilly, D.J. Owen, L.J. D'Souza, X.–Q. Tang, J. Yu, R. Nazarbaghi, A. Hunter, C.M. Anderson, S. Glasco, N.J. Ede, I.W. James, U. Maitra, S. Chandrasekaran, W.H. Moos and S.S. Ghosh, *J. Org. Chem*. 2003, 68, 92; (b) R.A. DeFronzo, *Ann. Intern. Med*. 1999, 131, 281; (c) J.M. Nuss and A.S. Wagman, *Annu. Rep. Med. Chem*. 2000, 35, 211; (d) A.J. Krentz, R.E. Ferner and C. Bailey, *J. Drug Safety* 1994, 11(4), 223; (e) C. B. Wollheim, *Diabetologia* 2000, 43, 265; (f) M. Prentki, *Eur. J. Endocrinol*. 1996, 134, 272; (g) H. Yoshida, E. Shirakawa, Y. Honda and T. Hiyama, *Angew. Chem., Int. Ed*., 2002, 41, 3247; (h) I.A. O'Neil, C.L. Murray, A.J. Potter and S.B. Kalindjian, *Tetrahedron Lett*. 1997, 38, 3609.

3 (a) K. Santa Deepthi and P.S.N. Reddy, *Synthesis* 2002, 15, 2168; (b) Y. Cheng, Q.-X. Liu and O. Meth-Cohn, *Synthesis* 2000, 640; (c) Y. Cheng, O. Meth-Cohn and D.L.Taylor, *J. Chem. Soc. Perkin Trans 1* 1968, 1257; (d) S. Eguchi, Y. Matsushita and H. Takeuchi, *J. Org. Chem*. 1992, *57*, 6975.

4 G. Schmitt, N. Dinh An, J.-P. Poupelin, J. Vebrel and B. Laude, *Synthesis* 1984, 758.

5 (a) J.-P. Poupelin, G. Saint-Ruf, J.-C. Perche, B. Laude, G. Narcisse, F. Bakri-Logeais and F. Hubert, *Eur. J. Med. Chem*. 1980, 15, 253; (b) J.-P. Poupelin, G. Saint-Ruf, J.-C. Perche, R. Lacroix, G. Uchida-Ernouf, G. Narcisse and F. Hubert, *Eur. J. Med. Chem*. 1979, 14, 171.

6 (a) D.A. Klumpp, S. Fredrick, S. Lau, K.K. Jin, R. Bau, G.K. Surya Prakash and G.A. Olah, *J. Org. Chem*. 1999, 64, 5152; (b) S.K. Kundu, A. Pramanik and A. Patra, *Synlett* 2002, 5, 823; (c) S.K. Kundu and A. Pramanik, *Indian J. Chem*. 2004, 43B, 595; (d) S.K. Kundu, A. Patra and A. Pramanik, *Indian J. Chem*. 2004, 43B, 604.

7 (a) S. Caddick, *Tetrahedron* 1995, 51, 10 403; (b) S.A. Galema, *Chem. Soc. Rev*. 1997, 26, 233; (c) A.K. Bose, B.K. Banik, N. Lavlinskaiz, M. Jayaraman and M. S. Manhas, *Chemtech* 1997, 27, 18.

8 (a) I. Heilbron and H.M. Bunbury, *Dictionary of Organic Compounds* London: Eyre & Spottiswoode, 1953, Vol. II; (b) I. Heilbron and H.M. Bunbury, *Dictionary of Organic Compounds* London: Eyre & Spottiswoode, 1953, Vol. IV.