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# A novel chemoselective synthesis of 3*H*-spiro[isobenzofuran-1,3'pyrazole] derivatives by oxidative cleavage of their corresponding dihydroindeno[1,2-*c*]pyrazoles

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Abstract This paper reports a new and simple procedure for the synthesis of 3H-spiro[isobenzofuran-1,3'-pyrazole] derivatives by reacting 1-benzylidene-2-phenylhydrazine derivatives with ninhydrin in acetic acid medium at room temperature followed by oxidative cleavage of their corresponding dihydroindeno[1,2-*c*]pyrazoles. 1-Benzylidene-2-phenylhydrazine derivatives were prepared via the reaction between phenylhydrazine and benzaldehyde derivatives. Easy procedure, mild reaction conditions, high yields in short reaction times, availability of starting materials, and no formation of by-product are the advantages of this approach.

**Keywords** 3*H*-spiro[isobenzofuran-1,3'-pyrazole] · Ninhydrin · 1-Benzylidene-2-phenylhydrazine · Dihydroindeno[1,2-*c*]pyrazole

### Introduction

Synthesis of compounds with specific chemical structures and biological properties may be important and has always been considered by chemists. Many efforts have been made to provide the efficient ways to produce a wide range of derivatives in each series. One of these compounds which has always been the focus of attention for various research groups is phthalide[1(3*H*)-isobenzofuranone] frameworks, a bunch of natural products possessing biological activity as well as synthetic goals [1–3]. 3-Substituted spiro-type phthalides are especially very important

M. R. Mohammadizadeh (⊠) · F. Basti Department of Chemistry, Faculty of Sciences, Persian Gulf University, Bushehr 75169, Iran e-mail: mrmohamadizadeh@pgu.ac.ir molecules as they possess antiepileptic, antibiotic and antidepressant activities as well as their presence in biologically active molecules [4–7]. On the other hand, pyrazole and its derivatives have also been focus of considerable attention due to their broad variety of properties. There is large variety of compounds having the pyrazole core structure that are of importance in agrochemical and pharmaceutical activities [8].

While isobenzofuranone and pyrazole derivatives have attracted significant attention, the preparation of spiroheterocyclic compounds incorporating isobenzofuranone and pyrazole motifs has not been the subject of much research.

We have been synthesizing numerous novel spiro-type molecules that have isobenzofuranone moiety through an oxidative cleavage strategy [9–11]. Herein, we apply this strategy to the synthesis of new spirocyclic compounds containing isobenzofuranone and pyrazole skeleton named 3H-spiro[isobenzofuran-1,3'-pyrazole].

### Experimental

#### General

Melting points were measured on an Electrothermal 9100 apparatus. IR spectra were recorded on A Jasco IR-460 Plus spectrometer. Mass spectra were recorded on an Agilent 8430 mass spectrometer operating at an ionization potential of 70 eV. <sup>1</sup>H and <sup>13</sup>C-NMR spectra were recorded at 500.1, 400.2 and 125.7, 100.6 MHz, respectively, on a BRUKER DRX 500 and 400-AVANCE FT-NMR instrument with CDCl<sub>3</sub> and DMSO as solvent. The reagents and solvents used in this work were obtained from Fluka, Merck and Aldrich companies and used without further

purification. The reaction monitoring was accomplished by TLC on silica gel PolyGram SILG/UV $_{254}$  plates.

General procedure for the preparation of 1-benzylidene-2-phenylhydrazine derivatives (**3a-j**)

To a mixture of phenylhydrazine (1 mmol) in ethanol (5 mL) aldehyde was added followed by some drops of acetic acid. The resulting mixture was disrupted under reflux conditions for 15 min using a magnetic stirrer. The reaction progress was looked for by TLC using a mixture of ethyl acetate/*n*-hexane (1:10). After completion of the reaction and cooling to room temperature, water (5 mL) was added. Pure product was obtained after filtration and washing with *n*-hexane ( $3 \times 5$  mL). All compounds were known and identified by comparison of their melting points with previously reported values [12–14].

General procedure for the preparation of 3*H*-spiro[isobenz ofuran-1,3'-pyrazole] derivatives in AcOH medium

A mixture of 1-benzylidene-2-phenylhydrazine **3** (1 mmol), and ninhydrin **4** (1 mmol) in acetic acid (3 mL), was stirred at room temperature for 3 h. Then, a solution of Pb(OAc)<sub>4</sub> (1 mmol) in acetic acid (2 mL) was added and the resulting mixture was allowed to rotate for additional 40 min at room temperature. After completion, confirmed by TLC, water (5 mL) was added to the reaction mixture and pure product was obtained after filtration and washing with a mixture of EtOAc/*n*-hexane (1:10,  $3 \times 5$  mL).

# 5'-(4-Chlorophenyl)-2'-phenyl-3H- spiro[isobenzofuran-1, 3'-pyrazole]-3,4'(2'H)-dione (5a)

Red powder; mp: 161–164 °C; IR (KBr),  $(\bar{v}_{max}, cm^{-1})$ : 1,789, 1,737, 1,597, 1,516, 1,497; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  7.07–7.11 (m, 3H, CH of Ar), 7.22–7.25 (m, 3H, CH of Ar), 7.49 (d, <sup>3</sup>J = 8.6 Hz, 2H, CH of Ar), 7.65–7.23 (m, 2H, CH of Ar), 8.06 (dd, <sup>3</sup>J<sub>1</sub> = 6.2 Hz, <sup>3</sup>J<sub>2</sub> = 1.9 Hz, 1H, CH of Ar), 8.16 (d, <sup>3</sup>J = 8.7 Hz, 2H, CH of Ar); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>),  $\delta$  90.6, 117.2, 122.0, 124.8, 126.6, 126.9, 127.1, 127.3, 129.2, 129.4, 131.7, 135.5, 136.0, 139.5, 139.9, 141.9, 167.0, 191.7. Anal. Calcd. for C<sub>22</sub>H<sub>13</sub>ClN<sub>2</sub>O<sub>3</sub> (388.80): C 67.96, H 3.37, N 7.21; Found: C 67.93, H 3.33, N 7.16. MS, *m*/*z* (%): 390 ([M<sup>+2</sup>]<sup>+</sup>, 20), 389 ([M<sup>+1</sup>]<sup>+</sup>, 15), 388 ([M]<sup>+</sup>, 66), 372 (14), 223 (98), 209 (96), 179 (base peak), 105 (99), 91 (43), 77 (61), 76 (29).

### 5'-(4-Nitrophenyl)-2'-phenyl-3H- spiro[isobenzofuran-1,3' -pyrazole]-3,4'(2'H)-dione (**5b**)

Red powder; mp: 214–217 °C; IR (KBr),  $(\bar{\upsilon}_{max}, cm^{-1})$ : 1,790, 1,732, 1,596, 1,523, 1,497; <sup>1</sup>H-NMR (400 MHz,

CDCl<sub>3</sub>), 7.12–7.17 (m, 3H, CH of Ar), 7.25–7.29 (m, 2H, CH of Ar), 7.30–7.31 (m, 1H, CH of Ar), 7.68–7.76 (m, 2H, CH of Ar), 8.12–8.14 (m, 1H, CH of Ar), 8.35–8.41 (m, 4H, CH of Ar); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>),  $\delta$  90.8, 117.6, 121.9, 124.2, 125.6, 126.4, 126.9, 127.1, 129.6, 131.9, 134.3, 135.7, 138.1, 139.5, 141.6, 148.1, 166.8, 191.0. Anal. Calcd. for C<sub>22</sub>H<sub>13</sub>N<sub>3</sub>O<sub>5</sub> (399.36): C 66.17, H 3.28, N 10.52; Found: C 66.13, H 3.25, N 10.49. MS *m*/*z* (%): 400 ([M<sup>+1</sup>]<sup>+</sup>, 1), 399 ([M]<sup>+</sup>, 3), 383 (20), 223 (43), 179 (base peak), 104 (39), 91 (40), 77 (86), 76 (66).

## 5'-(4-Fluorophenyl)-2'-phenyl-3H-spiro[isobenzofuran-1,3'pyrazole]-3,4'(2'H)-dione (**5c**)

Red powder; mp: 200–203 °C; IR (KBr),  $(\bar{v}_{max}, cm^{-1})$ : 1,794, 1,739, 1,597, 1,531, 1,496; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.10–7.15 (m, 3H, CH of Ar), 7.23–7.30 (m, 3H, CH of Ar), 7.67–7.75 (m, 2H, CH of Ar), 7.78 (d, <sup>3</sup>J = 8.8 Hz, 2H, CH of Ar), 8.12 (d, <sup>3</sup>J = 6.4 Hz, 1H, CH of Ar), 8.33 (d, <sup>3</sup>J = 8.4 Hz, 2H, CH of Ar); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>), 90.7, 112.9, 117.5, 118.6, 121.9, 125.5, 126.2, 126.9, 127.0, 129.6, 131.9, 132.5, 132.7, 135.6, 138.4, 139.5, 141.7, 166.8, 191.1. Anal. Calcd. for C<sub>22</sub>H<sub>13</sub>FN<sub>2</sub>O<sub>3</sub> (372.35): C 70.96, H 3.52, N 7.52; Found C 70.93, H 3.48, N 7.47. MS: *m/z*(%): 373 ([M<sup>+1</sup>]<sup>+</sup>, 22), 372 ([M]<sup>+</sup>, 98), 356 (16), 179 (99), 104 (73), 91 (37), 77 (88), 76 (base peak).

5'-(4-Bromophenyl)-2'-phenyl-3H-spiro[isobenzofuran-1,3'pyrazole]-3,4'(2'H)-dione (**5d**)

Red powder; mp: 158–161 °C; IR (KBr),  $(\bar{v}_{max}, cm^{-1})$ : 1,788, 1,737, 1,596, 1,514, 1,497; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  7.08–7.11 (m, 3H, CH of Ar), 7.22–7.26 (m, 3H, CH of Ar), 7.65 (d, <sup>3</sup>J = 8.6 Hz, 2H, CH of Ar), 7.68–7.73 (m, 2H, CH of Ar), 8.08–8.12 (m, 3H, CH of Ar); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>),  $\delta$  90.6, 117.2, 122.0, 124.4, 124.8, 126.9, 127.0, 127.1, 127.5, 129.4, 131.7, 132.2, 135.5, 139.6, 139.9, 141.9, 167.0, 191.6. Anal. Calcd. for C<sub>22</sub>H<sub>13</sub>BrN<sub>2</sub>O<sub>3</sub> (433.25): C 60.99, H 3.02, N 6.47; Found: C 60.95, H 2.99, N 6.45. MS, *m/z* (%): 435 ([M<sup>+2</sup>]<sup>+</sup>, 4), 434 ([M<sup>+1</sup>]<sup>+</sup>, 20), 433 ([M]<sup>+</sup>, 4), 416 (6), 223 (base peak), 179 (98), 104 (56), 91 (27), 77 (54), 76 (78).

# 4-(3,4'-Dioxo-2'-phenyl-2',4'-dihydro-3H- spiro[isobenzof uran-1,3'-pyrazole]-5'-yl)benzonitrile (5e)

Red powder; mp: 159–162 °C; IR (KBr), ( $\bar{v}_{max}$ , cm<sup>-1</sup>): 2,222, 1,786, 1,746, 1,597, 1,526, 1,497; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  7.00–7.09 (m, 3H, CH of Ar), 7.16–7.29 (m, 5H, CH of Ar), 7.55–7.72 (m, 2H, CH of Ar), 8.10–8.12 (m, 1H, CH of Ar), 8.19–8.23 (m, 2H, CH of Ar); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>),  $\delta$  90.6, 117.2, 122.0,

124.3, 124.4, 124.6, 126.9, 127.1, 128.1, 128.2, 129.4, 131.6, 135.5, 139.7, 140.0, 142.0, 162.6, 167.1, 191.9. Anal. Calcd. for  $C_{23}H_{13}N_3O_3$  (379.37): C 72.82, H 3.45, N 11.08; Found: C 72.79, H 3.43, N 11.06. MS m/z (%): 380 ([M<sup>+1</sup>]<sup>+</sup>, 3), 379 ([M]<sup>+</sup>, 11), 363 (26), 223 (61), 179 (base peak), 104 (24), 91 (11), 77 (54), 76 (45).

# 5'-(4-Methoxyphenyl)-2'-phenyl-3H-spiro[isobenzofuran-1, 3'-pyrazole]-3,4'(2'H)-dione (**5f**)

Red powder; mp: 148–151 °C; IR (KBr),  $(\bar{v}_{max}, cm^{-1})$ : 1,784, 1,745, 1,608, 1,578, 1,497; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  3.91 (s, 3H, CH<sub>3</sub>), 7.03–7.09 (m, 5H, CH of Ar), 7.21–7.29 (m, 3H, CH of Ar), 7.64–7.71 (m, 2H, CH of Ar), 8.09 (dd, <sup>3</sup>*J*<sub>1</sub> = 6.2 Hz, <sup>3</sup>*J*<sub>2</sub> = 1.6 Hz, 1H, CH of Ar), 8.16 (d, <sup>3</sup>*J* = 9.2 Hz, 2H, CH of Ar); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>),  $\delta$  55.4, 90.5, 114.4, 116.9, 120.6, 122.0, 124.0, 126.8, 127.2, 127.8, 129.3, 131.5, 135.4, 140.3, 140.6, 142.3, 161.2, 167.3, 192.3. Anal. Calcd. for C<sub>23</sub>H<sub>16</sub>N<sub>2</sub>O<sub>4</sub> (384.38): C 71.87, H 4.20, N 7.29; Found: C 71.84, H 4.17, N 7.26. MS: *m*/*z* (%): 385 ([M<sup>+1</sup>]<sup>+</sup>, 4), 384 ([M]<sup>+</sup>, 16), 368 (16), 301 (29), 223 (33), 179 (62), 104 (63), 90 (50), 77 (55), 76 (base peak).

### 2'-Phenyl-5'-(p-tolyl)-3H-spiro[isobenzofuran-1,3'-pyrazo le]-3,4'(2'H)-dione (**5g**)

Red powder; mp: 158–161 °C; IR (KBr),  $(\bar{v}_{max}, cm^{-1})$ : 1,787, 1,748, 1,596, 1,541,1,497; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  2.5 (s, 3H, CH<sub>3</sub>), 7.04–7.10 (m, 3H, CH of Ar), 7.21–7.28 (m, 3H, CH of Ar), 7.31–7.34 (m, 2H, CH of Ar), 7.64-7.71 (m, 2H, CH of Ar), 8.08–8.13 (m, 3H, CH of Ar), 1<sup>3</sup>C-NMR (100 MHz, CDCl<sub>3</sub>),  $\delta$  21.6, 90.6, 117.1, 122.0, 124.4, 125.3, 126.1, 126.8, 127.2, 129.4, 129.7, 131.5, 135.4, 140.2, 140.4, 140.7, 142.2, 167.2, 192.1. Anal. Calcd. for C<sub>23</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub> (368.38): C 74.99, H 4.38, N 7.60; Found: C 74.95, H 4.36, N 7.58. MS: m/z(%): 369 ([M<sup>+1</sup>]<sup>+</sup>, 18), 368 ([M]<sup>+</sup>, 79), 352 (17), 223 (base peak), 179 (99), 104 (55), 91 (36), 77 (67), 76 (81).

### 2',5'-Diphenyl-3H-spiro[isobenzofuran-1,3'-pyrazole]-3,4' (2'H)-dione (5 h)

Red powder; mp: 150–153 °C; IR (KBr),  $(\bar{v}_{max}, cm^{-1})$ : 1,786, 1,730, 1,599, 1,526,1,494; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  7.06–7.11 (m, 3H, CH of Ar), 7.22–7.27 (m, 3H, CH of Ar), 7.47-7.55 (m, 3H, CH of Ar), 7.65–7.72 (m, 2H, CH of Ar), 8.09–8.12 (m, 1H, CH of Ar), 8.21 (dd, <sup>3</sup>J<sub>1</sub> = 7.8 Hz, <sup>3</sup>J<sub>2</sub> = 1.6 Hz, 2H, CH of Ar); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>),  $\delta$  90.6, 117.1, 122.0, 124.6, 126.0, 126.8, 127.1, 128.1, 128.9, 129.4, 130.1, 131.6, 135.4, 140.1, 140.5, 142.2, 167.2, 191.9. Anal. Calcd. for C<sub>22</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub> (354.36): C 74.57, H 3.98, N 7.91; Found: C

74.52, H 3.94, N 7.87. MS: *m*/*z* (%): 355 ([M<sup>+1</sup>]<sup>+</sup>, 4), 354 ([M]<sup>+</sup>, 19), 338 (7), 223 (88), 179 (base peak), 104 (27), 91 (17), 77 (40), 76 (50).

# 2'-(4-Bromophenyl)-5'-(4-methoxyphenyl)-3H-spiro[isobe nzofuran-1,3'-pyrazole]-3,4'(2'H)-dione (**5i**)

Red powder; mp: 167–169 °C; IR (KBr),  $(\bar{v}_{max}, \text{ cm}^{-1})$ : 1,783, 1,746, 1,606, 1,536, 1,487; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  3.91 (s, 3H, CH<sub>3</sub>), 6.93 (dd,  ${}^{3}J_{1} = {}^{3}J_{2} = 2.6$  Hz, 1H, CH of Ar), 6.95 (dd,  ${}^{3}J_{1} = {}^{3}J_{2} = 2.6$  Hz, 1H, CH of Ar), 7.02 (dd,  ${}^{3}J_{1} = {}^{3}J_{2} = 2.4$  Hz, 1H, CH of Ar), 7.05 (dd,  ${}^{3}J_{1} = {}^{3}J_{2} = 2.4$  Hz, 1H, CH of Ar), 7.19–7.22 (m, 1H, CH of Ar), 7.33 (dd,  ${}^{3}J_{1} = {}^{3}J_{2} = 2.6$  Hz, 1H, CH of Ar), 7.35 (dd,  ${}^{3}J_{1} = {}^{3}J_{2} = 2.6$  Hz, 1H, CH of Ar), 7.66– 7.73 (m, 2H, CH of Ar), 8.09-8.12 (m, 1H, CH of Ar), 8.13 (dd,  ${}^{3}J_{1} = {}^{3}J_{2} = 2.4$  Hz, 1H, CH of Ar); 8.16 (dd,  ${}^{3}J_{1} = {}^{3}J_{2} = 2.4$  Hz, 1H, CH of Ar);  ${}^{13}$ C-NMR (100 MHz, CDCl<sub>3</sub>),  $\delta$  55.5, 90.3, 114.5, 117.0, 118.3, 120.3, 122.0, 126.9, 127.1, 127.9, 131.7, 132.3, 135.5, 139.4, 140.9, 141.9, 161.4, 166.9, 192.1. Anal. Calcd. for C<sub>23</sub>H<sub>15</sub>BrN<sub>2</sub>O<sub>4</sub> (463.28): C 59.63, H 3.26, N 6.05; Found: C 59.60, H 3.24, N 6.02. MS, *m*/*z* (%): 465 ([M<sup>+2</sup>]<sup>+</sup>, 8), 464 ([M<sup>+1</sup>]<sup>+</sup>, 35), 463 ([M]<sup>+</sup>, 8), 446 (20), 301 (97), 257 (49), 178 (46), 104 (68), 90 (56), 76 (base peak).

### 2'-(4-Bromophenyl)-5'-(p-tolyl)-3H-spiro[isobenzofuran-1, 3'-pyrazole]-3,4'(2'H)-dione (**5**j)

Red powder; mp: 189–192 °C; IR (KBr),  $(\bar{v}_{max}, cm^{-1})$ : 1,799, 1,747, 1,588, 1,535, 1,487; <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  2.43 (s, 3H, CH<sub>3</sub>), 6.92–6.94 (m, 2H, CH of Ar), 6.96–7.18 (m, 2H, CH of Ar), 7.26–7.31 (m, 3H, CH of Ar), 7.67–7.78 (m, 2H, CH of Ar), 8.05–8.07 (m, 3H, CH of Ar); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>),  $\delta$  22.7, 90.4, 114.6, 118.3, 119.5, 123.1, 125.1, 126.0, 127.3, 128.0, 130.8, 132.8, 133.4, 135.1, 136.6, 140.1, 141.9, 164.9, 192.1. Anal. Calcd. for C<sub>23</sub>H<sub>15</sub>BrN<sub>2</sub>O<sub>3</sub> (447.28): C 61.76, H 3.38, N 6.26; Found: C 61.73, H 3.34, N 6.22. MS, *m/z* (%): 449 ([M<sup>+2</sup>]<sup>+</sup>, 5), 448 ([M<sup>+1</sup>]<sup>+</sup>, 19), 447 ([M]<sup>+</sup>, 5), 432 (14), 301 (58), 257 (36), 178 (49), 104 (66), 90 (36), 76 (base peak).

#### **Results and discussion**

The synthesis of 3*H*-spiro[isobenzofuran-1,3'-pyrazole] derivatives from the reaction between 1-benzylidene-2-phenylhydrazine derivatives and ninhydrin followed by oxidative cleavage of their corresponding product was studied (Scheme 1).

As can be seen in Scheme 1, initially according to the previously reported procedure, the derivatives of

Scheme 1 Total pathway for the synthesis of 3*H*-spiro[isobenzofuran-1,3'pyrazole] derivatives



 
 Table 1
 Synthesis of new derivatives of 3H-spiro[isobenzofuran-1,3'-pyrazole]
 5a-j



5	$R^1$	$R^2$	Yield (%) <sup>a</sup>
a	Cl	Н	94
b	NO <sub>2</sub>	Н	97
c	F	Н	95
d	Br	Н	93
e	CN	Н	94
f	OCH <sub>3</sub>	Н	91
g	CH <sub>3</sub>	Н	91
h	Н	Н	92
i	OCH <sub>3</sub>	Br	89
j	CH <sub>3</sub>	Br	89

<sup>a</sup> Refers to isolated pure products

1-benzylidene-2-phenylhydrazine were prepared by the condensation reaction between phenylhydrazine and benzaldehyde derivatives (**3a-j**). These known compounds were identified by comparing their melting points with previously reported values. The reaction of these compounds with ninhydrin in acetic acid medium at room temperature followed by oxidative cleavage of their corresponding product by Pb(OAc)<sub>4</sub> was resulted in 3*H*-spiro[isobenzofuran-1,3'-pyrazole] (Table 1). The results show that the desired products were obtained in excellent yields and substituted groups on aromatic rings did not have any profound influence on the reactivity. Yet, oxidative cleavage step was very fast and clean and the pure products were precipitated at the end and extra action was not required for purification. Note that when periodic acid was used as oxidizing agent in the oxidative cleavage of vicinal diol **6a**, the product **5a** was obtained in only 55 % yield.

The molecular structures of all products **5a-j** were identified from their mass spectrometric analyses, IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR spectra and elemental analyses. Spectral data of compound **5a**, for instance, are as follows: The mass spectrum of **5a** displayed the molecular ion peak at m/z 372, which is in agreement with the proposed structure. The IR spectrum of this compound showed absorption bands due to the carbonyl groups of the lactone and ketone at 1,794, 1,739 cm<sup>-1</sup>, respectively, and at 1,597, 1,531, 1,496 cm<sup>-1</sup> for C=N, C=C and C–N bonds. The <sup>1</sup>H-NMR spectrum of this compound shows 12 protons in the aromatic region that correspond well with the structure of this compound. The <sup>1</sup>H-decoupled <sup>13</sup>C-NMR spectrum of **5a** showed 19 distinct resonances in agreement with the suggested structure.

For more information about the mechanism, in the synthesis of compound **5a**, the reaction was stopped before adding the  $Pb(OAc)_4$  and the product was isolated and identified on the basis of their IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR data and elemental analyses. Spectral data confirmed a vicinal cyclic diol structure in this step (Scheme 2).

The <sup>1</sup>H-NMR spectrum of **6a** in  $CDCl_3$  exhibited two single sharp signals at 3.58 and 4.19 ppm due to the hydroxyl protons, together with aromatic protons which

Scheme 2 Synthesis of vicinal diol **6a** by reaction of compound **3a** with ninhydrin





were resonated as multiplets in the region at  $\delta = 7.13$ –7.98 ppm. The <sup>1</sup>H decoupled <sup>13</sup>C-NMR spectrum of **6a** showed distinct signals in agreement with the proposed structure. (see Supplementary data).

A plausible mechanism for the synthesis of 3H-spiro[isobenzofuran-1,3'-pyrazole] derivatives is depicted in Scheme 3. At first, from the condensation reaction between phenylhydrazine and benzaldehyde derivatives, the corresponding 1-benzylidene-2-phenylhydrazines are obtained [15]. The 1-benzylidene-2-phenylhydrazine derivatives (phenylhydrazones) **3** act as enamines. In compound

**3**, due to the presence of nitrogen containing free electron pair conjugated with carbon–nitrogen double bond. This carbon is bearing some negative charge and nucleophilic attacks are firstly made through the carbon [16, 17]. Therefore, 1-benzylidene-2-phenylhydrazines **3** attack the ninhydrin and after passing the intermediate **8** followed by intramolecular attack of nitrogen to other carbonyl group of ninhydrin, dihydroindeno[1,2-*c*]pyrazole compounds **6a**–**j** are synthesized. Then, the oxidative cleavage of these cyclic diols by Pb(OAc)<sub>4</sub> produces the orthogonal intermediate **10** through intermediate **9**. Because of the strong intramolecular

interactions between the nitrogen and the carbonyl group next to it in such rings [18], a large positive charge assembled on the nitrogen in the intermediate 10. Hydrolysis of this intermediate produces the compound 11 which forms the final product by intramolecular sterification reaction.

#### Conclusion

In conclusion, this work described a novel method for the preparation of a wide variety of new spirocyclic compounds containing isobenzofuranone and pyrazole moieties, named 3H-spiro[isobenzofuran-1,3'-pyrazole] by oxidative cleavage of dihydroindeno[1,2-c]pyrazoles. This one-pot and simple procedure can be a convenient and effective method for the synthesis of a wide range of novel drug-like spiroindolines.

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