Iodo Cyclofunctionalization of 2,4-Dialkenyl-1,3-Dicarbonyl Compounds: Synthesis of Substituted 3-(2-furylidene)-2-furanones

Claudete J. Valduga* [a], Hélio A. Stefani [a],and Nicola Petragnani [b]

[a] Faculdade de Ciências Farmacêuticas, Universidade de São Paulo
[b] Instituto de Química, Universidade de São Paulo
Av. Prof. Lineu Prestes, 580 - CEP 05508-900 - São Paulo – Brasil
Received May 11, 2001

A facile method for the synthesis of substituted 3-(2-furylidene)-2-furanones has been developed using cyclofunctionalization reactions of 2,4-dialkenyl-1,3-dicarbonyl compounds and iodine as electrophile in the presence of Na_2CO_3, in refluxing chloroform. Compounds **4** are obtained in modest to good yields and their structural identification was established by ^{1}H NMR, ^{1}H COSY, ^{13}C NMR and ^{1}H-^{13}C COSY. A mechanism has been proposed to rationalize the formation of the ylidene furanone.

J. Heterocyclic Chem., **39**, 639 (2002).

Introduction.

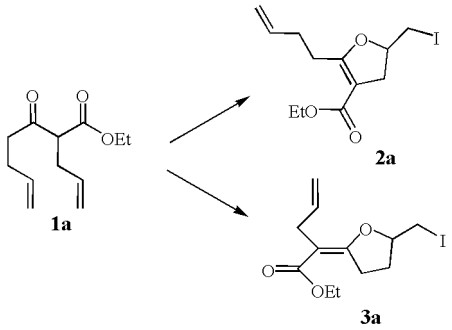
The word "cyclofunctionalization" was introduced by Clive [1] in 1977 to describe a process where the addition of an electrophile to an alkene bearing an internal nucleophile results in a cyclization. This electrophile remains connected to one of the carbons of the double bond involved in the reaction allowing for further modifications that will depend on the choice of the functionalization agent. Functional groups like OR, COOH, COO^-, $CONR_2$, NHR, SR, *etc*., will participate as internal nucleophiles in the process.

Based on the empirical Baldwin rules [2] governing ring closure reactions Cardillo and Orena [3] have emphasized that the 5-exo mode appears to be preferred in both the tetrahedral or trigonal ring closure under kinetic control, although several factors seem to promote the 5-exo or 6-endo process. Thus, in the lactonization reaction under kinetic control and in the absence of strong electronic factors, preference for formation of γ-lactones relative to δ-lactones can be observed [4]. Likewise a large number of examples are found in the literature focusing on the preference of 5 over 4 rings in the lactonization reactions under thermodynamic control as well as the 5-exo over the 6-endo mode cyclization process.

Results and Discussion.

Following an initial publication [5] describing the iodocyclization of 2,4-dialkenyl-1,3-dicarbonyl compounds (1 equivalent I_2/Na_2CO_3 in $CHCl_3$) we now report the reaction of other substrates under similar conditions. In all cases tetrahydrofuran derivatives with no pyran ring formation were obtained, confirming the preference for the five over the six-membered rings [3]. Iodoethers with endocyclic double bond are mainly formed with exception of the reactions with compounds **1a**, **1c** and **1f**. Compound **1a** gave rise only to a minor amount of the exocyclic derivative **3a** (10%), **1c** produced **3c** as the minor product (2.9:1 exo/endo), and **1f** formed exclusively the exo derivative **3f** (Scheme 1 and Table 1).

Scheme 1



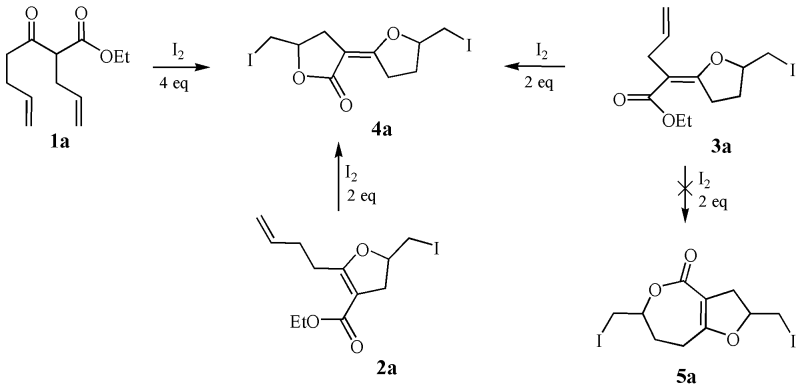
With the aim of synthesizing diiodocyclofunctionalized compounds, the monoiodocyclofunctionalized compounds **2a-e** and **2g-i** (with endocyclic double bond) and **3a**, **3c** and **3f** (with exocyclic double bond) were submitted to a second cyclization with iodine in excess/Na_2CO_3 in refluxing chloroform. The diiodocyclization was performed also in a "one pot" procedure by treating directly the starting dicarbonyl compounds (**1a-i**) with excess iodine. This "one pot" procedure is more suitable due to its experimental simplicity.

The monoiodo compounds with endocyclic double bond (**2a-e** and **2g-i**) were expected to produce the seven member lactones (ε-lactones), such as **5a**, fused to a dihydrofuranic ring. These seven-membered lactones should be obtained also by the "one pot" dicyclization procedure of the starting dicarbonyl substrates.

Likewise, five-membered lactones (γ-lactones) connected to a tetrahydrofuran ring by a C-C double bond (such **4a**) should be obtained by the iodocyclization of the exo-cyclic compound **3a**, **3c** and **3f**.

Contrary to our expectation the aforementioned five-membered lactones were the only products formed regardless of the method used, as exemplified in scheme 2 (see Table 1). These results confirm once more the preference toward the formation of five-membered over seven-membered lactones.

Scheme 2



These results can be rationalized by considering that under the employed conditions compounds **4** cannot be generated from **2** *via* the reverse sequence **2**→**1**→**4**.

Based on the fact that unsaturated ethers [6,7] and esters [8] are also susceptible to iodocyclization, it can be tentatively assumed that formation of **4** from **2** involves the intermediate iodonium salt **7**, or more probably the π complex **6** [9] which suffers the known lactonization step leading to the bicyclic compound **4**.

According to an earlier report [10], the lactonization step requires two equivalents of iodine on account of the formation of the π complex **6** followed by reaction with the second equivalent of iodine to generate the iodonium salt **7** and the I^- anion.

The conversion **3**→**2** by the iodine assisted antiperiplanar opening of the furan ring can be presumably attributed to the greater stability of the endocyclic olefins toward the exocyclic copartners [11]. Otherwise, the formation of **4** from **2** and from **1** by the two- or one-step procedure respectively, is supported by the previously mentioned preference for the five-membered over the seven-membered lactones (Scheme 3).

The low yield observed in the case of α-cyclohexenyl substituted compounds like **4b**, **4d** and **4i** (19%, 10% and 31%) can be attributed to the lack of anti-periplanarity in the iodine assisted opening of the furan ring (illustrative example **2b**→**4b**, figure 1).

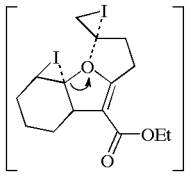


Figure 1. Cleavage of the dihydrofuran ring.

An alternative pathway to **2** can involve a direct cyclization of **1** by attack of the OH group on the other

Scheme 3

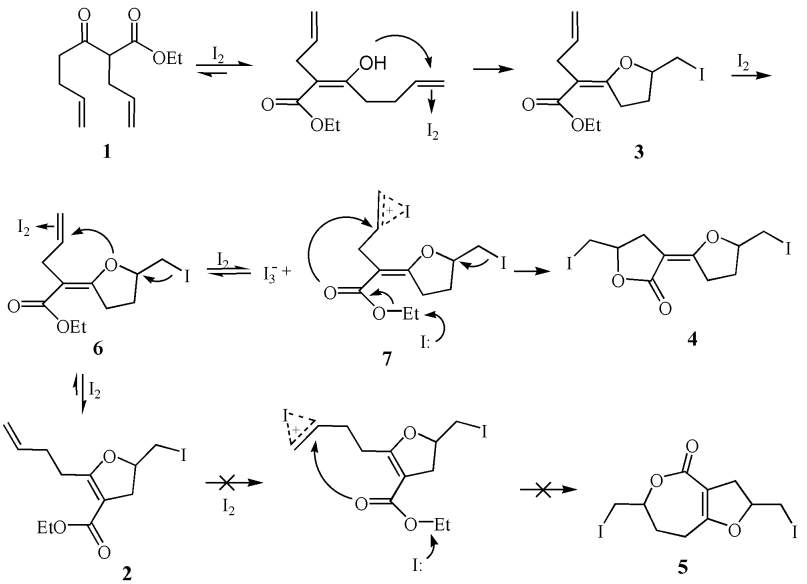


Table 1

Iodomono- and Iododicyclofunctionalized Products

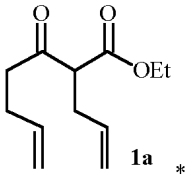
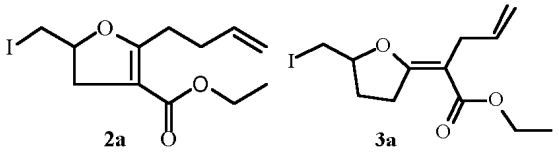
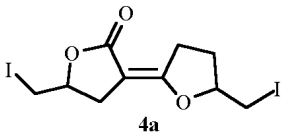
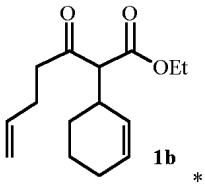
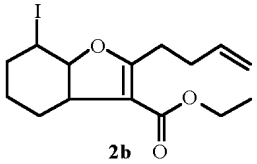
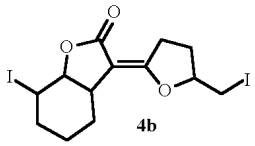
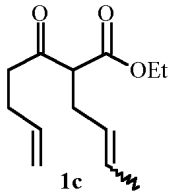
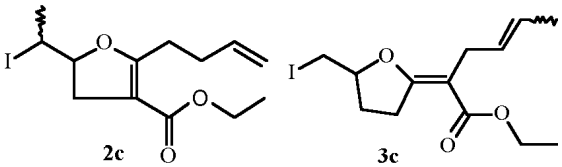
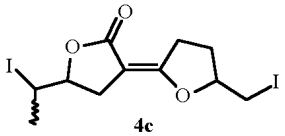
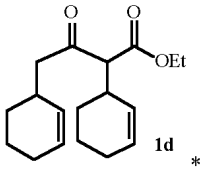
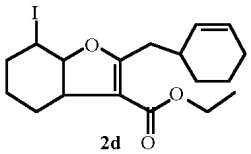
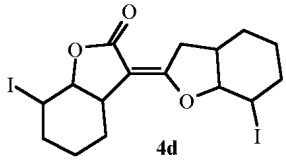
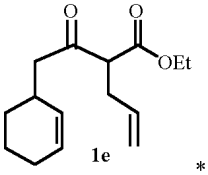
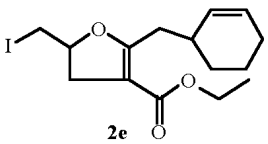
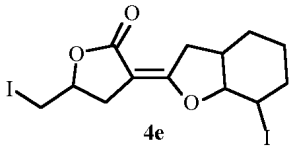
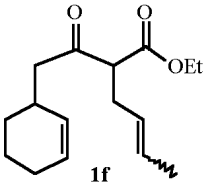
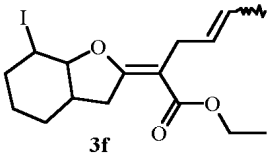
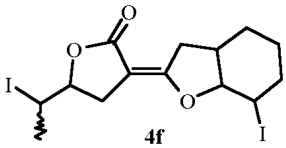
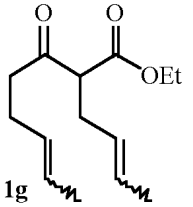
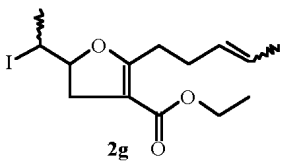
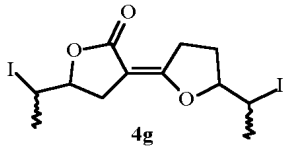
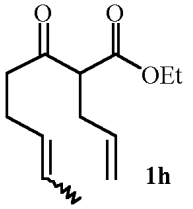
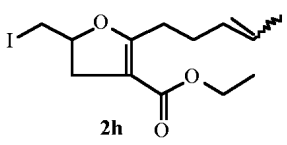
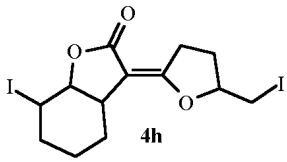
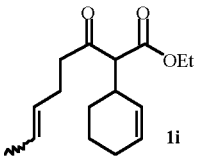
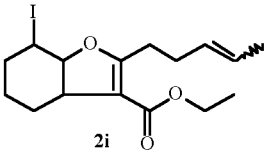
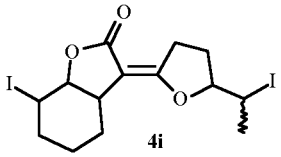
Substrate	Iodomonocyclofunctionalized Product (Yield %)	Iododicyclofunctionalized Product (Yield %)
 **1a** *	 **2a** (81) **3a**	 **4a** (78)
 **1b** *	 **2b** (72)	 **4b** (19)
 **1c**	 **2c** (68) **3c**	 **4c** (59)
 **1d** *	 **2d** (61)	 **4d** (10)
 **1e** *	 **2e** (73)	 **4e** (78)
 **1f**	 **3f** (65)	 **4f** (52)
 **1g**	 **2g** (62)	 **4g** (71)
 **1h**	 **2h** (50)	 **4h** (66)

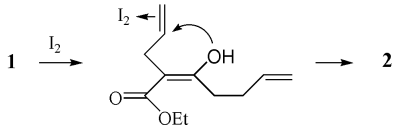
Table 1 (continued)

Substrate	Iodomonocyclofuntionalized Product (Yield %)	Iododicyclcofuntionalized Product Yield %)
 **1i**	 **2i** (54)	 **4i** (31)

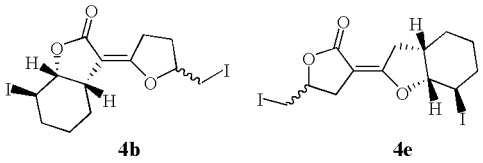
* Reported on the ref. 5.

iodine-π-complexed alkene at the 4 –position. Then **2** can be equilibrated with **6** giving **4**.

Scheme 4



The ring fusion in compounds **4b**, **4d**, **4e**, **4f** and **4i** is expected to be *cis* in accordance with literature data [12]. It was confirmed in the case of compounds **4b** and **4e** by NMR spectroscopy ^1H, ^{13}C, HETCOR and COSY and by X-ray in the case of compound **4e** [13].



4b **4e**

Figure 2

Conclusion.

We describe in this paper a simple one or two step procedure to synthesize 3-(2-furanylidene)-2-furanone compounds starting from the easily accessible 2,4-dialkenyl-1,3-dicarbonyl compounds.

EXPERIMENTAL

General.

^1H, COSY and HETCOR NMR spectra were recorded on a 300 MHz spectrometer using TMS as the internal standard and $CDCl_3$ as solvent. ^{13}C NMR spectra were recorded at 75 MHz on the same instrument with the solvent peak ($CDCl_3$) as the reference (In braces multiple signs correspond to diastereomeric mixture). GC/MS and elemental analysis (C, H) were performed at the Microanalytical Laboratory of the Chemistry Institute - USP. HPLC was performed on an HP 1100 instrument, with a β-cyclodextrin/carbamate column at 10° C, eluting with a mixture of methanol/water 22 % at 0.3 mL/minute (the diastereomeric ratio was identified in the case of the compounds **4a** and **4e**). Gas chromatography was carried out in an HP 6890 with methylsilicon column (30mX0.32mm). Flash chromatography was performed with Merck silica gel 60 (230-400 mesh ASTM). For thin-layer chromatography (TLC) analysis, Merck TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. All solvents and reagents were purified by conventional methods. Infrared spectra were recorded on a BOMEM-FTIR-MB 102 spectrometer using potassium bromide.

General Procedure.

Iodomonocyclization.

Compounds **4c**, **4f**, **4g**, **4h** and **4i** were prepared in accordance with the previously described method [5].

Iododicyclization.

2,4-Dialkenyl-1,3-dicarbonyl compounds (prepared by the previously described method [5]), (1 mmol), were treated with iodine (4 mmoles) and Na_2CO_3 (2 mmoles) in dry $CHCl_3$ (10 mL) at reflux. The reaction was stirred until the consumption of substrate (GC and TLC monitoring). Et_2O was added and the organic phase washed with aqueous sodium thiosulfate (10%), brine, and dried over Mg_2SO_4. The solvent was evaporated under vacuum and the crude reaction mixture was purified by flash chromatography on silica gel eluting with CH_2Cl_2 to give the product as a pale yellow oil or solid.

Ethyl 5-(3-Butenyl)-2-iodomethyl-2,3-dihydro-4-furancarboxylate (**2c**).

We are unable to purify this compound. MS: *m/z* 39, 55, 67, 79, 93, 107, 121, 135, 149, 177, 223(100), 251, 277, 305, 321, 350. Chromatographic yield: 17%.

Ethyl (*E*)-2-(5-Iodomethyltetrhydro-2-furylidene)-4-hexenoate (**3c**).

Compound **3c** was obtained in 49 % yield; ^1H NMR: δ 1.26 (t, *J*= 7.09 Hz, 3H), 1.61-1.63 (m, 3H), 1.84-1.90 (m, 1H), 2.25-2.36 (m, 1H), 2.97-3.08 (m, 3H), 3.22-3.37 (m, 3H), 4.17 (q, *J*= 7.09 Hz, 2H), 4.47 (ddd, *J*= 12.7, 8.6 and 4.9 Hz, 1H), 5.39-5.48 (m, 2H). ^{13}C NMR: δ 7.68, 14.61, 18.03, 29.31, 30.22, 31.14, 59.72, 81.89, 102.39, 125.05, 129.22, 168.79, 169.64. MS: *m/z* 39, 55, 67, 79, 93, 107, 121, 135, 149, 159, 177, 195, 223 (100), 263, 277, 305, 321, 350 (M^+). IR: 2976, 2930, 1694, 1635, 1443, 1368, 1303, 1187, 1110, 1056, 967, 887, 609 cm^{-1}.

Anal. Calcd. for $C_{13}H_{19}IO_3$: C, 44.59; H, 5.47. Found: C, 44.22; H, 5.58.

Ethyl (*E*)-2-(7-Iodoperhydrobenzo[*b*]-2-furylidene)-4-hexenoate (**3f**).

Compound **3f** was obtained in 65% yield; ^{1}H NMR: δ 1.28 (t, *J*= 7.05 Hz, 3H), 1.63 (dd, *J*= 3.3 and 1.15 Hz, 3H), 1.40-1.96 (m, 6H), 2.61 (dd, *J*= 13.08 and 6.4 Hz, 1H), 2.96 and 2.98 (s, 3H), 4.15 (*J*= 7.05 Hz, 2H), 4.42 (q, *J*= 5.20 Hz, 1H), 4.57 (t, *J*= 5.20 Hz, 1H), 5.44-5.48 (m, 2H). ^{13}C NMR: δ 14.46, 17.93, 21.33, 25.98, [29.01, 29.12], 32.40, 34.62, 37.09, 59.62, 85.79, 104.06, 124.88, 129.14, 168.68, 168.94. MS: *m/z* 39, 67, 77, 95, 123, 147, 189, 217 (100), 263, 291, 391 (M^+). IR: 2935, 1726, 1708, 1643, 1446, 1294, 1181, 1107, 1042, 875, 708, 622 cm^{-1}.

Anal. Calcd. for $C_{16}H_{23}IO_3$: C, 49.29; H, 5.94. Found: C, 49.40; H, 5.53.

Ethyl 2-(1-Iodoethyl)-5-(3-pentenyl)-2,3-dihydro-4-furancarboxylate (**2g**).

Compound **2g** was obtained in 62% yield; ^{1}H NMR: δ 1.28 (t, *J*= 7.0 Hz, 3H), 1.63 (d, *J*= 4.6 Hz, 3H), 1.90 (d, *J*= 6.8 Hz, 3H), 2.20-2.28 (m, 2H), 2.51-2.65 (m, 1H), 2.69-2.78 (m, 2H), 3.00 (dd, *J*= 15.0 and 10.9 Hz, 1H), 3.40-3.54 (m, 1H), 4.17 (q, *J*= 7.0 Hz, 2H), 4.33-4.42 (m, 1H), 5.43-5.54 (m, 2H). ^{13}C NMR: δ 14.34, 17.85, 23.48, 27.88, 29.78, 30.55, 35.77, 59.53, 101.62, 125.73, 129.74, 165.60, 170.05. MS: *m/z* 55 (100), 67, 95, 121, 189, 221, 237, 291, 365 (M^+). IR: 2971, 2926, 1725, 1443, 1362, 1227, 1115, 1035, 875, 597 cm^{-1}.

Anal. Calcd. for $C_{14}H_{21}IO_3$: C, 46.17; H, 5.81. Found: C, 46.22; H, 5.66.

Ethyl 2-Iodomethyl-5-(3-pentenyl)-2,3-dihydro-4-furancarboxylate (**2h**).

Compound **2h** was obtained in 50% yield; ^{1}H NMR: δ 1.28 (t, *J*= 7.11 Hz, 3H), 1.63 (d, *J*= 4.86 Hz, 3H), 2.21-2.33 (m, 2H), 2.55-2.73 (m, 3H), 3.03 (dd, *J*=10.48 and 6.43 Hz, 1H), 3.25-3.33 (m, 2H), 4.17 (q, *J*= 7.12 Hz, 2H), 4.64-4.70 (m, 1H), 5.42-5.47 (m, 2H). ^{13}C NMR: δ 9.11, 14.81, 18.27, 27.97, 30.19, 36.47, 59.96, 80.73, 101.95, 126.21, 130.08, 166.03, 170.52. MS: *m/z* 43 (100), 67, 81, 95, 113, 131, 149, 193, 223, 239, 253, 277, 293, 311, 321, 351 (M^+). IR: 2976, 2933, 1709, 1643, 1445, 1375, 1243, 1171, 1055, 971, 764, 522 cm^{-1}.

Anal. Calcd. for $C_{13}H_{19}IO_3$: C, 44.59; H, 5.47. Found: C, 44.52; H, 5.30.

Ethyl 7-Iodo-2-(3-pentenyl)-3a,4,5,6,7,7a-hexahydrobenzo[*b*]-3-furancarboxylate (**2i**).

Compound **2i** was obtained in 54 % yield; ^{1}H NMR: δ 1.28 (t, *J*= 7.01 Hz, 3H), 1.63 (d, *J*= 5.3 Hz, 3H), 1.42-2.04 (m, 6H), 2.24 (dd, *J*= 13.6 and 6.63 Hz, 2H), 2.54-5.63 (m, 1H), 2.67-2.75 (m, 1H), 3.18 (dd, *J*= 15.28 and 7.54 Hz, 1H), 4.13-4.22 (m, 2H), 4.56 (dd, *J*= 10.6 and 4.53 Hz, 1H), 4.69 (dd, *J*= 7,36 and 4.9 Hz, 1H), 5.30-5.53 (m, 2H). ^{13}C NMR: δ 14.39, 17.88, 20.70, 27.01, 28.06, 28.74, 29.86, 32.25, 39.24, 59.43, 87.01, 109.36, 125.88, 129.64, 165.64, 170.93. MS: *m/z* 55, 79, 91, 121, 139, 171, 189, 207, 217, 245, 263, 317, 345, 391(100) (M^+). IR: 2938, 1697, 1635, 1445, 1316, 1168, 1089, 972, 775, 620 cm^{-1}.

Anal. Calcd. for $C_{13}H_{19}IO_3$: C, 49.24; H, 5.94. Found: C, 50.02; H, 5.82.

5-Iodomethyl-3-(5-iodomethyltetrahydro-2-furylidene)tetrahydro-2-furanone (**4a**).

Compound **4a** was obtained in 78% yield; mp 89-90 °C. Diastereomeric ratio: 1:1. ^{1}H NMR: δ 1.88-1.95 (m, 1H), 2.25-2.42 (m, 1H), 2.51-2.65 (m, 1H), 2.85-3.09 (m, 2H), 3.16-3.37 (m, 5H), 4.41-4.57 (m, 2H). ^{13}C NMR: δ 6.75, 6.89, 9.09, 8.98, 29.23, 29.74, 29.59, 31.61, 31.67, 75.11, 75.07, 82.98, 83.09, 93.97, 168.91, 171.38. IR: 2930, 1741, 1674, 1432, 1302, 1255, 1186, 1008, 860, 750 cm^{-1}. MS: *m/z* 53, 79, 91, 125, 135, 147, 162, 179, 253, 265, 289, 321, 307 (100), 434 (M^+).

Anal. Calcd. for $C_{10}H_{12}I_2O_3$: C, 27.65; H, 2.79. Found: C, 27.95; H, 2.80.

7-Iodo-3-(5-iodomethyltetrahydro-2-furylidene)perhydrobenzo-[*b*]-2-furanone (**4b**).

Compound **4b** was obtained in 19% yield; ^{1}H NMR: δ 1.52-1.56 (m, 1H); 1.64-1.70 (m, 2H), 1.86-1.99 (m, 4H), 2.29-2.36 (m, 1H), 2.96-3.05 (m, 1H), 3.28-3.42 (m, 4H), 4.28-4.62 (m, 3H). ^{13}C NMR: δ [6.57, 7.40], [20.77, 21.11], [25.82, 26.12], [28.88, 29.12], [29.42, 29.49], 29.64, [31.40, 31.90], [35.99, 36.28], [81.26, 81.43], [82.52, 83.43], [99.78, 100.54], [168.44, 168.48], [171.59, 171.62]. IR: 2934, 2858, 1743, 1678, 1441, 1328, 1254, 1027, 915, 877,794, 738, 692, 628 cm^{-1}. MS: *m/z* 55 (100), 149, 165, 221, 331, 348, 475 (M^+).

Anal. Calcd. for $C_{13}H_{16}I_2O_3$: C, 29.49; H, 3.15. Found: C, 29.63; H, 3.18.

5-Iodomethyl-3-(5-iodomethyltetrahydro-2-furylidene)tetrahydro-2-furanone (**4c**).

Compound **4c** was obtained in 59% yield; ^{1}H NMR: δ 1.81-1.93 (m, 1H), 1.96 (d, *J*= 6.3 Hz, 3H), 2.31-2.45 (m, 1H), 2.62-2.72 (m, 1H), 2.94-3.08 (m, 2H), 3.29-3.43 (m, 3H), 4.10-4.35 (m, 2H), 4.56 (quint, *J*= 6,0 Hz, 1H). ^{13}C NMR: δ [6.76, 6.96], 23.95, [29.28, 29.31], [29.83, 29.85], [30.80, 30.94], 31.82, [80.18, 80.23], [83.03, 83.17], 94.41, [168.70, 168.73], [171.16, 171.57]. IR: 2942, 1740, 1674, 1334, 1253, 1187, 1083, 1010, 857, 751 cm^{-1}. MS: *m/z* 43, 55 (100), 69, 85, 113, 149, 181, 227, 267, 295, 321, 421, 448 (M^+).

Anal. Calcd. for $C_{11}H_{14}I_2O_3$: C, 29.49; H, 3.15. Found: C, 29.27; H, 3.05.

7-Iodo-3-(7-iodoperhydrobenzo[*b*]-2-furylidene)perhydrobenzo-[*b*]-2-furanone (**4d**).

Compound **4d** was obtained in 10% yield; ^{1}H NMR: δ 1.30-2.00 (m, 12H), 2.65-2.29 (m, 1H), 2.97-3.05 (m, 2H), 3.38-3.40 (m, 1H), 4.26-4.66 (m, 4H). ^{13}C NMR: δ [27.75, 27.89], [28.84, 28.92], [34.61, 34.65], 35.82, [81.22, 81.45], [87.02, 87.21], [102.41, 102.83], [168.00, 168.14], [171.55, 171.58]. IR: 2931, 2860, 1739, 1674, 1449, 1253, 1157, 1011, 911, 742, 527, 508 cm^{-1}. MS: *m/z* 41 (100), 55, 79, 91, 121, 165, 187, 207, 241, 259, 299, 387, 514 (M^+).

Anal. Calcd. for $C_{16}H_{20}I_2O_3$: C, 37.38; H, 3.92. Found: C, 37.56; H, 4.25.

5-Iodomethyl-3-(7-iodoperhydrobenzo[*b*]-2-furylidene)tetrahydro-2-furanone (**4e**).

Compound **4e** was obtained in 78% yield; mp 77-79 °C. Diastereomeric ratio: 1:1:1. ^{1}H NMR: δ 1.32-1.40 (m, 1H); 1.49-1.56 (m, 1H), 1.65-1.68 (m, 1H), 1.72-1.78 (m, 1H), 1.95 (q, *J*= 5.3 Hz, 2H), 2.62-2.64 (m, 1H), 2.69-2.75 (m, 1H), 2.96-2.98 (m, 1H), 3.04-3.10 (m, 2H), 3.25 (dd, *J*= 8.0 e 10.5 Hz, 1H), 3.39 (dd, *J*= 3.85 and 10.50 Hz, 1H), 4.45 (q, *J*= 5.1 Hz, 1H), 4.50-4.58 (m, 1H), 4.69 (t, *J*= 5.1 Hz, 1H). ^{13}C NMR: δ 9.17, 21.27, 25.99,

28.09, 31.88, 32.15, 34.48, 35.34, 75.39, 87.35, 95.88, 168.79, 171.67. IR: 2934, 2858, 1743, 1678, 1441, 1328, 1254, 1027, 915, 877, 794, 738, 692, 628 cm^{-1}. MS: *m/z* 43, 55, 67, 79, 95, 125, 139, 175, 221, 254, 303, 321, 347 (100), 375, 419, 448, 474 (M^+).

Anal. Calcd. for $C_{13}H_{16}I_2O_3$: C, 32.94; H, 3.40. Found: C, 33.23; H, 3.30.

5-(1-Iodoethyl)-3-(7-iodoperhydrobenzo[*b*]-2-furylidene)-tetrahydro-2-furanone (**4f**).

Compound **4f** was obtained in 52% yield; ^1H NMR: δ 1.30-1.77 (m, 6H), 1.92-1.97 (m, 3H), 2.65-2.71 (m, 2H), 2.99-3.07 (m, 3H), 4.16-2.26 (m, 1H), 4.42-4.54 (m, 1H), 4.68 (t, *J*= 4.45 Hz, 1H). ^{13}C NMR: δ 21.07, 23.97, 25.80, 27.88, 30.94, 31.81, 32.56, 34.28, 35.18, 75.58, 88.73, 95.54, 168.31, 171.64. IR: 2937, 1728, 1449, 1275, 1175, 1008, 765, 606 cm^{-1}. MS: *m/z* 32, 55, 79, 91, 121, 141, 187, 205, 233 (100), 265, 279, 313, 331, 359, 387, 405, 487 (M^+).

Anal. Calcd. for $C_{14}H_{18}I_2O_3$: C, 34.45; H, 3.72. Found: C, 34.39; H, 3.81.

5-(1-Iodoethyl)-3-[5-(1-iodoethyl)tetrahydro-2-furylidene]-tetrahydro-2-furanone (**4g**).

Compound **4g** was obtained in 71% yield; ^1H NMR: δ 1.83-1.97 (m, 5H), 2.30-2.47 (m, 1H), 2.64-2.70 (m, 1H), 2.94-3.07 (m, 2H), 3.35-3.45 (m, 1H), 4.15-4.29 (m, 4H). ^{13}C NMR: δ [23.91, 23.94], [24.30, 24.36], [28.65, 28.83], [29.20, 29.23], [29.46, 29.48, 29.52], [30.82, 31.76], [31.73, 31.76], [80.13, 80.16], [88.06, 88.37], [94.10, 94.18], [168.91, 168.89], [171.55, 171,73]. IR: 3443, 2932, 1743, 1676, 1447, 1379, 1333, 1253, 1192, 1081, 1012, 855, 779, 751, 700, 596, 516cm^{-1}. MS: *m/z* 41, 67, 95, 113, 127, 161, 179, 207, 241, 254, 321, 335 (100), 462 (M^+).

Anal. Calcd. for $C_{12}H_{16}I_2O_3$: C, 31.39; H, 3.49. Found: C, 31.63; H, 3.26.

3-[5-(1-Iodoethyl)tetrahydro-2-furylidene]-5-iodomethyltetrahydro-2-furanone (**4h**).

Compound **4h** was obtained in 66% yield; ^1H NMR: δ 1.91-1.94 (m, 1H), 1.95 (d, *J*= 6.3 Hz, 3H), 2.37-2.42 (m, 1H), 2.60-2.67 (m, 1H), 2.95-3.09 (m, 2H), 3.22-3.29 (m, 1H), 3.36-3.42 (m, 2H), 4.22-4.56 (m, 3H). ^{13}C NMR: δ [8.93, 9.13, 9.22, 9.28], [24.30], [28.75], [29.20, 29.25], [29.49, 29.48, 29.61], [31.62, 31.71], [75.22], [87.80, 87.86, 87.98, 88.05]; [93.74, 93.80], [169.11, 169.21, 169.25, 169.34], [171.51, 171.57]. IR: 3434, 2936, 1714, 1447, 1265, 861, 777, 752, 696, 611, 520 cm^{-1}. MS: *m/z* 67, 91, 125, 148, 176, 193, 253, 275, 303, 321 (100), 448 (M^+).

Anal. Calcd. for $C_{11}H_{14}I_2O_3$: C, 29.49; H, 3.15. Found: C, 29.35; H, 3.01.

7-Iodo-3-[5-(1-iodoethyl)tetrahydro-2-furylidene]perhydrobenzo[*b*]-2-furanone (**4i**).

Compound **4i** was obtained in 31% yield; ^1H NMR: δ 1.43-2.00 (m, 9H), 2.19-2.37 (m, 1H), 2.91-3.08 (m, 1H), 3.25-3.32 (m, 2H), 4.14-4.62 (m, 3H). ^{13}C NMR: δ 23.67, 29.64, 28.98, 29.64, 30.34, 34.91, 80.90, 82.30, 100.01, 168.83, 172.79. IR: 2934, 1726, 1446, 1361, 1247, 1169, 1016, 701 cm^{-1}. MS: *m/z* 41, 67, 79, 91, 121, 139, 167, 187, 205, 233 (100), 265, 279, 337, 361, 445, 463, 489 (M^+).

Anal. Calcd. for $C_{14}H_{18}I_2O_3$: C, 34.45; H, 3.72. Found: C, 34.73; H, 3.58.

Acknowledgement.

We thank the *FAPESP* (97/04222-3; 94/0712-8; 98/10821-0) and *CNPq* (520683/96-0) for financial support.

REFERENCES AND NOTES

* Author to whom correspondence should be addressed: E-mail: cvalduga@usp.br , Fax: (internat.) + 55 11 3815-4418.

[1] D. L. J. Clive, G. Chitattu, N. Curtis, W. A. Kiel and C. K., Wong, *J. Chem. Soc., Chem. Commun.*, 725, (1977).

[2] J. E. Baldwin, *J. Chem. Soc. Chem. Commun.*, 734 (1976).

[3] G. Cardillo and M. Orena, *Tetrahedron*, **46**, 3321 (1990) and references cited therein.

[4] C. Galli, G. Illuminati, L Mandolini and P. Tamborra, *J. Am. Chem. Soc.*, **99**, 2591 (1977).

[5] H. A. Stefani, N. Petragnani, C. J. Valduga and C. A. Brandt, *Tetrahedron Lett.*, **38**, 4977 (1997); see also Corrigendum in *Tetrahedron Lett*., **39**, 7624 (1998).

[6] S. D. Richnovsky and P. A. Bartlett, *J. Am. Chem. Soc*., **103**, 3963 (1981).

[7] P. A. Bartlett and P. C. Ting, *J. Org. Chem*., **51**, 2230 (1986).

[8] V. Jagër and H. J. Günther, *Tetrahedron Lett*., 2543 (1977).

[9] A. R. Chamberlin, R. L. Mulholland Jr, S. D. Kahn and W.J. Hehre, *J. Am. Chem. Soc.*, **109**, 672 (1987) and references cited therein.

[10] L. F. P. Amaral and S. C. Melo, *J. Org. Chem*., **38**, 800 (1973).

[11a] R. B. Turner and R. H. Garner, *J. Am. Chem. Soc.*, **79**, 253 (1957); [11b] R. B. Turner and R. H. Garner, *J. Am. Chem. Soc.*, **80**, 1424 (1958).

[12a] J. Klein, *J. Am. Chem. Soc*., **81**, 364 (1959); [11b] H. O. House, R. G. Carlson and H. Babad, *J. Org. Chem.*, **28**, 3359 (1963).

[13] J. Zukerman-Schpector, H. A. Stefani, C. J. Valduga, C. A. Brandt and I. Caracelli, *Z. Kristallogr.*, **213**, 733 (1998).