Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2011, **9**, 1474

www.rsc.org/obc

PAPER

Iodocyclization *versus* diiodination in the reaction of 3-alkynyl-4-methoxycoumarins with iodine: Synthesis of 3-iodofuro[2,3-*b*]chromones†

Guillaume Raffa, Sébastien Belot, Geneviève Balme and Nuno Monteiro*

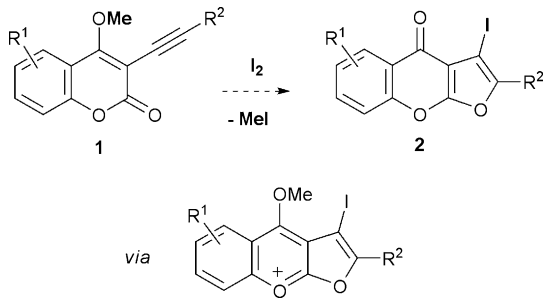
Received 26th October 2010, Accepted 2nd December 2010
DOI: 10.1039/c0ob00935k

The reaction of 3-alkynyl-4-methoxycoumarins with molecular iodine in chlorinated solvents allows access to 3-iodofurochromones in good to excellent yields as the result of a iodocyclization–demethylation process. Competitive diiodination of the coumarin acetylene moiety could be eliminated by simply performing the reactions in refluxing 1,2-dichloroethane, owing to the thermal instability of the resulting (*E*)-1,2-diiodoethenylcoumarins.

Introduction

The iodine-based activation of alkynes toward intramolecular addition of heteronucleophiles has proven to be an extremely effective and broadly applicable method to access a variety of heterocyclic compounds,[1] notably furan derivatives.[2] The introduction of a iodide functional group on the newly formed ring is of special interest as it can act as an effective chemical handle for further derivatization. Clearly, the main drawback of this method is the occasional difficulty in avoiding the competitive *trans*-addition of iodine across the triple bond, a relatively well-documented process that leads to the formation of (*E*)-1,2-diiodoalkenes.[3]

Recently, we became interested in developing a general and convenient method for the synthesis of 4*H*-furo[2,3-*b*][1]benzopyran-4-ones (furochromones).[4] The latter compounds have received little attention to date,[5] possibly because this heterocyclic system is not commonly encountered in nature.[6] Preliminary investigations based on previous work from this laboratory[7] suggested that these heterocycles (*i.e.* **2**) would be accessible *via* iodocyclization of readily available 3-alkynyl-4-methoxycoumarins (**1**) followed by the *in situ* demethylation of the methoxyl group (Scheme 1). We herein report on the scope and limitations of the method, and provide some mechanistic insight into plausible reaction pathways.



Scheme 1 An iodocyclization strategy toward 3-iodofuro[2,3-*b*]-chromones.

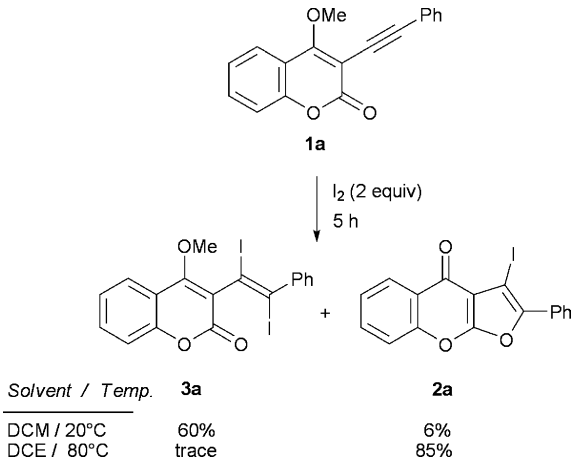
Results and discussion

Initially, we screened the reaction conditions for the electrophilic cyclization of substrate **1a**. As a preliminary experiment, **1a** was treated with two equivalents of I_2 in dichloromethane at room temperature. Disappointingly, the reaction essentially resulted in the formation of diiodoethenylcoumarin **3a** after stirring for 5 h (90% conversion as determined by ^{1}H NMR, 60% isolated yield), which was accompanied by only small amounts of the expected 3-iodofuran **2a** (*ca.* 6%) and remaining starting material. However, after further experimentation, we were pleased to discover that **1a** could be smoothly converted into the desired iodofurochromone by simply performing the reaction at higher temperatures. It is also interesting to note that the formation of the putative furochromenylium salt intermediate could not be observed under the reaction conditions. The best conditions consisted of heating **1a** in refluxing 1,2-dichloroethane (DCE) for 5 h, which furnished furan **2a** in 85% isolated yield (Scheme 2).

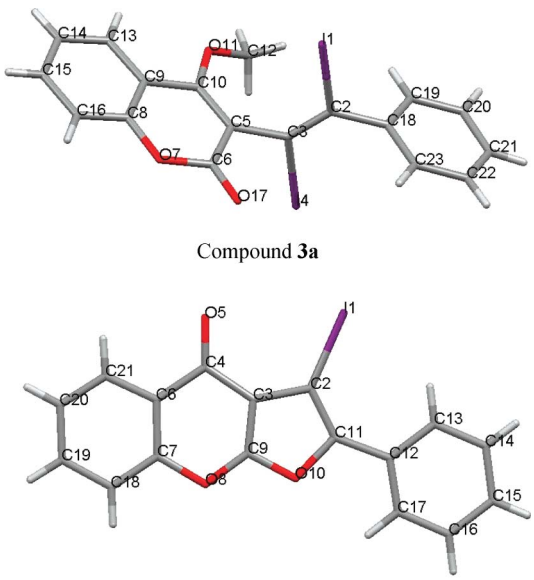
Although NMR and FT-IR spectroscopic data supported the formation of a linearly-fused furochromone **2a**, its structure was unambiguously secured by X-ray analysis. On the other hand, a crystal structure analysis of **3a** allowed us to establish the *E*-configuration of the diiodoalkene fragment (Fig. 1).

Université Lyon 1, Institut de Chimie et Biochimie Moléculaires et Supramoléculaires (ICBMS, UMR 5246 du CNRS), CPE Lyon, 43 Bd du 11 Novembre 1918, 69622, Villeurbanne Cedex, France. E-mail: monteiro@univ-lyon1.fr

† Electronic supplementary information (ESI) available: Experimental procedures and characterization data for new alkynylcoumarins **1**, copies of ^{1}H and ^{13}C NMR spectra of 3-iodofurans **2a–i** and **5**, and X-ray data for compounds **2a** and **3a** (CIF). CCDC reference numbers 798397 and 798398. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0ob00935k



Scheme 2 Reaction of **1a** with iodine at different temperatures.

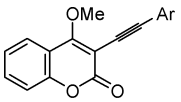
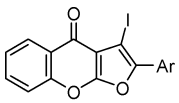
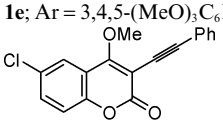
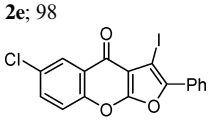
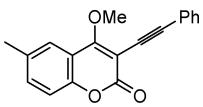
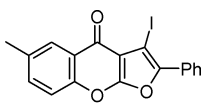
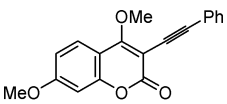
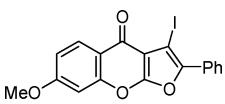
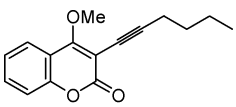
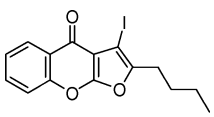
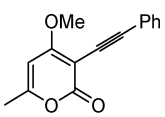
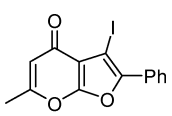


Compound **3a**

Compound **2a**

Fig. 1 X-Ray analyses of **3a** and **2a**.

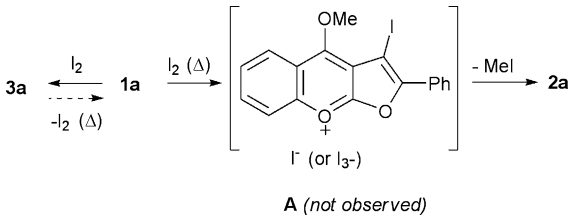
Table 1 Synthesis of diversely substituted 3-iodofurochromones **2** and related furopyranone **5**[a]

Entry	Starting alkyne	*t*/h	Product; yield (%)[b]
	 **1a-e**		 **2a-e**
1	**1a**; Ar = C_6H_5	5	**2a**; 85
2	**1b**; Ar = 4-FC_6H_4	5	**2b**; 89
3	**1c**; Ar = 4-$MeCO_2C_6H_4$	96	**2c**; 70[c]
4	**1d**; Ar = 4-$MeOC_6H_4$	0.5	**2d**; 92
5	**1e**; Ar = 3,4,5-$(MeO)_3C_6H_2$	0.5	**2e**; 98
6	 **1f**	72	 **2f**; 88
7	 **1g**	6	 **2g**; 89
8	 **1h**	6	 **2h**; 70
9	 **1i**	72	 **2i**; 60
10	 **4**	6	 **5**; 73

[a] All reactions were run on 0.1 mmol of the acetylene and 0.2 mmol of iodine in refluxing 1,2-dichloroethane. The synthesis of **2a** was also performed on a 2.1 mmol preparative scale (85% isolated yield). [b] Isolated yields (single runs). [c] 50% yield after 48 h.

The generality of the electrophilic cyclization process was then explored under the optimized reaction conditions. Aryl-substituted alkynylcoumarins **1a–h** (Table 1, entries 1–8) provided the corresponding 2-aryl-3-iodofurans in good to excellent yields. The nature of the arene attached to the triple bond had a significant impact on the rate of the reaction. As expected, electron-withdrawing groups, which are less capable of stabilizing the developing positive charge, decreased the reactivity of the triple bond dramatically, extending the reaction time up to several days, as illustrated by the reaction of (4-methoxycarbonyl)phenylacetylene **1c** (up to 4 days, 70% isolated yield). When the latter reaction was performed at room temperature, the product of the 1,2-diiodination of the triple bond (not shown) was formed in 81% yield, with only traces of the corresponding iodocyclization product (**2c**) being formed. In contrast, electron-rich arenes had a positive effect on the rate of the reaction, allowing the full and clean conversion of the starting materials within a few minutes (Table 1, entries 4 and 5). It is interesting to note that the iodocyclization of (3,4,5-trimethoxy)phenylacetylene **1e** also took place at room temperature. However, the reaction proved sluggish (85% conversion after 24 h) and led to the formation of some unidentified by-products. Alkyl-substituted alkyne **1i** also participated efficiently in the cyclization process (Table 1, entry 9). Interestingly, the same procedure applied well to the synthesis of 3-iodofuropyrone **5** (73% yield) (Table 1, entry 10).

From a mechanistic point of view, the cyclization process is supposed to proceed through iodonium-promoted nucleophilic attack of the coumarin carbonyl oxygen atom onto the triple bond to form furochromenylium **A**.[8] The latter would be unstable under the reaction conditions and thus would eliminate methyl iodide *via* S_N2 displacement to generate the furochromone ring system (Scheme 3).



Scheme 3 Diiodination as a 'reversible' competing process in the iodocyclization of **1a**.

^{1}H NMR monitoring of the iodocyclization reaction of **1a** by periodic aliquot removal[9] showed that the product of the 1,2-diiodination (**3a**) also formed at the early stage of the reaction and then gradually disappeared as the desired iodocyclization product **2a** formed. For instance, after 15 min, the reaction mixture was composed of 35% remaining starting material (**1a**), 40% diiodoalkene **3a** and 25% iodofuran **2a**. In light of this observation, it is reasonable to assume that **3a** exhibited a poor thermal stability and eliminated iodine upon heating to regenerate the original alkyne, thereby enabling the iodocyclization process to take place unhampered.[10] To confirm this assumption, a sample of **3a** was heated in refluxing DCE for several hours. Progress was monitored by crude ^{1}H NMR analysis, which showed the expected appearance and disappearance of the alkynyl coumarin (**1a**) as an intermediate in the conversion of **3a** into **2a**, thereby confirming that iodine was being eliminated and subsequently re-used in the next (cyclization) step.[11] Notably, if the reaction was terminated after 4 h,[12] the alkynyl coumarin **1a** was isolated in 40% yield. If the reaction was allowed to continue overnight, essentially all of the starting diiodoalkene was then converted into the iodocyclization product (**2a**), which was then obtained in an estimated 58% yield based on its crude weight and ^{1}H NMR analysis. Overall, these results demonstrate that—at least in some particular cases—the propensity of vicinal diiodoalkenes to undergo iodine elimination might be successfully exploited to hamper the diiodination of alkyne-containing derivatives, often reported as a predominant competing pathway in attempted iodocyclization processes.

Conclusions

In summary, we have developed an easy, straightforward access to 3-iodofurochromones based on iodine-promoted electrophilic cyclization/*O*-demethylation of 3-alkynyl-4-methoxycoumarins. An interesting feature of this process pertains the possibility of 'reversing' the competitive 1,2-diiodination of the coumarin acetylene moiety by simply increasing the reaction temperature.

Experimental section

Commercially available reagents and solvents were used as purchased without further drying. Acetylenic substrates **1a–i** and **4** were prepared from readily available 4-methoxy(benzo)pyrones and terminal acetylenes by following procedures previously developed in our laboratory.[13]

General procedure

A solution of the selected alkyne (0.1 mmol) in dichloroethane (1 mL) was treated with iodine (0.2 mmol) and left to stir under reflux for the indicated time (TLC). Unless otherwise stated, the reaction mixture was then diluted with dichloromethane and washed three times with aqueous $Na_2S_2O_3$. The aqueous layer was extracted twice with dichloromethane, and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography (silica gel, appropriate mixture of cyclohexane and ethyl acetate) to afford the desired 3-iodofuran.

3-Iodo-2-phenyl-4*H*-furo[2,3-*b*]benzopyran-4-one (2a)

(5 h, 85% yield), mp 175–177 °C (toluene/cyclohexane). FTIR (neat): ν_{max}/cm^{-1} 1660 (C═O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38–7.50 (m, 4H), 7.54 (dd, J = 8.5 and 0.7 Hz, 1H), 7.71 (ddd, J = 8.5, 7.1 and 1.7 Hz, 1H), 8.04 (dd, J = 8.4 and 1.5 Hz, 2H), 8.34 (dd, J = 7.9 and 1.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.2, 104.6, 117.6, 123.6, 125.8, 126.7, 126.8, 128.6, 128.7, 129.3, 133.7, 146.0, 152.7, 161.8, 173.3. HRMS (EI): M$^+$, 387.9596; calc. for $C_{17}H_9I0_3$: 387.9596. The synthesis of **2a** was also performed on a 2.1 mmol preparative scale (85% yield).

3-Iodo-2-(4-fluoro)phenyl-4*H*-furo[2,3-*b*]benzopyran-4-one (2b)

(6 h, 89% yield), white solid, mp 189–192 °C. FTIR (neat): ν_{max}/cm^{-1} 1657 (C═O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.16 (t, J = 8.6 Hz, 2H), 7.50 (m, 1H), 7.56 (br. d, J = 7.6 Hz, 1H), 7.73 (ddd, J = 8.5, 7.0 and 1.6 Hz, 1H), 8.00–8.07 (dd, J = 5.2 and 8.8, 2H), 8.36 (dd, J = 7.8 and 1.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.2, 104.6, 116.0 (d, J = 21.9 Hz), 117.9, 123.7, 124.9 (d, J = 3.6 Hz), 125.9, 126.9, 128.9 (d, J = 8.0 Hz), 133.8, 145.4, 152.7, 161.9, 163.2 (d, J = 249.4 Hz), 173.3. HRMS (ESI): MH$^+$, 406.9566; calc. for $C_{17}H_9FIO_3$: 406.9575.

3-Iodo-2-(4-methoxycarboxy)phenyl-4*H*-furo[2,3-*b*]benzo-pyran-4-one (2c)

After completion of the reaction (96 h), the precipitated furocoumarin was collected by filtration and recrystallized (AcOEt/cyclohexane). 70% yield, white solid, mp > 200 °C. FTIR (neat): ν_{max}/cm^{-1} 1716 and 1660 (C═O). ^{1}H NMR (100 MHz, $CDCl_3$): δ 3.95 (s, 3H), 7.48–7.51 (m, 1H), 7.58 (br. d, J = 8.0 Hz, 1H), 7.71–7.77 (m, 1H), 8.12–8.20 (m, 4H), 8.36 (dd, J = 8.0 and 1.4 Hz, 1H), ^{13}C NMR (75 MHz, $CDCl_3$): δ 52.5, 58.7, 105.01, 117.9, 123.6, 126.0, 126.3, 127.0, 130.0, 132.8, 134.0, 144.9, 152.8, 162.1, 166.6, 173.3. HRMS (ESI): MH$^+$, 446.9713; calc. for $C_{19}H_{12}IO_5$: 446.9724.

3-Iodo-2-(4-methoxy)phenyl-4*H*-furo[2,3-*b*]benzopyran-4-one (2d)

(0.5 h, 92% yield), white solid, mp > 200 °C. FTIR (neat): ν_{max}/cm^{-1} 1651 (C═O). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.87 (s, 3H), 7.00 (d, J = 9.0 Hz, 2H), 7.49 (m, 1H), 7.56 (br, d, J = 7.8 Hz, 1H), 7.72 (ddd, J = 8.6, 7.2 and 1.6 Hz, 1H), 7.98 (d, J = 9.0 Hz, 2H), 8.36 (dd, J = 7.9 and 1.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 54.5, 55.5, 104.6, 114.2, 117.8, 121.2, 123.7, 125.7, 126.9, 128.5, 133.6, 146.3, 152.7, 160.4, 161.7, 173.3. HRMS (ESI): MNa$^+$, 440.9587; calc. for $C_{18}H_{11}INaO_4$: 440.9594.

3-Iodo-2-(3,4,5-trimethoxy)phenyl-4*H*-furo[2,3-*b*]benzo-pyran-4-one (2e)

(0.5 h, 98% yield), white solid, mp 192–195 °C (dec.). FTIR (neat): ν_{max}/cm^{-1} 1656 (C═O). ^1H NMR (300 MHz, $CDCl_3$): δ 3.92 (s, 3H), 3.96 (br s, 6H), 7.32 (s, 2H), 7.50 (m, 1H), 7.56 (br. d, J = 8.3 Hz, 1H), 7.73 (ddd, J = 8.7, 7.3 and 1.7 Hz, 1H), 8.36 (dd, J = 8.0 and 1.7 Hz, 1H). ^{13}C (100 MHz, $CDCl_3$): δ 55.7, 56.4, 61.1, 104.1, 104.7, 117.8, 123.6, 123.8, 125.8, 126.7, 133.7, 139.0, 145.7, 152.6, 153.3, 161.6, 173.2. HRMS (EI): M^+, 477.9913; calc. for $C_{20}H_{15}IO_6$: 477.9913.

6-Chloro-3-iodo-2-phenyl-4*H*-furo[2,3-*b*]benzopyran-4-one (2f)

(72 h, 88% yield), white solid, mp 198–200 °C. FTIR (neat): ν_{max}/cm^{-1} 1660 (C═O). ^1H NMR (300 MHz, $CDCl_3$): δ 7.41–7.54 (m, 4H), 7.66 (dd, J = 9.0 and 2.5 Hz, 1H), 8.04 (dd, J = 8.2 and 1.5 Hz, 2H), 8.29 (d, J = 2.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.0, 104.8, 119.5, 124.7, 126.3, 126.8, 128.4, 129.5, 131.9, 133.8, 146.4, 161.9, 171.9. HRMS (EI): M^+, 421.9208; calc. for $C_{17}H_8ClIO_3$: 421.9207.

3-Iodo-6-methyl-2-phenyl-4*H*-furo[2,3-*b*]benzopyran-4-one (2g)

(6 h, 89% yield), white solid, mp 200–201 °C. FTIR (neat): ν_{max}/cm^{-1} 1648 (C═O). ^1H NMR (300 MHz, $CDCl_3$): δ 2.47 (s, 3H), 7.38–7.52 (m, 5H), 8.04 (dd, J = 8.6 and 1.6 Hz, 2H), 8.1 (d, J = 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.0, 56.3, 104.5, 117.5, 123.2, 126.2, 126.7, 128.6, 129.2, 134.7, 135.7, 145.7, 150.9, 161.8, 173.3. HRMS (EI): M^+, 401.9753; calc. for $C_{18}H_{11}IO_3$: 401.9753.

3-Iodo-7-methoxy-2-phenyl-4*H*-furo[2,3-*b*]benzopyran-4-one (2h)

After completion of the reaction (6 h), the precipitated furocoumarin was collected by filtration and recrystallized (AcOEt/cyclohexane). 70% yield, white solid, mp > 200 °C. FTIR (neat): ν_{max}/cm^{-1} 1639 (C═O). ^1H NMR (300 MHz, $CDCl_3$): δ 3.94 (s, 3H), 6.97 (d, J = 2.3 Hz, 1H), 7.04 (dd, J = 8.8 and 2.3 Hz, 1H), 7.42–7.51 (m, 3H), 8.05 (dd, J = 8.3 and 1.3 Hz, 2H), 8.26 (d, J = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.1, 56.5, 101.1, 104.4, 114.1, 117.3, 126.8, 128.1, 128.7, 128.8, 129.3, 145.8, 154.4, 161.8, 164.1, 173.1. HRMS (EI): M^+: 417.9702; calc. for $C_{18}H_{11}IO_4$: 417.9702.

2-Butyl-3-iodo-4*H*-furo[2,3-*b*]benzopyran-4-one (2i)

(72 h, 60% yield), white solid, mp 96–99 °C. FTIR (neat): ν_{max}/cm^{-1} 1656 (C═O). ^1H NMR (300 MHz, $CDCl_3$): δ 0.96 (t, J = 7.4 Hz, 3H), 1.40 (sext., J = 7.4 Hz, 2H), 1.68 (quint., J = 7.4, 2H), 2.77 (t, J = 2.4 Hz, 2H), 7.47 (t, J = 7.9 Hz, 1H), 7.52 (d, J = 7.9 Hz, 1H), 7.69 (m, 1H), 8.33 (dd, J = 8.0 and 1.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 22.1, 26.8, 29.9, 58.1, 103.3, 117.8, 123.8, 125.6, 126.8, 133.5, 141.4, 152.7, 161.7, 173.1. HRMS (EI): M^+, 367.9907; calc. for $C_{15}H_{13}IO_3$: 367.9909.

3-Iodo-6-methyl-2-phenyl-4*H*-furo[2,3-*b*]pyran-4-one (5)

(6 h, 73% yield), orange solid, mp 162–164 °C. FTIR (neat): ν_{max}/cm^{-1} 1649 (C═O). ^1H NMR (300 MHz, $CDCl_3$): δ 2.38 (s, 3H), 6.13 (s, 1H), 7.38–7.49 (m, 3H), 8.00 (dd, J = 8.5 and 1.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.3, 55.6, 107.1, 113.9, 126.8, 128.5, 128.7, 129.3, 145.9, 159.7, 161.9, 175.4. HRMS (EI): M^+, 351.9597; calc. for $C_{14}H_9IO_3$: 351.9596.

Acknowledgements

This research was assisted financially by a grant to G. R. from the French Ministry of Higher Education and Research (MESR). We thank Dr E. Jeanneau (Centre de Diffractométrie Henri Longchambon, Université Lyon 1) for the X-ray crystallographic analyses. I. Aillaud (Université Lyon 1) is acknowledged for preliminary experiments.

Notes and references

1 For reviews, see: (*a*) Y. Yamamoto, I. D. Gridnev, N. T. Patil and T. Jin, *Chem. Commun.*, 2009, 5075; (*b*) M. J. Mphahlele, *Molecules*, 2009, **14**, 4814; (*c*) H. Togo and S. Iida, *Synlett*, 2006, 2159.

2 For recent examples, see: (*a*) A. Arcadi, S. Cacchi, S. Di Giuseppe, G. Fabrizi and F. Marinelli, *Org. Lett.*, 2002, **4**, 2409; (*b*) Y. Liu and S. Zhou, *Org. Lett.*, 2005, **7**, 4609; (*c*) T. Yao, X. Zhang and R. C. Larock, *J. Org. Chem.*, 2005, **70**, 7679; (*d*) T. Yao, D. Yue and R. C. Larock, *J. Org. Chem.*, 2005, **70**, 9985; (*e*) D. Yue, T. Yao and R. C. Larock, *J. Org. Chem.*, 2005, **70**, 10292; (*f*) S. P. Bew, G. M. M. El-Taeb, S. Jones, D. W. Knight and W.-F. Tan, *Eur. J. Org. Chem.*, 2007, 5759; (*g*) C.-H. Cho, B. Neuenswander, G. H. Lushington and R. C. Larock, *J. Comb. Chem.*, 2008, **10**, 941; (*h*) Y.-X. Xie, X.-Y. Liu, L.-Y. Wu, Y. Han, L.-B. Zhao, M.-J. Fan and Y.-M. Liang, *Eur. J. Org. Chem.*, 2008, 1013; (*i*) S. Arimitsu, J. M. Jacobsen and G. B. Hammond, *J. Org. Chem.*, 2008, **73**, 2886; (*j*) T. Okitsu, D. Nakazawa, R. Taniguchi and A. Wada, *Org. Lett.*, 2008, **10**, 4967.

3 For leading references, see: (*a*) R. A. Hollins and M. P. A. Campos, *J. Org. Chem.*, 1979, **44**, 3931; (*b*) V. L. Heasley, D. F. Shellhamer, L. E. Heasley, D. B Yaeger and G. E. Heasley, *J. Org. Chem.*, 1980, **45**, 4649; (*c*) J. Barluenga, M. A. Rodriguez and P. J. Campos, *J. Org. Chem.*, 1990, **55**, 3104; (*d*) J. Duan, W. R. Dolbier Jr. and Q.-Y. Chen, *J. Org. Chem.*, 1998, **63**, 9486.

4 G. Raffa, M. Rusch, G. Balme and N. Monteiro, *Org. Lett.*, 2009, **11**, 5254.

5 (*a*) Y. R. Lee and J. Y. Suk, *Tetrahedron*, 2002, **58**, 2359; (*b*) S. Tollari, G. Palmisano, S. Cenini, G. Cravotto, G. B. Giovenzana and A. Penoni, *Synthesis*, 2001, 735; (*c*) K. Kobayashi, K. Sakashita, H. Akamatsu, K. Tanaka, M. Uchida, T. Uneda, T. Kitamura, O. Morikawa and H. Konishi, *Heterocycles*, 1999, **51**, 2881; (*d*) Y. R. Lee, B. S. Kim and H. C. Wang, *Tetrahedron*, 1998, **54**, 12215; (*e*) Y. R. Lee, M. W. Byun and B. S. Kim, *Bull. Korean Chem. Soc.*, 1998, **19**, 1080.

6 Benzo-fused furochromones possessing interesting biological properties have been recently isolated from plants used in Chinese folklore: (*a*) Q. Y. Shou, Q. Tan and Z. W. Shen, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 3389; A. Ahmed-Belkacem, S. Macalou, F. Borrelli, R. Capasso, E. Fattorusso, O. Taglialatela-Scafati and A. Di Pietro, *J. Med. Chem.*, 2007, **50**, 1933; Some naturally occurring dihydrofurochromone sesquiterpenes have been reported recently; for examples, see: (*b*) M. Iranshahi, F. Shaki, A. Mashlab, A. Porzel and L. A. Wessjohann, *J. Nat. Prod.*, 2007, **70**, 1240; (*c*) T. Motai and S. Kitanaka, *J. Nat. Prod.*, 2005, **68**, 1732; (*d*) B.-N. By Su, Y. Takaishi, G. Honda, M. Itoh, Y. Takeda, O. K. Kodzhimatov and O. Ashurmetov, *J. Nat. Prod.*, 2000, **63**, 520.

7 I. Aillaud, E. Bossharth, D. Conreaux, P. Desbordes, N. Monteiro and G. Balme, *Org. Lett.*, 2006, **8**, 1113.

8 Electrophilic activation of the triple bond occurs presumably *via* coordination to iodine to generate a cyclic iodonium ion. For a leading reference, see ref. 1*a*. See also: T. Okazaki and K. K. Laali, *J. Org. Chem.*, 2005, **70**, 9139and references therein.

9 Aliquots were submitted to ^1H NMR after work-up by treatment with aqueous bisulfite to remove any free iodine.

10 Vicinal diiodo compounds, including 1,2-diiodo*alkenes* but to a much lesser extent than 1,2-diiodo*alkanes*, have been reported as relatively

unstable compounds that may easily eliminate iodine: (*a*) M. Zanger and J. L. Rabinowitz, *J. Org. Chem.*, 1975, **40**, 248; (*b*) R. M. Pagni, G. W. Kabalka, R. Boothe, K. Gaetano, L. J. Stewart, R. Conaway, C. Dial, D. Gray, S. Larson and T. Luidhardt, *J. Org. Chem.*, 1988, **53**, 4477 See also ref. 3*b*.

11 It is likely that the elimination process is triggered by traces of iodine present as a contaminant in the starting diiodo compound. Studies on the iodine elimination reaction of 1,2-diiodoethylene by iodide ion catalysis have been published: S. I. Miller and R. M. Noyes, *J. Am. Chem. Soc.*, 1952, **74**, 3403.

12 At this point, the reaction mixture was composed of 42% remaining **3a**, 42% **1a** and 16% **2a**, as determined by ^{1}H NMR analysis.

13 D. Conreaux, S. Belot, P. Desbordes, N. Monteiro and G. Balme, *J. Org. Chem.*, 2008, **73**, 8619 and ref. 4.

