A novel iodine-induced sequential cyclization reaction of norbornene derivatives leading to the formation of novel iodo-cage compounds

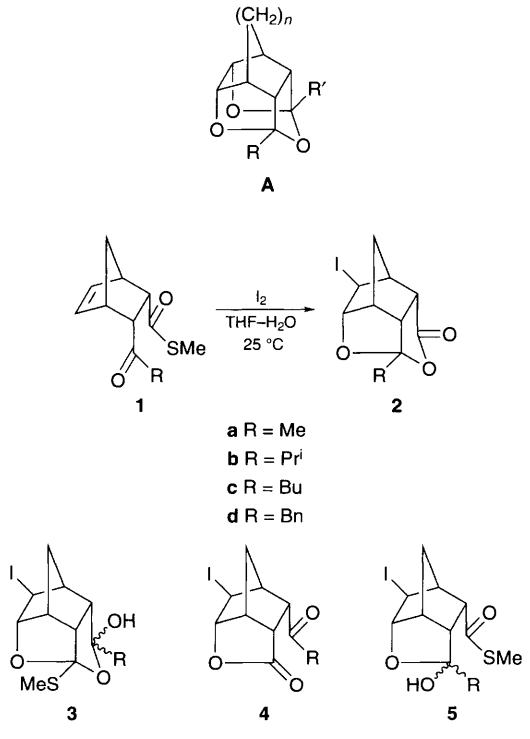
Hsien-Jen Wu,* Shih-Hwa Tsai and Wen-Sheng Chung*

Department of Applied Chemistry, National Chiao-Tung University, Hsinchu, Taiwan, R O China

Treatment of the bis-*endo*-thioester and acyl group substituted norbornenes 1a–d and 9a–c with iodine in aqueous tetrahydrofuran at 25 °C gave the novel iodo-cage compounds 2a–d and 10a–c in 80–90% yields respectively, the first example of sequential cyclization of norbornene derivatives induced by an iodine electrophile.

The halocyclization of an alkene bond is a powerful process in synthetic organic chemistry, especially for regio- and stereoselective functionalization of double bonds.[1] Usually, the ring closure takes place with participation of a number of electron-donating groups, such as OH, NHR, CO_2H, CO_2R, CONHR, *etc*. There are some reports regarding the electrophile-induced lactonization of norbornene derivatives.[2] We report here the first example of sequential cyclization of bis-*endo*-thioester and acyl group substituted norbornenes induced by an iodine electrophile, leading to the formation of novel iodo-cage compounds. To our knowledge, neither sequential heterocyclization induced by iodine nor the ring closure with participation of thioester and carbonyl groups has been reported.[1]

Treatment of the *endo* adducts **1a–d** with I_2 in aq. THF at 25 °C for 6 h gave the novel iodo-cage compounds **2a–d** as the major products in 80–85% yields respectively† (Scheme 1). No detectable amount of the other regioisomers **3a–d** was obtained. Also, no detectable amount of the monocyclization products **4** or **5** was obtained.

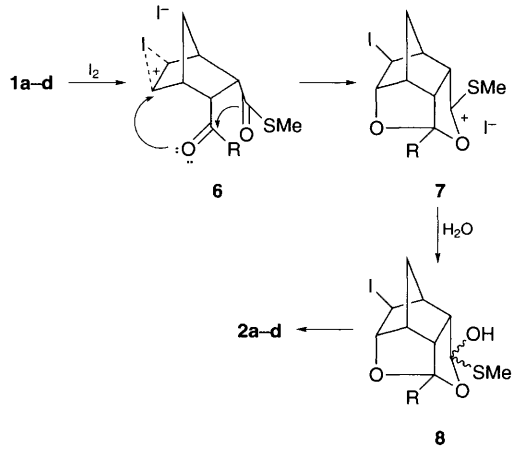


Scheme 1

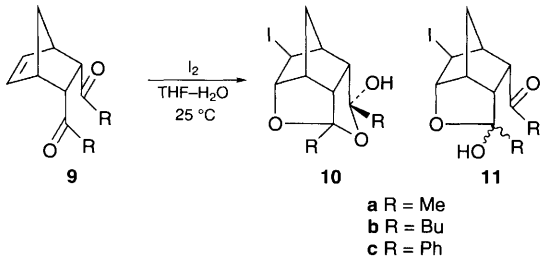
A mechanism is proposed for the formation of **2a–d** in Scheme 2. Electrophilic attack of an iodine molecule at the alkene bond of **1** from the *exo* face gives the iodonium ion **6**. Sequential intramolecular nucleophilic addition of the *endo* acyl and thioester groups to the iodonium ion followed by addition of water molecule gives the intermediate **8**. Loss of the methylsulfanyl group of **8** leads to the lactones **2a–d**. Since only the regioisomers **2a–d** are obtained, we propose here that the exclusive regioselective cleavage of the partial carbon–iodine bond of **6** is preferentially affected through space by the acyl carbonyl group rather than by the thioester group.

Treatment of the *endo* adducts **9a–c** with iodine in aqueous THF at 25 °C for 6 h gave the iodo-cages **10a–c** as the major products in 85–85% yields respectively‡ (Scheme 3). No detectable amount of the monocyclization product **11** was obtained. The stereochemistry of the hydroxy group of **10** was deduced by NOE experiments and further chemical transformation.

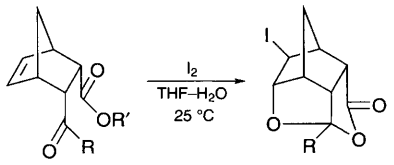
To compare the ability of nucleophilic cyclization of an ester group with that of an acyl group to the iodonium ion, compounds **12a** and **12b** were prepared. Iodocyclization of **12a** and **12b** under the same reaction conditions gives the iodo-cage compounds **2a** and **13** as the major products in 80% yields respectively (Scheme 4).



Scheme 2



Scheme 3



12 a R = R′ = Me
b R = Ph, R′ = Et

2a R = Me
13 R = Ph

Scheme 4

Thus, we have found a novel iodine-induced sequential cyclization of norbornene derivatives, leading to the formation of novel iodo-cage compounds. The application of these products to the synthesis of novel diacetal trioxa-cage compounds has been accomplished.§

We thank the National Science Council of Republic of China for financial support (Grant No. NSC83-0208-M009-012).

Footnotes

† *Selected data* for **2a** (*J* values in Hz): δ_H 4.94 (1 H, d, *J* 4.8), 4.01 (1 H, d, *J* 3), 3.19 (1 H, dd, J_1 9.9, J_2 4.5), 3.11 (1 H, dd, J_1 9.6, J_2 5.1), 3.01–3.04 (1 H, m), 2.92–2.94 (1 H, m), 2.46–2.50 (1 H, m), 2.01–2.05 (1 H, m) and 1.63 (3 H, s); δ_C 23.45, 27.88, 40.49, 48.33, 48.56, 49.61, 51.04, 91.31, 116.10 and 174.26; ν_{max}/cm^{-1} 1773. For **2b** δ_H 4.97 (1 H, d, *J* 5.1), 4.03 (1 H, d, *J* 2.1), 3.14–3.15 (2 H, m), 2.82–2.94 (2 H, m), 2.46–2.50 (1 H, m), 2.01–2.10 (2 H, m), 1.01 (3 H, d, *J* 6.6), 0.97 (3 H, d, *J* 6.6); δ_C 16.54, 16.71, 28.14, 33.88, 40.61, 47.72, 48.39, 49.26, 49.70, 91.07, 120.47 and 174.49; ν_{max}/cm^{-1} 1772. For **2c** δ_H 4.95 (1 H, d, *J* 4.4), 4.00 (1 H, d, *J* 2.9), 3.10–3.16 (2 H, m), 2.93–2.97 (2 H, m), 2.45–2.49 (1 H, m), 2.01–2.05 (1 H, m), 1.81–1.89 (2 H, m), 1.32–1.39 (4 H, m), 0.91 (3 H, t, *J* 6.6); δ_C 13.69, 22.22, 25.28, 28.08, 35.89, 40.40, 48.24, 48.62, 49.18, 49.35, 91.01, 118.05 and 174.23; ν_{max}/cm^{-1} 1772 cm^{-1}. For **2d** δ_H 7.23–7.33 (5 H, m), 4.90 (1 H, d, *J* 4.9), 4.03 (1 H, d, *J* 2.4), 3.07 and 3.26 (2 H, ABq, *J* 13.7), 3.07–3.10 (2 H, m), 2.89 (1 H, bs), 2.33–2.42 (2 H, m), 1.87–1.91 (1 H, m); δ_C 27.96, 40.64, 42.15, 48.33, 48.71, 49.12, 49.20, 91.28, 117.38, 127.20, 128.25 (2C), 130.32 (2C), 133.99 and 174.29; ν_{max}/cm^{-1} 1776.

‡ *Selected data* for **10a** δ_H 4.84 (1 H, d, *J* 4.4), 4.42 (1 H, d, *J* 1.5), 2.60–3.01 (5 H, m), 2.33–2.37 (1 H, m), 1.79–1.83 (1 H, m), 1.54 (6 H, s); δ_C 24.32, 25.75, 30.35, 39.56, 47.14, 49.62, 52.26, 56.81, 90.93, 103.98 and 116.83. For **10b** δ_H 4.83 (1 H, d, *J* 4.4), 4.42 (1 H, d, *J* 2.2), 2.98–3.03 (1 H, m), 2.78–2.82 (1 H, m), 2.55–2.59 (2 H, m), 2.29–2.36 (2 H, m), 1.27–1.82 (13 H, m), 0.86–0.96 (6 H, m); δ_C 13.95, 14.07, 22.75, 22.84, 26.10, 26.30, 31.08, 37.29, 38.80, 39.79, 46.99, 49.67, 50.60, 55.35, 90.78, 105.64 and 118.75. For **10c** δ_H 7.64–7.67 (4 H, m), 7.34–7.45 (6 H, m), 5.03 (1 H, d, *J* 5.1), 4.26 (1 H, d, *J* 2.2), 3.38–3.43 (1 H, m), 3.21–3.26 (1 H, m), 3.01–3.05 (1 H, m), 2.96 (1 H, s), 2.31–2.34 (2 H, m), 1.84–1.87 (1 H, m); δ_C 29.77, 39.71, 47.83, 50.34, 55.67, 58.18, 91.48, 106.02, 117.94, 126.01 (2C), 126.03 (2C), 128.08, (2C), 128.22, 128.51 (2C), 128.75, 140.96 and 141.19.

§ The synthesis of novel trioxa-cages **A** has been accomplished, and these results will be submitted for publication as a full paper soon.

References

1 For reviews of the halolactonization reaction, see: M. D. Dowle and D. I. Davies, *Chem. Soc. Rev.*, 1979, **8**, 171; Paul A. Bartlett, *Asymmetric Synthesis*, ed. J. D. Morrison, Academic, Orlando, 1983, vol. 3, pp. 411; G. Cardillo and M. Orena, *Tetrahedron*, 1990, **46**, 3321; Paul A. Bartlett, *Tetrahedron*, 1980, **36**, 2.

2 J. S. Meek and W. B. Trapp, *J. Am. Chem. Soc.*, 1957, **79**, 3909; A. Factor and T. G. Traylor, *J. Org. Chem.*, 1968, **33**, 2614; T. T. Tidwell and T. G. Traylor, *J. Org. Chem.*, 1968, **33**, 2607; R. M. Moriarty and K. Kapadia, *Tetrahedron Lett.*, 1964, 1165; R. M. Moriarty, H. G. Walsh and H. Gopal, *Tetrahedron Lett.*, 1966, 4363; R. M. Moriarty and H. Gopal, *Tetrahedron Lett.*, 1972, 347; A. McKillop and M. E. Ford, *J. Org. Chem.*, 1974, **39**, 2434; E. C. Taylor, G. E. Jagdmann, Jr. and A. McKillop, *J. Org. Chem.*, 1980, **45**, 3374.

Received, 27th September 1995; Com. 5/06364G