Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 48 (2007) 8747–8751
Tetrahedron Letters

Triiodoisocyanuric acid: a new and convenient reagent for regioselective coiodination of alkenes and enolethers with oxygenated nucleophiles

Rodrigo da S. Ribeiro, Pierre M. Esteves* and Marcio C. S. de Mattos*

Instituto de Química, Departamento de Química Orgânica, Universidade Federal do Rio de Janeiro, Cx. Postal 68545,
21945-970 Rio de Janeiro, Brazil

Received 17 April 2007; revised 1 October 2007; accepted 2 October 2007
Available online 6 October 2007

Abstract—The reaction of triiodoisocyanuric acid (prepared from I_2 and trichloroisocyanuric acid in 90% yield) with alkenes in the presence of oxygenated nucleophilic solvents (alcohols, AcOH and H_2O) led to the corresponding β-iodoethers, β-iodoacetates and iodohydrins, in 66–98% isolated yield. Enolethers reacted with triiodoisocyanuric acid in MeOH to produce dialkylacetals (70–83%).

The regioselective functionalization of alkenes is an important process in organic chemistry. Among the several methodologies, the so-called 'cohalogenation' (halogenation of an alkene in the presence of a nucleophilic solvent) provides vicinal halo-functionalized products regioselectively, which are useful intermediates for diverse synthetic applications.[1] Besides the large applicability in organic synthesis, the recent discovery of the bioactivity of naturally occurring organohalogen compounds has attracted the interest in such compounds.[2]

In contrast to other halogens, the simple iodination of an alkene is very slow and hence, the coiodination of alkenes is only effective using alternate sources of electrophilic iodine.[3] Traditional methodologies for the regioselective 1,2-alkoxy, -acetoxy and -hydroxy iodination of alkenes include the reaction of I_2 with an alkene in the presence of alcohols, acetic acid and water, respectively, mediated by diverse heavy metal salts[4] or oxidizing reagents.[5] Alternative methodologies are the reactions of alkenes with excess iodine,[6] I_2/clays,[7] diacetoxyiodine(I) complexes,[8] in situ generated acyl hypoiodite,[9] IPy_2BF_4,[10] I_2/ultrasound[11] or iodide/H_2O_2[12] in the presence of the nucleophilic solvent, to name a few.

N-Haloimides[13] and *N*-halosaccharins[14] are mild electrophilic halogenating agents, which can be used under neutral conditions. The halogen in those of compounds has a greater electrophilic character than in X_2 and the representative iodination reagents are *N*-iodosuccinimide (NIS)[15] and *N*-iodosaccharin (NISac).[15c,16]

Recent papers have demonstrated that trihaloisocyanuric acids (Fig. 1), such as trichloroisocyanuric[17] (TCCA) and tribromoisocyanuric acids[18] (TBCA), are efficient halogenating agents, due to their capability of halenium ('X^+') atoms transfer to unsaturated substrates. These trihaloisocyanuric acids are also very interesting from the green chemistry point of view,[19] as they can introduce halogen atoms in organic compounds without using toxic and corrosive X_2 and also present good atom economy.

Triiodoisocyanuric acid (TICA), an analogue of TCCA and TBCA, synthesized by Gottardi more than 35 years ago,[20] has not yet been reported as an iodination reagent

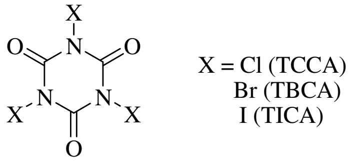
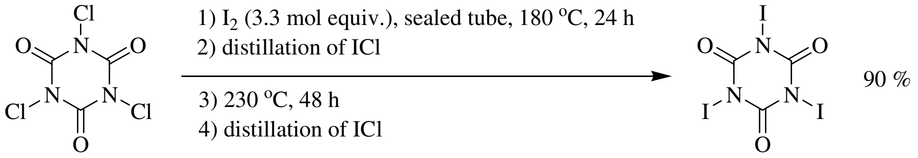


Figure 1. The trihaloisocyanuric acids.

Keywords: Triiodoisocyanuric acid; Alkenes; Cohalogenation; Enolethers; Iodohydrins.

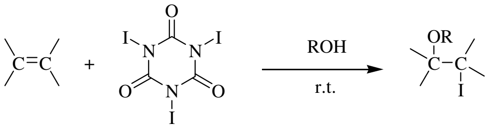
* Corresponding authors. Fax: +55 21 25627133 (M.C.S.M.); e-mail addresses: pesteves@iq.ufrj.br; mmattos@iq.ufrj.br

0040-4039/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2007.10.011



Scheme 1. Preparation of TICA.

Table 1. Coiodination of alkenes with TICA and oxygenated nucleophiles



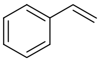
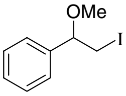
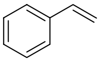
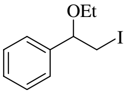
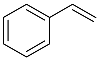
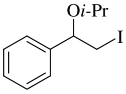
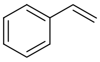
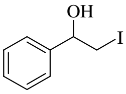
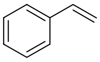
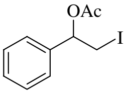
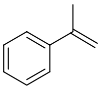
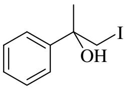
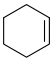
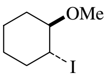
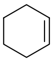
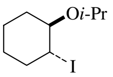
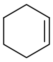
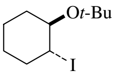
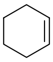
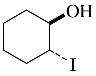
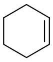
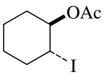
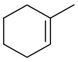
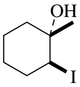
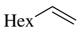
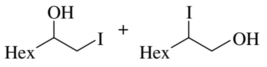
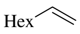
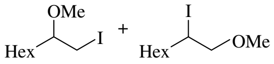
Entry	Alkene	Product	Reaction condition	Yield[a] (%)	Ref. to Product
1			MeOH, 15 min	90	24
2			EtOH, 30 min	84	25
3			*i*-PrOH, 60 min	90	25
4			$Me_2CO–H_2O$ (2:1), 60 min	88	25
5			$AcOH–Ac_2O$ (1:1), 40 min	73	4
6			$Me_2CO–H_2O$ (2:1), 20 min	98	26
7			MeOH, 5 min	89	27
8			*i*-PrOH, 20 min	74	28
9			*t*-BuOH, 150 min	66	28
10			$Me_2CO–H_2O$ (2:1), 5 min	77	24
11			$AcOH–Ac_2O$ (1:1), 30 min	79	4
12			$Me_2CO–H_2O$ (2:1), 10 min	93	6

Table 1 (*continued*)

Entry	Alkene	Product	Reaction condition	Yield[a] (%)	Ref. to Product
13		 (75 : 25)[b]	$Me_2CO–H_2O$ (2:1), 10 min	88	26
14		 (80 : 20)[b]	MeOH, 90 min	88	29

[a] Isolated yield, based on alkene.
[b] Determined by HRGC–MS.

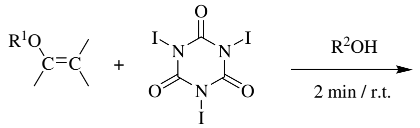
and this motivated us to use it in our studies of iodination reactions. Furthermore, TICA has also the advantage of transferring 3 equiv of iodine atom to the substrate, representing an atom economy of 75%. In the present work, we studied the regioselective coiodination of alkenes and enolethers using TICA as the source of I^+ in the presence of oxygenated nucleophiles (water, alcohols and acetic acid).

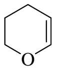
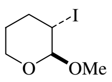
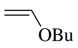
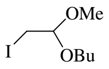
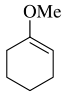
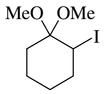
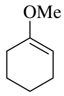
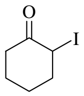
In a previous study, Gottardi demonstrated that the reaction between dichloroisocyanuric acid and I_2 for three days at 180–230 °C produces a mixture of triiodoisocyanuric acid and ICl, which can be separated through evaporation of ICl under reduced pressure.[20] Herein, we have prepared TICA substituting dichloroisocyanuric acid by the readily available and inexpensive trichloroisocyanuric acid employing 3.3 mol equiv of I_2. The product, a brown solid, was obtained in 90% yield after 24 h at 180 °C followed by 48 h at 230 °C in a sealed tube and distillation of ICl under reduced pressure (Scheme 1).[21]

In this study, alkenes (cyclohexene, 1-methylcyclohexene, styrene, α-methylstyrene and 1-octene) and activated alkenes that possess an enolethers moiety (butyl vinyl ether, dihydropyran and 1-methoxycyclohexene) were used as substrates and acetic acid, alcohols and acetone/water system as nucleophilic solvents. The scope of the coiodination reactions using TICA is indicated by the examples listed in Tables 1 (alkenes) and 2 (enolethers).

The reactions were carried out with 2 mmol of alkene and 0.67 mmol of TICA at room temperature (Table 1).[22] Iodohydrins were rapidly obtained in good yields using a mixture of acetone/water (2:1). The iodination of alkenes with TICA in the presence of alcohols (MeOH, EtOH, *i*-PrOH, *t*-BuOH) and acetic acid/acetic anhydride resulted in the respective β-iodoethers and β-iodoacetates, in good yields. The reactions with styrene, α-methylstyrene and 1-methylcyclohexene were highly regioselective, following Markovnikoff fashion (Table 1, entries 1–6 and 12) and no regioisomers were detected

Table 2. Coiodination of enolethers with TICA and oxygenated nucleophiles



Entry	Enolether	Product	R^2OH	Yield[a] (%)	Ref. to Product
1			MeOH	83	5c
2			MeOH	83	—
3			MeOH	70	31
4			H_2O	69	32

[a] Isolated yield, based on enolether.

on the crude reaction products by the analytical procedures employed (HRGC–MS, ^{1}H NMR and ^{13}C NMR spectroscopy). As previously observed,[23] exceptions were observed in the reactions with 1-octene that produced a mixture of regioisomers in which the primary iodide predominated (Table 1, entries 13 and 14). High trans-stereoselectivity was also observed for additions to cyclohexene and 1-methycyclohexene (Table 1, entries 7–12).

Enolethers (2 mmol) reacted quickly and smoothly with TICA (0.67 mmol) at room temperature in MeOH to produce the corresponding iodo-dialkylacetals (Table 2, entries 1–3).[30] However, if the reaction was performed with 1-methoxycyclohexene in water, the hemiacetal was very unstable and 2-iodocyclohexanone was obtained in 69% yield (entry 4).

In conclusion, we have presented an efficient and eco-friendly alternative reagent for the regioselective coiodination of alkenes, affording good to excellent yields of iodohydrins, β-iodoethers and β-iodoacetates under mild conditions.

Acknowledgements

The authors thank CNPq, CAPES and FAPERJ for the financial support. We also thank Professor Vitor Francisco Ferreira and Mrs. Sabrina Baptista Ferreira (Instituto de Química/UFF) for the kind donation of butyl vinyl ether. One of the referees is also acknowledged for useful suggestions.

References and notes

1. Rodrigues, J.; Dulcere, J.-P. *Synthesis* **1993**, 1177; Sanseverino, A. M.; da Silva, F. M.; Jones, J., Jr.; de Mattos, M. C. S. *Quim. Nova* **2001**, *24*, 637; da Silva, F. M.; Jones, J., Jr.; de Mattos, M. C. S. *Curr. Org. Synth.* **2005**, *2*, 393.
2. Gribble, G. W. *Acc. Chem. Res.* **1998**, *31*, 141; Gribble, G. W. *Chemosphere* **2003**, *52*, 289.
3. De Mattos, M. C. S.; Sanseverino, A. M. *J. Chem. Res. (S)* **1994**, 440.
4. Sanseverino, A. M.; de Mattos, M. C. S. *J. Chem. Res.* **2004**, 638, and references cited therein.
5. (a) Ogata, Y.; Aoki, K. *J. Org. Chem.* **1966**, *31*, 1625; (b) Antonioletti, R.; D'Auria, M.; De Mico, A.; Piancatelli, G.; Scettri, A. *Tetrahedron* **1983**, *39*, 1765; (c) Jereb, M.; Zupan, M.; Stavber, S. *Green Chem.* **2005**, *7*, 100.
6. Sanseverino, A. M.; de Mattos, M. C. S. *Synthesis* **1998**, 1584.
7. Villegas, R. A. S.; Santo, J. L. E., Jr.; de Mattos, M. C. S.; de Aguiar, M. R. M. P.; Guarino, A. W. S. *J. Braz. Chem. Soc.* **2005**, *16*, 565.
8. Kirschning, A.; Kunst, E.; Ries, M.; Rose, L.; Schönberger, A.; Wartchow, R. *ARKIVOC* **2003**, 145.
9. Goosen, A.; Hoffmann, E.; Taljaard, B. *J. Chem. Soc., Perkin Trans. 1* **1994**, 41.
10. Barluenga, J.; González, J. M.; Campos, P. J.; Asensio, G. A. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 319.
11. Rama, K.; Pasha, M. A. *Ultrason. Sonochem.* **2005**, *12*, 437; Fernandes, V. S.; Barboza, J. C. S.; Serra, A. A. *Synth. Commun.* **2007**, *37*, 1433.
12. Barluenga, J.; Marco-Arias, M.; Gonzáles-Bobes, F.; Ballesteros, A.; Gonzáles, J. M. *Chem. Eur. J.* **2004**, *10*, 1677.
13. Kolvani, E.; Ghorbani-Choghamarani, A.; Salehi, P.; Shirini, F.; Zolfigol, M. A. *J. Iran. Chem. Soc.* **2007**, *4*, 126.
14. de Souza, S. P. L.; da Silva, J. F. M.; de Mattos, M. C. S. *Quim. Nova* **2006**, *29*, 1061.
15. (a) Vankar, Y. D.; Kumaravel, G. *Tetrahedron Lett.* **1984**, *25*, 233; (b) Sniady, A. *Synlett* **2006**, 960; (c) de Mattos, M. C. S.; Bernini, R. B. *Heterocycl. Commun.* **2006**, *12*, 411.
16. Dolenc, D. *Synlett* **2000**, 544; Urankar, D.; Rutar, I.; Modec, B.; Dolenc, D. *Eur. J. Org. Chem.* **2005**, 2349.
17. Mendonça, G. F.; Magalhães, R. M.; de Mattos, M. C. S.; Esteves, P. M. *J. Braz. Chem. Soc.* **2005**, *16*, 695; Mendonça, G. F.; Sanseverino, A. M.; de Mattos, M. C. S. *Synthesis* **2003**, 45; Wengert, M.; Sanseverino, A. M.; de Mattos, M. C. S. *J. Braz. Chem. Soc.* **2002**, *13*, 700.
18. De Almeida, L. S.; Esteves, P. M.; de Mattos, M. C. S. *Synlett* **2006**, 1515; de Almeida, L. S.; Esteves, P. M.; de Mattos, M. C. S. *Synthesis* **2006**, 221; Tozetti, S. D. F.; de Almeida, L. S.; Esteves, P. M.; de Mattos, M. C. S. *J. Braz. Chem. Soc.* **2007**, *18*, 675; de Almeida, L. S.; Esteves, P. M.; de Mattos, M. C. S. *Synlett* **2007**, 1687.
19. Sanseverino, A. M. *Quim. Nova* **2000**, *23*, 102.
20. Gottardi, W. *Monatsh. Chem.* **1970**, *101*, 655.
21. *Procedure for the preparation of TICA*. Iodine (184.6 mmol, 46.85 g) and trichloroisocyanuric acid (55.93 mmol, 13.00 g) were added to a 100 mL sealed tube and heated in a sand bath at 180 °C. After 24 h, the ICl produced was distilled off under reduced pressure and the sealed tube was heated again at 230 °C during 48 h. Evaporation of ICl under reduced pressure and heating gave triiodoisocyanuric acid as a brown solid in 90% yield. At room temperature TICA decomposes slowly with the formation of I_2. On the other hand, in the presence of light the decomposition is very fast. However, if stored in dark in a freezer, TICA proved to be stable for at least one year. IR (cm^{-1}): ν 3211, 3053, 2884, 2830, 2780, 1700, 1665, 1459, 1372, 1145, 1061, 1051, 732, 663, 533.[20]
22. *General procedure for coiodination of alkenes*. To a stirred solution of the alkene (2 mmol) in an appropriated solvent (8 mL of acetone and 4 mL of H_2O for iodohydrins, or 10 mL of alcohols or acetic acid for β-iodoethers and β-iodoacetates), TICA (0.67 mmol) was added at room temperature. The reaction was monitored by HRGC–MS. After the specified time shown in Table 1 (for alkenes), CH_2Cl_2 (10 mL) was added, cyanuric acid was filtered off and the resulting solution was treated with 10% aq $NaHSO_3$ (50 mL). The aqueous phase was washed with CH_2Cl_2 (2 × 10 mL), the organic extract was dried (anhydrous Na_2SO_4) and filtered. The solvent was evaporated on a rotatory evaporator to give the pure product.
23. Sanseverino, A. M.; de Mattos, M. C. S. *Synth. Commun.* **1998**, *28*, 559.
24. Barluenga, J.; Rodriguez, M. A.; Campos, P. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2807.
25. Villegas, R. A. S.; Santo, J. L. E., Jr.; de Mattos, M. C. S.; Aguiar, M. R. M. P.; Guarino, A. W. S. *Catal. Commun.* **2007**, *8*, 97.
26. Villegas, R. A. S.; de Mattos, M. C. S.; de Aguiar, M. R. M. P.; Guarino, A. W. S.; Barbosa, L. M.; Assumpção, L. C. F. N. *J. Braz. Chem. Soc.* **2004**, *15*, 150.
27. Cambie, R. C.; Hayward, R. C.; Roberts, J. L.; Rutledge, P. S. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1858.
28. Villegas, R. A. S.; Santo, J. L. E., Jr.; Sanseverino, A. M.; de Mattos, M. C. S.; de Aguiar, M. R. M. P.; Guarino, A. W. S. *Synth. Commun.* **2005**, *35*, 1627.

29. Davidson, R. I.; Kropp, P. J. *J. Org. Chem.* **1982**, *47*, 1904.
30. *General procedure for coiodination of enolethers*. To a stirred solution of the enolether (2 mmol) in MeOH (10 mL), TICA (0.67 mmol) was added at room temperature. After 2 min, CH_2Cl_2 (10 mL) was added, cyanuric acid was filtered off and the solution was extracted with CH_2Cl_2 (2×10 mL). The organic extract was dried (anhydrous Na_2SO_4), filtered and the solvent was evaporated on a rotatory evaporator to give the pure product. Selected spectroscopic data for 1-(2-iodo-1-methoxyethoxy)butane: ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.93 (t, 3H), 1.35–1.59 (m, 4H), 3.20–3.22 (d, 2H), 3.37 (s, 3H), 3.47–3.63 (m, 2H), 4.54 (br s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 4.9, 13.9, 19.4, 31.8, 53.5, 66.8, 102.7. MS (70 eV): *m*/*z* 227 ($M^+ - OMe$), 201, 185, 171, 170, 141, 117, 61 (100%), 41.
31. D'Auria, M.; D'Onofrio, F.; Piancatelli, G.; Scettri, A. *Synth. Commun.* **1982**, *12*, 1127.
32. Dolenc, D. *Synth. Commun.* **2003**, *33*, 2917.