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An unusual decarboxylative benzannulation and biaryl formation during copper(I)-promoted halogen atom transfer radical cyclization of 2-allylaryl trichloroacetates

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Abstract—CuCl/bpy-promoted halogen atom transfer radical cyclization of 2-allylaryl trichloroacetates in refluxing benzene gave benzannulated chloroarenes and benzannulated symmetrical biaryls along with reductive dehalogenation products. The unusual decarboxylative benzannulation and biaryl formation might be explained by a further intramolecular radical addition on the benzene ring of the eight-membered lactone intermediate, initially formed through 8-*endo*-*trig* halogen atom transfer radical cyclization, followed by decarboxylation, radical dimerization and dehydrochlorination reactions.

1. Introduction

The transition metal catalyzed intramolecular addition of a carbon–halogen bond across a carbon–carbon multiple bond through a redox process, known as halogen atom transfer radical cyclization (HATRC), has emerged as a useful alternative to the tributyltin hydride-mediated reductive radical cyclization reaction.[1] The reaction is applicable to substrates having a carbon (sp^3)-halogen bond, weak or activated by adjacent halogen atom(s) or other radical stabilizing groups which efficiently add to a nucleophilic carbon–carbon multiple bond. Notwithstanding these limitations, the reaction has many advantages over tin hydride mediated cyclizations. It is catalytic involving a transition metal (most popularly Cu(I)-tertiary base chelate), generates no toxic byproducts and can be performed at relatively high substrate concentrations without much problem of reductive dehalogenation and telomerization. The transition metal is inexpensive, purification of the product is much easier and the product retains the valuable halogen functionality for further elaboration. A new dimension has been added to the reaction where Grubbs' catalyst catalyzes HATRC along with a preceding alkene metathesis step in a single pot reaction,[2] thus further enhancing its synthetic potential. The reaction, particularly that of *gem*-trichloro and *gem*-dichloro compounds, has found applications in the synthesis of several five-membered lactones, lactams and lactols, some of which could be elaborated further leading to the synthesis of natural,[3] bioactive and other valuable products.[4]

The efficacy of the reaction has also been demonstrated for the synthesis of medium- and large-sized monocyclic lactones and lactams.[1a,5] However, until recently (vide infra) the transition metal catalyzed HATRC has not been applied to the synthesis of medium-sized benzene ring fused lactones or lactams, though cyclization in such a situation is expected to be more favourable due to less conformational flexibility imparted by the benzene ring. In fact, 2-allylaryl monohaloacetates are known to undergo bis(tributyltin)-catalyzed[6] and organophosphorus-promoted[7] facile 8-*endo*-*trig* radical cyclization to give eight-membered benzolactones. These benzolactones, that is, 3,4,5,6-tetrahydro-[2*H*]-benzo[*b*]-oxocin-2-ones, are rare in the literature.[6–9] Recently, during an investigation on HATRC for the synthesis of medium-sized lactones, Quayle et al.[10] reported an efficient benzannulation of several 2-allylaryl trichloroacetates to chloroarenes in high yields on microwave irradiation in DCE in the presence of catalytic amounts of CuCl (5 mol %) and a specially synthesized ligand, 1,3-bis(2-pyridylmethyl)imidazolium chloride (5 mol %).

Keywords: Benzannulation; Biaryls; Chloroarenes; HATRC; Decarboxylation; CuCl/bpy.
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They proposed a mechanism involving initial formation of the expected eight-membered benzo[*b*]lactone intermediates which reacted further under the reaction conditions by 4-*exo*-*trig* radical cyclization onto the benzene ring followed by decarboxylation and dehydrohalogenation to give the final products (vide infra).

2. Results and discussion

Our interest in the Cu(I)/bpy-catalyzed HATRC of *gem*-trichloro compounds and related reactions[4i,11] had also led us to explore Cu(I)/bpy-catalyzed HATRC of 2-allylaryl trichloroacetates with a view to prepare more functionalized eight-membered benzo[*b*]lactones of the type mentioned above. Herein, we wish to report our observations under a different set of reaction conditions, which are similar but potentially complementary to those reported by Quayle et al.[10] When the readily available 2-allylaryl trichloroacetates **1** (Scheme 1) were treated with CuCl/bpy (1:1 molar ratio, 1 equiv) in refluxing benzene under a nitrogen atmosphere, we also could not isolate the expected 8-*endo* (or 7-*exo*) radical cyclization products. Rather, small amounts of chloroarenes **2**, observed as the sole products by Quayle et al.,[10] and, most significantly, biaryls **3** were isolated along with varying amounts of the reductive dechlorination products **4**. The relevant details are given in Table 1. The yields of the reduction products **4** were found to be rather high for a transition metal-catalyzed HATRC, particularly in benzene as the reaction medium.[12]

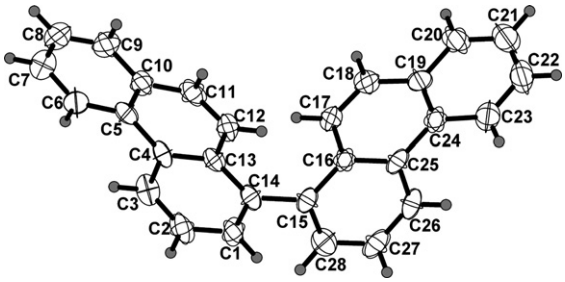
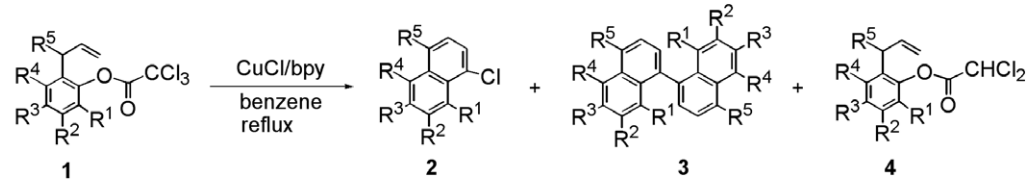


Figure 1. ORTEP diagram of **3a**.

The structures of the products were supported by IR, ^{1}H and ^{13}C NMR, DEPT, and mass spectrometry/elemental analysis/comparison of the melting points with reported values. The structures of biaryls **3a**, **3c** and **3e** were also established by single crystal X-ray diffraction spectroscopy. The ORTEP diagram of **3a** as a representative example is shown in Figure 1.[13]

The reaction required about one equivalent of CuCl/bpy for completion. With dichloroethane (DCE) as the reaction medium, the reduction products **4** predominated. Thus, the reaction of **1a** in refluxing DCE for 1 h gave 1-chlorophenanthrene, **2a** (15%), and the reduction product, **4a** (50%); 1,1′-biphenanthrenyl, **3a**, was not obtained. An acetyl group at the *ortho*, *meta* or *para* position to the ester group makes the substrate susceptible to hydrolysis. Reaction of these compounds did not lead to the formation of compounds **2** or **3** in our hands as against Quayle's observations but resulted



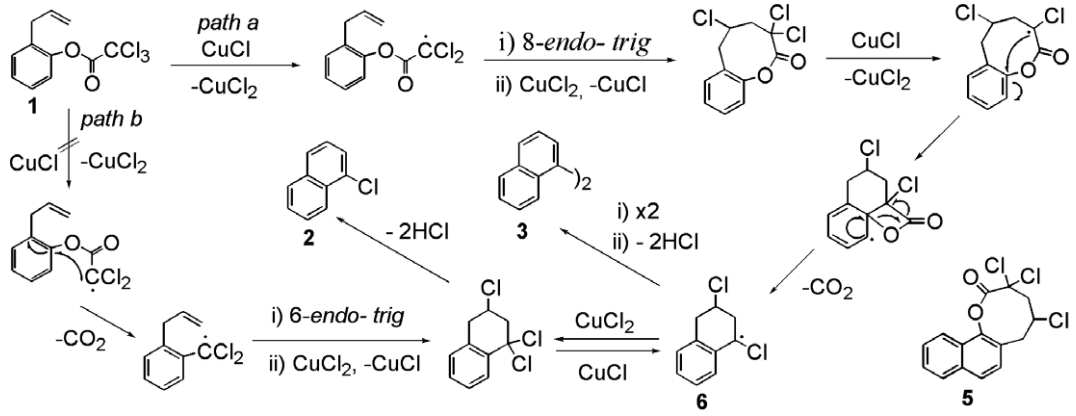
a: R^1= H, R^2= H, R^3R^4= CH=CH-CH=CH, R^5= H
b: R^1R^2= CH=CH-CH=CH, R^3= H, R^4= H, R^5= H
c: R^1= H, R^2= H, R^3= Cl, R^4= H, R^5= H
d: R^1= H, R^2= H, R^3= Cl, R^4= H, R^5= Ph
e: R^1= H, R^2= H, R^3= Me, R^4= H, R^5= H
f: R^1= OMe, R^2= H, R^3= H, R^4= H, R^5= H
g: R^1= H, R^2= Me, R^3= H, R^4= H, R^5= H
h: R^1= H, R^2= H, R^3= H, R^4= Me, R^5= H

Scheme 1. Reactions of 2-allylaryl trichloroacetates **1** with CuCl/bpy.

Table 1. Reactions of 2-allylaryl trichloroacetates **1** with CuCl/bpy[a]

Entry	Ester **1**	Time (h)	Product		
			2 yield (%)	**3** yield (%)	**4** yield (%)
1	**1a**	1	20	40	30
2	**1b**	1	20	—	—
3	**1c**	6	12	32	50
4	**1d**	2	30	—	25[b]
5	**1e**	2	—	46	30
6	**2f**	1	10	30	—
7	**1g** + **1h**	5	15 (**2g** + **2h**)	23 (**3g** + **3h**)	50 (**4g** + **4h**)

[a] The reactions were performed under a nitrogen atmosphere in a Schlenk tube with **1** (1 g, 3–3.5 mmol), CuCl (3–3.5 mmol, 1 equiv) and bpy (3–3.5 mmol, 1 equiv) in refluxing benzene (15 mL).
[b] Deacylated product of **1d**.



Scheme 2. Proposed mechanism for the formation of chloroarenes **2** and biaryls **3**.

in the formation of the reduction products **4** and/or hydrolysis products to give the original phenols. The reduction products **4** in these cases were also susceptible to hydrolysis.

A mechanism (Scheme 2, *path a*) similar to that proposed by Quayle et al.[10] is also favoured by us for the formation of the products on the basis of the following observations: (i) When the reaction of the 1-naphthyl ester **1b** was performed by warming the reaction mixture at 50 °C for a shorter time (15 min), chlorophenanthrene **2b** (15%) and a moisture- senstive product (50%) were isolated. The latter appeared to be the 8-*endo-trig* cyclization product **5**, by its ^{1}H NMR and IR spectral analysis.[14] This product is analogous to the one isolated and shown by Quayle et al. to be converted to the corresponding benzannulated chloroarene under the reaction conditions employed. (ii) The reaction of 1-prenyl-2-naphthyl trichloroacetate, 1-propyl-2-naphthyl trichloroacetate and 1- and 2-naphthyl trichloroacetates having 3,3-disubstituted allyl groups or no allyl group did not proceed to completion with one equivalent of CuCl/bpy and did not give any decarboxylation/cyclization products after completion of the reaction using two equivalents of CuCl/bpy. These results indicate that decarboxylation probably requires the presence of an unhindered olefinic bond. Thus, the mechanism involving initial decarboxylation (Scheme 2, *path b*) via a radical *ipso* attack[15] seems unlikely. Furthermore, the *ipso* radical attack through a 4-*exo-trig* cyclization[1a,16] and subsequently a 6-*endo-trig* radical cyclization[17] reaction required by this mechanism *en route* to the final products are rare occurrences that require special structural features.

According to this mechanism, the formation of biaryls **3** and the reduction products **4** both require one equivalent of the copper complex, while the formation of chloroarenes **2** requires catalytic amounts. Since the latter is a minor product in all the cases, nearly one equivalent of the copper complex is consumed in the reaction. Plausibly, under the present heterogeneous reaction conditions, the transfer of chlorine atom from the sparingly soluble $CuCl_2$/bpy to the radical intermediate **6** is a slower process than that under the homogeneous conditions used by Quayle et al., thus allowing the dimerization of the radical intermediate **6** to compete effectively with the chlorine atom transfer.

In conclusion, the reaction described herein might stimulate further research to develop into a useful method for biaryl synthesis. This would add a new dimension to the Ullmann type biaryl coupling for a one-pot benzannulation–biaryl synthesis from simple, easily available starting materials. Biaryl sub-units occur as building blocks in several bioactive natural products, pharmaceuticals and agrochemicals and find potential applications in the areas of organometallic catalysis, materials science and supramolecular chemistry.[18]

3. Experimental

3.1. Typical experimental procedure

Reaction of 1-allyl-2-naphthyl trichloroacetate ***1a*** *with CuCl/bpfy*: A two-neck round-bottomed flask containing a magnetic bar and connected to a Schlenk line through a condenser was charged with CuCl (306.0 mg, 3 mmol), 2,2′-bipyridyl (473 mg, 3 mmol) and benzene (8 mL). The heterogeneous mixture was heated at 50 °C with stirring for 30 minutes under a nitrogen atmosphere to ensure the formation of the brown copper–bpy complex. Ester **1a** (1 g, 3 mmol) in benzene (7 mL) was then injected into the flask and the reaction mixture was heated at reflux with stirring under a slow and continuous flow of nitrogen. The initial brown colour of the reaction mixture faded as the reaction progressed. After completion of the reaction as indicated by TLC monitoring (1 h), the greenish reaction mixture was cooled and filtered through a Celite pad. The insoluble green solid on the Celite pad was washed thoroughly with benzene and the light brown filtrate was evaporated under reduced pressure. The residual mass was subjected to column chromatography using silica gel as the solid support and *n*-hexane and its mixture with chloroform as the solvent for elution. 1-Chlorophenanthrene **2a** (127 mg, 20%) was eluted first followed by 1,1′-biphenanthrenyl **3a** (212 mg, 40%) with *n*-hexane as white solids. The reduced ester **4a** (265 mg, 30%) was obtained afterward as a colourless thick liquid by elution with *n*-hexane–chloroform mixture (95:5 v/v).

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Supplementary data

IR, ^{1}H and ^{13}C NMR data of products **2**–**5**, copies of ^{1}H and ^{13}C NMR spectra of the biaryls **3**, single crystal X-ray diffraction data (CIF files) and ORTEP diagrams of **3a**, **3c** and **3e** are available. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.09.058.

References and notes

1. For reviews, see (a) Clark, A. J. *Chem. Soc. Rev.* **2002**, *31*, 1–11; (b) Majumdar, K. C.; Basu, P. K.; Mukhopadhyay, P. P. *Tetrahedron* **2005**, *61*, 10603–10642; For some recent references, see (c) Clark, A. J.; Geden, J. V.; Thom, S. *J. Org. Chem.* **2006**, *71*, 1471–1479; (d) Motoyama, Y.; Hanada, S.; Shimamoto, K.; Nagashima, H. *Tetrahedron* **2006**, *62*, 2779–2788; (e) Motoyama, Y.; Hanada, S.; Niibayashi, S.; Shimamoto, K.; Takaoka, N.; Nagashima, H. *Tetrahedron* **2005**, *61*, 10216–10226; (f) Wetter, C.; Studer, A. *Chem. Commun.* **2004**, 174–175; (g) Quayle, P.; Fengas, D.; Richards, S. *Synlett* **2003**, 1797–1800.
2. (a) Edlin, C. D.; Faulkner, J.; Quayle, P. *Tetrahedron Lett.* **2006**, *47*, 1145–1151; (b) Seigal, B. A.; Fajardo, C.; Snapper, M. L. *J. Am. Chem. Soc.* **2005**, *127*, 16329–16332; (c) Schmidt, B.; Pohler, M. *J. Organomet. Chem.* **2005**, *690*, 5552–5555.
3. (a) Buyck, L. D.; Forzato, C.; Ghelfi, F.; Mucci, A.; Nitti, P.; Pagnoni, U. M.; Parsons, A. F.; Pitacco, G.; Roncaglia, F. *Tetrahedron Lett.* **2006**, *47*, 7759–7762; (b) Bellesia, F.; Danieli, C.; Buyck, L. D.; Galeazzi, R.; Ghelfi, F.; Mucci, A.; Orena, M.; Pagnoni, U. M.; Parsons, A. F.; Roncaglia, F. *Tetrahedron* **2006**, *62*, 746–757; (c) Helliwell, M.; Fengas, D.; Knight, C. K.; Parker, J.; Quayle, P.; Raftery, J.; Richards, S. N. *Tetrahedron Lett.* **2005**, *46*, 7129–7134; (d) Buyck, L. D.; Danieli, C.; Ghelfi, F.; Pagnoni, U. M.; Parsons, A. F.; Pattarozzi, M.; Roncaglia, F. *Tetrahedron* **2005**, *61*, 2871–2877; (e) Matsunaga, H.; Ishizuka, T.; Kunieda, T. *Tetrahedron* **2005**, *61*, 8073–8094; (f) Iwamatsu, S.-i.; Matsubara, K.; Nagashima, H. *J. Org. Chem.* **1999**, *64*, 9625–9631; (g) Hirai, Y.; Hagiwara, A.; Tereda, T.; Yamazaki, T. *Chem. Lett.* **1987**, *16*, 2417–2418.
4. (a) Edlin, C. D.; Faulkner, J.; Helliwell, M.; Knight, C. K.; Parker, J.; Quayle, P.; Raftery, J. *Tetrahedron* **2006**, *62*, 3004–3015; (b) Ghelfi, F.; Stevens, C. V.; Laureyn, I.; Meenen, E. V.; Rogge, T. M.; Buyck, L. D.; Nikitin, K. V.; Grandi, R.; Libertini, E.; Pagnoni, U. M.; Schenetti, L. *Tetrahedron* **2003**, *59*, 1147–1157; (c) Broadhurst, M. D.; Gless R. D., Jr. Eur. Pat. Appl. EP 129296 Al 19841227, 1984; (d) Broadhurst, M. D.; Gless, R. D., Jr. *Chem. Abstr.* **1985**, *102*, 184971; (e) Rempfler, H.; Meyer, W. Eur. Pat. Appl. EP 55215 A1 19820630, 1982; (f) Rempfler, H.; Meyer, W. *Chem. Abstr.* **1982**, *97*, 182204c; (g) Broadhurst, M. D. U.S. Patent 4,132,713, 1977; (h) Broadhurst, M. D. *Chem. Abstr.* **1977**, *90*, 137672y; (i) Ram, R. N.; Charles, I. *Chem. Commun.* **1999**, 2267–2268.
5. For a review, see (a) Yet, L. *Tetrahedron* **1999**, *55*, 9349–9403; For some other references, see (b) Campo, F. D.; Lastecoueres, D.; Verlhac, J.-B. *J. Chem. Soc., Perkin Trans. 1* **2000**, 575–580; (c) Campo, F. D.; Lastécouères, D.; Verlhac, J.-B. *Chem. Commun.* **1998**, 2117–2118; (d) Pirrung, F. O. H.; Hiemstra, H.; Speckamp, W. N.; Kaptein, B.; Schoemaker, H. E. *Synthesis* **1995**, 458–472; (e) Pirrung, F. O. H.; Hiemstra, H.; Speckamp, W. N.; Kaptein, B.; Schoemaker, H. E. *Tetrahedron* **1994**, *50*, 12415–12442, and references cited therein.
6. Wang, J.; Li, C. *J. Org. Chem.* **2002**, *67*, 1271–1276.
7. Lang, S.; Corr, M.; Muir, N.; Khan, T. A.; Schonebeck, F.; Murphy, J. A.; Payne, A. H.; Williams, A. C. *Tetrahedron Lett.* **2005**, *46*, 4027–4030.
8. (a) Moody, C. J.; Taylor, R. J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 721–731; (b) Yokota, K.; Kaneko, N.; Iwata, J.; Komuro, K.; Takada, Y. *Polym. J.* **1979**, *11*, 929–935; (c) Dean, F. M.; Park, B. K. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1260–1268; (d) Clinging, R.; Dean, F. M.; Houghton, L. E. *J. Chem. Soc., Perkin Trans. 1* **1974**, 66–73.
9. The structures of the bioactive natural products puerosides A, B and sophoroside A as the 5,6-dihydro-2*H*-benzo[*b*]oxocin-2-one derivatives (a) Barrero, A. F.; Sanchez, J. F.; Barron, A.; Rodriguez, I. *J. Nat. Prod.* **1989**, *52*, 1334–1337; (b) Shirataki, Y.; Tagaya, Y.; Yokoe, I.; Komatsu, M. *Chem. Pharm. Bull.* **1987**, *35*, 1637–1640; (c) Kinjo, J.-e.; Furusawa, J.-i.; Nohara, T. *Tetrahedron Lett.* **1985**, *26*, 6101–6102, have been shown to be in error and were subsequently assigned butenolide structures; (d) Nohara, T.; Kinjo, J.; Furusawa, J.; Sakai, Y.; Inoue, M.; Shirataki, Y.; Isibashi(nee Tagaya), Y.; Yokoe, I.; Komatsu, M. *Phytochem.* **1993**, *33*, 1207–1210.
10. Bull, J. A.; Hutchings, M. G.; Quayle, P. *Angew. Chem., Int. Ed.* **2007**, *46*, 1869–1872.
11. Ram, R. N.; Meher, N. K. *Org. Lett.* **2003**, *5*, 145–147.
12. An attempted 7-*exo*-*trig* HATRC of 2,2,2-trichloroethyl *N*-(2-cyclohexenyl)carbamate catalyzed by first generation Grubbs' ruthenium catalyst in toluene is known to give only the reduction product in 83% yield (Ref. 2b).
13. CCDC No. 619577.
14. Eight-membered γ-iodolactones and to some extent the corresponding benzo[*b*]lactones are known to be hydrolytically unstable (see Ref. 6).
15. For a similar mechanism during an attempted Cu(I)-catalyzed 8-*endo*-*trig* HATRC of N-(4-pentenyl),*N*-trichloroacetyltosyl amide resulting into radical *ipso*-attack on benzene ring carbon followed by rearrangement with extrusion of SO_2, see Clark, A. J.; Campo, F. D.; Deeth, R. J.; Filik, R. P.; Gatard, S.; Hunt, N. A.; Lastecoueres, D.; Thomas, G. H.; Verlhac, J.-B.; Wongtap, H. *J. Chem. Soc., Perkin Trans. 1* **2000**, 671–680.
16. Srikrishna, A. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, Germany, 2001; Vol. 2, pp 151–187.
17. For reviews, see (a) Schiesser, C. H.; Wille, U.; Matsubara, H.; Ryu, I. *Acc. Chem. Res.* **2007**, *40*, 303–313; (b) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3071–3100; For some other references, see (c) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925–3941; (d) Gomez, A. M.; Company, M. D.; Uriel, C.; Valverde, S.; Lopez, J. C. *Tetrahedron Lett.* **2007**, *48*, 1645–1649, and references cited therein; (e) Quirante, J.; Vila, X.; Paloma, L.; Guiu, J. M.; Bonjoch, J. *Tetrahedron* **2007**, *63*, 1372–1379; (f) Bennasar, M.-L.; Roca, T.; Ferrando, F. *J. Org. Chem.* **2006**, *71*, 1746–1749.
18. For leading references, see Ram, R. N.; Singh, V. *Tetrahedron Lett.* **2006**, *47*, 7625–7628.