JOC Article

Single-Isomer Iodochlorination of Alkynes and Chlorination of Alkenes Using Tetrabutylammonium Iodide and Dichloroethane

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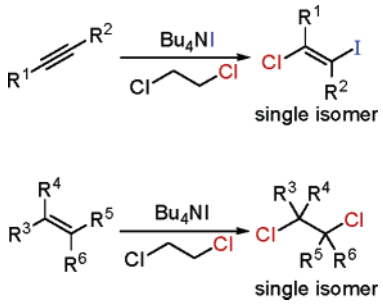

The efficient formation of single-isomer, differentially halogenated alkenes and alkanes is described. These structures were generated by treatment of the appropriate alkyne or alkene with tetrabutylammonium iodide in refluxing dichloroethane. This process is highly selective as evidenced by control experiments using ICl. Treatment of the same alkenes and alkynes directly with iodine monochloride resulted in complex, inseparable mixtures of regio- and stereoisomers. Mechanistic studies indicated that the Bu_4NI reaction most likely proceeded through the slow generation of ICl. Complexation of ICl with Bu_4NI is also a key controlling element that leads to perfect regio-, chemo-, and stereoselectivity in these processes.

Introduction

Halogenation reactions feature prominently in the toolbox of the organic chemist. Bromination and chlorination are straightforward processes. Iodination is frequently more difficult because the reaction proceeds very slowly and is often reversible under standard conditions.[1] Because of these reactivity challenges, additives are typically required to promote iodination of alkenes and alkynes. Halogenation using iodine monochloride is more facile because a permanent dipole exists in the reagent that greatly facilitates electrophilic attack.[2] Unfortunately, this process usually produces regio- and stereoisomers that are difficult to separate and purify. Use of iodine monochloride for iodination of aromatic compounds frequently gives mixtures of mono-, di-, and tri-iodinated arene products.[3] To overcome these selectivity and reactivity difficulties, a variety of conditions have been developed for the more efficient and selective iodination of alkenes[4] and aromatic compounds,[5] and many of these involve generation of ICl in situ. For example, halogenation of alkenes can be done using iodine and copper(II) chloride, but the method tends to give mixtures of iodochlorinated regioisomers and dichlorinated products.[4a,b] Thallium(I) azide has been employed as an additive in combination with iodine and gives predominantly anti addition products.[4c] As in the case of other methods, control of the regioselectivity and stereoselectivity are significant issues associated with this technique.

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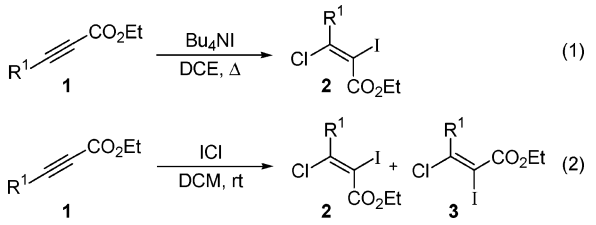
SCHEME 1



Iodination of silyl enol ethers has been accomplished using a combination of NaI and $FeCl_3$.[1a] Aromatic compounds have been iodinated with moderate selectivity for the para position using combinations of ammonium iodide and oxone,[5a] tetrabutylammonium peroxydisulfate and iodine,[5b] iodine and copper(II) chloride,[5c] and hypervalent iodine.[5d] Iodination of aromatic heterocycles has been reported using aqueous potassium dichloroiodate.[5e] Anilines have been iodinated with high para selectivity using benzyltriethylammonium dichloroiodate and sodium bicarbonate.[5f] Iodination of phenols is selective for the ortho position when thallium acetate is used in combination with iodine.[5g]

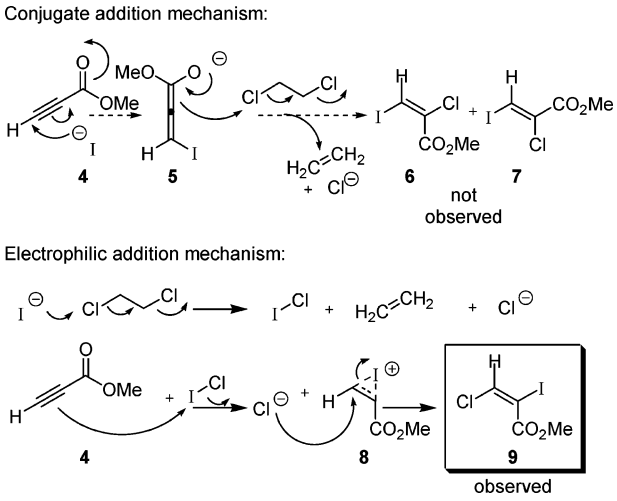
Iodochlorination of alkynes also remains problematic. Addition of ICl to alkynes provides the desired iodochlorinated alkenes; unfortunately mixtures of regio- and stereoisomers are normally observed.[6] This is somewhat inefficient because the products can be extremely difficult to separate and purify. Because of their use in the production of asymmetrically substituted olefins,[7,8] methods to prepare single-isomer iodochlorinated products are highly desirable. In this paper we describe a simple method that leads to complete regio- and stereocontrol during additions to alkynes. Chemoselectivity is also realized by suppressing the normal reactivity of ICl toward electrophilic aromatic substitution. Reactions with olefins produce exclusively the dichlorinated products in an extremely clean and selective process. Mechanistic studies of the Bu_4NI method and applications to various substrates are also described.

Results and Discussion

As part of a study directed toward generation of single-isomer tetrasubstituted olefins, we recently disclosed an efficient method for generation of single-isomer iodochlorinated alkenes by exposure of the appropriate alkynes to tetrabutylammonium iodide in refluxing dichloroethane (DCE) (Scheme 1, eq 1).[8] This method was highly efficient in converting 2-alkynyl esters such as **1** into the corresponding *E*-β-chloro-α-iodo-α,β-unsaturated ester compounds **2**, giving the products as single isomers. Use of ICl directly generated the same regioisomers but produced an equimolar mixture of *E* and *Z* stereoisomers **2** and **3**, respectively (eq 2).

Two plausible mechanisms can be proposed for the combination of tetrabutylammonium iodide with an alkynyl ester such as **4** and DCE (Scheme 2). The first involves conjugate addition

SCHEME 2. Plausible Mechanisms for the Iodochlorination of 4 with Bu_4NI and DCE



of iodide to the β position of the α,β-unsaturated ester **4**. The resulting allenoate **5** would then react with dichloroethane, thereby generating ethene and producing stereoisomeric α-chloro-β-iodo-α,β-unsaturated esters **6** and **7**. The second possible mechanism involves initial attack of the iodide onto dichloroethane, generating iodine monochloride and ethene. Alkyne **4** could then react with the electrophilic iodine to generate cyclic iodonium **8**.[6] This intermediate would undergo backside attack by the chloride at the more electropositive β-position to generate the *E*-β-chloro-α-iodo-α,β-unsaturated ester **9**. The first mechanism was ruled out by establishing the identity of the isomer produced. Carbon and DEPT NMR analysis of the product showed a chemical shift of 129.4 ppm for the CH carbon, consistent with chlorine substitution at the β position of an α,β-unsaturated ester. A strong upfield chemical shift of 84.3 ppm was observed for the quaternary olefinic carbon, consistent with iodine substitution at that position.[8] The configuration of the alkene products was determined using NMR methods.[9] These results confirmed that the only product produced was olefin **9**, proving the conjugate addition mechanism to be inoperative and clearly supporting the electrophilic addition mechanism.[8]

The electrophilic addition mechanism was tested by parallel experiments performed using ICl. Exposure of **4** to ICl in DCE gave a mixture of alkenes **6**, **7**, **9**, and **10** (Scheme 3).[10] This reaction using ICl was completely nonselective as the products were formed as a mixture of regioisomers and mixtures of *E*

SCHEME 3

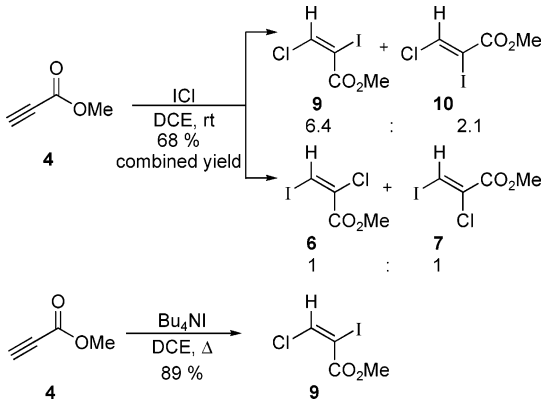


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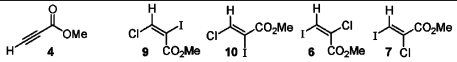
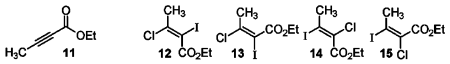
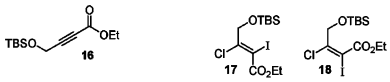
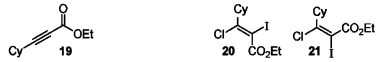
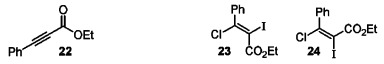
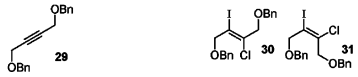
TABLE 1. Conversion of Alkynes to Single-Isomer Products with Bu_4NI in DCE, and Comparison to Analogous Reaction with ICl Alone

Entry	Substrate	Products	Bu_4NI/DCE		ICl	
			Product	Yield[a] (%)	Products (Ratio)	Yield[b] (%)
1			**9**	89	**9, 10, 6, 7**[d] (6:2:1:1)	68
2			**12**[c]	91	**12,13,14,15**[d] (5:6:1.5:1)	90
3			**17**[c]	92	**17, 18**[d] (2:1)	67
4			**20**[c]	75	**20, 21**[d] (1:1)	99
5			**23**	76	**23, 24**[d] (3:1)	93
6			**26**[c]	92	**26**	99
7			**28**	97	**28**	92
8			**30**	93	**30, 31** (1:1)	99

[a] Isolated yield. [b] Combined isolated yield. [c] These products were successfully generated on >5 g scale. [d] Mass spectrum shows the presence of diiodinated compounds.

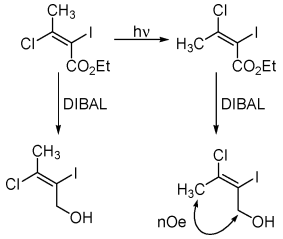
and *Z* isomers **6**, **7**, **9**, and **10**. In contrast, exposure of alkyne **4** to Bu_4NI in refluxing DCE gave *E*-alkene **9** as the only product.

The clear superiority of the Bu_4NI/DCE method led us to examine the process with other substrates. To our delight, use of Bu_4NI in refluxing DCE with a variety of alkynes gave single isomers in every reaction. In contrast, control reactions employing direct use of ICl gave mixtures in almost every case. This completely regio- and stereoselective Bu_4NI/DCE reaction tolerates a variety of substituents on the alkyne terminus, including a hydrogen (Table 1, entry 1) and a simple alkyl group (entry 2). In contrast, treatment of these substrates (**4**, **11**) with ICl gave mixtures of at least three chloroiodinated products as mixtures of regio- and stereoisomers. Mass spectral analysis of these mixtures also indicated that small amounts of diiodinated products were present. The Bu_4NI/DCE reaction was very successful if the substituent was a functionalized alkyl chain (entry 3) or a branched alkyl group (entry 4) as a single isomer was obtained in each case (**17** entry 3, **20** entry 4). Inseparable mixtures were obtained upon exposure of the same substrates (**16**, **19**) to ICl. The Bu_4NI/DCE reaction of an alkyne bearing a phenyl substituent (entry 5) followed the same trend, producing a single isomer (**23**) in good yield. This same substrate **22**, when treated with ICl alone, afforded an inseparable mixture of products.

The Bu_4NI/DCE reaction could be extended to other carbonyl derivatives, such as alkynyl amides (entry 6), with perfect control of selectivity. Exposure of unconjugated alkyne **27** to Bu_4NI in DCE gave a single-isomer product in excellent yield (entry 7). A single isomer was obtained from use of ICl in only this case in which symmetry in the substrate most likely controlled the outcome of the process. Functionalized alkyne **29** was cleanly converted to *E*-isomer **30** using Bu_4NI in DCE, whereas this same compound gave a mixture of *E* and *Z* products, **30** and **31**, when ICl was used. The reliability, selectivity, and effectiveness of the Bu_4NI/DCE reactions were remarkable, and this method enabled efficient generation of single-isomer chloroiodinated alkenes, a class of compounds whose utility has until now been limited by preparative challenges.[7,8]

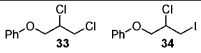
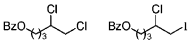
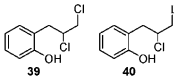
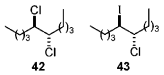
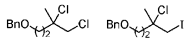
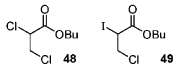
Use of Bu_4NI in refluxing DCE with related alkene substrates such as **32** did not give the anticipated iodochlorinated products. Instead, single-isomer dichlorinated products such as **33** were cleanly obtained (Table 2, entry 1).[11] Once again, this was in stark contrast to the results obtained by use of ICl with the same

(9) The *E*-esters were briefly photolyzed to generate the corresponding *Z*-isomers, and then the esters were reduced with DIBAL, giving the corresponding alcohols. Consistent with the structural assignments shown, nOe enhancements were observed between the methyl and methylene of the *Z*-isomer whereas these interactions were lacking in the *E*-isomer. See ref 8 for details.



(10) Diiodinated products were also detected by mass spectroscopy.

TABLE 2. Conversion of Alkenes to Single Isomer Dichlorinated Products Using Bu_4NI in DCE, and Comparison to Reaction of the Same Alkenes with ICl That Gave Mixtures of Halogenated Products

Entry	Substrate	Products	Bu_4NI		ICl[a]	
			Product	Yield[b] (%)	Product(s) (Ratio)	Yield[c] (%)
1	 **32**	 **33** **34**	**33**	99	**33**, **34** (1:1)	99
2	 **35**	 **36** **37**	**36**	99	**36**, **37** (1:1)	92
3	 **38**	 **39** **40**	**39**	89	**39**, **40** (1:1)	99
4	 **41**	 **42** **43**	**42**	78	**43**	66
5	 **44**	 **45** **46**	-	NR[d]	**45**, **46** (1:1)	14[e]
6	 **47**	 **48** **49**	**48**	20[f]	**48**, **49** (5.3:1)	61

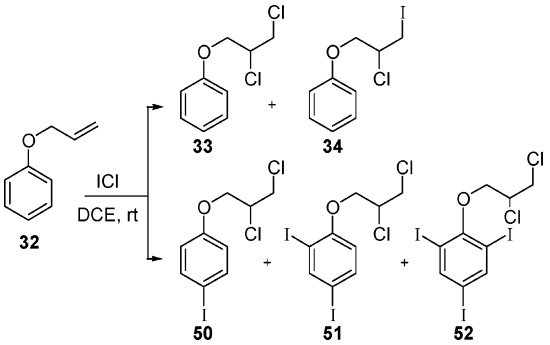
[a] All reactions performed with 0.98 equiv of ICl. [b] Isolated yield. [c] Combined isolated yield. [d] NR = no reaction. [e] Reaction performed in DCE at reflux. [f] Reaction time was 4 days.

substrate, a procedure that gave a mixture of dichlorinated (**33**) and iodochlorinated (**34**) compounds. While many reactions have been reported in which iodine monochloride has been found to give chlorinated products, these materials are typically only minor components in the reaction mixture.[2] Clean production of dichlorinated products using the Bu_4NI/DCE method was a surprising and useful result.

The remarkable selectivity of halogenations using Bu_4NI in refluxing DCE was further investigated using a variety of alkenes as substrates. An alkene bearing a substituted alkyl chain (**35**, entry 2) gave single-isomer dichlorinated product **36** using Bu_4NI/DCE. In contrast, treatment of the same alkene with ICl gave an inseparable mixture of dichlorinated and iodochlorinated products. Thus, reaction of ICl with compound **35** gave a mixture of **36** and **37**. An alkene tethered to an unprotected phenol (entry 3) cleanly reacted with Bu_4NI/DCE to give compound **39** exclusively and in high yield. Reaction of the same substrate with ICl gave a mixture of products (**39**, **40**) as with other examples. Internal trans alkene **41** (entry 4) reacted very well under the Bu_4NI/DCE conditions to give a single-isomer **42** as evidenced by both ^1H and ^{13}C NMR spectra. In contrast, treatment of alkene **41** with ICl gave the iodochlorinated compound **43**. A 2,2-disubstituted alkene proved to be completely unreactive toward Bu_4NI/DCE (entry 5). A low yield was also observed in the corresponding ICl reaction of **44** under forcing conditions in which a mixture of products **45** and **46** was obtained. An electron-deficient alkene (entry 6) reacted sluggishly under refluxing conditions with Bu_4NI in DCE but nevertheless produced a single product **48**. Treatment of the same Michael acceptor with ICl produced a mixture of products **48** and **49** in moderate yield.

While the Bu_4NI/DCE system was highly selective for iodochlorination of alkynes with a wide variety of substitution patterns and for chlorination of monosubstituted alkenes, aromatic rings were completely unreactive. Anisole did not react upon exposure to Bu_4NI in DCE even after several days at reflux. However, anisole reacted readily upon exposure to ICl at room temperature, giving a mixture of multiple addition products. *N*,*N*-Dimethylaniline was completely unreactive upon exposure to Bu_4NI in refluxing DCE but rapidly gave a mixture of multiple addition products in the related ICl reaction. Even the electron-rich 1,3-dimethoxybenzene was unreactive in the presence of Bu_4NI/DCE and again readily gave a mixture of products in the presence of ICl. This property of the Bu_4NI/DCE system allowed for selective reaction at alkenyl or alkynyl functional groups in the presence of electron-rich aromatic systems while leaving the aromatic moieties untouched. Thus, allyloxybenzene **32** was cleanly converted to dichloride **33** with Bu_4NI/DCE, leaving the aromatic group undisturbed (Table 2, entry 1). This is in contrast to treatment of the same substrate (**32**) with ICl which gave inseparable mixtures of products bearing mono-, di-, and trisubstitution (**50**−**52**) of the aromatic ring even if only a slight excess of ICl was employed (Scheme 4). Many conditions have been developed for halogenation of aromatic compounds, but the current Bu_4NI method is remarkable for the chemoselectivity demonstrated toward the electro-

SCHEME 4



(11) A control reaction performed by refluxing allyloxybenzene in DCE gave no reaction. This illustrated that the tetrabutylammonium iodide was an essential component of this process.

philic addition to alkenes and alkynes rather than electrophilic aromatic substitution.

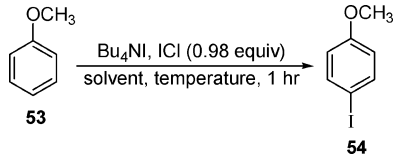
Mechanistic Considerations. The notable selectivity of the Bu_4NI/DCE method warranted an investigation of the mechanism. As noted above, the regioselectivity in the reaction with alkynyl substrates such as **1**, producing products such as **2**, suggested that ICl was involved in the process. As this intermediate was presumably formed by reaction between Bu_4NI and DCE, it was reasonable to assume that similar reactivity could be realized with other electropositive chloride sources.

Treatment of alkyne **11** with Bu_4NI and *N*-chlorosuccinimide (NCS) in refluxing CH_2Cl_2 gave product **12** exclusively in 85% yield. This supported the supposition that ICl was being formed slowly in situ by the reaction between Bu_4NI and electrophilic chloride sources such as DCE or NCS. However, this in situ generation of ICl could not by itself explain the remarkable selectivity observed when using Bu_4NI. If the effect was due to slow generation of ICl, then presumably the selectivity of the Bu_4NI/DCE was simply the result of a low concentration of ICl. This was examined by adding ICl via syringe-pump to a solution of alkyne **11** in CH_2Cl_2 over 24 h. The reaction resulted in excellent conversion to products **12**, **13**, **14**, and **15**, but virtually no selectivity was observed, thus ruling out this possible concentration effect.

Another possible explanation for the Bu_4NI selectivity could be a buffering effect. In other words, the ICl reactions may have given poor selectivity because of an acid-catalyzed isomerization of the alkenes. To test this hypothesis, compound **11** was exposed, in separate reactions, to ICl in the presence of an excess of the bases imidazole and lutidine. Despite this precaution, these reactions again gave mixtures of isomeric products **12** to **15** as before. If Bu_4NI was reacting with DCE to generate ICl, it was possible that the Bu_4NCl generated as a byproduct was somehow modulating the reactivity of the ICl. To test this hypothesis, alkyne **11** was treated with ICl in the presence of excess Bu_4NCl. Once again the outcome of the reaction was indistinguishable from the results obtained using ICl alone.

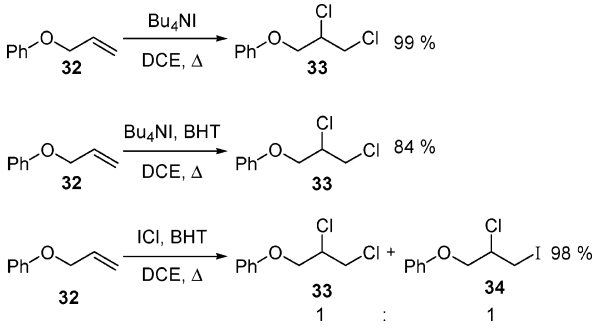
Two significant observations led us to suspect that a $Bu_4NI-ICl$ complex was forming and that this complex was responsible for the remarkable selectivity achieved with Bu_4NI. The first was the low reactivity of the Bu_4NI/DCE system toward electrophilic aromatic substitution when all other reactions clearly showed that ICl was implicated in the transformations. Given the high reactivity of ICl toward electrophilic aromatic substitution with electron-rich substrates such as anisole, an attenuating factor must have been operative if ICl was being slowly generated to account for the lowered reactivity when Bu_4NI was used. The second observation was the fact that slow introduction of ICl into a solution of alkene **32** did not result in a selective reaction. Control reactions were performed using anisole to investigate the role of complexation. Exposure of anisole (**53**) to 0.98 equiv of ICl in DCE gave *p*-iodoanisole **54** in 90% yield after 1 h at room temperature (Table 3, entry 1). Adding small amounts of Bu_4NI to the mixture suppressed the reactivity of ICl, resulting in yield decreases that were dependent on the amount of ICl present. Thus, addition of 0.25 equiv of Bu_4NI gave a drop in yield from 90% to 54% (entry 2). Recovery of **54** was reduced to 14% when 0.5 equiv of Bu_4NI was present (entry 3), and the reaction was effectively suppressed when 1 equiv of Bu_4NI was introduced (entry 4). Increasing the temperature of the reaction did not restore the reactivity of ICl when Bu_4NI was present,

TABLE 3. Reaction of 53 with ICl in the Presence of Varying Amounts of Bu_4NI



entry	equiv Bu_4NI	solvent	temp. (°C)	yield (%)
1	0	DCE	22	90
2	0.25	DCE	22	56
3	0.5	DCE	22	14
4	1.05	DCE	22	3
5	3.0	DCE	22	trace
6	3.0	DCE	83	trace
7	3.0	benzene	80	trace

SCHEME 5



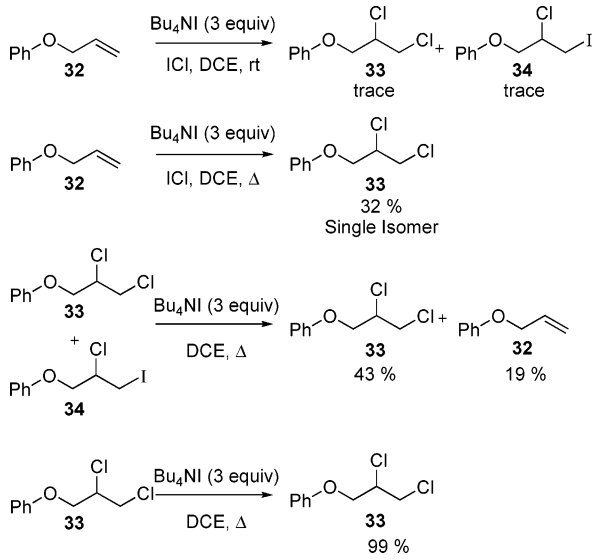
regardless of the solvent used (entries 5−7). These results strongly suggested that complexation between ICl and Bu_4NI was responsible for the reactivity control observed when Bu_4NI was used in DCE.

Control reactions performed with alkyne **11** further confirmed that a complex was involved in the stereocontrol of the reaction.[12] Adding increasing amounts of Bu_4NI to a reaction mixture containing alkyne **11** and ICl suppressed the reactivity of ICl. Decreases in yield were strongly dependent on the amount of Bu_4NI present. The reaction was completely suppressed when alkyne **11** was treated with 3.0 equiv of Bu_4NI at room temperature in DCE in the presence of ICl. In contrast to the reaction with anisole, reactivity returned when the reaction was heated to reflux, giving a 30% conversion to single-isomer product **12**. This indicated that Bu_4NI exerted strong stereocontrol over the reaction, presumably through complexation with the ICl present.

Formation of dichlorinated products from reaction of Bu_4NI with alkenes in DCE could also be accounted for by formation of a $Bu_4NI-ICl$ complex, which presumably was modulating the reactivity of ICl. Disproportionation and radical mechanisms are the typical means by which the chlorination of alkenes is thought to occur in the presence of ICl.[2] In the case of Bu_4NI/DCE, the radical mechanism was ruled out by adding the radical inhibitor 3,5-di-*tert*-butyl-4-hydroxytoluene (BHT) to a reaction of alkene **32** and Bu_4NI in DCE (Scheme 5).[13] The results of this reaction were comparable to those obtained without BHT as dichloride **33** was obtained in 84% yield. Similarly, use of BHT had no effect on the reaction of alkene **32** with ICl, as a

(12) Full reaction details are described in the Supporting Information.
(13) BHT (20 mol %) was added to a mixture of alkene **32** (1 equiv) and Bu_4NI (3 equiv) in DCE. The solution was heated at reflux until consumption of starting material was complete as indicated by TLC.

SCHEME 6. Investigation of a Complexation Effect of Bu_4NI with ICl



mixture of products **33** and **34** was obtained. As this radical scavenger did not inhibit the reactions, the process was most likely proceeding via the disproportionation of complexed ICl rather than by the intermediacy of free radicals.

A series of reactions was performed to confirm whether the chlorination reaction resulted from a disproportionation of ICl. Thus, ICl was added to reaction mixtures of alkene **32** containing increasing amounts of Bu_4NI (Scheme 6). Utilization of 3 equiv of Bu_4NI and 1 equiv of ICl in DCE at room temperature gave only traces of isomers **33** and **34**. The same reagents, in the same relative proportions, gave dichlorinated compound **33** as the exclusive product when the reaction was heated to reflux. Exposure of an equimolar mixture of dichlorinated ether **33** and chloroiodinated ether **34** to Bu_4NI in refluxing dichloroethane gave essentially quantitative recovery of dichlorinated ether **33**. No chloroiodinated compound **34** was recovered; however, alkene **32** was now present in the mixture. This suggested that the chloroiodinated compound **34** underwent an elimination to give alkene **32** which could then be dichlorinated. Formation of **33** was consistent with a disproportionation mechanism. Support for this was obtained by refluxing dichlorinated ether **33** with Bu_4NI in DCE. After 3 days at reflux, dichloride **33** was recovered in quantitative yield, showing that **33** was stable under the reaction conditions.[14]

Conclusion

Exposure of a wide variety of alkynes to Bu_4NI in refluxing DCE gave single-isomer *E*-*β*-chloro-α-iodo-α,*β*-unsaturated ester products in every instance. This method is far superior to the direct use of ICl, which gave mixtures of stereoisomers. Treatment of alkenes with Bu_4NI in refluxing DCE cleanly gave single-isomer dichloroalkane products, representing a useful and convenient method for formation of such materials. The same alkenes, when treated with ICl, gave inseparable mixtures of dichlorinated and regioisomeric chloroiodinated alkanes. Most notable was the selectivity for reactions at the alkynyl and alkenyl functions rather than electrophilic aromatic substitutions.

Mechanistic experiments using NCS indicated that ICl was being slowly generated in the Bu_4NI/DCE system and that this species could explain the observed regioselectivity. A series of experiments in which Bu_4NI was found to attenuate the reactivity of ICl toward electrophilic aromatic substitution indicated that a complex between Bu_4NI and ICl was responsible for the modulation of reactivity in these processes. This was confirmed for the alkyne series by experiments using alkynyl ester **11** and alkene **32**, which indicated that the $Bu_4NI-ICl$ complex was responsible for the extreme selectivity in this process. This complex also appeared to moderate the reactivity of the ICl during additions to alkenes such that dichlorinated products were obtained rather than the expected chloroiodinated derivatives. This reagent combination will undoubtedly be frequently utilized to access these single-isomer substrates cleanly and in preparatively useful quantities.

Experimental Section

General Procedure for the Halogenation of Alkenes and Alkynes Using Bu_4NI.[15] **(*E*)-Methyl 3-Chloro-2-iodoacrylate (9).**[8] A solution of methyl-2-propiolate **4** (250 mg, 2.98 mmol, 1.0 equiv) and tetrabutylammonium iodide (3.25 g, 8.95 mmol, 3.0 equiv) in dichloroethane (25 mL) was heated at reflux for 18 h. The reaction mixture was cooled, diluted with Et_2O, and washed with $NaHSO_3$ (20 wt % solution), saturated $NaHCO_3$, and brine. The organic phase was then dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The pure product was obtained by flash chromatography eluting with hexanes and then 5% EtOAc in hexanes to give the title product as a colorless oil (528 mg, 72%). ^1H NMR (300 MHz, $CDCl_3$) δ 7.00 (s, 1H), 3.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6 (C), 129.4 (CH), 84.3 (C), 53.2 (CH_3); IR (neat) 1728, 1567 cm^{-1}; MS (EI) 246 (M^+); HRMS calcd for $C_4H_4ClIO_2$ (M^+) 245.8945, found 245.8926.

(*E*)-Ethyl 4-(*tert*-Butyldimethylsilyloxy)-3-chloro-2-iodobut-2-enoate (17). Prepared from ethyl 4-(*tert*-butyldimethylsilyloxy)-but-2-ynoate (100 mg, 0.41 mmol) using a procedure similar to that described above for compound **9** that provided the title compound as a colorless oil (152 mg, 92%). ^1H NMR (400 MHz, $CDCl_3$) δ 4.53 (s, 2H), 4.31 (q, $J = 7.2$ Hz, 2H), 1.34 (t, $J = 7.2$ Hz, 3H), 0.93 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6 (C), 137.1 (C), 80.1 (C), 68.6 (CH_2), 62.6 (CH_2), 25.8 (CH_3), 18.3 (C), 13.9 (CH_3); IR (neat) 2956, 1733, 1472 cm^{-1}; HRMS calcd for $C_8H_{13}ClIO_3Si$ ($M^+ - t$-Bu) 346.9367, found 346.9352; calcd for $C_{11}H_{19}ClIO_3Si$ ($M^+ - CH_3$) 388.9837, found 388.9830.

***N*-Methoxy-*N*-Methylnon-2-ynamide (25).** To a solution of 1-hexyne (2.6 mL, 17.7 mmol, 1.0 equiv) in hexanes (150 mL) at −78 °C was added a solution of butyllithium (2.26 M in THF, 8.63 mL, 19.5 mmol, 1.1 equiv). After 1 h a solution of *N*-methoxy-*N*-methylcarbamoyl chloride[16] (2.40 g, 19.4 mmol, 1.1 equiv) in THF (20 mL) was slowly added via canula. The reaction was stirred for 1 h at −78 °C and then allowed to warm to room temperature for 1 h. The reaction was quenched by the dropwise addition of 10% HCl and diluted with ether. The organic layer was washed sequentially with a saturated solution of sodium bicarbonate and brine and then dried over anhydrous $MgSO_4$, filtered, and concentrated. The pure product was obtained by chromatography eluting with 5% EtOAc in hexanes and then 20% EtOAc in hexanes to give the title product as a pale yellow oil (3.02 g, 77%). ^1H NMR (400 MHz, $CDCl_3$) δ 3.40 (s, 3H), 2.94 (s, 3H), 2.03 (t, $J = 6.4$ Hz, 2H), 1.36−1.14 (m, 8H), 0.93 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 73.0 (CH_3), 61.8 (CH_3), 31.1 (CH_2), 30.8

(14) Exposure of an *E*:*Z* mixture of *β*-chloro-α-iodo-α,*β*-unsaturated esters **12** and **13** (2.8:1) to Bu_4NI in refluxing DCE for 18 h returned the material in an unaltered ratio (95 %, **12**:**13**, 2.8:1).

(15) Detailed descriptions of the preparation of compounds **9**, **12**, **20**, and **23** are found in ref 8.

(16) Smith, A. B., III; Beiger, J. J.; Davulcu, A. H.; Cox, J. M. *Org. Synth.* **2005**, *82*, 147.

(CH_2), 28.4 (CH_2), 27.6 (CH_2), 22.4 (CH_2), 18.8 (CH_2), 13.6 (CH_3); IR (neat) 2237, 1644 cm^{-1}; HRMS calcd for $C_{11}H_{19}NO_2$ (M^+) 197.1416, found 197.1405.

(*E*)-3-Chloro-2-iodo-*N*-methoxy-*N*-methylnon-2-enamide (26). Prepared from *N*-methoxy-*N*-methylnon-2-ynamide (3.02 g, 15.3 mmol) using a procedure similar to that described above for compound **9** that provided the title compound as a colorless oil (5.05 g, 92%). ^1H NMR (400 MHz, C_6D_6) δ 3.22 (s, 3H), 2.82 (s, 3H), 2.46 (br s, 2H), 1.48−1.45 (m, 2H), 1.19−1.14 (m, 6H), 0.84 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 166.3 (C), 135.1 (C), 82.7 (C), 60.8 (CH_3), 40.4 (CH_2), 32.4 (CH_3), 31.8 (CH_2), 28.3 (CH_2), 27.1 (CH_2), 22.8 (CH_2), 14.1 (CH_3); IR (neat) 2954, 2930, 2858, 1654, 1459 cm^{-1}; HRMS calcd for $C_{11}H_{10}ClIO_2$ (M^+) 359.0149, found 359.0201.

(*E*)-5-Chloro-6-iododec-5-ene (28). Prepared from 5-decyne (0.13 mL, 0.76 mmol) using a procedure similar to that described above for compound **9** that provided the title compound as a colorless oil (210 mg, 92%). ^1H NMR (400 MHz, acetone-d_6) δ 2.68 (t, $J = 7.2$ Hz, 4H), 1.60−1.48 (m, 4H), 1.39−1.32 (m, 4H), 0.94 (t, $J = 7.2$ Hz, 3H), 0.93 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ 133.0 (C), 100.6 (C), 44.3 (CH_2), 43.2 (CH_2), 32.2 (CH_2), 30.9 (CH_2), 23.3 (CH_2), 23.0 (CH_2), 15.2 (CH_3), IR (neat) 2957, 2860, 1623, 1464 cm^{-1}; MS (EI) 300 (M^+); HRMS calcd for $C_{10}H_{18}ClI$ (M^+) 300.0142, found 300.0132.

(*E*)-(2-Chloro-3-iodobut-2-ene-1,4-diyl)bis(oxy)bis(methylene)dibenzene (30). Prepared from 1,4-bis(benzyloxy)but-2-yne[17] (50 mg, 0.19 mmol) using a procedure similar to that described above for compound **9** that provided the title compound as a colorless oil (75 mg, 93%). ^1H NMR (400 MHz, acetone-d_6) δ 7.42−7.29 (m, 10 H), 4.57 (s, 2H), 4.55 (s, 2H), 4.51 (s, 2H), 4.44 (s, 2H); ^{13}C NMR (100 MHz, acetone-d_6) δ 139.9 (C), 139.8 (C), 132.7 (C), 130.03 (CH), 130.01 (CH), 129.63 (CH), 129.56 (CH), 129.41 (CH), 129.38 (CH), 102.6 (C), 77.9 (CH_2), 74.8 (CH_2), 73.5 (CH_2), 73.2 (CH_2); IR (nujol) 2957, 1640, 1458 cm^{-1}; MS (EI) 428 (M^+); HRMS calcd for $C_{18}H_{18}ClIO_2$ (M^+) 428.0040, found 428.0043.

(2,3-Dichloropropoxy)benzene (33).[18] Prepared from allyloxybenzene (100 mg, 0.75 mmol) using a procedure similar to that described above for compound **9** that provided the title compound as a colorless oil (151 mg, 99%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.34−7.31 (m, 2H), 7.05−6.94 (m, 3H), 4.41−4.35 (m, 1H), 4.30 (dd, $J = 6.4$, 1.2 Hz, 2H), 4.02−3.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9 (C), 129.6 (CH), 121.6 (CH), 114.7 (CH), 68.1 (CH_2), 57.3 (CH), 45.0 (CH_2); IR (neat) 2959, 2933, 1599, 1496 cm^{-1}; MS (EI) 204 (M^+); HRMS calcd for $C_9H_{10}Cl_2O$ (M^+) 204.0109, found 204.0105.

4,5-Dichloropentyl benzoate (36). Prepared from pent-4-enyl benzoate[19] (100 mg, 0.53 mmol) using a procedure similar to that described above for compound **9** that provided the title compound as a colorless oil (118 mg, 99%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, $J = 6.4$, 1.2 Hz, 2H), 7.55−7.54 (m, 1H), 7.44 (dd, $J = 8.0$, 1.6 Hz, 2H), 4.38−4.35 (m, 2H), 4.13−4.10 (m, 1H), 3.79 (dd, $J = 11.0$, 5.0 Hz, 1H), 3.66 (dd, $J = 11.4$, 7.8 Hz, 1H), 2.22−1.84 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4 (C), 132.9 (CH), 130.0 (C), 129.5 (CH), 128.3 (CH), 63.9 (CH_2), 60.4 (CH), 47.9 (CH_2), 31.7 (CH_2), 25.2 (CH_2); IR (neat) 2956, 2849, 1718, 1451 cm^{-1}; MS (EI) 260 (M^+); HRMS calcd for $C_{12}H_{14}ClO_2$ ($M^+ - Cl$) 225.0682, found 225.0700.

2-(2,3-Dichloropropyl)phenol (39). Prepared from 2-allylphenol[20] (100 mg, 0.74 mmol) using a procedure similar to that described above for compound **9** that provided the title compound as a colorless oil (135 mg, 89%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.23−7.16 (m, 2H), 6.94 (dd, $J = 7.4$, 7.4 Hz, 1H), 6.79 (d, $J = 8.0$ Hz, 1H), 5.42 (br s, 1H), 4.53−4.66 (m, 1H), 3.78 (dd, $J = 11.7$, 5.5 Hz, 1H), 3.76 (dd, $J = 11.7$, 5.36 Hz, 1H), 3.35 (dd, $J = 14.0$, 6.0 Hz, 1H), 3.09 (dd, $J = 14.0$, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6 (C), 131.8 (CH), 128.6 (CH), 123.1 (C), 120.9 (CH), 115.5 (CH), 60.3 (CH), 48.4 (CH_2), 36.5 (CH_2); IR (neat) 3540, 2951, 1609, 1502 cm^{-1}; MS (EI) 204 (M^+); HRMS calcd for $C_9H_{10}Cl_2O$ (M^+) 204.0109, found 204.0121.

Butyl 2,3-dichloropropanoate[21] (48). Prepared from *n*-butyl acrylate (50 mg, 0.39 mmol) using a procedure similar to that described above for compound **9** that provided the title compound as a colorless oil (15.5 mg, 20%). ^1H NMR (400 MHz, $CDCl_3$) δ 4.42 (dd, $J = 8.7$, 5.2 Hz, 1H), 4.24 (t, $J = 6.8$ Hz, 2H), 3.96 (dd, $J = 11.1$, 8.7 Hz, 1H), 3.80 (dd, $J = 11.1$, 5.2 Hz, 1H), 1.71−1.64 (m, 2H), 1.44−1.39 (m, 2H), 0.95 (t, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1 (C), 66.5 (CH_2), 55.1 (CH), 43.9 (CH_2), 30.4 (CH_2), 18.9 (CH_2), 13.6 (CH_3); IR (neat) 2936, 1750 cm^{-1}.

General Procedure for the Halogenation of Alkenes and Alkynes Using ICl. Reaction of Methyl-2-propiolate with ICl. To a solution of methyl-2-propiolate **4** (50 mg, 0.60 mmol, 1.0 equiv) in dichloroethane (25 mL) was added iodine monochloride (1.0 M solution in DCM, 0.60 mL, 0.60 mmol, 1 equiv), and the resulting mixture was stirred for 2 h. The reaction was diluted with Et_2O and washed sequentially with $NaHSO_3$ (20 wt % solution), saturated $NaHCO_3$, and brine. The organic phase was then dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The pure product was obtained by flash chromatography eluting with hexanes and then 5% EtOAc in hexanes to give an inseparable mixture of compounds **9**, **10**, **6**, and **7** as a pale yellow oil (100 mg, 68%).

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Supporting Information Available: ^1H NMR spectra for compounds **9**, **12**, **17**, **19**, **20**, **23**, **25**, **26**, **29**, **30**, **33**, **35**, **36**, **39**, **48**, and **54**; summary of ICl control reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

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