Addition of Bromine Chloride and Iodine Monochloride to Carbonyl-Conjugated, Acetylenic Ketones: Synthesis and Mechanisms†

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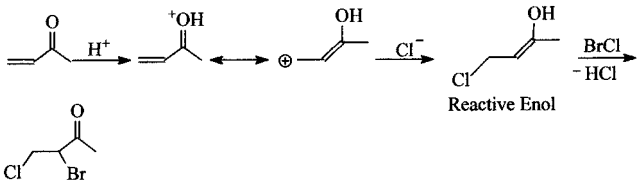
The reactions of 3-butyn-2-one (**1**), 3-hexyn-2-one (**2**), and 4-phenyl-3-butyn-2-one (**3**) with bromine chloride (BrCl) and iodine monochloride (ICl) in CH_2Cl_2, CH_2Cl_2/pyridine, and MeOH are described. The data show that the major products in CH_2Cl_2 are (*Z*)-AM (anti-Markovnikov) regioisomers. With the exception of **3** and ICl, the (*E*)-AM regioisomers predominate when pyridine was added as an acid scavenger. Minor amounts of the M regioisomers were formed with **1** and **2** and BrCl. The percentage of M regioisomer increased significantly with **1** and BrCl in MeOH, but MeOH had little affect on the other reactions. Isolation and stability of the products are discussed. Detailed evidence for the structures of the products, involving a combination of MS, ^{1}H and ^{13}C NMR, and IR, is presented; HRMS analyses are provided as proofs for all of the products. The acid-catalyzed mechanism and the halonium ion mechanism are considered as possible pathways in the formation of the products.

Across the past few years, we have reported on the addition of several unsymmetrical halogen electrophiles to α,*β*-unsaturated olefinic ketones, esters, and aldehydes: Br_2/MeOH,[1] Cl_2/MeOH,[2] *N*-bromosuccinimide (NBS)/MeOH,[3] and BrCl.[4] In these studies, we observed that the amount of anti-Markovnikov (AM)[5] regioisomer was unexpectedly high and was reduced significantly when the reaction was carried out in the presence of an acid scavenger. We attributed the formation of AM regioisomer to an acid-catalyzed mechanism (See Scheme 1, using methyl vinyl ketone), a mechanism that begins with Michael addition of acid (from a trace of acid present in solution) to the carbonyl-conjugated bond via a reactive enol intermediate that is rapidly attacked by halogen leading to AM product and halide ion. Acid scavengers remove the acid, permitting a conventional attack by halogen on the carbon, carbon *π*-bond, via a halonium ion, leading to the anticipated formation of Markovnikov

Scheme 1



(M) regioisomer. Recently, we reported on the reaction of NBS and *N*-iodosuccinimide (NIS) with carbonyl-conjugated alkynes.[6]

In the current investigation, we report on the addition of BrCl and ICl to the following carbonyl-conjugated acetylenic ketones: 3-butyn-2-one (**1**), 3-hexyn-2-one (**2**) and 4-phenyl-3-butyn-2-one (**3**). Our goal was to examine the mechanism of addition, the stability of the vinyl bromo/iodo, chloro ketones and the potential of the reactions for synthesis of these products. None of the products has been reported previously. If the reaction proceeds via an acid-catalyzed mechanism, it would necessitate the involvement of an allenic enol intermediate (see Scheme 3, using 3-butyn-2-one), resulting in a mixture of *E*-/*Z*-, AM regioisomers, because the allenic intermediate would show *E*-/*Z*-stereochemistry. Although the M-regioisomer predominated (90%) with exclusive *E*-stereochemistry in the addition of BrCl to 1-hexyne via a bromonium ion,[7] we anticipated an increase in AM regiochemistry at least with alkynes **1** and BrCl since the bridging in the intermediate halonium ion should be more symmetrical because of the electron-withdrawing effect of the carbonyl group. Schmid et al.[8] have shown

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(1) Heasley, V. L.; Louie, J. T.; Luttrull, D. K.; Millar, M. D.; Moore, H. B.; Nogales, D. F.; Sauerbrey, A. M.; Shevel, A. B.; Shibuya, T. Y.; Stanley, M. S.; Shellhamer. D. F. *J. Org. Chem.* **1988**, *53*, 2199.

(2) Heasley, V. L.; Elliott, S. L.; Erdman, P. E.; Figueroa, D. E.; Krosley, K. W.; Louie, J. T.; Moore, H. B.; Mudge, B. P.; Nogales, D. F.; Nordeen, J.; Oakes, M. L.; Rosbrugh, J. W., Jr.; Sauerbrey, A. M.; Shibuya, T. Y.; Stanley, M. S.; Stewart, C. C.; Shellhamer, D. F.; Heasley, G. E. *J. Chem. Soc., Perkins Trans. 2* **1988**, 393.

(3) Heasley, V. L.; Wade, K. E.; Aucoin, T. G.; Gipe, D. E.; Shellhamer, D. F.; Heasley, G. E. *J. Org. Chem.* **1983**, *48*, 1377.

(4) Heasley, V. L.; Elias, D. S.; Erdman, P. E.; Van Horn, D.; Whitelaw, P. M.; Shellhamer, D. F. *J. Chem. Soc., Perkins Trans. 2* **1996**, 761.

(5) We have used the terms Markovnikov (M) and anti-Markovnikov (AM) as follows: the M regioisomer refers to compounds where the electrophile (Br with BrCl and I with ICl) is on the carbon which is *β* to the carbonyl group; the AM regioisomer has the electrophile on the α carbon.

(6) Heasley, V. L.; Shellhamer, D. F.; Chappell, A. E.; Cox, J. M.; Hill, D. J.; McGovern, S. L.; Eden, C. C.; Kissel, C. L. *J. Org. Chem.* **1998**, *63*, 4433.

(7) Heasley, V. L.; Shellhamer, D. F.; Iskikian, J. A.; Street, D. L.; Heasley, G. E. *J. Org. Chem.* **1978**, *43*, 3139.

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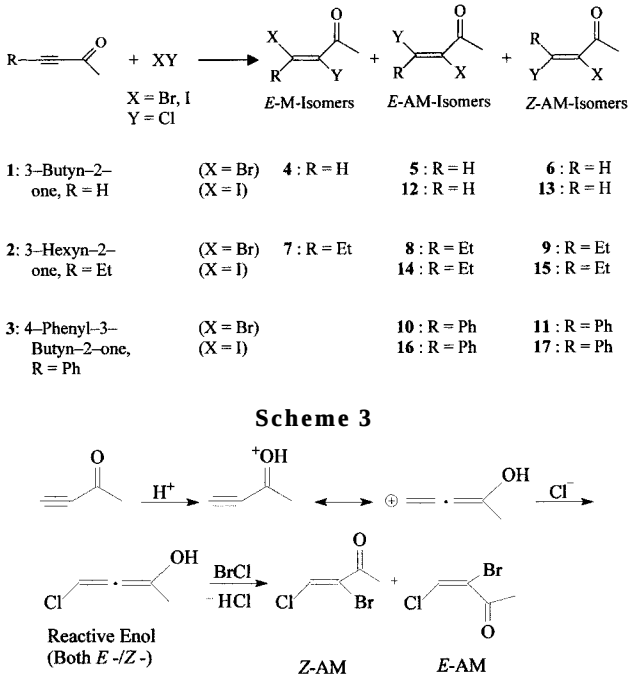
Scheme 2



Scheme 3

that additions of sulfenyl halides to alkynes, which are known to involve symmetrical bridging in the episulfide intermediates, give exclusively AM regioisomers with *E*-stereochemistry. The symmetry of the bridging should be the least with **3** where the benzylic cation should require little bridging for stabilization. Generally speaking, the iodonium ions should have greater symmetry than the bromonium ions, and therefore should give a higher percentage of AM regioisomer.[9,10]

A possible complication in our investigation involved the projected stereochemical instability of the *E*-isomer of the vinyl bromo/iodo, chloro ketones since studies of the analogous dibromide of 3-butyn-2-one (**1**)[11] have shown that the *E*-isomer rearranged readily to the more stable *Z*-isomer. Another study[12] on the bromination of alkynes reported that the *E*-stereoisomer was essentially the only product when the reaction was carried out in the presence of graphite; without graphite or if the products were heated, the *E*-isomer rearranged rapidly to the *Z*-isomer.

Carbonyl-conjugated acetylenic ketones **1**−**3** were not investigated in these studies.[11,12] We were interested in determining whether graphite would have the same effect with BrCl and ketones **1**−**3**, yielding only *E*-stereoisomers. The authors[12] of the study involving graphite suggested that the rearrangement during bromination resulted from a concomitant radical reaction, but they did not probe radical involvement. We intended to use radical inhibitors to examine this aspect of the reaction of BrCl with our alkynes.

Table 1. Products in the Reactions of Alkynes with BrCl and ICl

			products (%)		
alkyne	halogen	conditions	(*E*)-M	(*E*)-AM	(*Z*)-AM
1	BrCl	CH_2Cl_2	6 (**4**)[a]	37 (**5**)	57 (**6**)
1	BrCl	CH_2Cl_2, pyridine	8 [a]	76	16
1	BrCl	CH_2Cl_2, pyridine, heatedst	0	2	98 [a]
1	BrCl	CH_2Cl_2, HCl[b]	0.6	44.2	55.2
1	BrCl	MeOH	49 [c]	35	16
2	BrCl	CH_2Cl_2	4 (**7**)[d]	30 (**8**)	66 (**9**)
2	BrCl	CH_2Cl_2, pyridine	4 [d]	85	11
2	BrCl	MeOH	<1 [d]	80	19
3	BrCl	CH_2Cl_2	0	28 (**10**)	72 (**11**)
3	BrCl	CH_2Cl_2, pyridine	0	64	36
3	BrCl	MeOH	0	27	73
1	ICl	CH_2Cl_2	0	25 (**12**)	75 (**13**)
1	ICl	CH_2Cl_2, pyridine	0	98	2
1	ICl	MeOH	0	62	38
2	ICl	CH_2Cl_2	0	49 (**14**)	51 (**15**)
2	ICl	CH_2Cl_2, pyridine	0	72	28
2	ICl	MeOH	0	80	20
3	ICl	CH_2Cl_2	0	89 (**16**)[c]	11 (**17**)
3	ICl	CH_2Cl_2, pyridine	0	91	9
3	ICl	MeOH	0	41	59

[a] The percentage of (*Z*)-M, based on the ^{1}H NMR of a crude sample, was ca. 2%. [b] HCl ranged in concentration from 0.1 to 0.7 M. M regioisomer decreased with increased acidity. [c] The percentage of (*Z*)-M, based on the ^{1}H NMR of a crude sample, was ca. 10%. [d] The stereochemistry of **7** is uncertain; see the Experimental Section.

Results and Discussion

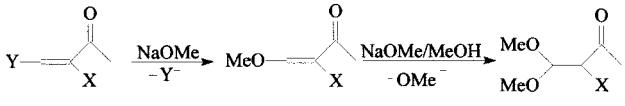
The reactants and the products from our study are summarized in Scheme 2. The percentages of products and the reaction conditions are presented in Table 1. In all cases, the percentages were determined by gas chromatography (GC); many of the isomer ratios were confirmed by NMR analysis on crude samples, establishing that rearrangement was minimal, if at all, in the GC. The structures of products were confirmed by their mass spectra (GC−MS), a combination of ^{1}H, ^{13}C NMR and IR spectra (GC−FTIR) of either individual compounds or isomeric mixtures and exact mass determinations. These data and the proofs for individual structures are described in detail in the Experimental Section. With the exception of **3** and ICl, the data show that the alkynes with BrCl and ICl in CH_2Cl_2 give *Z*-AM regioisomers (*E*- and *Z*- are defined as having the halogens trans and cis, respectively) as the major products, but when pyridine was added as an acid scavenger, the *E*-AM isomer predominated. Methanol (MeOH) as the reaction solvent had a minor affect on several of the product ratios, but in the case of **1** and BrCl the effect was major with a significant increase in *E*-M regioisomer (**4**). The presence of HCl (added as a gas) diminished the amount of M regioisomer (**4**) in the addition of BrCl to **1**. BrCl reacted more rapidly with **1** in CH_2Cl_2/HCl (added as a gas) than with neat CH_2Cl_2. In general, HCl (added as a gas) caused a rearrangement of *E*- to *Z*- stereoisomers.

None of the products reported in Table 1 was stable to distillation, but, with the exception of the products from **3** with BrCl and ICl, compounds could be isolated in high purity by GC collection. At the temperature of the GC collection column, products of **4**/**5**/**6** and **12**/**13** rearranged to give neat **6** and **13**, respectively; the **8**/**9** product mixture enriched during collection to 85% of **9**.

All of the product mixtures were stable to silica chromatography, although some rearrangement occurred. In certain situations, the rearrangement during silica chromatography led to significant enrichment in a par-

(8) Schmid, G. J.; Modro, A.; Lenz, F.; Garratt, D. G.; Yates, K. *J. Org. Chem.* **1978**, *41*, 2331.
(9) Heasley, V. L.; Berry, B. R.; Holmes, S. L.; Holstein, L. S., III; Milhoan, K. A.; Sauerbrey, A. M.; Teegarden, B. R.; Shellhamer, D. F. *J. Org. Chem.* **1988**, *53*, 198.
(10) Shellhamer, D. F.; Allen, J. L.; Allen, R. D.; Bostic, M. J.; Miller, E. A.; O'Neill, C. M.; Powers, B. J.; Price, E. A.; Probst, J. W.; Heasley, V. L. *J. Fluorine Chem.* **2000**, *106*, 103.
(11) Burreson, B. J.; Moore, R. E. *Tetrahedron Lett.* **1975**, *No. 7*, 473.
(12) Kodomari, M.; Sakamoto, T.; Yoshitomi, S. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 4053.

Scheme 4



18: X = Cl
20: X = Br
22: X = I

19: X = Cl
21: X = Br
23: X = I

4: X = Cl; Y = Br: **18**: trace; **19**: 17%

5/6: X = Br; Y = Cl: **20**: 15%; **21**: 68%

12/13: X = I; Y = Cl; **12**: 19%; **23**: 31%

Table 2. Abundancies of Acylium Ions and Vinyl Ions

	ions[a]			ions[a]	
compd	$RC{\equiv}O^+$	R^+	compd	$RC{\equiv}O^+$	R^+
4	2.1	3.7	7	1.0	0.24
5	4.1	4.4	8	4.6	0.73
6	3.5	4.3	9	4.4	0.73

[a] Abundancies of ions are expressed as percentages of the base peaks.

ticular isomer as listed here: product **4/5/6 (**from CH_2Cl_2/pyridine) with hexane gave **5**, 75%/**6**, 25%; product **12**/**13** with hexane produced **12**, 5%/**13**, 95% and with CH_2Cl_2 **12**, 72%/**13**, 28%; product **14**/**15** with hexane yielded **14**, 28%/**15**, 72% and with CH_2Cl_2 **14**, 72%/**15**, 28%. The iodo chloro products after chromatography showed a slight purple color due to loss of iodine.

Surprisingly, the presence of graphite in CH_2Cl_2, which led to almost exclusively *E*-stereoisomers with Br_2 and several alkynes,[12] had no affect on the product composition from **1** and BrCl. Also, the percentage of isomers for **1** and BrCl was unaffected by the presence of the radical inhibitors oxygen (O_2) and 1,3-dinitrobenzene, suggesting that a radical mechanism is not involved in the addition reactions.

The ratios of M/AM regioisomers from the addition of BrCl and ICl to **1** were established by a Michael addition of methoxide (NaOMe) to the vinyl dihalide products (See Scheme 4). Initially, a loss of the β-halogen occurred to give a vinyl methoxy, α− halo ketone, and then (with BrCl products) a second addition of methoxide formed a dimethoxy, α-halo ketone; both the mono- and dimethoxy compounds were present in the product from BrCl. The remaining halogen in the α-position confirmed the M and AM orientation in the original regioisomers (see Scheme 4). This procedure worked only with **1**. The vinyl dihalide from **2** and **3** gave complex mixtures without evidence of Michael addition products. Additional proof for the regiochemistry of the products from alkynes **1** and **2** with BrCl is shown by the abundancies of the acylium and vinyl ions in their mass spectra (Table 2). The abundancies are consistently lower where a chlorine atom with its greater electronegativity is situated adjacent to the charge (acyclium ion) or directly bonded to the vinyl cation. We have no direct proof for the regiochemistry of the products from alkyne **3** and for ICl with alkyne **2**. Our assumption is that these products all have AM regiochemistry. The bases for these assumptions are given in the Experimental Section.

We conclude that our data does not clearly distinguish between the involvement of the acid-catalyzed mechanism and a halonium ion mechanism. For example, the data support the halonium mechanism to some extent with **1** and **2** and BrCl, since the M-regioisomers (**4** and **7**) cannot result from the acid-catalyzed mechanism. On the other hand, the mixture of *E*-/*Z*-AM regioisomers (**5**/**8** and **6**/**9**, respectively) could be derived either directly from the acid-catalyzed mechanism or indirectly from rearrangement of initially formed *E*-AM regioisomer (**5** and **8**) from the halonium ion mechanism. Therefore, the product compositions do not assist in establishing the mechanism. Furthermore, the effect of pyridine can also be interpreted in either of two ways: pyridine may remove acid and eliminate rearrangement of the less stable *E*-AM regioisomer to the more stable *Z*-AM regioisomer; it may prevent the acid-catalyzed mechanism by removing acid which is necessary for the mechanism to occur. The only direct support for involvement of the acid-catalyzed mechanism arises from two sources: the presence of acid increases the rate of reaction and decreases the formation of M-regioisomer.

The greater production of *E*-M regioisomer **5** from the reaction of **1** with BrCl in MeOH must result from an open cation or from a halonium ion, which is weakly bridged with major charge on the α-carbon, with the charge stabilized by MeOH even though the charge is adjacent to the carbonyl group. Apparently the same stabilization by MeOH is not operative in the reaction of **2** with BrCl in MeOH where there is no increase in the *E*-M regioisomer **7**. This lack of effect by MeOH with **2** is probably the result of alternative stabilization of the intermediate ion by the ethyl cation. The intermediate ion from **3** and BrCl should be strongly stabilized by the adjacent phenyl group. The intermediate ion from **1** and ICl is probably stabilized by the greater bonding from iodine in the iodonium ion, and, therefore, does not require stabilization from MeOH.

Experimental Section

Materials. The alkynes **1** and **3**, iodine monochloride (1 M), and methanol (anhydrous) were obtained from Aldrich; **2** was purchased from Lancaster. BrCl was synthesized as reported previously.[4]

Instrumentation. ^{13}C NMR spectra were obtained at 75.4 MHz. Mass spectra data are expressed as *m*/*z* and as relative intensity (%). GC and GC−MS analyses were done with a 25 m ultraperformance column of internal diameter 0.20 mm with a methyl silicone stationary phase of 0.33 mm firm thickness. All IR spectra were prepared in the vapor phase. CG collection was accomplished on a 2.6 m × 1 cm glass column packed with DC 550 on Chromasorb W at 150 °C with a He flow rate of 100 mL/min.

Reaction Conditions and Information. General reaction conditions: 0.5 mmol (0.5) of BrCl (approximately 1 M) or ICl (1 M) in CH_2Cl_2, to avoid the reaction of halogen with the products, was added to 1 mmol of alkyne in 1 mL of CH_2Cl_2. After the reaction was completed (approximately 10−15 min), the product was analyzed directly by GC, GC−MS, and GC−FTIR. Products from reactions in CH_2Cl_2 were prepared as follows for NMR spectra: the solvent was removed under vacuum; except for **3** with BrCl and ICl, products were isolated by GC collection; because of decomposition, $CDCl_3$ was added directly to the products from **3** with BrCl and ICl. In several cases, the *E*-stereoisomer, or enriched *E*-stereoisomers, were obtained by conducting the reaction directly in $CDCl_3$ with pyridine, and obtaining ^1H NMR spectra of these solutions. Yields (%), which were determined by NMR with an internal standard, ranged from 68 to 95 with an average of 82.

Determination of the Effect of Acid (HCl) on the Rate of Reaction of 1 and BrCl. Amounts of **1** and BrCl, comparable to a normal reaction, were dissolved in CH_2Cl or CH_2Cl_2/HCl (gas) and the BrCl remaining after 3 min was

determined iodometrically. The results showed that **1** and BrCl in CH_2Cl_2/HCl reacted approximately twice as rapidly.

Products from 3-Butyn-2-one (1) and BrCl. Compound **4** (*E*-M): the MS of **4**, which is essentially identical to **5** and **6** except for differences in abundancies (Table 2), confirms that **4**−**6** are isomers: GC−MS *m*/*z* (EI) 186, 184, 182 (M, 2.1, 9.0, 6.8), 171, 169, 167 (M − Me, 0.60, 2.5, 2.1) 143, 141, 139, (M − MeCO, 1.1, 4.9, 3.7), 43 (MeCO, 100). The HRMS indicates that the presence of **4** in the isomer mixture does not cause deviation from the correct value. The elimination products resulting from the reaction of methoxide with the regioisomers from the addition in MeOH, which shows a small amount of α-chloro product (ca. 20%), confirms that the M-product is the minor isomer (see Scheme 4). By analogy to the ^{1}H NMR chemical shift of the vinyl proton (6.96 ppm) in the *E*-regioisomer of the dibromide[11] of **1**, we have assigned *E*-stereochemistry to **4**: ^{1}H NMR (300 Hz) δ 2.52 (s, 3H), 6.92 (s, 1H). The ^{1}H NMR spectrum of **4** was prepared on a crude sample also containing **5** and **6** that was obtained from addition of BrCl to **1** in MeOH and isolated as follows without the application of heat: the reaction product in MeOH was added to H_2O, extracted with $CDCl_3$, and an NMR spectrum made directly on this dried solution; the methyl protons of **4** and **6** have identical chemical shifts. Additional proof for the regiochemistry of **4** is shown in Table 2 where a comparison of the abundancies (stabilities) of the acyclium ions and vinyl cations for **4**, **5** and **6** are shown. It is clear that the ions derived from **4** with the chlorine closer to the charge are less stable (less abundant) than those from **5** and **6** where bromine is closer to the charge. The IR spectrum, which is a combination of **4**, **5** and **6** is compatible with the structure of **4**. Regioisomer **4** showed much greater stability to acid than **5** and did not rearrange after standing for several days in HCl/CH_2Cl_2. It decomposed when heated lightly at 65 °C. The proof for the structure of *Z*-M (*Z*-4-bromo-3-chloro-3-butyn-2-one), a minor component, consists entirely of the chemical shift (7.79 ppm) for the vinyl proton in the ^{1}H NMR spectrum. This assignment is based on the fact that the chemical shift is comparable to the vinyl proton in the *Z*-AM regioisomer **6** and that the peak is much larger in the MeOH product. The HRMS supports the *Z*-M regioisomer as an isomer since it does not cause deviation from the correct value.

5 (*E*-AM). The MS of **5**, which is identical to **6**, confirms that it is an isomer: GC−MS *m*/*z* (EI): 186, 184, 182 (M, 2.1, 7.6, 6.2), 171, 169, 167, (M − Me, 1.0, 5.0, 4.1), 143, 141, 139 (M − MeCO, 1.5, 5.0, 4.4), 43 (MeCO, 110). The HRMS indicates that the presence of **5** in the isomer mixture does not cause deviation from the correct value. Since **5** rearranges to **6** in the presence of acid or when heated, by analogy to the stabilities of the *E*-/*Z*-stereoisomers of the dibromides[11] of **1** where the *Z*-stereoisomer is most stable, we have assigned *E*-stereochemistry to **5**. The stereoisomeric assignment of **5** is also supported by its ^{1}H NMR spectrum; the chemical shift of the vinyl proton of **5** and that of the *E*-dibromide[11] of **1** are, respectively: 6.97 and 6.96 ppm. The methyl protons for **5** cannot be specifically confirmed in the spectrum of a mixture of **4**, **5** and **6** and starting material. AM regiochemistry is established by the elimination product from reaction with methoxide in MeOH (Scheme 4) where the α-bromo isomer is major and by the stabilities of the ions in Table 2. The IR spectrum, which is a mixture of **4**−**6**, is compatible with the structure of **5**.

6 (*Z*-AM). The MS (identical with **5**) and ^{1}H and ^{13}C NMR spectra of **6** confirm that it is an isomer: ^{1}H NMR (300 MHz) δ 2.52 (s, 3H), 7.81 (s, 1H); ^{13}C NMR δ 27.2, 128.7, 135.5, 190.1. (The ^{1}H and ^{13}C NMR spectra were made from the GC-collected (heated) sample where **6** is the sole component). The HRMS indicates that the presence of **6** in the isomer mixture does not cause deviation from the correct value. Since **6** is the more stable of the **5**/**6** pair, by analogy to the stabilities of the dibromides[11] of **1**, we have assigned *Z*-stereochemistry to **6**. The stereoisomeric assignment of **6** is also supported by its ^{1}H NMR; the chemical shift of the vinyl proton of **6** and that of the *Z*-dibromide[11] of **1** are, respectively: 7.82 and 8.10 ppm. AM regiochemistry is established by the elimination product with methoxide in MeOH where the α -bromo isomer is major, and by the stabilities of the ions in Table 2. The IR spectrum, which is a mixture of **4**, **5** and **6**, is compatible with structure of **6**. Data for the mixtures of **4**−**6**: IR (cm^{-1}) CO, 1716, C=C, 1565; HMRS (EI) with **4**−**6** present calcd for C_4H_4BrClO 181. 9134, found 181.9129. GC analysis conditions: programmed from 45 to 180 °C at 3 °C/min; retention times (min) for **4**, **5**, and **6**, respectively: 11.3, 11.5, and 11.8.

Products from the Michael Addition/Elimination Reactions of 4−6 with Sodium Methoxide (NaOMe). (See Scheme 4.) The following compounds were identified in product mixtures by EI GC−MS, in two cases by CI GC−MS, and GC−FTIR. **3-Chloro-4-methoxy-3-butyn-2-one (18):** GC−MS *m*/*z* (EI) 136, 134 (M, 12, 36), 121, 119 (M − Me, 27, 82), 43 (MeCO, 100); GC analysis conditions are identical to **4**−**6**, retention time (min) 14.92. **3-Chloro-4,4-dimethoxybutan-2-one (19):** GC−MS *m*/*z* (EI) 137, 135 (M − OMe, 2.2, 6.6), 131 (M − Cl, 37), 75 ($CH(OMe)_2$) 100, 43 (MeCO, 97); GC−MS *m*/*z* (CI) MNH_4 166; IR (cm^{-1}) MeO, 2845, CO, 1740; GC analysis conditions are identical to **4**−**6**, retention time (min): 14.88.

3-Bromo-4-methoxy-3-butyn-2-one (20): GC−MS *m*/*z* (EI) 180, 178 (M, 28, 31), 165, 163 (M − Me, 71, 73), 137, 135 (M − MeCO, 3.0, 2.9), 43 (MeCO, 100); IR (cm^{-1}) MeO, 2852, CO, 1700, C=C,1614; GC analysis conditions are identical to **4**−**6**, retention time (min) 19.2.

3-Bromo-4,4-dimethoxybutan-2-one (21): GC−MS *m*/*z* (EI) 181, 179 (M − OMe, 5.3, 5.3), 131 (M − Br, 3.7), 75 ($CH(OMe)_2$), 100, 43 (MeCO, 97); GC−MS *m*/*z* (CI) MNH_4 210; IR (cm^{-1}) MeO, 2844, CO, 1736; GC analysis conditions are identical to **4**−**6**, retention time (min) 18.6.

Products from 3-Hexyn-2-one (2) and BrCl. 7 (*E*-M): the major proof for the structure of **7** is the MS, which is similar to the mass spectrum of **7** and **8** confirming that is an isomer: GC−MS *m*/*z* (EI) 214, 212, 210 (M, 0.24, 1.2, 0.26) 199, 197, 195 (M − Me, 0.39, 0.90, 1.0), 171, 169, 167 (M − MeCO, 0.37, 0.63, 0.24) 133, 131 (M − Br, 6.3. 18). 43 (MeCO, 100). The HRMS indicates that the presence of **7** in the isomer mixture does not cause deviation from the correct value. The regiochemistry of **7** is supported by the stabilities of the acyclium and vinyl cations as shown in Table 2; again, the cations with the charges located adjacent to chlorine are less stable.

We have no direct proof for the stereochemistry of **7**. Since it is a minor product and was not isolated, the suggestion of *E*-stereochemistry for **7** was based on the fact that it is formed when the reaction is done in the presence of pyridine, and our data show that pyridine leads primarily to *E*-stereochemistry.

8 (*E*-AM): the mass spectrum of **8**, which is essentially identical to **9** and establishes that they are stereoisomers, confirms that it is an isomer: GC−MS *m*/*z* (EI): 214, 212, 210 (M, 2.4, 9.6, 7.7), 199, 197, 195 (M − Me, 1.4, 6.0, 4.6) 171, 169, 167 (M − MeCO, 0.04, 0.70, 0.54), 133, 131 (M − Br, 0.024, 0.042), 43 (MeCO, 100). The ^{1}H NMR spectrum of **8**, (some of **9** is present) obtained from a crude sample by addition of BrCl to **2** in $CDCl_3$ and pyridine with minimal rearrangement, supports the proposed structure: ^{1}H NMR (300 MHz) δ 1.20 (t, 3H, J = 7.5 Hz), 2.48 (s, 3H), 2.67 (q, 2H, J = 7.5 Hz). The ^{13}C NMR spectrum, obtained from a GC-collected sample, contained a mixture of both **8** and **9**: ^{13}C NMR δ 11.0, 12.9, 28.9, 30.2, 31.6, 32.3, 114.4, 118.8, 136.5, 150.0, 194.9, 195.4. The regiochemistry of **8** and **9** is supported by the stabilities of the acyclium and vinyl cations in Table 2. By analogy to the results from alkyne **1** and BrCl, the *E*-stereochemistry for **8** is suggested by the data showing that it becomes the major isomer when the reaction is conducted in the presence of pyridine and rearranges to **9** when heated.

9 (*Z*-AM). The MS (reported with **8**) and the ^{1}H and ^{13}C NMR spectra (reported with **8**) support the structure: ^{1}H NMR (300 MHz) (a mixture with **8**) 1.21 (t, 3H, J = 7.2 Hz), 2.52 (s, 3H), 2.74 (q, 2H, J = 7.2 Hz). Heating during GC collection increased the amount of *Z*-AM (**9**) by 20%, indicating the greater stability of the *Z*-isomer. The IR spectra of **8** and **9** are, respectively: **8** (cm^{-1}) CO, 1710; C=C, 1580; **9** (cm^{-1}) CO, 1726; C=C, 1614. The HRMS for **7**/**8**/**9**: HRMS M^+ calcd for C_6H_8BrClO 209.9447, found 209.9446. GC analysis condi-

tions: programmed from 45 to 200 °C at 5 °C/min; retention times (min) for **7**, **8** and **9**, respectively: 11.6, 11.7 and 11.3.

Products from 4-Phenyl-3-butyn-2-one (3) and BrCl. The mass spectra of **10** and **11** are essentially identical, suggesting that they are stereoisomers: GC−MS *m/z* (EI) 262, 260, 258 (M, 31, 100, 76), 247, 245, 243 (M − Me, 16, 19), 217, 215 (M − MeCO, 5.8 5.9), 182, 180 (M − MeCO, − Cl, 35, 38), 138,136 (M − MeCO, − Cl, 15, 38) 43 (MeCO, 83). Attempts to identify the β-halogen (chloride) by solvolysis in MeOH/H_2O, MeOH, MeOH/Ag^+ failed because of nonreactivity. The assumption was made that **10**/**11** are AM regioisomers since the major isomers from alkynes **1** and **2** have AM regiochemistry, and there is no reason for M regioisomer to predominate here since an acid-catalyzed mechanism would produce AM regioisomers and involvement of a stable benzylic cation (or a partially bridged bromonium ion) would lead to chloride ion attack at the β-position, giving an AM regioisomer. By analogy to the results from alkyne **1**, the *E*-stereochemistry for **10** is suggested by the data showing that it becomes the major isomer when the reaction is conducted in the presence of pyridine. All attempts at obtaining a ^{1}H NMR spectrum of the *E*-stereoisomer from a crude sample, obtained by addition of BrCl to **3** in $CDCl_3$ with pyridine without further workup, failed because of rapid rearrangement to the equilibrium mixture. The ^{1}H and ^{13}C NMR spectra for **10**/**11**, prepared on a crude sample because of extensive decomposition during GC collection, showed a mixture of isomers: ^{1}H NMR (300 MHz) (isomers) δ 2.07 (s, 3H), 2.11 (s, 3H), 7.37−7.42 (m, 5H); ^{13}C NMR δ 27.5, 29.3, 29.4 (impurity or starting compound for one of the peaks), 121.3, 126.9, 127.2, 128.2, 128.5, 128.6, 129.6, 129.8, 130.0, 130.4, 130.6, 130.9, 131.1, 136.3, 136.5, 140.5, 141.2 (impurity or starting compound for one of the peaks), 193.8, 195.5; IR (cm^{-1}) for a mixture of **10**/**11** CO, 1723, C═C, 1584; HRMS (EI) for a mixture of **10**/**11** M^+ − 1(H) calcd for $C_{10}H_7BrClO$ 256.9369, found 256.9371; GC analysis conditions are identical to **7**−**9**, retention times (min) 23.7 and 23.8.

Products from 3-Butyn-2-one (1) and ICl. The mass spectra of **12** and **13** are essentially identical, suggesting that they are stereoisomers: GC−MS *m/z* (EI) 230, 232 (M, 5.1, 15), 217, 215 (M − Me, 2.9, 8.8), 189, 187 (M − MeCO, 1.9, 5.5), 105, 103 (M − Cl, 1.2, 3.6), 43 (MeCO, 100). The elimination product from the addition in CH_2Cl_2 showed only α-iodo product and, therefore, confirmed the exclusive formation of AM-regioisomer. Since **12** readily rearranges to **13**, by analogy to the stabilities of the *E*-/*Z*-stereoisomers of the dibromides of **1** where the *Z*-stereoisomer is most stable and the relative positions of the vinyl protons in the dibromides,[11] we have assigned *E*-stereochemistry to **12**. The ^{1}H NMR spectrum of **12** was made on a sample from the addition of ICl to **1** in $CDCl_3$ without further workup: ^{1}H NMR (60 MHz) spectrum for **12** 2.56 (s, 3H), 7.01 (s,1H). The percentages of **12**/**13** in the ^{1}H NMR spectrum was the same as in the GC analysis confirming no rearrangement during GC analysis. Because of rearrangement in the hot GC detector (GC collected), only **13** was present in the sample used for ^{1}H and ^{13}C NMR spectra: ^{1}H NMR (300 MHz) δ 2.58 (s, 3H), 7.80 (s, 1H); ^{13}C NMR 26.4, 113.3, 142.3, 191.0; IR (cm^{-1}) for a mixture of **12**/**13** CO, 1709, C═C, 1551; HRMS (EI) for a mixture of **12**/**13** calcd for C_4H_4ClIO 229.9008, found 229.9007; GC analysis conditions are identical to **7**−**9**, retention times (min) 10.2 and 11.2.

Products from the Michael Addition/Elimination Reactions of 12 and 13 with NaOMe. (See Scheme 4.) The following compounds were both identified in product mixtures by EI GC−MS. **3-Iodo-4-methoxy-3-butyn-2-one (22):** GC−MS *m/z* (EI) 226 (M, 74), 211 (M − Me, 97), 183 (M − MeCO, 7.3), 99 (M − I, 38), 43 (MeCO, 100). GC analysis conditions: programmed from 45 to 200 °C at 5 °C/min; retention time (min): 16.0. **3-Iodo-4,4-dimethoxybutan-2-one (23):** GC−MS *m/z* (EI) 227 (M − MeO, 11) 185 (M − MeO, − C_2H_2O, 14) 169 (M − MeO, − C_2H_2O, − CH_4, 32), 131 (M − I, 41), 75 CH(OMe)$_2$, 100) 43 (MeCO, 19); GC analysis conditions are identical to 3-iodo-4-methoxy-3-butyn-2-one; retention time (min) 16.9.

Products from 3-Hexyn-2-one (2) and ICl. The mass spectra of **14** and **15** are essentially identical, suggesting that they are stereoisomers: 260, 258 (M, 5.9, 22), 245, 243 (M − Me, 1.2, 4.9) 223 (M − Cl, 2.7), 180 (M − Cl, − MeCO, 3.3), 133, 132 (M − I, 3.3 10.9), 43 (MeCO, 100).

The assumption was made that **14** and **15** are AM stereoisomers since the major isomers from alkynes **1** and **2** with BrCl and **1** with ICl were AM, and there is no reason for M regioisomer to predominate here since an acid-catalyzed mechanism would produce AM regioisomers and involvement of a relatively stable ethyl cation (or a partially bridged iodonium ion) would lead to chloride ion attack at the β-position, giving an AM regioisomer. By analogy with the stabilities of the products from the other alkynes where the *E*-isomer is less stable than the *Z*-isomer, *E*-stereochemistry is assumed for **14** since it is the major isomer when the reaction is conducted with pyridine. The^{1}H NMR (300 MHz) spectrum of a crude sample (mainly **14** with some **15** also present) from addition of ICl to **2** in $CDCl_3$ with pyridine is: ^{1}H NMR 1.18 (t,3H, J = 9.0 Hz), 2.45 (s, 3H), 2.63 (q, 2H, J = 9.3 Hz). Heating during GC collection increased the amount of *Z*-AM (**15**) by approximately 10%, indicating the greater stability of the *Z*-isomer. The ^{1}H NMR (300 MHz) spectrum of **15** in a mixture with **14**: 1.19 (t, 3H, J = 9.3 Hz), 2.56 (s, 3H), 2.72 (q, 2H, J = 9.0 Hz). ^{13}C NMR spectra of a mixture of **14** and **15**: 11.3, 13.2, 27.6, 29.5, 31.3, 35.4, 90.7 97.3, 136.4, 151.1, 197.6, 197.9. IR (cm^{-1}) of **14**: CO, 1723; C═C, 1600. IR (cm^{-1}) of **15**: CO, 1710; C═C, 1579. HRMS (EI) of a mixture of **14**/**15**: M^+ calcd for C_6H_8ClIO 257.9308, found 257.9305. GC analysis conditions are identical to **7**−**9**: retention times (min) for **14** and **15**, respectively, 14.4 and 14.8.

Products from 4-Phenyl-3-butyn-2-one (3) and ICl. The mass spectra of **16** and **17** are essentially identical, suggesting that they are stereoisomers: GC−MS *m/z* (EI): 308, 306 (M, 0.25, 0.77), 307, 305 (M − H, 40, 100), 293, 291 (M − Me, 8.1, 24), 271 (M − Cl, 2.2), 228 (M − Cl, − MeCO, 45), 138, 136 (M − I, − MeCO, 7.3, 22), 43 (MeCO, 100). Attempts to identify the β-halogen (chloride) by solvolysis in MeOH/H_2O, MeOH, MeOH/Ag^+ failed because of nonreactivity. The assumption was made that **16** and **17** are AM regioisomers since the major isomers from alkynes **1** and **2** with BrCl and **1** with ICl were AM, and there is no reason for M-regioisomer to predominate here since an acid-catalyzed mechanism would produce AM regioisomers and involvement of a stable benzylic cation (or a partially bridged iodonium ion) would lead to chloride ion attack at the β -position, giving an AM regioisomer. The stereochemistry is uncertain for **16** and **17**. *E*-Stereochemistry has been assigned to product **16** because it is the major product in pyridine, although pyridine has little affect on this reaction. The ^{1}H and ^{13}C NMR spectra, prepared on a crude reaction product without further workup because of extensive decomposition during GC collection, showed only one isomer, presumably **16**: ^{1}H NMR (300 MHz) δ 2.54 (s, 3H), 7.39−7.41 (m, 5H); ^{13}C NMR δ 27.3, 92.3, 128.4, 128.8, 129.8, 130.9, 138.2, 198.0; IR (cm^{-1}) of **16** CO, 1725, C═C, 1590; IR (cm^{-1}) of **17** CO, 1717, C═C, 1575; HRMS (EI) of a mixture of **16**/**17** M^+ − 1(H), calculated for $C_{10}H_7ClIO$, 304.9230, found 304.9244. GC analysis conditions; programmed from 100 to 200 °C and 5 °C/min; retention times (min) for **16** and **17**, respectively: 15.5 and 15.7.

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Supporting Information Available: NMR, IR, and mass spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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