A Novel Regio- and Stereospecific Hydrohalogenation Reaction of 2-Propynoic Acid and Its Derivatives

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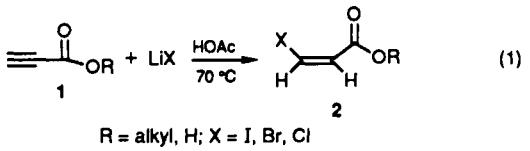
2-Propynoic acid and its derivatives are hydrohalogenated regio- and stereospecifically by reaction with lithium halides in acetic acid, or preferably with 1 equiv of acetic acid in refluxing CH_3CN, to afford the thermodynamically unfavorable (*Z*)-3-halopropenoic acids and their derivatives as sole products. A rationale for the regio- and stereospecificity is briefly discussed.

Introduction

Selectivity provides a formidable challenge for synthetic chemists. Thus, a new synthesis of pure geometrical isomers at a double bond, especially those in the thermodynamically unfavorable *Z* configuration, would be a significant advance. 3-Halopropenoic acids and their derivatives have proved to be valuable intermediates in organic synthesis owing to the presence of three functional groups, i.e., the C—X bond, the conjugated C=C bond, and the carbonyl group.[1] Usually such compounds are prepared as *Z* and *E* isomeric mixtures. Only a few stereoselective synthetic methods have been reported, most of which are for *E* isomers. During our study of palladium(II)-catalyzed cyclization reaction of 4'-iodobut-2'-enyl 2-propynoate,[2] we found that addition of lithium iodide in acetic acid to the reaction mixture gave (*Z*)-3-halopropenoate.[3] Similarly ethyl 2-propynoate (**1a**) with lithium iodide afforded ethyl (*Z*)-3-iodopropenoate (**2a**) with or without the use of palladium(II) acetate.[3] In this paper, we wish to describe in detail the hydrohalogenation reaction of 2-propynoate esters and 2-propynoic acid along with other 2-propynoic acid derivatives.

Results and Discussion

Reaction of 2-Propynoates with Lithium Halides. Reaction of ethyl 2-propynoate (**1a**) with lithium halides in acetic acid at 70 °C (method A) gave *Z* isomers (**2**) stereospecifically, eq 1, though results with substituted 2-alkynoates were poor.[3] Reaction of 2-propynoic acid with lithium halides in acetic acid also afforded (*Z*)-halopropenoic acids,[3] compounds reported to have defoliating and plant growth regulating activities.[4]

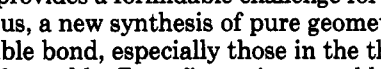


1 2 (1)

R = alkyl, H; X = I, Br, Cl

Further studies showed that both the stereoselectivity and yield depended on the reaction temperature. The reaction occurred slowly at ambient temperature and more efficiently at 50–70 °C; at temperatures above 90 °C, a minute amount of the *E* isomer could be detected and the yields were lower.

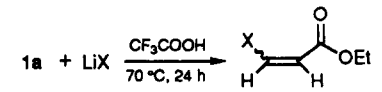
Table I. Reaction of 1a with Lithium Bromide and Acetic Acid in Different Solvents[a]



entry	solvent	reaction condition	convn (%)
1	C_6H_6	70 °C	38
2	$CHCl_3$	70 °C	44
3	THF	reflux	44
4	1,4-dioxane	70 °C	22
5	CH_3CN	reflux	82
6	HOAc	70 °C	85
7	DMF	70 °C	11[b]
8	HMPA	70 °C	<3[b]

[a] Mole ratio of 1a:LiBr:HOAc = 1:1.1:1.1, solvent: 1 mL. [b] A complicated mixture of products was obtained.

Reactions in trifluoroacetic acid gave 3-halopropenoates as mixtures of *Z* and *E* isomers in low yields as shown in eq 2. In contrast, both TLC and ^1H NMR spectra showed that no detectable *E* isomer was formed during the reaction in acetic acid.



(2)

	yield (%)	*Z*/*E* (isolated)
X = I	30	5/2
Br	22	5/3

Reaction of **1a** with lithium bromide in aprotic solvents for 24 h followed by hydrolysis with dilute HOAc did not afford the expected product, ethyl (*Z*)-3-bromopropenoate (**2b**). When the reaction was carried out in the presence of 1.1 equiv of HOAc, **2b** was formed in some solvents as shown in Table I. Especially in refluxing CH_3CN, the preparation of **2b** occurred smoothly with high conversion and high stereoselectivity (method B). For 2-propynoic acid, the reaction proceeded smoothly even in the absence of HOAc. This synthesis of (*Z*)-3-halopropenoic acids and their derivatives (method B) is preferred to the former one (method A) in which a large amount of alkali must be employed to neutralize the solvent acetic acid. Table II shows that method B can be used to prepare a wide range of (*Z*)-halopropenoic acids and (*Z*)-3-propenoates.

Reaction of 2-Propynamides with Lithium Halides. Aminolysis of the corresponding acyl chlorides (prepared from 3-halopropenoic acids[5,6]) gives *Z* and *E* isomeric

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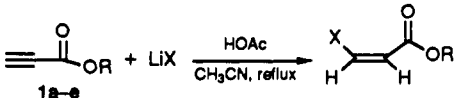
Table II. Reaction of 2-Propynoic Acid or 2-Propynoates with Lithium Halides and Acetic Acid in Refluxing Acetonitrile (Method B)

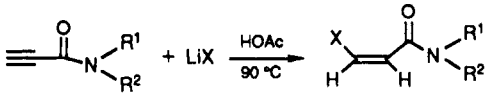


1a–e 2a–n

entry	substrate no.	R	time (h)	product no.	X	isolated yield (%)
1	1a	Et	21	2a	I	87 (91)[3]
2	1a		22	2b	Br	82 (85)[3]
3	1a		24	2c	Cl	80 (80)[3]
4	1b	Me	20	2d	I	91 (94)
5	1b		23	2e	Br	75 (99)
6	1c	allyl	21	2f	I	88 (97)[15]
7	1c		23	2g	Br	86 (94)[15]
8	1c		25	2h	Cl	82 (78)[15]
9	1d	propargyl	20	2i	I	67[a] (11)[15]
10	1d		21	2i	I	79[b] (78)[15]
11	1d		22	2j	Br	99 (99)[15]
12	1d		26	2k	Cl	75 (75)[15]
13	1e	H	24	2l	I	81 (89)[3]
14	1e		24	2m	Br	93 (93)[3]
15	1e		24	2n	Cl	85 (89)[3]

[a] 2,3-Diiodoprop-2-en-1-ol was isolated in 8% yield.[15] [b] The reaction was carried out in the atmosphere of nitrogen.[15] [c] The figures in the parentheses represent the yields using method A.

Table III. Synthesis of (*Z*)-3-Halopropenamides (4) by Hydrohalogenation of 2-Propynamides (3) with Lithium Halides in Acetic Acid at 90 °C (Method A)



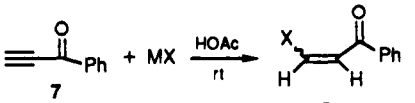
3a–c 4a–l

entry	reactant no.	R^1	R^2	time (h)	product no.	X	yield (%)[a]
1	3a	H	H	22	4a	I	98
2	3a			22	4a		79[b] (80)
3	3a			22	4b	Br	95
4	3a			22	4b		85[b] (79)
5	3a			22	4c	Cl	98
6	3a			22	4c		80[b] (75)
7	3b	H	Et	24	4d	I	91
8	3b			24	4e	Br	85
9	3b			24	4f	Cl	91
10	3c	Me	Me	24	4g	I	67 (52)
11	3c			36	4g		65[c]
12	3c			24	4h	Br	49
13	3c			48	4i	Cl	36

[a] The figures in the parentheses represent the yield using method B. [b] The reaction was carried out at 70 °C. [c] 2.2 equiv of LiI was used.

mixtures of 3-halopropenamides. Reaction of 3-(dimethylamino)prop-2-yn-1-al with HX (X = Br or Cl), followed by rearrangement was reported to afford *N,N*-dimethyl-(*E*)-3-halopropenamides.[7] (*Z*)-3-Halopropenamides could also be prepared by hydrolysis of (*Z*)-3-halo-2-propenenitriles.[8] To our knowledge, direct hydrohalogenation of 2-propynamides has been reported only once in the literature.[6] We found that the reaction of 2-propynamides (3) with lithium halides in acetic acid at 90 °C also afforded (*Z*)-3-halopropenamides (4) with high stereoselectivity in good yields (Table III).

Table IV. Reaction of 1-Phenyl-2-propynone (7) with Metal Halides in Acetic Acid at rt



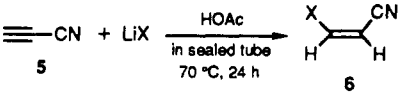
7 8a–c

entry	MX	time	product no.	X	isolated yield (%) *Z* isomer	*E* isomer
1	LiI	12 h	8a	I	6	60
2	NaI	50 min	8a		24	30
3	NaI	2 h	8a		8	50
4	NaI	24 h	8a		0	35
5	LiBr	33 h	8b	Br	27	15
6	LiCl	26 h	8c	Cl	45	9
7[a]	LiCl	24 h		–	0	0

[a] The reaction was carried out at 70 °C.

At 70 °C, hydrohalogenation was stereospecific but slower than at 90 °C (Table III, entries 2, 4, and 6). Assignment of stereochemistry of (*Z*)-3-halopropenamides 4 is based on the coupling constant of the two vicinal vinyl protons (J = 8.4 Hz) shown in 200-MHz ^{1}H NMR spectra and by comparison of their melting points with the literature values.[5b,8] The *E* isomers were not detected. Generally, (*Z*)-3-iodopropenamides are not easily prepared, but using the present methodology, **4a**, **4d**, and **4g** can be obtained conveniently (Table III, entries 1, 2, 7, 10, and 11). Although reaction of *N,N*-dimethyl-2-propynamide (**3c**) with lithium halides gave the products in lower yields (Table III, entries 10–13), the stereoselectivity was still high and no other products were detected. Using method B, (*Z*)-3-halopropenamides were obtained in lower yields (Table III).

Reaction of 2-Propynenitrile with Lithium Halides. (*E*)-3-Iodo-2-propenenitrile has been prepared from reaction of 1,2-diiodoethylene with copper(I) cyanide.[9] Hydrohalogenation of 2-propynenitrile (**5**) with lithium halides in acetic acid also gave (*Z*)-3-halopropenenitriles (**6**) exclusively in good yields (eq 3). Because of the regio- and stereospecificity, simple procedure, and high yields, this method is superior to hydrohalogenation of 2-propynenitrile with HX (X = Br, Cl)[10] or dehydration of the corresponding amides.[5] The stereochemistry of **6** was assigned by ^{1}H NMR spectral analysis as previously described for the analogous compounds (**4**).



5 6 (3)

	yield (%)
a: X = I	98
b: X = Br	86
c: X = Cl	85

Reaction of 1-Phenyl-2-propynone with Metal Halides. Reaction of 1-phenyl-2-propynone (**7**) with metal halides occurred at rt (Table IV). Reaction of **7** with lithium chloride in acetic acid at 70 °C did not afford the expected product, 3-chloro-1-phenylpropenone (**8c**) (Table IV, entry 7), probably owing to the polymerization of both **8c** and **7**. The same reaction at rt proceeded with high *Z*

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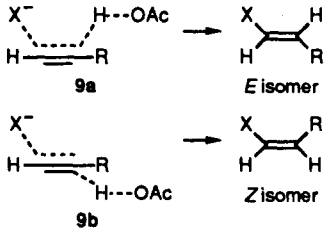
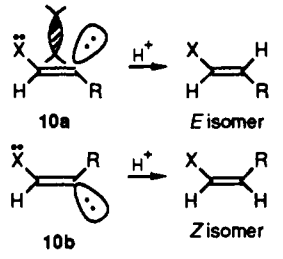
Scheme I



Scheme II



selectivity (Table IV, entry 6). Using NaI or LiI, the reaction at rt afforded both *Z* and *E* isomers of 3-iodo-1-phenyl-2-propenone (**8a**). With longer reaction time, the *Z* isomer converted gradually to the thermally more stable *E* isomer. The results are similar to that reported by Taniguchi et al.[11]

Mechanism. The high stereospecificity of this reaction ruled out the possibility of direct HX addition to the propynoates in HOAc, which is reported to show low stereoselectivity.[5a,6,10,12] On the other hand, the regiospecific attack of halide ion at C-3 carbon atom of the electron-deficient carbon–carbon triple bond indicates a nucleophilic addition mechanism.[13,14] This nucleophilic addition mechanism is also consistent with the different reactivities of the carbon–carbon multiple bonds in allyl or propargyl 2-propynoates toward lithium halides in acetic acid, in which the electron-deficient carbon–carbon triple bond is hydrohalogenated while the electron-rich multiple bond remains intact.[15]

A mechanism involving contact ion pairs between Li^+ and X^- and the coordination of Li^+ with the carbonyl oxygen atom has been postulated to explain the stereospecificity.[3] When less easily coordinated cations, such as sodium bromide or tetrabutylammonium bromide were used, the reaction of **1a** still afforded **2b** with high stereoselectivity. Furthermore, it is very difficult to imagine a six-membered transition state[3] for the reaction of 2-propynenitrile (**5**) with lithium halides. The above two observations indicate that the stereospecificity cannot be attributed to a simple coordination effect.

In both methods A and B the use of terminal electron-deficient acetylene derivatives, lithium halides, and acetic acid are all crucial; thus, a termolecular transition state might be responsible for the high *Z* stereospecificity. The transition state, in which the halide ion and acetic acid are on the same side of the carbon–carbon triple bond, i.e., **9a**, is considered to be unfavorable owing to steric hindrance. Thus, the reaction might occur through the less crowded transition state **9b**, in which the halide ion and acetic acid are on opposite sides of the carbon–carbon triple bond to form the *Z* isomer (Scheme I).

On the other hand, the postulated stereoelectronic effect of the vinyl anion intermediate,[16] formed by the nucleophilic addition of halide ion to the electron-deficient carbon–carbon triple bond, may be responsible for the observed stereospecificity. Repulsion of the electron pairs on the halogen atom and the electron pair of the carbanion makes the *E* intermediate **10a** unstable, while in *Z* intermediate **10b** the two relevant pairs are far away from each other. Thus, the reaction occurs through the more stable *Z* intermediate **10b** to form the *Z* isomer as the sole product (Scheme II).

In the case of the propynones, it seems unlikely that the *Z* and *E* mixtures might result from isomerization of allenol intermediates formed by the Michael addition of the halide ion to the carbon–carbon triple bonds, followed by protonation.[11] Usually, the isomerization of allenols gives the thermally stable *E* isomer instead of a *Z* and *E* mixture. We propose that the *Z* isomer might also be formed initially during the reaction by a mechanism similar to that of the 2-propynoates. However, the *Z* isomers might isomerize to *E* isomers when heated in the presence of an acid.[17] The experiments show that the 1-phenyl-3(*Z*)-iodo-2-propenone ((*Z*)-**8a**) is transformed into the *E* isomer slowly on standing at 35 °C and somewhat faster in HOAc. After 4 h in the presence of 9% of NaI in HOAc, the *E* isomer was isolated in 77% yield along with 3% of *Z* isomer recovered.

Experimental Section

Materials. 2-Propynoic acid,[18] ethyl or methyl 2-propynoate,[19] 2-propynamide,[19] *N*-ethyl-2-propynamide,[20] *N,N*-dimethyl-2-propynamide,[20] 2-propynenitrile,[19] and ethynyl phenyl ketone[21] were prepared by literature methods. Allyl or propargyl 2-propynoates were synthesized by azeotropic distillation of 2-propynoic acid and allyl or propargyl alcohol under the catalysis of concentrated H_2SO_4 in benzene in 57% and 66% yield, respectively.

All salts were dried at 100 °C over P_2O_5. All compounds were obtained as colorless liquids unless a melting point is given. The analytical samples of liquid were further purified by Kugelrohr distillation at the specified oven temperature (ot).

Reaction of Lithium Halides with 2-Propynoates in Acetic Acid (Method A). Typical Procedure. Ethyl (*Z*)-3-Iodopropenoate (2a). A mixture of ethyl 2-propynoate (100 mg, 1 mmol) and LiI (150 mg, 1.1 mmol) in acetic acid (1 mL) was stirred and heated at 70 °C. The reaction was monitored by GLC (after neutralization). After 15 h, water (5 mL) was added. The mixture was neutralized with solid K_2CO_3 until no CO_2 was evolved and then extracted with ether (3 × 10 mL). The extracts were dried ($MgSO_4$), and the product **2a** was obtained by preparative TLC on silica gel using petroleum ether/ethyl acetate (10:1) as the

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solvent; yield 210 mg (91%). Spectral data are identical with the reported data.[22]

Reaction of 2-Propynoates and Lithium Halides and Acetic Acid in Refluxing CH_3CN (Method B). Typical Procedure. Ethyl (*Z*)-3-Iodopropenoate (2a). A mixture of ethyl 2-propynoate (100 mg, 1 mmol), LiI (150 mg, 1.1 mmol), and acetic acid (65 mg, 1.1 mmol) was refluxed in CH_3CN (1 mL) for 21 h. A similar workup procedure as above gave **2a** in pure form; yield 200 mg (87%).

The following compounds were prepared similarly. The *Z* and *E* isomers of ethyl 3-halopropenoates could be separated either by TLC using petroleum ether/ethyl acetate (10:1) as the eluent or GC analysis with a column of OV-1 at 70 °C. Spectral data of ethyl (*E*)-3-iodopropenoate,[22] ethyl (*Z*)-3-bromopropenoate (**2b**),[22] ethyl (*E*)-3-bromopropenoate,[22] ethyl (*Z*)-chloropropenoate (**2c**),[22] methyl (*Z*)-iodopropenoate (2d),[23] and methyl (*Z*)-3-bromopropenoate (**2e**)[23] are identical with those in the literature.

Allyl (*Z*)-3-iodopropenoate (2f): ot 90–92 °C (7 mmHg); IR (neat) 3050, 1710, 1625, 1600, 1195, 1150 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 7.47 (d, J = 8.40 Hz, 1 H), 6.90 (d, J = 8.40 Hz, 1 H), 6.40–5.00 (m, 3 H), 4.60 (d, 2 H); MS m/e (%) 240 (4.62), 239 (M^+ + 1, 21.45), 238 (M^+, 25.46), 195 ($M^+ - C_3H_7$, 8.38), 182 ($M^+ - OC_3H_4$, 100.00), 153 ($M^+ - CO_2C_3H_5$, 12.89), 111 ($M^+ - I$, 9.66). Anal. Calcd for $C_6H_7IO_2$: C, 30.28; H, 2.96. Found: C, 30.04; H, 2.78.

Allyl (*Z*)-3-bromopropenoate (2g): ot 65–67 °C (7 mmHg); IR (neat) 3050, 1715, 1625, 1605, 1200, 1160 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.03 (d, J = 8.40 Hz, 1 H), 6.60 (d, J = 8.40 Hz, 1 H), 6.43–5.00 (m, 3 H), 4.60 (d, 2 H); MS m/e (%) 193 ($M^+(^{81}Br)$ + 1, 25.99), 191 ($M^+(^{79}Br)$ + 1, 25.39), 134 ($M^+ - OC_3H_4$, 100.00), 111 (M^+ - Br, 10.06). Anal. Calcd for $C_6H_7BrO_2$: C, 37.73; H, 3.69. Found: C, 37.70; H, 3.33.

Allyl (*Z*)-3-chloropropenoate (2h): ot 100–102 °C (15 mmHg); IR (neat) 3080, 1730, 1650, 1620, 1220, 1165 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 6.55 (d, J = 8.40 Hz, 1 H), 6.40–5.00 (m, 4 H), 4.60 (d, 2 H); MS m/e (%) 149 ($M^+(^{37}Cl)$ + 1, 14.52), 148 ($M^+(^{37}Cl)$, 3.85), 147 ($M^+(^{35}Cl)$ + 1, 35.05), 146 ($M^+(^{35}Cl)$, 2.63), 131 ($M^+(^{37}Cl)$ - OH, 3.17), 129 ($M^+(^{35}Cl)$ - OH, 10.56), 111 (M^+ - Cl, 3.91), 91 ($M^+(^{37}Cl) - OC_3H_5$, 47.30), 89 ($M^+(^{35}Cl) - OC_3H_5$, 100.00). Anal. Calcd for $C_6H_7ClO_2$: C, 49.07; H, 4.81. Found: C, 48.43; H, 4.47.

Propargyl (*Z*)-3-iodopropenoate (2i): ot 83–85 °C (2 mmHg); IR (neat) 3225, 2100, 1710, 1600, 1190, 1150 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.55 (d, J = 8.40 Hz, 1 H), 6.90 (d, J = 8.40 Hz, 1 H), 4.70 (d, 2 H), 2.40 (t, 1 H); MS m/e (%) 237 (M^+ + 1, 1.35), 236 (M^+, 20.19), 192 ($M^+ - CO_2$, 7.07), 182 (3.36), 181 ($M^+ - OC_3H_3$, 100.00), 153 ($M^+ - CO_2C_3H_3$, 26.30), 127 (I^+, 26.60), 109 (M^+ - I, 4.19). Anal. Calcd for $C_6H_5IO_2$: C, 30.54; H, 2.14. Found: C, 31.01; H, 2.12.

Propargyl (*Z*)-3-bromopropenoate (2j): ot 80–82 °C (3 mmHg); IR (neat) 3220, 2100, 1710, 1605, 1200, 1160 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.05 (d, J = 8.40 Hz, 1 H), 6.60 (d, J = 8.40 Hz, 1 H), 4.70 (d, 2 H), 2.35 (t, 1 H); MS m/e (%) 191 ($M^+(^{81}Br)$ + 1, 1.83), 190 ($M^+(^{81}Br)$, 0.96), 189 ($M^+(^{79}Br)$ + 1, 1.96), 188 ($M^+(^{79}Br)$, 1.12), 135 ($M^+ - OC_3H_3$, 100.00), 109 (M^+ - Br, 6.36), 107 ($M^+(^{81}Br) - CO_2C_3H_3$, 15.28), 105 ($M^+(^{79}Br) - CO_2C_3H_3$, 15.17). Anal. Calcd for $C_6H_5BrO_2$: C, 38.13; H, 2.67. Found: C, 38.38; H, 2.53.

Propargyl (*Z*)-3-chloropropenoate (2k): ot 75–77 °C (4 mmHg); IR (neat) 3300, 2100, 1720, 1610, 1210, 1160 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 6.58 (d, J = 8.00 Hz, 1 H), 6.03 (d, J = 8.0 Hz, 1 H), 4.58 (d, 2 H), 2.36 (t, 1 H); MS m/e (%) 147 ($M^+(^{37}Cl)$ + 1, 2.87), 146 ($M^+(^{37}Cl)$, 0.82), 145 ($M^+(^{35}Cl)$ + 1, 9.95), 109 (M^+ - Cl, 3.15), 93 (8.18), 91 ($M^+(^{37}Cl) - OC_3H_3$, 46.09), 89 ($M^+(^{35}Cl) - OC_3H_3$, 100.00). Anal. Calcd for $C_6H_5ClO_2$: C, 49.85; H, 3.49. Found: C, 49.63; H, 3.49.

Preparation of (*Z*)-3-Halopropenoic Acids. Typical Procedure. (*Z*)-3-Iodopropenoic Acid (21): Method A. A mixture of 2-propynoic acid (70 mg, 1 mmol) and LiI (150 mg, 1.1 mmol) in acetic acid (1 mL) was heated at 70 °C with stirring. The reaction was monitored by TLC. After 24 h, acetic acid was removed under vacuum, and subsequent purification by preparative TLC (solvent: petroleum ether/ethyl acetate 1:1) afforded **21**: yield 175 mg (89%); mp 63–64 °C (lit.[24] mp 63–65 °C). The spectral data are identical with those reported.[24]

Method B. A mixture of 2-propynoic acid (70 mg, 1 mmol) and LiI (150 mg, 1.1 mmol) was refluxed in CH_3CN (1 mL) for 24 h. The mixture was acidified with 2 N HCl and extracted with ethyl acetate (4 × 10 mL). After drying ($MgSO_4$), removal of solvent, and purification by preparative TLC, **21** was obtained in pure form; yield 160 mg (81%).

(*Z*)-3-Bromopropenoic acid (2m): mp 53–54 °C (lit.[12c] mp 54–55 °C); IR (neat) 3400, 1720, 1600, 1160 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 11.31 (bs, 1 H), 7.23 (d, J = 8.60 Hz, 1 H), 6.66 (d, J = 8.60 Hz, 1 H); MS m/e (%) 153 ($M^+(^{81}Br)$ + 1, 5.17), 152 ($M^+(^{81}Br)$, 92.09), 151 ($M^+(^{79}(Br)$ + 1, 6.70), 150 ($M^+(^{79}Br)$, 100.00), 135 ($M^+(^{81}Br)$ - OH, 56.51), 133 ($M^+(^{79}Br)$ - OH, 54.26), 124 ($M^+(^{81}Br)$ - CO, 12.87), 122 ($M^+(^{79}Br)$ - CO, 13.62), 107 ($M^+(^{81}Br) - CO_2H$, 29.46), 105 ($M^+(^{79}Br) - CO_2H$, 31.67), 71 (M^+ - Br, 79.30), 45 (CO_2H^+, 70.00).

(*Z*)-3-Chloropropenoic acid (2n): mp 58–59 °C (lit.[25] mp 61–62 °C). Spectral data are identical with those reported.

Preparation of (*Z*)-3-Halopropenamides. Typical Procedure. (*Z*)-3-Iodopropenamide (4a): Method A. A mixture of 2-propynamide (70 mg, 1 mmol) and lithium iodide (150 mg, 1.1 mmol) in acetic acid (1 mL) was heated at 90 °C. After 22 h, the reaction was complete as monitored by TLC. The mixture was diluted with water (5 mL), neutralized with solid K_2CO_3 until no CO_2 was evolved, and extracted with ethyl acetate (4 × 10 mL). The organic layer was dried ($MgSO_4$). **4a**[26] was obtained by purification with preparative TLC (solvent: petroleum ether/ethyl acetate 1:1); yield 195 mg (98%).

Method B. A mixture of 2-propynamide (70 mg, 1 mmol) and lithium iodide (150 mg, 1.1 mmol) was refluxed in CH_3CN (1 mL). After 24 h, the reaction was complete as monitored by TLC. **4a** was obtained after similar workup as above; yield 160 mg (80%).

Spectral data of **4b**,[5b] **4g**,[27] **4h**,[27] and **4i**[27] are identical with those reported.

(*Z*)-3-Iodopropenamide (4a):[26] mp 98–102 °C; IR (KCl) 3250, 3100, 1660, 1580, 1380, 1280, 1050, 800, 600 cm^{-1}; ^1H NMR (200 MHz, CD_3COCD_3) δ 7.22 (d, J = 8.50 Hz, 1 H), 7.04 (d, J = 8.50 Hz, 1 H); MS m/e (%) 198 (M^+ + 1, 2.53), 197 (M^+, 42.48), 181 ($M^+ - NH_2$, 18.62), 153 ($M^+ - CONH_2$, 8.06), 151 ($M^+ - CONH_2$ - 2H, 14.10), 43 ($CONH^+$, 100.00). Anal. Calcd for C_3H_4INO: C, 18.29; H, 2.05; N, 7.11. Found: C, 18.63; H, 1.98; N, 7.15.

(*Z*)-3-Bromopropenamide (4b): mp 92–94 °C (lit.[5b] mp 90–90.5 °C).

(*Z*)-3-Chloropropenamide (4c): mp 108–110 °C (lit.[8] mp 111–112 °C); IR (KCl) 3350, 3150, 1660, 1610, 1400, 1300, 1260, 1210, 1100, 800, 700 cm^{-1}; ^1H NMR (200 MHz, CD_3COCD_3) δ 6.72 (d, J = 8.40 Hz, 1 H), 6.19 (d, J = 8.40 Hz, 1 H); MS m/e (%) 108 $M^+(^{37}Cl)$ + 1, 11.63), 107 ($M^+(^{37}Cl)$, 20.54), 106 ($M^+(^{35}Cl)$ + 1, 36.91), 105 ($M^+(^{35}Cl)$, 59.15), 91 ($M^+(^{37}Cl) - NH_2$, 40.47), 89 ($M^+(^{35}Cl) - NH_2$, 95.92), 79 ($M^+(^{37}Cl)$ - CO, 5.46), 77 ($M^+(^{35}Cl)$ - CO, 16.23), 43 ($CONH^+$, 100.00).

***N*-Ethyl (*Z*)-3-iodopropenamide (4d)**:[28] oil; IR (neat) 3300, 3080, 1650, 1600, 1540, 1220, 800, 700 cm^{-1}; ^1H NMR (200 MHz, CD_3COCD_3) δ 7.13 (d, J = 8.70 Hz, 1 H), 6.96 (d, J = 8.70 Hz, 1 H), 3.15 (m, 2 H), 1.11 (t, 3 H); MS m/e (%) 226 (M^+ + 1, 12.50), 225 (M^+, 33.71), 210 (M^+ - Me, 8.09), 197 (M^+ + 1 - Et, 1.79), 182 (M^+ + 1 - NHEt, 3.17), 180 (M^+ - 1 - NHEt, 100.00), 98 (M^+ - I, 80.21), 44 ($CONH_2^+$, 52.44).

***N*-Ethyl (*Z*)-3-bromopropenamide (4e)**:[29] oil; IR (neat) 3300, 3060, 1640, 1540, 1250, 1200, 800, 700 cm^{-1}; ^1H NMR (200 MHz, CD_3COCD_3) δ 6.83 (d, J = 8.10 Hz, 1 H), 6.70 (d, J = 8.10 Hz, 1 H), 3.15 (m, 2 H), 1.10 (t, 3 H); MS m/e (%) 180 ($M^+(^{81}Br)$ +

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1, 35.63), 179 ($M^+(^{81}Br)$, 11.73), 178 ($M^+(^{79}Br)$ + 1, 31.54), 177 ($M^+(^{79}Br)$, 9.88), 164 ($M^+(^{81}Br)$ - Me, 8.18), 162 ($M^+(^{79}Br)$ - Me, 8.46), 135 ($M^+(^{81}Br)$ - NHEt, 69.05), 133 ($M^+(^{79}Br)$ - NHEt, 68.31), 107 ($M^+(^{81}Br)$ - CONHEt, 15.04), 105 ($M^+(^{79}Br)$ - CONHEt, 14.72), 98 (M^+ - Br, 100.00).

***N*-Ethyl (*Z*)-3-chloropropenamide (4f)**:[28] oil; IR (neat) 3300, 3060, 1640, 1540, 1260, 1200, 810, 700 cm^{-1}; ^1H NMR (200 MHz, CD_3COCD_3) δ 6.64 (d, J = 8.10 Hz, 1 H), 6.32 (d, J = 8.10 Hz, 1 H), 3.15 (m, 2 H), 1.10 (t, 3 H); MS m/e (%) 271 (2 $M^+(^{37}Cl)$ + 1, 1.05), 270 (2 $M^+(^{37}Cl)$, 0.87), 269 (2 $M^+(^{37}Cl)(^{35}Cl)$ + 1, 6.00), 268 (1.53), 267 (2 $M^+(^{35}Cl)$ + 1, 10.62), 137 (0.80), 136 ($M^+(^{37}Cl)$ + 1, 94.15), 135 ($M^+(^{37}Cl)$, 76.49), 134 ($M^+(^{35}Cl)$ + 1, 26.43), 133 ($M^+(^{35}Cl)$, 6.25), 120 ($M^+(^{37}Cl)$ - Me, 3.81), 118 ($M^+(^{35}Cl)$ - Me, 13.16), 106 ($M^+(^{37}Cl)$ - Et, 1.13), 105 (1.34), 104 (0.40), 99 (M^+ + 1 - Cl, 80.79), 98 (M^+ - Cl, 33.15), 97 (M^+ - HCl, 6.64), 92 ($M^+(^{37}Cl)$ + 1 - NHEt, 2.04), 91 ($M^+(^{37}Cl)$ - NHEt, 9.67), 90 ($M^+(^{35}Cl)$ + 1 - NHEt, 100.00), 89 (28.31), 63 ($M^+(^{37}Cl)$ - CONHEt, 10.25), 61 ($M^+(^{35}Cl)$ - CONHEt, 28.40).

Preparation of (*Z*)-3-Halo-2-propenenitrile. Typical Procedure. (*Z*)-3-Iodopropenenitrile (6a). A mixture of 2-propynenitrile (50 mg, 0.98 mmol), LiI (150 mg, 1.1 mmol), and acetic acid (1 mL) in a sealed tube was stirred and heated at 70 °C for 24 h. Through a procedure similar to that of (*Z*)-3-halopropenoates, **6a** was isolated in pure form: yield 175 mg (98%); IR (neat) 3050, 2200, 1570 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.63 (d, J = 8.60 Hz, 1 H), 6.75 (d, J = 8.60 Hz, 1 H); MS m/e (%) 180 (M^+ + 1, 3.50), 179 (M^+, 60.50), 128 (11.58), 127 (I^+, 28.46), 52 (M^+ - I, 100.00), 51 (M^+ - HI, 49.01); HRMS calcd for C_3H_2IN 178.9231. Found: 178.9231.

Spectral data of (*Z*)-3-bromopropenenitrile (**6b**)[5b] are identical with those reported.

(*Z*)-3-Chloropropenenitrile (6c). The reaction was carried out on a scale of 16 mmol of 2-propynenitrile (**5**), and the product was purified by distillation: bp 78–80 °C (90 mmHg) (lit.[5b] bp 145–146 °C); IR (neat) 3050, 2200, 1560 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 7.00 (d, J = 8.0 Hz, 1 H), 5.85 (d, J = 8.0 Hz, 1 H); MS m/e (%) 90 ($M^+(^{37}Cl)$ + 1, 5.94), 89 ($M^+(^{37}Cl)$, 31.26), 88 ($M^+(^{35}Cl)$ + 1, 21.58), 87 ($M^+(^{35}Cl)$, 100.00), 63 ($M^+(^{37}Cl)$ - CN, 1.10), 62 ($M^+(^{37}Cl)$ - 1 - CN, 4.06), 61 ($M^+(^{35}Cl)$ - CN, 4.18), 60 ($M^+(^{35}Cl)$ - 1 - CN, 14.60), 53 (3.18), 52 (M^+ - Cl, 85.60), 51 (M^+ - HCl, 31.04).

Reaction of 1-Phenyl-2-propynone with Metal Halides in Acetic Acid. The reaction was carried out at rt and the procedure was similar to that of 2-propynoate (method A).

Spectral data of the *E* isomer of **8a**, **8b**, and **8c** are identical with the reported data,[30] and those of *Z* isomers are given below.

1-Phenyl-3-iodo-2-propenone (8a) (*Z* isomer):[11] IR (neat) 3030, 1660, 1600, 1560, 1220, 1000, 940, 730, 680 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.90 (m, 2 H), 7.88 (d, J = 8.40 Hz, 1 H), 7.55 (m, 3 H), 7.45 (d, J = 8.40 Hz, 1 H); MS m/e (%) 391 (3.55), 390 (2 M^+ + 1 - I, 11.79), 313 (2 M^+ + 1 - I - Ph, 14.16), 286 (1.65), 285 (2 M^+ + 1 - I - PhCO, 7.24), 259 (M^+ + 1, 0.28), 258 (M^+, 0.30), 257 (M^+ - 1, 0.97), 127 (I^+, 3.17), 105 ($PhCO^+$, 100.00), 77 (Ph^+, 45.76).

1-Phenyl-3-bromo-2-propenone (8b) (*Z* isomer):[31] IR (neat) 3050, 1660, 1580, 1230, 1000, 730, 695 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.95 (m, 2 H), 7.70–7.30 (m, 4 H), 6.95 (d, J = 8.20 Hz, 1 H); MS m/e (%) 213 ($M^+(^{81}Br)$ + 1, 3.25), 212 ($M^+(^{81}Br)$, 10.74), 211 ($M^+(^{79}Br)$ + 1, 4.08), 210 ($M^+(^{79}Br)$, 12.27), 135 ($M^+(^{81}Br)$ - Ph, 8.24), 133 ($M^+(^{79}Br)$ - Ph, 8.28), 132 (5.00), 131 (M^+ - Br, 42.85), 106 (8.07), 105 ($PhCO^+$, 100.00), 77 (Ph^+, 67.51).

1-Phenyl-3-chloro-2-propenone (8c) (*Z* isomer):[32] IR (neat) 3050, 1660, 1590, 1230, 1000, 880, 740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.80 (m, 2 H), 7.30 (m, 3 H), 6.80 (d, J = 8.20 Hz, 1 H), 6.53 (d, J = 8.20 Hz, 1 H); MS m/e (%) 171 (4.00), 170 (1.58), 169 ($M^+(^{37}Cl)$ + 1, 8.64), 168 ($M^+(^{37}Cl)$, 4.11), 167 ($M^+(^{35}Cl)$ + 1, 19.21), 166 ($M^+(^{35}Cl)$, 4.60), 131 (M^+ - Cl, 19.80), 105 ($PhCO^+$, 26.15).

Isomerization of (*Z*)-8a in the Presence of NaI in HOAc. A mixture of (*Z*)-**8a** (65 mg, 0.25 mmol) and NaI (3.5 mg, 0.023 mmol) in HOAc (0.25 mL) was stirred at 35 °C for 4 h. Through direct preparative TLC using petroleum ether/ethyl acetate (10:1) as the solvent, 50 mg of (*E*)-**8a** was isolated (yield 77%) along with 2 mg of (*Z*)-**8a** recovered (3%).

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Registry No. **1a**, 623-47-2; **1b**, 922-67-8; **1c**, 14447-00-8; **1d**, 4383-39-5; **1e**, 471-25-0; (*Z*)-**2a**, 31930-36-6; (*Z*)-**2b**, 31930-34-4; (*Z*)-**2c**, 16490-99-6; (*Z*)-**2d**, 6214-23-9; (*Z*)-**2e**, 6214-22-8; (*Z*)-**2f**, 132973-27-4; (*Z*)-**2g**, 132973-28-5; (*Z*)-**2h**, 132973-29-6; (*Z*)-**2i**, 132973-25-2; (*Z*)-**2j**, 132973-26-3; (*Z*)-**2k**, 35227-67-9; (*Z*)-**2l**, 6214-35-3; (*Z*)-**2m**, 1609-92-3; (*Z*)-**2n**, 1609-93-4; **3a**, 7341-96-0; **3b**, 2682-33-9; **3c**, 2682-34-0; (*Z*)-**4a**, 137627-61-3; (*Z*)-**4b**, 41866-46-0; (*Z*)-**4c**, 78708-26-6; (*Z*)-**4d**, 137627-63-5; (*Z*)-**4e**, 72261-36-0; (*Z*)-**4f**, 137627-64-6; (*Z*)-**4g**, 68596-67-8; (*Z*)-**4h**, 68596-66-7; (*Z*)-**4i**, 68596-65-6; (*Z*)-**6a**, 137627-62-4; (*Z*)-**6c**, 3721-37-7; **7**, 3623-15-2; (*Z*)-**8a**, 108161-49-5; (*E*)-**8a**, 24883-49-6; (*Z*)-**8b**, 137627-65-7; (*E*)-**8b**, 34237-40-6; (*Z*)-**8c**, 15724-79-5; (*E*)-**8c**, 15724-86-4; NaI, 7681-82-5; LiI, 10377-51-2; LiBr, 7550-35-8; LiCl, 7447-41-8; 2-propynenitrile, 1070-71-9; 2,3-diiodoprop-2-en-1-ol, 1779-30-2.

Supplementary Material Available: ^1H NMR spectra for compounds **2h**, **2i**, and **6a** (3 pages). Ordering information is given on any current masthead page.

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