

Stereoselective Bromination of Acetylenes with Bromine in the Presence of Graphite

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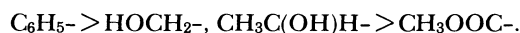
Synopsis. Acetylenes were stereoselectively brominated with molecular bromine adsorbed on graphite in dichloromethane to produce (*E*)- α,β -dibromoalkenes; isomerization of the *E*-isomer to the *Z*-isomer, usually catalyzed by bromine, did not occur in the presence of graphite.

The use of inorganic solid supports has been attracting widespread interest in organic synthesis.^{1,2)} Significant improvements of reagent activity or regioselectivity has been achieved in a wide variety of organic reactions by the use of supported reagents formed by the adsorption of reagent molecules onto the surface of a solid support. However, only a few studies on stereoselective control using supported reagents have been reported.³⁾ In a previous paper,⁴⁾ we reported that graphite inhibits the bromine-catalyzed isomerization of (*E*)- α,β -dibromostyrene to the *Z*-isomer, and that the addition of bromine to phenylacetylene produces (*E*)- α,β -dibromostyrene exclusively in the presence of graphite. We further found that the addition of graphite is also effective in the bromination of several other acetylenes. In the present paper we describe these recent results.

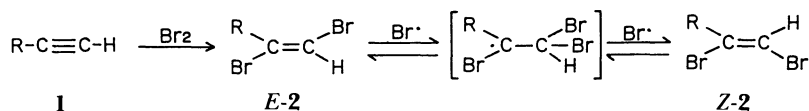
Results and Discussion

The bromination of acetylenes with bromine usually produces a mixture of two isomeric dibromoalkenes due to the reversible addition of a halogen atom to the double bond.^{5–7)} Thus, the *E/Z* ratio depends on the reaction conditions; namely, the *E/Z* ratio decreases when a prolonged reaction time, higher temperature, and a higher molar ratio of bromine relative to acetylenes are employed. We found, however, that acetylenes are stereoselectively brominated by molecular bromine adsorbed on graphite in dichloromethane to give (*E*)- α,β -dibromoalkenes.

The *E/Z* ratio in the products mixture was almost independent of the reaction conditions. The results are summarized in Table 1. For example, the treatment of propargyl bromide with 0.5-equiv of bromine in dichloromethane at 20°C gave a mixture of two isomeric 1,2,3-tribromo-1-propene; the *E/Z* ratio was 76/24, and with 1.1-equiv of bromine, the *E/Z* ratio was 46/54. In contrast, an appreciable difference in the isomer ratio between a reaction with 0.5-equiv and 1.1-equiv of bromine was hardly observed when the reaction was carried out in the presence of graphite under similar conditions. (*E*)-1,2,3-Tribromo-1-propene was obtained in high yield stereoselectively. The *E/Z* ratio was 96/4. The rate of bromination in the presence of graphite was slower than that without graphite. The electron-withdrawing group (*R*) decreased the reactivity of the acetylenes toward bromine as follows:



The results show that the bromine-catalyzed isomerization of (*E*)- α,β -dibromoalkenes to the *Z*-isomer does not occur in the presence of graphite.⁷⁾ To make sure of the role of graphite, the bromine-catalyzed isomerization of (*E*)- or (*Z*)- α,β -dibromoalkenes was carried out in the presence or in the absence of graphite. Both bromine-catalyzed isomerization of the *E*- to the *Z*-isomer and the *Z*- to the *E*-isomer in dichloromethane readily occurred. In contrast, neither the *E*- nor the *Z*-isomer was isomerized in the presence of graphite under similar conditions. The results are summarized in Table 2. We previously explained the role of graphite on the basis of a heterogeneous reaction on the surface of a solid support. Recently, however, we observed that the photostimulated bromination of toluene with bromine in the presence of



Scheme 1.

Table 1. Stereoselective Bromination of Acetylenes with Bromine^{a)}

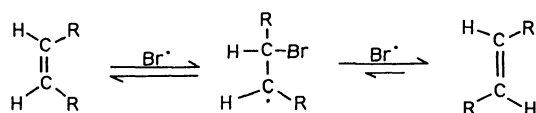
H-C≡C-R (1)	Temp/Time (°C/h)	Composition/% ^{b)}	
		With graphite <i>E-2</i> : <i>Z-2</i>	Without graphite <i>E-2</i> : <i>Z-2</i>
R: C ₆ H ₅	20/2	94:6	20:80
CH ₂ Br	20/4	96:4	46:54
CH ₂ OH	20/2	100:0	91:9
CH(OH)CH ₃	20/2	100:0	66:34
COOCH ₃	30/10	97:3	12:88

a) The molar ratio of bromine/acetylenes was 1.1. b) Yields were almost quantitative.

Table 2. Bromine-Catalyzed Isomerization of α,β -Dibromoalkenes^{a)}

RBrC=CHBr (2)	Temp/Time (°C/h)	Composition/%	
		With graphite E-2: Z-2	Without graphite E-2: Z-2
E-, R: C ₆ H ₅	20/2	100:0	36:64
E-, CH(OH)CH ₃	20/2	100:0	66:34
E-, CH ₂ OH	20/2	100:0	67:33
Z-, CH ₂ OH	20/2	0:100	65:35
E-, CH ₂ Br	20/4	100:0	48:52
Z-, CH ₂ Br	20/4	0:100	47:53
E-, COOCH ₃	30/5	100:0	58:42
Z-, COOCH ₃	30/5	0:100	55:45

a) All reactions were carried out in dichloromethane. The molar ratio of bromine/2 was 0.2.



R = C₆H₅, CH₃COO.

Scheme 2.

graphite occurs by electrophilic substitution rather than free-radical substitution.⁸⁾ This observation suggests that a bromine radical may not be generated in the presence of graphite. Therefore, the inhibition of the isomerization by graphite is more likely to be due to the fact that no bromine radical is generated in the presence of graphite, rather than to a restriction of the rotation around the C-C bond in the radical intermediate adsorbed on graphite, as was previously presumed. Isomerization of (Z)-stilbene to the E-isomer and dimethyl maleate to dimethyl fumarate are usually catalyzed by bromine. These bromine-catalyzed isomerizations are attributed to the reversible addition of a bromine radical to the double bond. If graphite inhibits the formation of a halogen atom, bromine-catalyzed isomerization of (Z)-stilbene and dimethyl maleate as well as α,β -dibromoalkenes may not occur. In fact, these bromine-catalyzed isomerizations did not proceed at all in the presence of graphite.

Experimental

(E)-1,2,3-Tribromo-1-propene. General Procedure for Bromination of Acetylenes. Graphite (5 g) was added to a solution of bromine (11 mmol, 1.76 g) in dichloromethane (50 ml), and stirred at room temperature for 0.5 h. To the resulting mixture was added a solution of propargyl bromide (10 mmol, 1.19 g) in dichloromethane (10 ml), and stirring was continued at 20 °C for 4 h. Aqueous sodium thiosulfate was then added, and the mixture was filtered. The organic layer was separated, washed with water and dried. The residue, after evaporation of the solvent, was analyzed by GLC and ¹H NMR. The yield of 1,2,3-tribromo-1-propene was 98%, the E:Z ratio 94:6.

Isomerization of (E)-1,2,3-Tribromo-1-propene: General Procedure for Isomerization of α,β -Dibromoalkenes. Graphite (5 g) was added to a solution of (E)-1,2,3-tribromo-1-propene (0.66 mmol, 0.184 g) in dichloromethane (20 ml),

and stirred at 20 °C for 0.2 h. To the resulting mixture was added a solution of bromine (0.132 mmol, 0.02 g) in dichloromethane (10 ml), and stirring was continued at 20 °C for 4 h. Aqueous sodium thiosulfate was added, and the mixture was filtered. The organic layer was separated, washed with water and dried. The residue, after evaporation of the solvent under reduced pressure, was analyzed by ¹H NMR.

Isomerization of Dimethyl Maleate. The isomerization was carried out as above using dimethyl maleate (1 mmol, 0.144 g) and bromine (0.1 mmol, 0.016 g) in dichloromethane (30 ml) with or without graphite (5 g) at 50 °C for 5 h under a nitrogen atmosphere and irradiation with a tungsten lamp (30 W). Isomerization without graphite gave dimethyl fumarate in 98% yield; graphite dimethyl maleate was recovered quantitatively.

Isomerization of (Z)-Stilbene: (a) Without Graphite. A mixture of (Z)-stilbene (1 mmol, 0.180 g) and bromine (0.2 mmol, 0.050 g) in hexane (30 ml) was stirred at 50 °C for 3 h. Aqueous sodium thiosulfate was then added in order to remove bromine. The organic layer was separated, washed with water and dried. The residue, after evaporation of the solvent under reduced pressure, was analyzed by GLC. The E:Z ratio of the isomers was 86:14.

(b) With Graphite. The isomerization was carried out as described above using graphite (5 g). (Z)-Stilbene was recovered in 97% yield after 5 h.

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- 8) Bromination of toluene (10 mmol) with bromine (5 mmol) in carbon tetrachloride was carried out at 50 °C for 1 h in the presence of graphite (5 g) under irradiation with a tungsten lamp (30 W), and bromotoluene was obtained in 84% yield (p/o=2.6). The reaction without graphite under similar conditions gave benzyl bromide in 87% yield.