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Electrochemical Conjugate Additions of the Allyl Groups in Substituted Allyl Halides to α,β-Unsaturated Esters

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Electrolysis of allyl halides and diethyl fumarate (**2**) in *N,N*-dimethylformamide containing 0.2 M† tetraethylammonium tosylate gave a conjugate addition product, ethyl 3-(ethoxycarbonyl)-5-hexenoate, in a moderate yield. The electrochemical reaction of 1-chloro-3-methyl-2-butene (**4**) with **2**, that of allyl chloride **4** with methyl crotonate (**6**), and that of methyl 4-halo-2-butenoate with **2** likewise gave the corresponding conjugate addition products, ethyl 3-(ethoxycarbonyl)-6-methyl-5-heptenoate, methyl 3,4,4-trimethyl-5-hexenoate, and ethyl 3-(ethoxycarbonyl)-4-(methoxycarbonyl)-5-hexenoate, respectively. The addition reaction of **4** to **2** takes place at the α-carbon terminus of **4** exclusively, whereas the addition of **4** to **6** at the γ-carbon terminus of **4**. These regioselectivities of the additions and pathways of the reactions are discussed.

The electrochemical reduction of organic halides has been extensively studied, but most of these studies have been concerned with the elucidation of the mechanism of the cleavage of the carbon-halogen bond.[1] These studies have shown that the electrochemical reduction of carbon-halogen bonds generally gives radical or carbanion intermediates[2] which result in the formation of dimers or hydrocarbons.[1]

Although these species generated by ordinary chemical reaction are widely used in a variety of organic syntheses, only a limited number of investigations have been reported on the application of these species generated by the electrochemical reduction of organic halides to the formation of the carbon-carbon bond. These electrochemical investigations include ones on the cyclization of α,ω-dihalides,[3] cyclization of acetylenic halides,[4] alkylation of substrates containing an acidic hydrogen by alkyl halides,[5] acylation of benzyl halides,[6] and addition of alkyl halides to carbon-carbon[7] or to carbon-nitrogen double bonds.[8] The electrochemical addition of allyl bromide to acrylonitrile, ethyl acrylate, or diethyl maleate has also been reported to give a conjugate addition products.[7a]

In this paper we report a conjugate addition of the allyl group in allyl halides to α,β-unsaturated esters by the electrochemical reduction. The electrochemical conjugate additions of the allyl groups in substituted allyl halides to α,β-unsaturated esters were found to take place in a regioselective manner at either their α- or γ-carbon terminus.

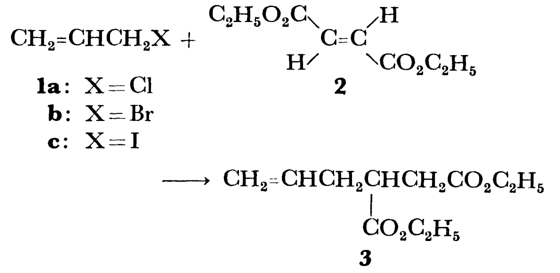
Results and Discussion

The electrolysis of allyl chloride (**1a**), allyl bromide (**1b**), or allyl iodide (**1c**) together with diethyl fumarate (**2**) in *N,N*-dimethylformamide (DMF) containing 0.2 M tetraethylammonium tosylate as a supporting electrolyte gave a conjugate addition product, ethyl 3-(ethoxycarbonyl)-5-hexenoate (**3**), in the yields shown in Table 1. Electrolyses were carried out at a constant current in a normal undivided cell with two platinum plate electrodes. Electrolysis of **1b** in the presence of tenfold excess of **2** gave **3** in a 70% yield, although electrolysis of **1a** or **1c** under the same conditions gave a lower yield of **3**.

TABLE 1. RESULTS OF ELECTROCHEMICAL ADDITIONS OF ALLYL GROUPS IN ALLYL HALIDES (**1a**, **1b**, AND **1c**) TO DIETHYL FUMARATE (**2**)[a)]

	1 (mmol)	**2** (mmol)	*F*/mol	Conv./% of **1**	Yield/%[b)] of **3**
1a	1.7	15	2	—	15
1b	1.5	1.5	4	100	36
	1.5	3	2	68	58
	1.5	3	4	75	61
	1.5	15	2	85	70
1c	1.5	15	2	90	39

a) Conducted at 5 mA/cm² in DMF containing 0.2 M Et_4NOTs. b) Yields are based on **1** consumed.



Scheme 1.

When substituted allyl halides are used in this electrolysis, the formation of a mixture of two isomers arising from the combination of the allyl halides at their α- and γ-carbon termini to α,β-unsaturated ester might be expected. The electrochemical reaction of a substituted allyl chloride, 1-chloro-3-methyl-2-butene (**4**), with a two-fold excess of diethyl fumarate (**2**) at 0 °C, however, gave exclusively ethyl 3-(ethoxycarbonyl)-6-methyl-5-heptenoate (**5**) in a 15% yield, in which a less heavily substituted carbon terminus of the allyl group was attached to the α,β-unsaturated ester. The electrolysis was conducted in DMF containing 0.2 M tetraethylammonium tosylate at a constant current of 25 mA/cm². Electricity passed was 2 Faraday per mole of **4**. On the other hand, the electrochemical reaction of **4** with methyl crotonate (**6**) gave methyl 3,4,4-trimethyl-5-hexenoate (**7**) as a single product, in which a more heavily substituted

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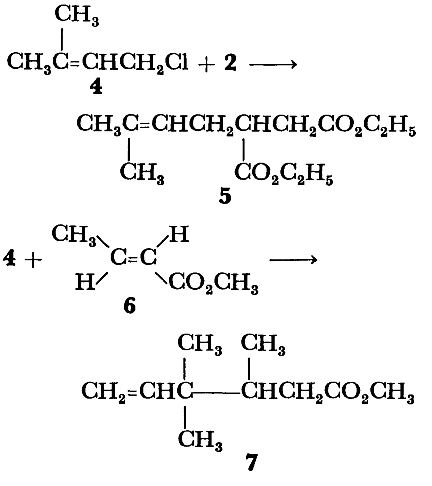
† 1 M = 1 mol dm⁻³.



$$\mathrm{CH_3\overset{CH_3}{\overset{|}{C}}{=}CHCH_2Cl} + \mathbf{2} \longrightarrow$$

4

$$\mathrm{CH_3\underset{CH_3}{\underset{|}{C}}{=}CHCH_2\underset{CO_2C_2H_5}{\underset{|}{C}H}CH_2CO_2C_2H_5}$$

5

6

$$\mathrm{CH_2{=}CH\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}\!-\!\overset{CH_3}{\overset{|}{C}}HCH_2CO_2CH_3}$$

7

Scheme 2.

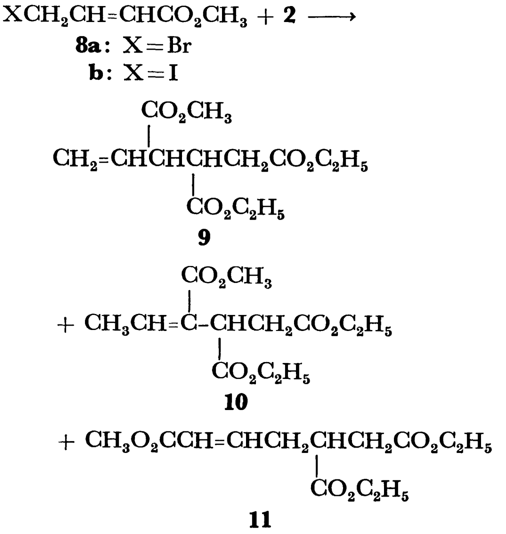
Table 2. Results of electrochemical additions of methyl 4-halo-2-butenoate (**8**) to diethyl fumarate (**2**)[a]

	8 (mmol)	**2** (mmol)	Curr. dens. / mA cm^{-2}	F/mol	Yield/%[b] of **9**
8a	1.5	15	5[c]	2	16
	1.5	15	5	2	39
	1.5	15	5	4	18
	1.5	15	25	2	14
	1.5	5	5	2	20
	1.5	15	5[d]	2	27
	1.5	15	5[d]	4	31
8b	1.5	15	5	2	11
	1.5	15	5[d]	2	11

a) Conducted at −40 °C in DMF containing 0.2 M Et_4NOTs using a platinum cathode. b) Yields are based on **8** used. c) Conducted at 0 °C. d) Mercury pool was used as a cathode.

carbon of the allyl group was attached to the α,β-unsaturated ester, in a 22% yield. The structures of **5** and **7** were determined by elemental analyses and spectroscopies. The ^{1}H NMR spectrum of **7** gave well-resolved signals consistent with the assigned structure by an addition of 40 mol% of tris(dipivaloylmethanato)europium.

Electrolysis of methyl 4-bromo- (**8a**) or methyl 4-iodo-2-butenoate (**8b**) with ten-fold excess of **2** gave ethyl 3-(ethoxycarbonyl)-4-(methoxycarbonyl)-5-hexenoate (**9**) as the major product, in which the allyl group was again combined to the α,β-unsaturated ester with an allylic rearrangement. The structure of **9** was confirmed by the elemental analysis and spectroscopy. Traces of two isomeric products (**10** and **11**) were also obtained in this electrolysis. Table 2 shows the yields of **9** under various conditions. When electrolysis was conducted at −40 °C, **9** was obtained in a higher yield than at 0 °C. This is probably due to the decomposition or the condensation of the anion generated from **8** at room temperature. It is also seen that platinum is better than mercury as a cathode material.



$$\mathrm{XCH_2CH{=}CHCO_2CH_3} + \mathbf{2} \longrightarrow$$

8a: X=Br

b: X=I

$$\mathrm{CH_2{=}CH\overset{CO_2CH_3}{\overset{|}{C}}H\underset{CO_2C_2H_5}{\underset{|}{C}}HCH_2CO_2C_2H_5}$$

9

$$+\ \mathrm{CH_3CH{=}\overset{CO_2CH_3}{\overset{|}{C}}\!-\!\underset{CO_2C_2H_5}{\underset{|}{C}}HCH_2CO_2C_2H_5}$$

10

$$+\ \mathrm{CH_3O_2CCH{=}CHCH_2\underset{CO_2C_2H_5}{\underset{|}{C}}HCH_2CO_2C_2H_5}$$

11

Scheme 3.

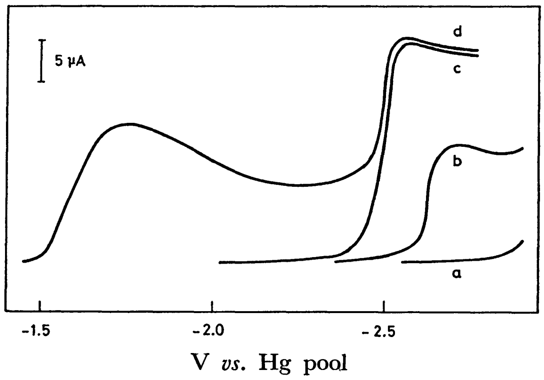


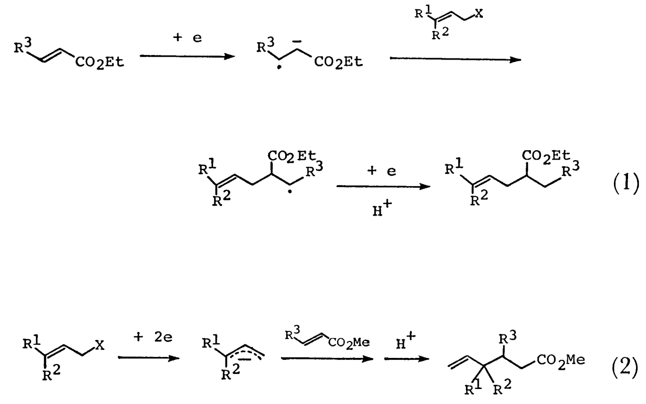
Fig. 1. Linear-sweep voltammograms of **4**, **2**, and **6** with a platinum disc electrode. Sweep rate, 0.023 V s^{-1}.

(a): 0.2 M Et_4NOTs in DMF, (b): 0.018 M **6** in 0.2 M Et_4NOTs–DMF, (c): 0.017 M **4** in 0.2 M Et_4NOTs–DMF, (d): 0.013 M **2** and 0.017 M **4** in 0.2 M Et_4NOTs–DMF.

The allyl groups were thus regioselectively combined to the two different α,β-unsaturated esters **2** and **6** at different sites. These regioselectivities can be interpreted by assuming the involvement of two different mechanisms. The reaction pathway of each electrochemical addition may be determined by whether a more readily reducible species in the electrolysis is α,β-unsaturated esters or allyl halides. Linear sweep voltammetry showed that allyl halides **4** and **8a** are reduced at about −2.5 and −1.1 V *vs.* Hg, while α,β-unsaturated esters **2** and **6** are reduced at −1.7 and −2.7 V *vs.* Hg, respectively (Fig. 1).

Therefore, in the electrochemical reaction of **4** with **2**, a preferential one-electron reduction of **2** generates an anion radical which reacts with the carbon atom of **4** carrying chlorine in an S_N2 fashion to give an intermediary radical species. A further reduction of the radical followed by a protonation of the resulting carbanion would give the observed addition product **5** [Scheme 4, (1)].

In the reaction of either **4** with **6** or **8** with **2**, however, a two-electron reduction of allyl halides **4** or



4: $R^1=R^2=CH_3$, X=Cl

8: $R^1=CO_2Me$, $R^2=H$, X=Br, I

2: $R^3=CO_2Et$

6: $R^3=CH_3$

Scheme 4.

8 may take place to generate allylic carbanions which then add to α,β-unsaturated esters to afford the observed addition products **7** or **9** [Scheme 4, (2)].

The aforementioned explanations are further supported by the results of ordinary chemical reactions. Several carbanions such as 2-substituted allyllithium,[9] dienolate anions derived from α,β-unsaturated acids,[10,11] or α-phenylsulfonyl carbanions[12] always undergo nucleophilic substitution on **4** at the less heavily substituted carbon terminus. On the other hand, the addition reactions of allylic carbanions derived from 3,3-dimethylallyl compounds to carbonyl group,[13] acyl halide,[14] acetal,[15] or α,β-unsaturated carbonyl compounds[16] take place at the more heavily substituted carbon terminus of **4** exclusively. Moreover, lithium dienolates derived from α,β-unsaturated esters undergo alkylation reactions at the α carbon of the ester almost exclusively.[10]

The formation of the addition product such as **5** having an allylic unit attached at a less heavily substituted carbon in the present electrochemical reaction is worth noting, since allylic organometallics always gave the addition products having the allyl groups at a more highly substituted carbon terminus.[16]

Experimental

All the products were isolated and purified by distillation and by preparative GLPC with a JEOL JGC-20K instrument. IR spectra were obtained with a Hitachi EPI-22 spectrometer, and NMR spectra in CCl_4 were measured with a Hitachi R-22 high-resolution spectrometer (90 MHz) using TMS as an internal reference. Mass spectra were obtained with a Hitachi RM-50GC mass spectrometer. Quantitative GLPC analyses were carried out with a Hitachi 063 instrument by an internal standard method.

Materials. *N,N*-Dimethylformamide (DMF) was shaken with phosphorus pentaoxide and then stirred overnight with potassium hydroxide. It was distilled under a reduced pressure of nitrogen atmosphere and then distilled over picric acid. The allyl halides used were washed with sodium thiosulfate solution, dried over calcium chloride, and then distilled.

1-Chloro-3-methyl-2-butene (**4**) was prepared from isoprene by the described procedure.[17] Dry hydrogen chloride (183 g) was added to isoprene (344 g) over a period of 2.5 h at −40 °C, and the resulting mixture was refluxed for 1 h. Distillation of the reaction mixture gave **4** (228 g, 43%): bp 107—109 °C; NMR δ 1.74 (3H), 1.78 (3H), 4.02 (2H), 5.44 (1H).

Methyl 4-bromo-2-butenoate (**8a**) was prepared from methyl crotonate by the described procedure.[18] To methyl crotonate (24 g) in carbon tetrachloride (100 ml) was added *N*-bromosuccinimide (25 g) and benzoyl peroxide (0.2 g) and the mixture was refluxed for 7 h. The usual work up and a distillation of the reaction mixture gave **8a**: bp 88—89° C/15 mmHg[††] (lit,[18] 83—85 °C/13 mmHg); NMR δ 3.70 (3H, s), 3.98 (2H, m), 5.99 (1H, m), 6.96 (1H, m); MS *m/e* 180 (M^++2), 178 (M^+).

Methyl 4-iodo-2-butenoate (**8b**) was prepared from **8a** and sodium iodide by a literature procedure;[19] bp 108 °C/19 mmHg; MS *m/e* 266 (M^+).

General Procedure of Electrolysis. For most of the preparative electrolysis, a normal undivided cell (2.8 cm dia.) equipped with a magnetic stirrer, a reflux condenser, and a serum cap for introduction of nitrogen gas was used. Electrolysis was carried out under nitrogen atmosphere at a constant current using two platinum plate electrodes (2×2 cm²). Amounts of the substrates in each electrolysis are shown in Tables 1 and 2. After electrolysis, the reaction mixture was dissolved in diethyl ether and the solution was washed with sodium thiosulfate solution and water, and dried over magnesium sulfate. The usual work up of the solution gave a product mixture which was subjected to distillation and preparative GLPC with a JEOL-20K instrument to give pure products.

Some physical properties of the products are recorded below.

*Ethyl 3-(Ethoxycarbonyl)-5-hexenoate (**3**)*: Bp 101—103 °C/18 mmHg; n_D^{24} 1.4330; IR (neat) 3090, 1735, 1645, and 925 cm⁻¹; NMR δ 1.24 (6H, t, $CO_2CH_2C\underline{H}_3$), 2.5 (5H, m, C-2H, C-3H, and C-4H), 4.10 (2H, q, $CO_2C\underline{H}_2CH_3$), 4.13 (2H, q, $CO_2C\underline{H}_2CH_3$), 5.05 (2H, m, C-6H), and 5.7 (1H, m, C-5H); MS *m/e* (rel intensity) 169 ($M^+-OC_2H_5$, 46), 140 (56), 123 (40), 95 (44), 67 (100), and 41 (42). Found: C, 61.29; H, 8.34%. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47%.

*Ethyl 3-(Ethoxycarbonyl)-6-methyl-5-heptenoate (**5**)*: Bp 118—119 °C/19 mmHg; n_D^{24} 1.4422; IR (neat) 3050, 1730, and 855 cm⁻¹; NMR δ 1.24 (6H, t, $CO_2CH_2C\underline{H}_3$), 1.61 (3H, s, $-C\underline{H}_3$), 1.70 (3H, s, $-C\underline{H}_3$), 2.5 (5H, m, C-2H, C-3H, and C-4H), 4.10 (2H, q, $CO_2C\underline{H}_2CH_3$), 4.12 (2H, q, $CO_2C\underline{H}_2CH_3$), and 5.07 (1H, m, C-5H); MS *m/e* (rel intensity) 242 (M^+, 12), 197 ($M^+-OC_2H_5$, 38), 168 (97), and 95 (78). Found: C, 64.13; H, 9.06%. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15%.

*Methyl 3,4,4-Trimethyl-5-hexenoate (**7**)*: Bp 117—120 °C/48 mmHg; IR (neat) 3090 and 1745 cm⁻¹; NMR δ 0.88 (3H, d, C-3-$C\underline{H}_3$), 0.97 and 0.99 (each 3H, s, $-C(C\underline{H}_3)_2$), 2.0 (3H, m, $-C\underline{H}C\underline{H}_2CO_2$), 3.62 (3H, s, $CO_2C\underline{H}_3$), 4.9 (2H, m, $C\underline{H}_2$=CH), and 5.80 (1H, m, =$C\underline{H}$); NMR (CCl_4, 40 mol% of $Eu(DPM)_3$ added) δ 1.79 and 1.84 (each 3H, s, $C(C\underline{H}_3)_2$), 3.41 (3H, d, C-3-$C\underline{H}_3$), 5.3—5.7 (2H, m, $C\underline{H}_2$=CH), 6.3—6.7 (1H, m, $-C\underline{H}$), 6.57—6.9 (1H, m, =$C\underline{H}$), 7.02 (1H, dd, $J=10$ Hz, $J=15$ Hz, $-C\underline{H}_2CO_2$), 7.54 (1H, dd, $J=4$ Hz, $J=15$ Hz, $-C\underline{H}_2CO_2$); MS *m/e* (rel intensity) 170 (M^+, 3), 96 (59), and 69 (100). Found: C, 70.33; H, 10.37%. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66%.

*Ethyl 3-(Ethoxycarbonyl)-4-(methoxycarbonyl)-5-hexenoate (**9**)*: Bp 67 °C/1 mmHg; n_D^{21} 1.4492; IR (neat) 3090, 1740,

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[††] 1 mmHg≈133.322 Pa.

1640, 935, and 860 cm^{-1}; NMR δ 1.26 (6H, t, $CO_2CH_2C\underline{H}_3$), 2.5 (2H, m, C-2H), 3.2 (2H, m, C-3H and C-4H), 3.70 (3H, s, $CO_2C\underline{H}_3$), 4.12 (4H, q, $CO_2C\underline{H}_2CH_3$), 5.2 (2H, m, C-6H), and 5.8 (1H, m, C-5H); MS *m/e* (rel intensity) 241 (M^+-OCH_3, 21), 240 (47), 227 ($M^+-OC_2H_5$, 82), 226 (44), 167 (56), 166 (53), 99 (68), 67 (65), and 29 (100). Found: C, 57.36; H, 7.37%. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40%.

*Ethyl 3-(Ethoxycarbonyl)-4-(methoxycarbonyl)-4-hexenoate (**10**)*: NMR δ 1.28 (6H, t, $CO_2CH_2C\underline{H}_3$), 1.97 (3H, d, J=7.5 Hz, C-6-$C\underline{H}_3$), 2.8 (3H, m, C-2H and C-3H), 3.78 (3H, s, $CO_2C\underline{H}_3$), 4.19 (4H, q, two $CO_2C\underline{H}_2CH_3$), and 7.07 (1H, q, J=7.5 Hz, C-5H). MS *m/e* 227 ($M^+-OC_2H_5$).

*Methyl Ethyl 5-(Ethoxycarbonyl)-2-heptene-1,7-dioate (**11**)*: NMR δ 1.24 and 1.26 (each 3H, s, $CO_2CH_2C\underline{H}_3$), 2.7 (5H, m, C-4H, C-5H, and C-6H), 3.71 (3H, s, $CO_2C\underline{H}_3$), 4.13 and 4.17 (each 2H, q, $CO_2C\underline{H}_2CH_3$), 5.85 (1H, d, J= 16 Hz, C-2H), and 6.85 (1H, dt, J=16 Hz, J=8 Hz, C-3H). MS *m/e* 227 ($M^+-OC_2H_5$).

Voltammetry. Voltammetry was carried out with a Yanaco V8 potentionstat at a sweep rate of 0.023 V s^{-1} using a platinum disc electrode (1 mm dia.) in DMF containing 0.2 M Et_4NOTs. A potential was measured in V *vs.* Hg pool.

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