by rubber septa, under argon, was charged with the appropriate phenol (3 mmol) and dry ether (6 mL). To this stirred solution, at room temperature (23 °C), 1.5 M *n*-BuLi (6 mL, 9 mmol) was added dropwise (4 min) via syringe. The mixture was magnetically stirred for up to 48 h, cooled to 0 °C, and finally carefully quenched with water. The standard workup yielded a residue which was then examined by gas chromatographic analysis against authentic samples. Quantitative results are given in the text.

**Acknowledgment**. Financial support by the DGICYT (PB87-0019) is gratefully acknowledged. We are indebted to Professor S. Olivella (University of Barcelona, Spain) for helpful discussions and also for making available to us his modified version of MOPAC. Time allocation for calculations, performed with VAX 11/750 and VAX 8820 computers, was generously provided by the Centre de Càlcul de la Universitat de les Illes Balears. Thanks are also due to Dr. G. Tojo (University of Santiago de Compostela) for obtaining our high-resolution mass spectra.

**Registry No.** **1a**, 150-76-5; **1b**, 127087-14-3; **1c**, 123-31-9; **1d**, 127087-15-4; **1e**, 127087-16-5; **2a**, 5307-05-1; **2b**, 127087-17-6; **2c**, 127087-18-7; **2d**, 127087-19-8; **3a**, 150-19-6; **3b**, 19555-09-0; **3c**, 33617-66-2; **3d**, 108-46-3; **3e**, 127087-20-1; **3f**, 127087-21-2; **3g**, 127087-22-3; **4a**, 90-05-1; **4b**, 127087-23-4; **4c**, 38377-31-0; **4d**, 120-80-9; **4e**, 127087-24-5; **5a**, 91-10-1; **5b**, 127087-25-6; **5c**, 127087-26-7; **5d**, 127087-27-8; **5e**, 87-66-1; **6a**, 634-36-6; **6b**, 5150-42-5; **7a**, 91-16-7; **7b**, 90-05-1; **8a**, 100-66-3; **8b**, 500-99-2; **9b**, 108-95-2.

**Supplementary Material Available:** Listing of Cartesian coordinates of the optimized molecular structures (16 pages). Ordering information is given on any current masthead page.

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# Electrochemical Hydrotrifluoromethylation of Fumaronitrile

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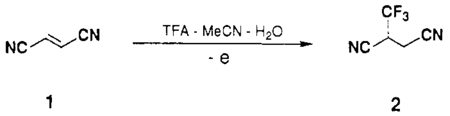
Electrooxidation of trifluoroacetic acid in the presence of fumaronitrile (1) in an MeCN–$H_2O$–(Pt) system provides 2-(trifluoromethyl)succinonitrile (2) in a 65% yield. The electrochemical reaction is remarkably affected by the reaction temperature. That is, at the ice-cooling temperature, a simple hydrogenation of 1 predominates, while at 50–55 °C, the desired hydrotrifluoromethylation proceeds exclusively. The anodically generated trifluoromethyl radicals recombine with the succinonitrile radicals produced at the cathode, leading to the formation of 2.

Scheme I



Because of the increasing attention to trifluoromethyl compounds for medicines and material science,[1,2] trifluoromethyl metal complexes have been extensively employed for trifluoromethylation of carbonyl compounds[3-5] and aryl halides.[6-8] Perfluoroalkanoyl peroxide,[9-11] *N*-(trifluoromethyl)-*N*-nitrosotrifluoromethanesulfonamide-,[12,13] and xenon difluoride–trifluoroacetic acid[14] can trifluoromethylate aromatic compounds. Recently, electrochemical trifluoromethylation of olefins has been recognized as a useful method for the preparation of aliphatic trifluoromethylated compounds since electrochemical oxidation of trifluoroacetic acid (TFA) in an MeCN–$H_2O$–(Pt) system generates trifluoromethyl radicals almost quantitatively[15] and TFA is one of the economically feasible trifluoromethyl sources. Renaud,[17,18] Brookes,[19,20] Muller,[21,22,24] and our group[15,16] have demonstrated the usefulness of electrochemical trifluoromethylation. Trifluoromethyl-dimerization of methyl acrylate,[15] bistrifluoromethylation of acrylamide,[16] diethyl fumarate, and maleimide,[18] and trifluoromethyl–acetamidation of methyl methacrylate[23] are typical examples which are not realized by conventional chemical reactions. On the other hand, hydrotrifluoromethylation of olefins sometimes occurs as a side reaction[17-20] but does not predominate in most electrochemical trifluoromethylations. Judging from the reported results so far, the electronic and steric features of the substituents attached to the carbon–carbon double bond of the reactant olefins are intensively influential toward the chemical and electrochemical fate of the initially formed trifluoromethylated radical intermediates and thus to the final products. Among the nitrogen-containing functional groups, both carbamoyl groups of acrylamide[16] and maleimide[18] enhance bistrifluoromethylation while the cyano group in acrylonitrile promotes trifluoromethyl–dimerization.[20] Generalization on the substituent effect of the electrochemical trifluoromethylation of olefins re-

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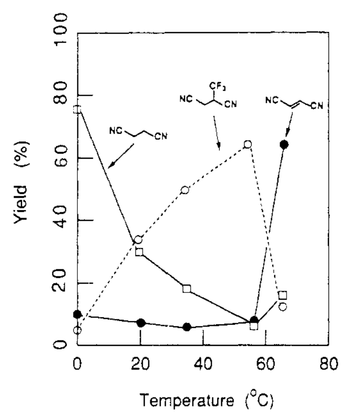


**Figure 1.** Temperature dependence of the product yield.

mains to be clarified at the present stage until further extensive studies are accumulated. On this basis, fumaronitrile (1) as a symmetric nitrile has been chosen. This paper describes optimization of the hydrotrifluoromethylation of 1 and the reaction mechanism (Scheme I).

## Results and Discussion

Electrochemical reaction of 1 was conducted in an MeCN-$H_2O$-NaOH system (1-TFA, 1:4) using platinum electrodes in an undivided beaker type cell. 2-(Trifluoromethyl)succinonitrile (2) was produced as a major product, and succinonitrile (3) and 1,2,3,4-tetracyanobutane (8) were produced as byproducts. The proton-decoupled $^{13}C$ NMR spectrum of 2 showed two quartets at 34.6 ppm ($J$ = 34.1 Hz, $CCF_3$) and 121.8 ppm ($J$ = 281.2 Hz, $CF_3$) and three singlets at 16.2, 111.5, and 113.6 ppm attributed to methylene and two cyano groups, respectively. The $^{19}F$ NMR spectrum showed one doublet at 92.3 ppm ($J$ = 7.0 Hz), suggesting a partial structure of $CF_3CH$. The mass spectrum showed a parent peak ($m/e$ 148). The yield of 2 was markedly temperature dependent, as shown in Figure 1. At around 50–55 °C, the yield became optimum (65%) after 1.5 F/mol of charge to TFA was passed. In contrast, the yield of 2 decreased gradually and that of 3 increased sharply as the temperature was lowered. This result is quite contrary to the fact that the current efficiency of the generation of trifluoromethyl radicals is better at the lower temperature (Figure 2) and reached 95% yield at 0 °C.[25] At around 65 °C, which is almost the boiling point of TFA, TFA and its sodium salt would not be oxidized due to desorption from the anode. However, gas evolution was observed at the anode. Therefore, most of the anode reaction at 65 °C would arise from oxidation of water. The low current efficiency of TFA consumption (Figure 2) and the high recovery of 1 at 65 °C suggest the hypothesis.

The area of the electrodes and the distance between the anode and the cathode also slightly affected the yield of 2. A shorter electrode distance and a larger cathode area compared to that of the anode favored the formation of 2 (Figure 3).

The product 2 would arise from the formal 1,2-addition of trifluoromethyl and hydrogen to fumaronitrile. However, 1,2-addition of trifluoromethyl and hydrogen to a double bond is quite unusual so far as the reported literature is concerned. In most of the cases, the trifluoromethyl-hydrogenated products are obtained as minor products. For instance, the electrochemical trifluoromethylation of methyl acrylate, acrylonitrile, and methallyl cyanide provided methyl 4,4,4-trifluorobutanoate (5%),[19] and 4,4,4-trifluorobutyronitrile (5%),[19] and a mixture of 3-methyl-5,5,5-trifluoropentanonitrile and isomeric 3-methyl-5,5,5-trifluoropentenonitriles,[24] respectively. The question is whether or not the electrophilic trifluoromethyl radicals can attack exclusively at the electron-deficient carbon–carbon double bond of 1, generating the radical intermediate **7b**, which would subsequently abstract hydrogen from poor-hydrogen-donor solvents such as water and acetonitrile (Scheme II).

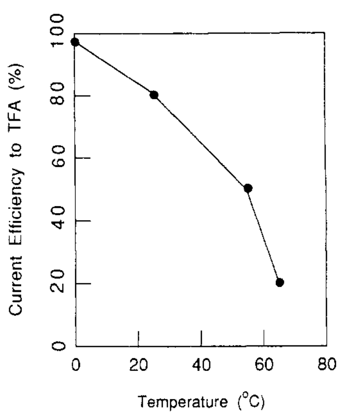


**Figure 2.** Temperature dependence of the current efficiency of TFA.[25]

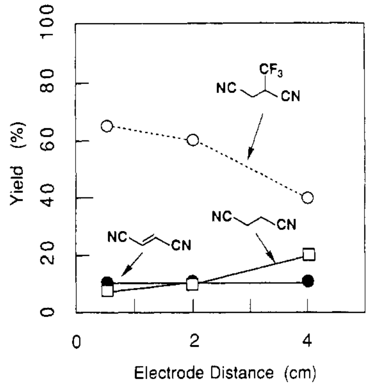
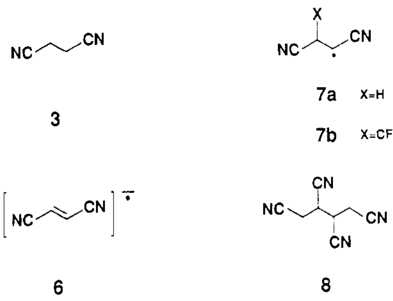


**Figure 3.** Dependence on electrode distance of the product yield.

### Scheme II



Some experiments were performed in order to elucidate the reaction mechanism. At first, the electrolysis of 2 was conducted in an MeCN-$H_2O$-TFA-NaOH-(Pt) system in a divided cell separated with a sintered-glass filter. The substrate 1 was supplied in both compartments and electrolyzed. The starting material 1 was recovered completely, and no desired 2 was obtained from the anodic compartment, in contrast to the predominant formation of 2 in an undivided cell. Meanwhile, succinonitrile (3)

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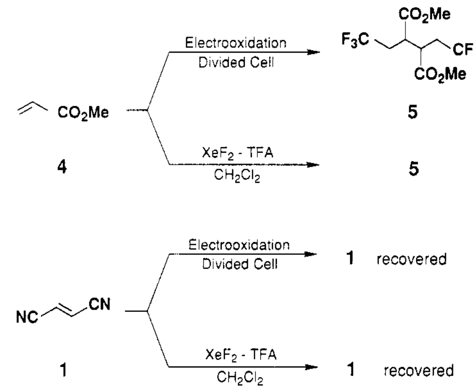
(25) The remaining TFA was quantitatively analyzed by $^{19}F$ NMR.

(26) We are grateful to CIBA-GEIGY Foundation, The Asahi Glass Foundation, and the Ministry of Education, Culture and Science of Japan for financial support (a Grant-in-Aid for Scientific Research (No. 01550675) and Priority Area (No. 01607001 and 63607521)) and the SC-NMR Laboratory of Okayama University for 500-MHz NMR analysis.

Scheme III

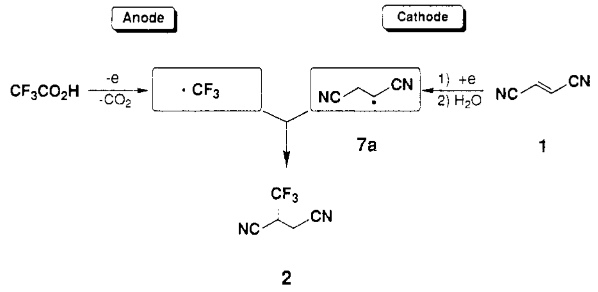


was obtained as a major product from the cathodic compartment, suggesting that **1** was electrochemically reduced to **3**. Then, both methyl acrylate and **1** were supplied in the anodic compartment and electrolyzed under the same conditions. In this case, **1** was again recovered completely, but methyl acrylate was converted to dimethyl 2,3-bis(2,2,2-trifluoroethyl)succinate (**5**) in 50% yield, which must arise from the addition of the trifluoromethyl radicals to methyl acrylate followed by dimerization of the resulting radical intermediate as already clarified.[15] This result indicates clearly that even in a divided-cell system the trifluoromethyl radicals are generated electrochemically and attack methyl acrylate, but not **1** (Scheme III).

The reactivity of the trifluoromethyl radicals to a carbon–carbon double bond was next examined in an $XeF_2$–TFA–$CH_2Cl_2$ system. The xenon system is useful for generation and homogeneous reaction of trifluoromethyl radicals.[14] A mixture of fumaronitrile, $XeF_2$, and TFA dissolved in methylene chloride was stirred at room temperature. However, **1** was recovered quantitatively. In contrast to this, methyl acrylate was cleanly transformed to the trifluoromethylated dimer **5** (50%) under the same reaction conditions. Then, a mixture of **1** and methyl acrylate was subjected to the xenon system. Here again, **1** was recovered intact and methyl acrylate was converted to **5**. These results apparently reveal that the trifluoromethyl radicals attack methyl acrylate but not the electron-deficient carbon–carbon double bond of **1**. Taking into account the following facts, it is postulated that both anodic and cathodic reactions must cooperate to form **2** in an undivided cell: (a) **2** forms electrochemically only in an undivided cell and not in a divided cell, (b) **1** is reduced at the cathode to **3**, and (c) trifluoromethyl radicals do not attack **1**. Fumaronitrile is reduced cathodically to the anion radical **6**, which abstracts a proton from the solvent (water), forming the succinonitrile radical **7a**. The isolation of **8** (dimer of **7a**) supports the existence of the radical **7a** in the electrolysis system. The succinonitrile radical **7a** combines with the anodically generated trifluoromethyl radical, leading to **2**, and partially dimerizes to **8** under high temperature electrolysis conditions. This type of radical recombination reaction would predominate in a poor hydrogen donor solvent as a mixture of water and acetonitrile (Scheme IV).

The anodically generated trifluoromethyl radicals could migrate to the cathode and be reduced to the trifluoromethyl carbanions, which undergo Michael-type addition to **1**. However, the explanation is unreasonable on taking into account that, firstly, the trifluoromethyl carbanions would be spontaneously protonated in an MeCN–$H_2O$–TFA solvent system and, secondly, hydrotrifluoromethylation is a minor reaction pathway in the electrolysis of methyl acrylate,[15] diethyl fumarate,[18] and acrylonitrile,[20] all of which are good Michael acceptors.

Scheme IV



The present hydrotrifluoromethylation is remarkably temperature dependent (Figure 2). At lower temperatures, the radical anion **6** and the radical **7a** would adsorb on the electrode surface more tightly and thus diffuse less to the bulk solution. As a result, they would mainly undergo subsequent chemical and electrochemical reactions at the cathode surface (proton abstraction/one-electron reduction of **7a**/proton abstraction), leading to **3**.

## Experimental Section

The boiling points are indicated by the temperature of a glass tube oven. Infrared spectra were taken on a Hitachi 270-30 spectrometer. The $^1H$, $^{13}C$, and $^{19}F$ NMR spectra were measured on a Varian VXR-500 instrument using TMS as internal standards for $^1H$ and $^{13}C$ NMR and $C_6F_6$ for $^{19}F$ NMR. Mass spectra (MS) were obtained with a Hitachi M-80 spectrometer.

**2-(Trifluoromethyl)succinonitrile (2).** A mixture of **1** (156 mg, 2.0 mmol), trifluoroacetic acid (0.62 mL, 8.0 mmol), NaOH (32 mg, 0.8 mmol), MeCN (6 mL), and $H_2O$ (1 mL) was electrolyzed at 50 °C in an undivided beaker-type cell (10 cm tall and 1.8 cm in diameter) fitted with platinum foils (1.5 × 1 $cm^2$ for an anode and 1.5 × 2 $cm^2$ for a cathode) as the electrodes. A constant current (50 mA/$cm^2$) was supplied until the charge reached 1.5 faraday/mol of TFA. The solvent was evaporated under reduced pressure, and the organic residue was extracted with AcOEt, washed with brine, dried over $Na_2SO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (hexane–AcOEt), to give **2** (193 mg, 65%) as a slightly green liquid, **3** (11 mg, 7%), and **8** (12 mg, 8%, a mixture of *dl* and meso) as colorless crystals.

**2**: bp 135 °C (5 mmHg); IR (neat) 2952, 2268 (CN), 1366, 1258, 1198, 1142 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 3.03 (d, $J = 6.9$ Hz, 2 H, $CH_2CN$), 3.83 (dq, $J_1 = 6.9$ Hz, $J_2 = 6.9$ Hz, 1 H, $CHCF_3$); $^{13}C$ NMR ($CDCl_3$) $\delta$ 16.2 ($CH_2$), 34.6 (q, $J_{C-C-F} = 34.1$ Hz), 111.5 ($CF_3CHCN$), 113.6 ($CH_2CN$), 121.8 (q, $J_{C-F} = 281.2$ Hz, $CF_3$); $^{19}F$ NMR ($CDCl_3$) $\delta$ 92.3 (d, $J = 7.0$ Hz); MS, *m/e* (relative intensity) 148 ($M^+$, 4), 79 (8), 69 ($CF_3$, 100), 53 (9), 40 (15). Anal. Calcd for $C_5H_3N_2F_3$: C, 40.55; H, 2.04; N, 18.92. Found: C, 40.32; H, 1.94; N, 18.73.

**8**: mp 120 °C; IR (Nujol) 2256 $cm^{-1}$ (CN); $^1H$ NMR (DMSO-$d_6$) $\delta$ 3.14–3.26 (m, 2 H, $CH_2CN$), 3.88–3.92, 4.03–4.07 (m, 1 H, CHCN); $^{13}C$ NMR (DMSO-$d_6$) $\delta$ 17.8, 18.8 ($CH_2CN$), 29.2, 29.9 (CHCN), 116.5, 116.6 (CHCN), 116.7 (2 C, $CH_2CN$); MS, *m/e* (relative intensity) 157 (M – 1, 0.1), 131 (M – HCN, 0.1), 118 (M – $CH_2CN$, 12), 91 (8), 80 (100), 79 (75), 53 (20), 52 (14), 41 (23), 40 (15). Anal. Calcd for $C_8H_6N_4$: C, 60.75; H, 3.82; N, 35.42. Found: C, 60.80; H, 3.85; N, 35.35.

**Electrolysis of 1 and 4 in a Divided Cell.** A mixture of **1** (312 mg, 4 mmol), **4** (0.36 mL, 4 mmol), TFA (1.24 mL, 16 mmol), and NaOH (64 mg, 1.6 mmol) in MeCN (12 mL) and $H_2O$ (2 mL) was added in both compartments of a divided cell separated by sintered glass fitted with platinum foils as electrodes and was electrolyzed at 50 °C. A constant current (50 mA/$cm^2$) was supplied until the charge reached 1.5 faraday/mol of TFA. The solvent was evaporated under reduced pressure, and the organic residue was extracted with AcOEt, washed with brine, dried over $Na_2SO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (hexane–AcOEt), providing **1** (312 mg, 100%) and dimethyl 2,3-bis(2,2,2-trifluoroethyl)succinate (**5**) (310 mg, 50%) from the anodic compartment and succinonitrile (**3**)

(176 mg, 55%) and **1** (62 mg, 20%) from the cathodic compartment. The spectral data of **5** were consistent with those of an authentic sample.[15]

**Reaction of 1 and 4 with $XeF_2$–TFA.** A mixture of **1** (78 mg, 1 mmol) and TFA (0.23 mL, 3 mmol) in $CH_2Cl_2$ (2 mL) was added to $XeF_2$ (254 mg, 1.5 mmol) and then stirred at room temperature for 2 h. The solvent was evaporated under reduced pressure. The organic residue was extracted with AcOEt, washed with brine, dried over $Na_2SO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel (hexane–AcOEt), recovering **1** (55 mg, 70%). By the same procedure, **4** was converted to **5** (202 mg, 65%).

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# Intramolecular Diels–Alder Approach to Cadinane and Amorphane Sesquiterpenes

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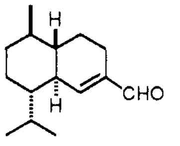
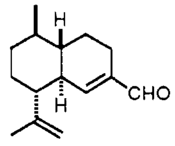
*Received June 26, 1989*

A synthetic route to both cadinane and amorphane type sesquiterpenes is described. Successful implementation of this route showed the structures previously considered for cadinenal (**1**) and dehydrocadinenal (**2**) to be incorrect, but confirmed both the relative and absolute configurations proposed for pernetic acid C (**3**) and pernetic acid B (**4**).

Plant metabolites have often been postulated to provide defense against herbivores. Numerous essential oils have been found to contain terpenes which exhibit insect-repellent activity.[1] The essential oil from the grass *Vetiveria zizanoides* (L.) Nash, known largely because of its use in perfumery, is purportedly repellent to insects. Bioassays using Javanese oil of vetiver showed that the potent topical irritant activity of this oil on flies and cockroaches was attributable to its carbonyl-containing components.[2] Among the minor carbonyl components from this oil, two new sesquiterpene aldehydes, cadinenal (**1**) and dehydrocadinenal (**2**), have been tentatively assigned cadinane-based structures containing four contiguous asymmetric centers, largely on the basis of spectroscopic data.[3]



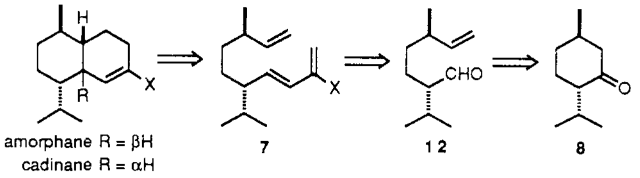
**1**

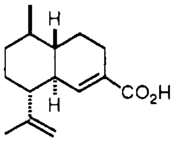


**2**

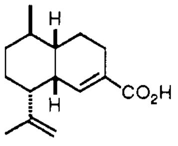
In addition, fruit of the Chilean plant *Pernettya furens* has yielded pernetic acid C (**3**) and pernetic acid B (**4**), which have been assigned structures based on the cadinane and closely related amorphane system, respectively.[4] This fruit, called *hysh-hued* or *hierba-loca*, is toxic to humans and is reported to cause mental confusion and madness.[5] During the characterization of these compounds, both acids were partially hydrogenated over Wilkinson's catalyst to form the corresponding dihydropernetic acids C and B, formulated as **5** and **6**. We have undertaken syntheses of compounds **1**, **5**, and **6** in order to confirm the structural and stereochemical assignments.

**Scheme I**

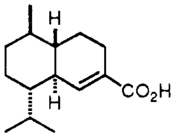




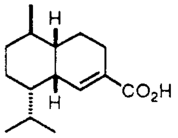
**3**



**4**



**5**



**6**

## Results and Discussion

We sought to establish the four contiguous stereogenic centers in the target compounds by an intramolecular Diels–Alder reaction[6] of an appropriate acyclic triene, as outlined in Scheme I, where X is a suitable precursor to the aldehyde and carboxylic acid functionalities. Consideration of molecular models showed the likelihood of forming both cadinane and amorphane ring systems. We felt that triene **7** could be prepared from aldehyde **12**, which could in turn be formed from (−)-menthone (**8**). This approach would establish the relative stereochemistry of the isopropyl and methyl groups early in the synthesis and would also provide a method by which to determine or confirm the absolute configurations of the natural products.

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