Electrochemical Synthesis of (Phenylseleno)benzophenones and (Phenyltelluro)benzophenones by the $S_{RN}1$ Mechanism, Using a Redox Catalyst

Chantal Degrand* and Rita Prest

Laboratoire de Synthèse et d'Electrosynthèse Organométalliques associé au CNRS (UA 33), Faculté des Sciences Gabriel, 21000 Dijon, France

Paul-Louis Compagnon

Laboratoire de Chimie Organique, Faculté de Pharmacie, 21000 Dijon, France

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Benzophenone derivatives substituted by *o*-, *m*-, or *p*-phenyltelluro and *m*- or *p*-phenylseleno groups have been synthesized in acetonitrile by the mediated cathodic reduction of bromobenzophenone in the presence of an equivalent amount of $PhTe^-$ or $PhSe^-$ initially prepared by electrochemical reduction of the corresponding diphenyl dichalcogenide. Azobenzene (0.1 equiv) was utilized as redox catalyst. Sonication was maintained during electrolysis and an acid such as fluorene or malononitrile (0.5 equiv) was present to avoid the formation of $^-CH_2CN$ and its addition upon the bromo or chalcogeno ketones. Under such conditions, the chalcogeno ketones were isolated in 44–86% yields. In the case of the *m*- and *p*-telluro ketones whose yields are moderate (48% and 44%), the formation of $(PhCOC_6H_4)_2Te$ proceeded simultaneously (31% and 36%).

A convenient method to prepare substituted aromatic compounds is the $S_{RN}1$ aromatic nucleophilic substitution.[1] A large variety of nonsymmetrical diaryl selenides and tellurides has thus been prepared by photochemical stimulation in liquid ammonia[2] and electrochemical stimulation in acetonitrile,[3] from aryl halides and $PhSe^-$ or $PhTe^-$ anions (eq 1–4; E = Se or Te). An advantage of the

$$ArX + \text{electron donor} \rightleftarrows (ArX)^{\bullet -} + \text{residue} \quad (1)$$

$$(ArX)^{\bullet -} \rightarrow Ar^\bullet + X^- \quad (2)$$

$$Ar^\bullet + PhE^- \rightarrow (ArEPh)^{\bullet -} \quad (3)$$

$$(ArEPh)^{\bullet -} + ArX \rightarrow ArEPh + (ArX)^{\bullet -} \quad (4)$$

$$Ar^\bullet + e \rightarrow Ar^- \quad (5)$$

$$med + e \rightleftarrows med^{\bullet -} \quad (6)$$

$$med^{\bullet -} + ArX \rightleftarrows med + (ArX)^{\bullet -} \quad (7)$$

electrochemical method is that the energy involved in the induction step (eq 1) is controlled by the value of the applied potential; however, a disadvantage is that the yields of substitution products can be lower than in the photochemical method, due to a further cathodic reduction (eq 5) of the intermediate aryl radical.[1b,4,5] It explains the moderate yields of *o*-, *m*-, and *p*-(phenylseleno)benzonitrile (36%, 42%, and 59%, respectively) isolated from the partial cathodic reduction of bromobenzonitrile in the presence of an equivalent amount of electrochemically generated $PhSe^-$.[3b] The cathodic side reaction (eq 5) is hindered when the cleavage reaction (eq 2) does not occur close to the electrode or, in other words, when this reaction is not very rapid.[1b,4] Thus, the yield of *p*-(benzeneseleno)benzonitrile increased from 59% to 70% when *p*-chlorobenzonitrile was used instead of *p*-bromobenzonitrile in the $S_{RN}1$ mechanism.[3b] Another means to promote the coupling reaction 3 at the expense of eq 5 is to add an electron donor, a redox catalyst,[1b,e,4f–h,6] which is easier to reduce than ArX, and to perform the electrolysis at potentials where this mediator is the only electroactive species. Under such conditions, the electrochemical synthesis proceeds according to eq 6, 7, and 2–4.

Indeed, the addition of benzonitrile as mediator has allowed the electrochemical synthesis in DMSO of diphenyl sulfide in 67% yield from bromobenzene and PhS^-, whereas in the absence of catalyst, the yield dropped to 8%.[6] We wish to report the results of a study of the large-scale electrochemical synthesis of the phenylchalcogeno ketones **1a–e**. This study was carried out in acetonitrile which is a very versatile solvent, on a graphite tissue cathode, with sonication as stirring. None of these compounds has been described previously. An attempt to synthetize the seleno ketone **1d** by photostimulated $S_{RN}1$ substitution in liquid ammonia failed[2e] since $PhSe^-$ was observed to add upon the carbonyl group of *p*-chlorobenzophenone (**2d**). The multiple step chemical synthesis in moderate yield of **1f** from *o*-(chloroseleno)benzoyl chloride and Ph_2Cd has been reported previously,[7] and so we have not examined the electrochemical synthesis of this compound. It will be shown that the best yields of substituted ketones (57–77%) were obtained when a mediator such as azobenzene was present and when an acid such as fluorene or malononitrile was added to avoid the

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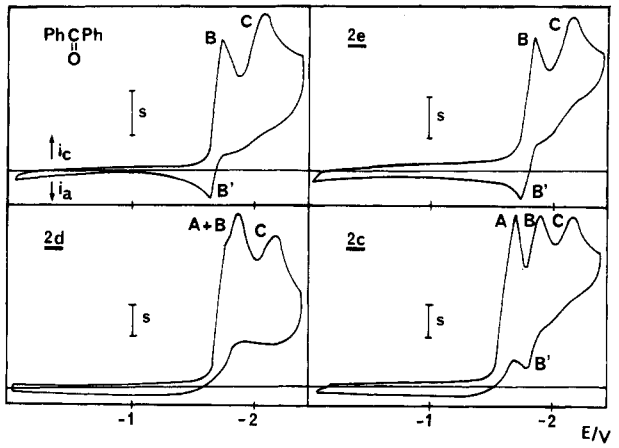


Figure 1. Cyclic voltammograms of **2c–e** (2 mM) and benzophenone (2 mM). The scan rate is 0.1 V s^{-1}, and $s = 2 \times 10^{-5}$ A.

Table I. Cyclic Voltammetric Data for the Ketones 2a–f (2 mM) and Benzophenone (2 mM) at a Glassy Carbon SDE in MeCN[a]

	$-E_p$, V			
ketone	peak A	peak B	peak B′	peak C
2a	1.65	1.87	1.79	2.15
2b	1.70	1.86	1.78	2.14
2c	1.69	1.89	1.78	2.14
2d	1.79	1.87		2.17
2e		1.74	1.66	2.07
2f		1.86		2.14
benzophenone		1.86	1.77	2.14

[a] The peak potential values E_p refer to a SCE.

formation of $^-CH_2CN$ and its further addition upon carbonyl groups.

1a: R = *p*-TePh
b: R = *m*-TePh
c: R = *o*-TePh
d: R = *p*-SePh
e: R = *m*-SePh
f: R = *o*-SePh

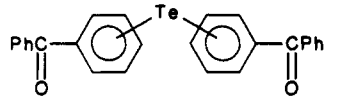
2a: X = *p*-Br
b: X = *m*-Br
c: X = *o*-Br
d: X = *p*-Cl
e: X = *m*-Cl
f: X = *o*-Cl

Results and Discussion

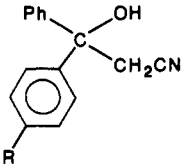
Bromobenzophenones as well as chlorobenzophenones can be considered a priori as precursors in the electrochemical synthesis of the chalcogeno ketones **1**, according to eq 1–4. However, as shown below, the cathodic behavior of the chloro ketones shows that they cannot be utilized.

Cathodic Behavior of the Halogenobenzophenone Derivatives 2a–f. In nonaqueous media, the cathodic reduction of some of the ketones **2a–f** has been described previously.[5,8] In MeCN, the results of a cyclic voltammetric study performed at a stationary glassy carbon disc electrode (SDE) are shown in Figure 1 and summarized in Table I. In the case of the bromo ketones **2a–c**, the first irreversible reduction step (peak A of Figure 1) was a two-electron reductive cleavage[8] which gave the anion $PhCOC_6H_4^-$ according to eq 1, 2, and 5. A fast protonation of this anion led to benzophenone which was further reduced reversibly to its radical anion (peaks B and B′ of Figure 1) and irreversibly to its dianion (peak C). In the presence of benzenechalcogenate PhE^-, the intermediately generated radical $PhCOC_6H_4^{\bullet}$ is expected to be trapped according to eq 3 before its further reduction (eq 5). Since Br^- is a better leaving group than Cl^-, the electrochemical synthesis of the chalcogeno derivatives **1** would proceed a priori in better yields with the chloro ketones **2d–f** as precursors. As expected, the reductive cleavage of the C–Cl bond occurred at more negative potentials than in the preceding case, but the peaks A and B/B′ collapsed in the case of the ortho and para isomers **2d** and **2f** (Figure 1), and therefore they cannot be utilized. Furthermore the radical anion $PhCOC_6H_4Cl^{\bullet-}$ of the meta isomer **2e** was stable.[8]

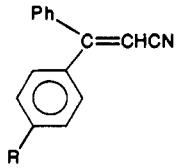
Large-Scale Electrolyses of *p*-Bromobenzophenone (2a) in the Presence of $PhTe^-$ and $PhSe^-$. The electrolyses were carried out in a two-step process. First, diphenyl dichalcogenide (1 mmol) was reduced to benzenechalcogenate PhE^- with sonication in a H-type cell equipped with ion-exchange membranes. Such conditions facilitated stirring and avoided anodic migration of PhE^-. In a second step, the ketone **2a** (2 mmol) was added, and the applied potential was changed toward negative values where the first reduction step of **2a** took place. When electrogenerated $PhTe^-$ was present and the ketone **2a** partially reduced (50%), the substituted telluro ketones **1a** and **3a** were isolated in low yields (entry 1 of Table II), together with benzophenone, starting materials **2a**, PhTeTePh, and nitriles **4b**[16] and **5b**[16] in low yields. When **2a** is totally reduced, the yields of the nitriles **4b** and **5b** increased, whereas those of **1a** and **3a** decreased significantly. The total electrolysis of **2a** in the presence of $PhSe^-$ led to a moderate yield of the substituted ketone **1d** (entry 2 of Table II) and again to nitrile derivatives, mainly **4c** and **5c**. This shows that, in both electrolyses, MeCN molecules were involved. Deprotonation of the solvent ($pK_A = 25$) by cathodically generated $PhCOC_6H_4^-$ anion provided $^-CH_2CN$ which is known[9,10] to react with aromatic ketones. In the case of benzophenone, the saturated and unsaturated nitrile adducts **4a** and **5a** are thus isolated.[9] Addition of a weak acid such as fluorene ($pK_A = 22.6$[11]) or malononitrile ($pK_A = 11.0$[11]) at the second stage of the electrolysis would hinder the formation of the conjugated base of the solvent and therefore of nitrile derivatives. Addition of an equivalent of fluorene improved the yield of the seleno ketone **1d** by suppressing the formation of nitrile derivatives (entry 3 of Table II).



3a: *p,p′*-Te
b: *m,m′*-Te



4a: R = H
b: R = Br
c: R = SePh



5a: R = H
b: R = Br (cis + trans)
c: R = SePh (cis + trans)

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Table II. Large-Scale Reduction with Sonication of 2a (2 mmol) in the Presence of PhE⁻ (2 mmol; 1 equiv)

electrolysis	PhE⁻	added acid (equiv)	charge consumed, mmol of e	e-equiv consumed	substd products	yield,[a] %
1	PhTe⁻		0.50[b]	0.50[c]	1a	17[c]
					3a	6[c]
2	PhSe⁻		0.66	0.33	1d	49
					4c	5
					5c	7
3	PhSe⁻	fluorene (1)	0.84	0.42	1d	61 (44[d])

[a] Isolated yields. [b] Partial reduction of 2a (50%). [c] Taking into account the partial reduction of 2a. [d] Yield after crystallization.

Table III. Large-Scale Reduction with Sonication of the Bromo Ketones 2a–c (4 mmol) in the Presence of an Equivalent Amount of PhE⁻[g]

electrolysis	ketone	PhE⁻	added acid	charge consumed, mmol of e	n_1[a]	theor substn yield, %	substd products	yields,[b] %
1	2a	PhSe⁻	fluorene	1.18	0.19	90.5	1d	86 (57)
2	2a	PhSe⁻		0.92	0.18[c]	91	1d	64 (48)
							4c	9 (3)
							5c	1[d]
3	2a	PhTe⁻	fluorene	0.75	0.11	94.5	1a	45 (43)
							3a	36 (34)
4	2a[e]	PhTe⁻	fluorene	1.26	0.21	89.5	1a	44[e] (43)
							3a	23[e] (22)
5	2b	PhTe⁻	malononitrile	1.08	0.17	92.5	1b	48
							3b[f]	31
6	2b	PhSe⁻	malononitrile	1.42	0.25	87.5	1e	62
7	2c	PhTe⁻	malononitrile	1.27	0.22	89	1c	75 (60)

[a] Electron-equivalent consumed in the $S_{NR}1$ mechanism; see the text. [b] Isolated yields; the values in parentheses are the yields after crystallization. [c] 0.05 equiv of azobenzene in this experiment. [d] Cis/trans in 1/1 ratio from ^{1}H NMR determination. [e] Magnetic stirring instead of sonication. [f] This compound contained an impurity. [g] The reduction of the ketones was mediated by azobenzene (0.4 mmol; 0.1 equiv), and an acid (2 mmol; 0.5 equiv) was present during the second stage of the electrolysis.

During the electrochemical synthesis of the telluro ketone **1a** (entry 1 of Table II), the concomittant formation of **3a** suggests a partial decomposition of the intermediate $\mathbf{1a}^{\bullet-}$ radical anion (eq 8). Since diphenyl telluride was not

$$(PhC(=O)C_6H_4TePh)^{\bullet-} \rightarrow PhC(=O)C_6H_4Te^- + Ph^{\bullet} \quad (8)$$

isolated, it suggests that the phenyl radicals generated in eq 8 would be reduced to Ph^- more rapidly than they would be trapped by $PhTe^-$ anion. The decomposition of $\mathbf{1a}^{\bullet-}$ would impede the formation of **1a** and promote that of **3a** since the telluride anion thus generated would be involved in the $S_{RN}1$ mechanism.

The above results show that the first electron uptake by the bromo ketone **2a** was rapidly followed by a cleavage of the C–Br bond and so the $PhCOC_6H_4^{\bullet}$ radical thus generated close to the electrode was mainly reduced to its anion according to eq 5, whose protonation by MeCN or fluorene led to benzophenone. Addition of a mediator prevents the cathodic reduction (eq 5) as shown below.

Mediated Electrochemical Reduction of the Bromo Ketones 2a–c in the Presence of PhTe⁻ and PhSe⁻. Azobenzene which is reversibly reduced at potentials positive of bromophenone was observed to mediate the electrochemical reduction of the ketones **2a–c**. In cyclic voltammetry at a SDE, the cathodic current of azobenzene was increased at the expense of the anodic current when bromobenzophenone was added. No more anodic peak was observed when the ketone was in excess (Figure 2).

Large-scale mediated electrochemical synthesis of the ketones **2a–c** was performed under the following conditions. Electrochemical synthesis of PhE^- was followed by the addition of azobenzene (0.1 equiv), fluorene or malononitrile (0.5 equiv), and bromobenzophenone (1 equiv). The second stage of the electrolysis was then carried out at potentials where the mediator is the only electroactive species. The ketones **1a–e** could thus be isolated in good

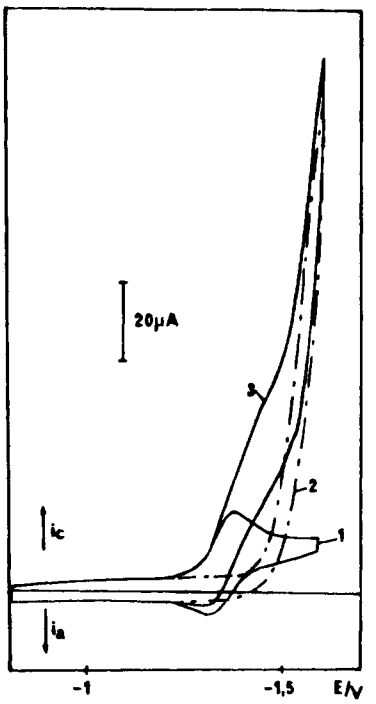

Figure 2. Cyclic voltammograms of (1) azobenzene (0.4 mM), (2) **2a** (4 mM), (3) azobenzene (0.4 mM) + **2a** (4 mM). The scan rate is 0.1 V s^{-1}.

yields (Table III). Let us consider the results presented in electrolysis 1 of Table III. Since the electrolysis was stopped after total depletion of the faradaic current and 1.16 mmol of electrons was consumed in the mediated reduction of **2a**, it can be concluded that 0.76 mmol of electron was first involved in the $S_{RN}1$ process then 0.40 mmol in the monoelectronic reduction of azobenzene to its radical anion (this species is oxidized to azobenzene

Table IV. Physical and Spectroscopic Data of Aryl Selenides and Tellurides

compd	mp, °C	IR, cm^{-1}	NMR[a]	MS, m/e (relative intensity)
1a	78[b]	1651 (C=O)	7.88–7.21 (m, 14 H)	388 (M, 52),[c] 181 ($PhCOC_6H_4$, 100)
1b	oil	1655 (C=O)	8.05 (s, 1 H), 7.90–7.13 (m, 13 H)	388 (M, 100), 105 (PhCO, 52)
1c	75[b]		8.05–7.17 (m, 14)	388 (M, 100), 311 ($PhCOC_6H_4Te$, 99)
1d	78[b]	1655 (C=O)	7.81–7.32 (m, 14 H)	338 (M, 32),[d] 105 (PhCO, 100)
1e	oil	1658 (C=O)	7.86–7.20 (m, 14 H)	338 (M, 100), 105 (20)
3a	134[e]	1652 (C=O)	7.86–7.36 (m, 18 H)	492 (M, 22),[c] 105 (PhCO, 100)
3b	oil[f]	1658 (C=O)	8.10 (s, 2 H), 8.00–7.15 (m, 16 H)	492 (M, 100), 105 (PhCO, 59)
4c	101[b]	2264 (C≡N)	7.31 (s, 5 H), 7.60–7.10 (m, 9 H), 3.20 (s, 2 H), 2.90 (s, 1 H)	379 (M, 6),[d] 105 (PhCO, 100)
5c[g]		2211 (C≡N), 1650 (C=C)	7.62–7.09 (m, 14 H), 5.70 and 5.68 (s, 1 H)[h]	361 (M, 94),[d] 281 (M – Se, 100)

[a] Solvent is $CDCl_3$. [b] Solvent of crystallization is ether–pentane. [c] The isotopic distribution in tellurium containing fragments is as follows: ^{120}Te, 0.26; ^{122}Te, 7.54; ^{123}Te, 2.52; ^{124}Te, 13.37; ^{125}Te, 20.27; ^{126}Te, 54.26; ^{128}Te, 92.19; based on the most abundant ^{130}Te peak which was taken into account for the description of the MS spectra. [d] The isotopic distribution in selenium containing fragments is as follows: ^{74}Se, 1.8; ^{76}Se, 18.1; ^{77}Se, 15.2; ^{78}Se, 47.2; ^{82}Se, 18.5; based on the most abundant ^{80}Se peak which was taken into account for the description of the MS spectra. [e] Solvent of crystallization is dichloromethane–pentane. [f] An impurity was present (see the text). [g] This compound was isolated in too low yield to allow its complete characterization. [h] Cis/trans in 1/1 ratio.

during treatment of the cathodic solution). In other words, the amount n_1 of electron-equivalent consumed per mole of **2a** is 0.19, which indicates an excellent theoretical yield of substitution products (90.5% if we consider the bielectronic reduction of **2a** to benzophenone). A comparison of entries 1 and 2 of Table III shows, once more, that in the absence of fluorene, the formation of $^-CH_2CN$ occurred, its addition upon the seleno ketone **1d** diminishing its yield at the benefit of the saturated and unsaturated nitrile adducts **4c** and **5c**. The assisted reduction of **2a** in the presence of $PhTe^-$ gave a high total yield (77%) of the telluro derivatives **1a** and **3a** (electrolysis 3). This yield was slightly decreased with magnetic stirring instead of sonication (electrolysis 4). Again a mixture of telluro ketone **1b** and diketone **3b** was obtained when **2b** was reduced in the presence of $PhTe^-$. It was not possible to isolate **3b** as the pure oil since its ^1H NMR and IR spectra revealed the presence of traces of an unidentified unsaturated nitrile derivative (olefinic proton at 5.7 ppm and C≡N bond at 2251 cm^{-1}). Several other electrolyses described in Table III led to traces of unidentified nitrile derivatives. The physical and spectroscopic data of the chalcogeno derivatives **1a–e**, **3a,b**, **4c**, and **5c** are summarized in Table IV. A detailed study of the electrochemical behavior of the chalcogeno ketones **1a–e** and **3a–b** will be presented later. At a SDE electrode, their first reduction step was observed at potential values negative of –1.74 V, so their electrochemical reduction did not interfere in the $S_{RN}1$ mechanism, since the values are more negative than in the case of the bromo ketone **2a–c** (Table I).

Conclusions

The mediated electrochemical reduction of bromobenzophenone in the presence of PhE^- has allowed the synthesis of the chalcogeno ketones **1a–e** in satisfactory yields in acetonitrile although this versatile solvent is known to be a good H-atom[1,4,8,12] as well as proton donor. The H-atom-donating ability of the solvent did not prevent the formation of the chalcogeno benzophenone since the results of Table III indicate theoretical yields of substituted ketones of about 90%. The acidic properties of the solvent were overcome by addition of a carbon acid such as fluorene or malonitrile, which hindered the formation of $^-CH_2CN$. However, traces of nitrile derivatives were isolated in a few cases, suggesting that deprotonation of the carbon acids was not rapid enough and that hetero acids would be more efficient. The addition of $^-CH_2CN$ upon the carbonyl function was thus avoided in a large extent. On the another hand, it has to be borne in mind that $^-CH_2CN$ is a nucleophile which is known to be involved in $S_{NR}1$ mechanism.[1] However, no nitrile derivative corresponding to this substitution process was isolated. Similarly the conjugated bases of the added carbon acids were not observed to interfere. Sonication has been shown to increase the yield of substituted derivatives (compare electrolyses 3 and 4 of Table III). The role of ultrasound has not yet been fully established although it may affect mass transport.[13,14] A detailed study of the influence of sonication and the concentration of mediator upon the electrochemically induced $S_{RN}1$ mechanism will be published later.

Experimental Section

Compounds **2a,d–f**, diphenyl diselenide, and diphenyl ditelluride are commercially available. The ketones **2b,c** were prepared according to ref **15**. Analytical grade acetonitrile (Spectrosol SDS) was carefully dried on neutral alumina.

Elemental analyses were performed by Service Central d'Analyse, CNRS, Lyon. Spectra were recorded by means of the following instruments: infrared, Perkin-Elmer 580 B; ^1H NMR, JEOL FX 100.

Cyclic voltammograms at a stationary glassy carbon disk electrode (V 25 Carbone Lorraine; diameter = 3 mm) were obtained with a Tacussel UAP 4 unit and a GSTP function generator and were recorded on an Ifelec 2025 C *X–Y* recorder. An Amel 552 potentiostat (output voltage 200 V at full load) and a Tacussel IG 5-N integrator were used in coulometry and preparative electrolysis. All the potentials referred to the aqueous saturared calomel electrode (SCE). Large-scale electrolyses were performed in a H-type cell, the three compartments of which were separated by ion-exchange membranes Ionac 3475 (anodic side) and MC 3470 (cathodic side) and filled with acetonitrile containing 0.1 M Bu_4NPF_6. The cathode was a graphite cloth of cylindric shape and the anode a Pt grid. The cathodic solution was dearerated with argon before electrolysis. The volume of the cathodic compartment was 25 (Table II) or 100 mL (Table III). The cell was immersed in a sonic cleaning bath (vat Sonoclean or Bransonic) filled with cold water. Sonication and an argon atmosphere were maintained during electrolysis and for 10 min. Afterward, oxygen was introduced before treatment of the cathodic solution.

The electrolyses of Table II were carried out as follows. Diphenyl dichalcogenide (1 mmol) was introduced and reduced to PhE^-. The potential had to be changed from –1.20 to –2.35 V (E = Te) and –1.10 to –2.10 V ((E = Se), whereas the faradaic

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current dropped from 100 mA (initial value) to a negligible value after consumption of 193 C (2 mmol of electrons). The electrolysis was interrupted, and **2a** (2 mmol) was added; then a working potential of −1.6 ± 0.1 V was applied. The electrolysis was stopped after partial (electrolysis 1) or total depletion (electrolyses 2 and 3) of the faradaic current. Fluorene (2 mmol) was present during the second stage of electrolysis 3. The cathodic solution was diluted with water, and the electrolysis products were extracted with diethyl ether. After the solution was dried, the ether was removed. The crude product was separated by column chromatography with 2/8 diethyl ether/hexane or 1/9 acetone/hexane as eluant and 70–230-mesh silica gel.

The electrolyses of Table III were performed as follows. Diphenyl dichalcogenide (2 mmol) was reduced to PhE^- as above, and then a mixture of azobenzene (0.4 mmol), **2** (4 mmol), and fluorene or malononitrile (2 mmol) was introduced. A working potential of −1.25 ± 0.05 V was applied, and the second stage of the electrolysis was carried out until total depletion of the faradaic current. Treatment of the cathodic solution was performed as above.

The physical and spectroscopic data of the isolated chalcogeno derivatives are summarized in Table IV. Satisfactory analytical data (0.4% for C and H) were reported for all compounds listed in this table, except for **3b** which contained an impurity as mentioned in the text.

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Registry No. **1a**, 110589-51-0; **1b**, 110589-52-1; **1c**, 106467-87-2; **1d**, 110589-53-2; **1e**, 110589-54-3; **2a**, 90-90-4; **2b**, 1016-77-9; **2c**, 13047-06-8; **2d**, 134-85-0; **2e**, 1016-78-0; **2f**, 5162-03-8; **3a**, 110589-57-6; **3b**, 110589-58-7; **4c**, 110589-56-5; *cis*-**5c**, 110589-55-4; *trans*-**5c**, 110589-59-8; PhTeTePh, 32294-60-3; PhSeSePh, 1666-13-3; $PhSe^-$, 14971-39-2; $PhTe^-$, 65081-67-6; azobenzene, 103-33-3; fluorene, 86-73-7; malononitrile, 109-77-3; benzophenone, 119-61-9.

Studies on the Synthesis of Morphinan and Its Related Compounds: Construction of Morphinan Skeleton

Tetsuji Kametani,* Masato Nishimura, Katsuyuki Higurashi, Yukio Suzuki, Masayoshi Tsubuki, and Toshio Honda

Institute of Medicinal Chemistry, Hoshi University, Ebara 2-4-41, Shinagawa-ku, Tokyo 142, Japan

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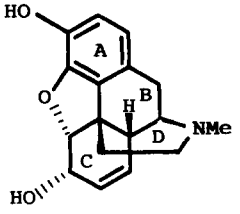
Diels–Alder reaction of the cyclohexadiene derivatives **1** and **2** with α-chloroacrylonitrile afforded the adducts **7** and **8**, whose hydrolysis, followed by the fragmentation reaction, gave rise to the cyanides **13** and **14**. Since these compounds were transformed into mesembrine (**15**) and *O*-methyljoubertiamine (**16**), this synthesis constitutes their formal synthesis. Furthermore, the cyanide **13** was converted to the alcohol **24**, whose Claisen rearrangement furnished the aldehyde **29**. After formation of the B ring of the morphinan skeleton by dehydration of **29**, the olefin **30** was transformed into the amine **32**, whose cyclization through the aminylium ion intermediate, followed by demethoxylation under the Birch reduction condition, provided the morphinan **34**.

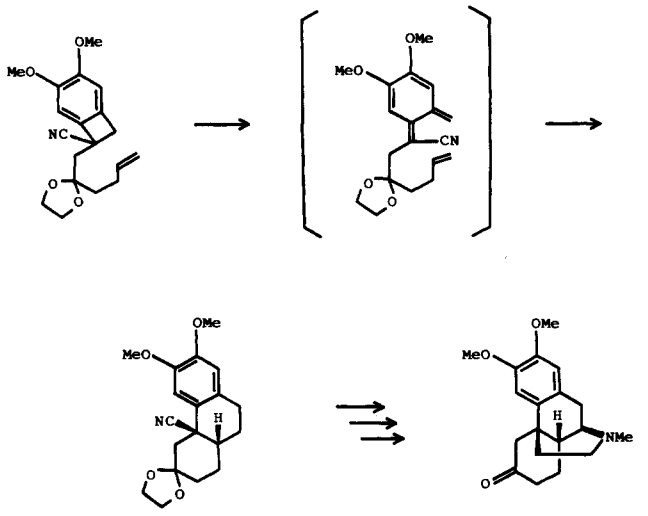
Morphine is the major constituent of opium, and its structure has been established[1] from spectroscopic characteristics including X-ray technique[2] and by syntheses.[1] Since this class of alkaloids exhibits important physiological activities, a number of synthetic routes have been elaborated in a variety of ways.[1]



morphine

During the last several years, we have been involved in the development of a general route to morphinans and have reported the stereoselective synthesis of the morphinan ring skeleton employing an intramolecular [4 + 2]-cycloaddition reaction of *o*-quinodimethane generated in situ by thermolysis of a corresponding benzocyclobutene as a key step to control the stereochemistry of its B/C ring juncture[3] (Scheme I). Here we report an alternative synthetic approach to morphinans.

Scheme I



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