# Comparative Studies of Cathodically-Promoted and Base-Catalyzed Michael Addition Reactions of Levoglucosenone

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Regioselective Michael addition of nitro and heterocyclic compounds to levoglucosenone, **1**, is effectively catalyzed by amines and also by cathodic electrolysis. In comparison to the base-catalyzed reaction, it was found that under electrochemical conditions the reaction proceeds under milder conditions and with higher yields. Cathodically-initiated Michael addition of thiols to levoglucosenone using small currents produces the previously unknown *threo* addition product in several instances. The normal *erythro* isomer, identified as the kinetic product, tends to be formed when large currents are used. In contrast, slow, low current electrolyses promote equilibration of the two forms so that *erythro* can be converted to *threo* by the retro reaction and readdition. Addition of 2-naphthalenethiol to (*R*)-(+)-apoverbenone is also reported.

## Introduction

Levoglucosenone (**1**) is an interesting starting material because it is chiral and contains an activated double bond. Moreover, this compound can be obtained from biomass by pyrolysis of wood wastes.[1] An improved method of pyrolysis of cellulose now allows the preparation of **1** in higher yield than previously achievable.[2] Levoglucosenone has been successfully used as a chiral starting material for syntheses of a variety of natural and unnatural compounds such as food toxins,[3] alkaloids,[4] antibiotics,[5] anhydrosugars,[6] prostaglandin analogues,[7] herbicides,[8] etc.

One of the most attractive reactions for modification of the carbohydrate skeleton of **1** is Michael addition.[9−11] By base-catalyzed reaction of **1** with alcohols and thiols, the corresponding alkoxy and alkylthioderivatives have been obtained in good yields.[1a,9] However, in the case of the addition of malonate and cyanoacetate, the yields were moderate (49−54%), and a yield of 70% could be achieved for malonate only by use of Ni(II) complexes as catalysts.[11] It is probable that the suppressed yields were caused by oligomerization of **1** under the basic conditions used in the reaction.[11] It should be noted that in all cases only exo-addition was observed to occur forming the 4-axial derivatives, *i.e., anti* to the 1,6-anhydro bridge as in compounds **3** below.

The presence of a nitro group in a 4-substitutent of **1** would be interesting owing to the possibility of further transformation of the nitro group (*e.g.*, reduction to the amine) as well as the formation of new C−C bonds at its activated α-carbon. In the literature, only the Michael addition of 2-nitropropane and nitromethane to **1** have been reported.[10,12] It is interesting to consider the addition of ethyl nitroacetate and its derivatives to **1**,[13] which allows the introduction of carbethoxy, nitro, alkyl, and other functional groups to levoglucosenone. Subsequent transformation of these functionalities can be used for the synthesis of both unnatural amino acids and heterocycles. In this work we summarize our comparative studies of the Michael addition reactions of different kinds of organic acids to levoglucosenone under electrochemical and purely chemical conditions.

It is known that the Michael addition reaction is effectively promoted by electrogenerated bases[14] or by direct cathodic electrolysis.[15] Recently, it was shown that ethyl nitroacetate and its derivatives electrocatalytically react under mild conditions with Michael acceptors to form coupling products in high yield.[16a] This approach has been successfully applied for functionalization of **1**.

## Results and Discussion

**Reaction of Levoglucosenone with Nitro Compounds.**[17] The anions of nitro compounds can be formed

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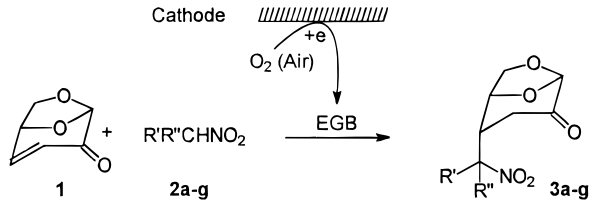
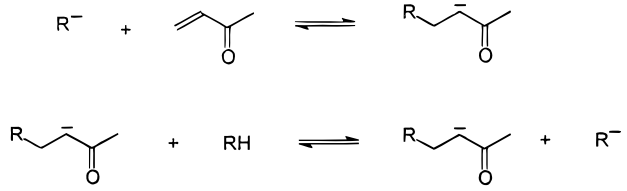
**Scheme 1**




| 2 | R' | R" | Yield of 3, % |
|---|---|---|---|
| a | H | $CO_2Et$ | 85 |
| b | Me | $CO_2Et$ | 89 |
| c | $CO_2Et$ | $CH_2CH_2CO_2Et$ | 82 |
| d | Me | Me | 93 |
| e | -$(CH_2)_5$- | | 96 |
| f | $CO_2Et$ | $CH_2CH{=}CH_2$ | 89 |
| g | H | $NO_2$ | 88 |

**Scheme 2**

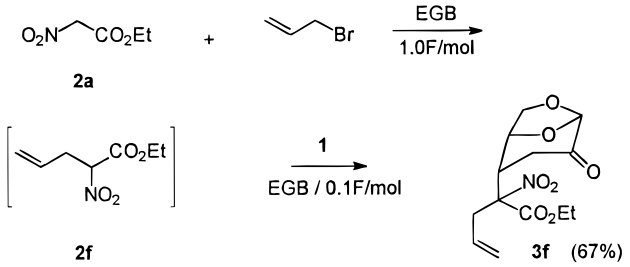



by direct reduction at the cathode with concomitant discharge of hydrogen. However, when the nitro compound contains a second electron-withdrawing group, it has been found[16] that production of the anion is accompanied by elimination of the nitro group, even in the case of relatively strong organic acids as, for example, ethyl nitroacetate[16a] (p$K_a$($H_2O$)[18a] = 5.75; p$K_a$(DMSO)[18b] = 9.2). Thus, the desired anion, necessary for catalytic addition to **1**, is not formed efficiently. This difficulty was easily overcome when electrogenerated superoxide was used as an electrogenerated base (EGB) for generation of the carbanion of nitro compounds.[16a]

Cathodic electrolysis of ethyl nitroacetate (**2a**) in the presence of an equimolar amount of levoglucosenone in an air-saturated solution of 0.01 M $Bu_4NBr$ in MeCN produced **3a** (Scheme 1) in 85% isolated yield. Only 0.10 F/mol of electricity was consumed, and the reaction was completed in 1 h at room temperature (see general catalytic Scheme 2).[19] Isolation of the product was very simple: a solution of the crude product was filtered through a layer of silica gel, and after evaporation of the solvent, the analytically pure product was obtained.

The key step of the reaction is the cathodic generation of EGB, which deprotonates ethyl nitroacetate with formation of the corresponding carbanion. The use of tetraalkylammonium salts as supporting electrolyte results in a very high reactivity of this carbanion.[20] Therefore,

**Scheme 3**




the anion reacts rapidly with **1** with the result that the reaction medium remains essentially neutral, thus circumventing the base-catalyzed oligomerization of **1**.

In an analogous fashion, the coupling products of **1** with ethyl 2-nitropropionate (**3b**), diethyl 2-nitroglutarate (**3c**), 2-nitropropane (**3d**), nitrocyclopentane (**3e**), ethyl 2-nitro-4-pentenoate (**3f**), and dinitromethane (**3g**) were obtained (Scheme 1) in practically quantitative yields (82−96% isolated).

It should be noted that in all cases exclusively exo addition of the nitro-containing substituent was observed, giving the *erythro* stereoisomers shown in Scheme 1.

Electrochemical syntheses are often amenable to multistep reactions without isolation of intermediate products. In earlier work,[16a] it was shown that under electrochemical conditions alkylation of ethyl nitroacetate and further Michael addition can be carried out in a one-pot procedure. This approach was used for synthesis of **3f**. Electrochemical alkylation of ethyl nitroacetate with allyl bromide was first carried out to form ethyl 2-nitro-4-pentenoate (**2f**). Levoglucosenone was then added, and the cathodically-promoted Michael reaction resulted in formation of **3f** in moderate yield (Scheme 3).

In contrast to the present electrochemical method, the reported chemical version[10] of the reaction of 2-nitropropane with **1** required heating for 48 h and was accompanied by side reactions, the yield of **3d** being only 15%. A higher yield (67%) was achieved by using 2-nitropropane as solvent, but the isolation of the product required column chromatography due to the presence of byproducts.

In general, the most effective bases for catalyzing Michael addition to **1** have proven to be nitrogen-containing bases such as triethylamine, piperidine, or tetramethylguanidine. For purposes of comparison with the electrochemical method, we treated **1** with ethyl nitroacetate at 20−25 °C in acetonitrile in the presence of a catalytic amount of triethylamine. The exo-derivative **3a** was obtained with an isolated yield of only 38%. Under the same conditions, the products of condensation of **1** with ethyl 2-nitropropionate (**3b**) and diethyl 2-nitroglutarate (**3c**) were obtained with isolated yields of 35 and 37%, respectively. The use of Triton B, piperidine, or tetramethylguanidine as well as increasing the temperature did not improve the yield of the products.

Only when the reaction was carried out in $CHCl_3$ at 40−50 °C for 48 h were the yields of **3a** (75%), **3b** (86%), and **3c** (83%) comparable to those obtained by the electrochemical method.

Interesting results have been reported for the condensation of **1** with nitromethane. Forsyth *et al.*[12] reported that the reaction of nitromethane and **1** in the presence of tetramethylguanidine led to excellent yields of either a coupling product with two molecules of **1** and one of nitromethane (**3h**) or one with one **1** and two molecules

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(19) The two reactions in Scheme 2 constitute a chain process by which a small amount of anion initiates the catalytic addition of RH to the acceptor. The term F/mol denotes the number of equivalents of electrical charge per mole of reactant. In the limit of infinitely effective catalysis, this quantity approaches zero.

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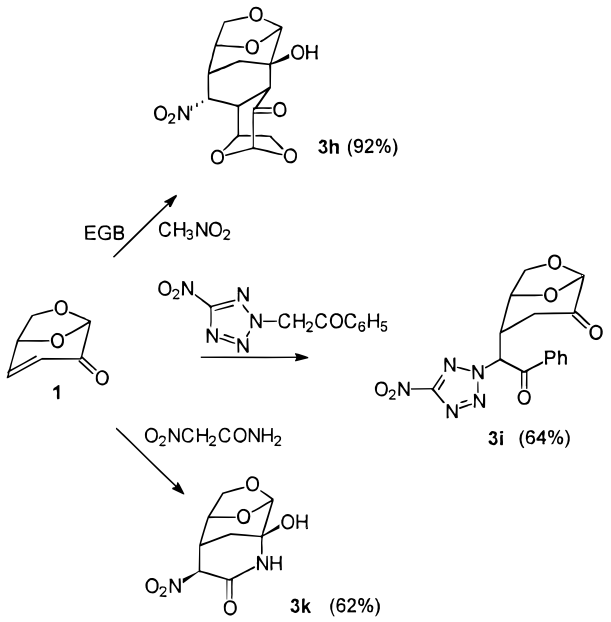
**Scheme 4**

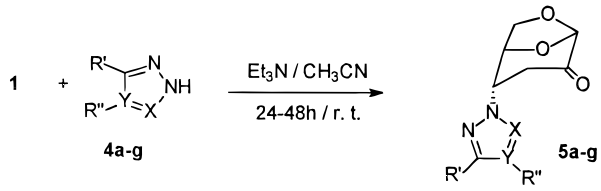



of nitromethane, depending upon the ratio of reactants. When an equimolar mixture was used, a mixture of the two products was obtained with yields of 18% and 61% yields, respectively. Results from the electrochemical method were more selective. Electrolysis of an equimolar mixture of nitromethane and **1** gave exclusively **3h** (isolated yield of 92% based on **1** Scheme 4).

It should be noted that stereoselectivity at the carbon center attached to **1** is low and identical for both the electrochemical and chemical reactions. According to $^1$H-NMR data the ratio of diastereomers for the compound **3a** is close to 1:1 (structures not assigned). For other compounds (**3b**,**c**,**f**) the ratio was 3:4. The same ratio was obtained when 5-nitro-2-phenacyltetrazole, **2i**, was chemically added to **1** (the yield of **3i** was 64%). So, the stereoselectivity is low both for compounds with an acidic proton (where epimerization is possible) and those with much less acidic protons. The situation was different when addition was accompanied by cyclization. As was already mentioned, in the case of nitromethane only one stereoisomer (**3h**) is formed. It was found that chemical addition of the amide $O_2NCH_2CONH_2$ (**2j**) to **1** also is accompanied by cyclization and formation of only one stereoisomer (**3j**) in 62% yield (Scheme 4).

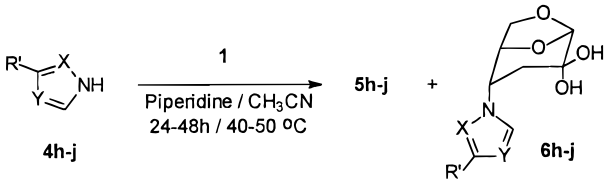
**Reaction of Levoglucosenone with Nitrogen-Containing Heterocycles.** Nitrogen-containing 5-membered heterocyclic compounds substituted on nitrogen by a carbohydrate moiety could be interesting as biologically active compounds due to a structural analogy with nucleosides. These kinds of compounds can be easily synthesized by Michael addition of NH-azoles to the activated double bond of LG in the presence of bases. It was found that NH-heterocycles that are relatively strong acids react with **1** smoothly in 24−48 h at room temperature in the presence of triethylamine. The yields of isolated products were 67−81% (see Scheme 5) except in the case of the reaction of **1** with 3-nitro-1,2,4-triazole (**4e**) where only 52% was obtained. This example was selected for comparison with the electrochemical version of the reaction. Cathodic electrolysis of a mixture of **1** and **4e** resulted in formation of addition product **5e** in good isolated yield (85%). In this reaction, electrogenerated superoxide ion was used as an EGB.

**Scheme 5**




| 4 | X | Y | R' | R'' | Yield of **5**, % |
|---|---|---|---|---|---|
| **a** | CH | C | $NO_2$ | H | 81 |
| **b** | CH | C | $NO_2$ | $NO_2$ | 80 |
| **c** | CH | C | H | $NO_2$ | 79 |
| **d** | CH | C | $CH_3$ | $NO_2$ | 72 |
| **e** | CH | N | $NO_2$ | H | 52 |
| **f** | N | C | $CO_2CH_3$ | $CO_2CH_3$ | 67 |
| **g** | N | N | $NO_2$ | – | 74 |

**Scheme 6**




| 4 | X | Y | R' | Yield, % 5 | 6 |
|---|---|---|---|---|---|
| **h** | N | CH | $CH_3$ | 70* | traces |
| **i** | N | CH | H | 33 | 32 |
| **j** | CH | N | H | 60 | 20 |

*)Mixture of 1-N- (59%) and 2-N-addition (11%) products

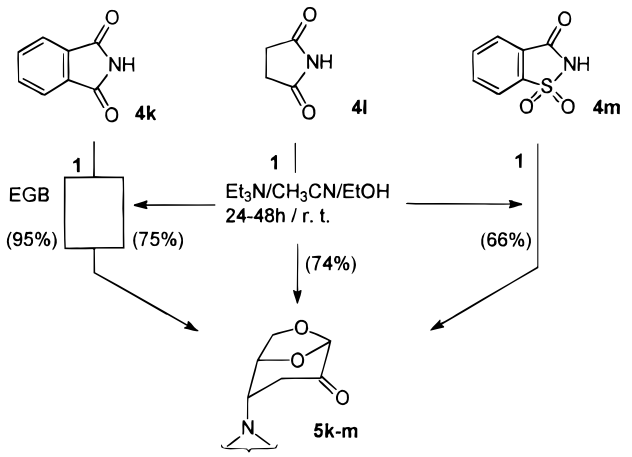
Less acidic heterocycles require stronger base and higher temperature. Thus, for **4h**−**j**, piperidine was used as a base and the reaction was carried out at 40−50 °C for 24−48 h. It was found that the reaction is accompanied by addition of residual water to **5h**−**j**, either during the electrolysis or during workup, forming *gem*-diols **6h**−**j** (Scheme 6). It has been shown previously that the carbonyl group of compounds with a 1,6-anhydrohexos-2-ulose structure (such as **5**) can be easily hydrated, giving an equilibrium mixture of hydrate and starting carbonyl compound.[1b]

Addition of phthalimide (**4k**) to **1** (MeCN/EtOH 3:1; room temperature) in the presence of triethylamine also proceeds with formation of product **5k** in relatively good yield. But once again the electrochemical version of that reaction gave a significantly higher yield, 95% (Scheme 7). Succinimide (**4l**) and saccharin (**4m**) can also be added to **1** in the presence of triethylamine with formation of **5l** and **5m** (74% and 66% yields, respectively).

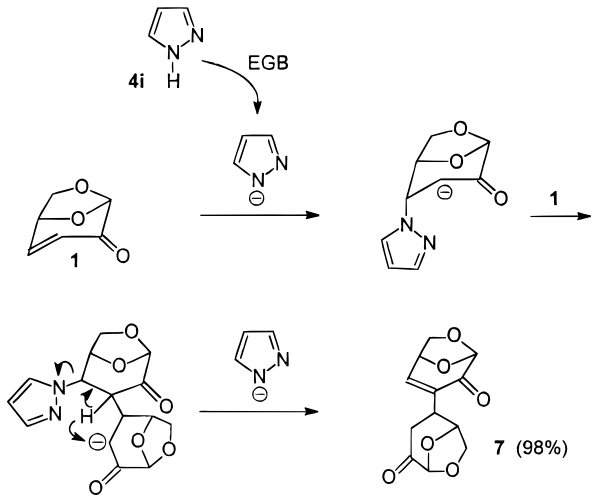
Interesting results were obtained with pyrazole under electrochemical conditions. The chemical addition of that compound to **1** in MeCN in the presence of piperidine resulted in formation of **5i** (33%) and the hydration product **6i** (32%) (Scheme 6). By contrast, the cathodically-promoted addition produced a selective self-coupling of **1**, giving dimer **7** in quantitative yield (Scheme 8). This product was previously found in low yield (8%) after heating **1** in aqueous triethylamine.[11]

The behavior of the diols **6** was dependent on structure. **6h** was formed in only trace amounts but was detectable by $^{13}$C-NMR. Hydration of **5i** was more extensive, and substantial amounts of **6i** were detected during attempts

**Scheme 7**




**Scheme 8**




to purify **5i**. Likewise, we were unable to separate **6j** from **5j**, and the yield is based on NMR analysis. In the case of the nitropyrazole adduct **5c**, it was found that some hydrate **6c** was formed upon storing **5c** in acetone solution for a long time (90 days). The $^{13}$C-NMR spectra of diols **6** feature a signal for the *gem*-diol carbon at ~90 ppm and absence of the characteristic signal for the carbonyl carbon at ~195−200 ppm. In the IR spectra, a broad band at 3300−3500 cm$^{-1}$ replaces the characteristic carbonyl absorption. Apparently, the diols **6** are formed by reaction[1b,21] of the carbonyl group of **5** with residual water present in the solvent, silica gel, air, etc.

As with the nitro derivatives **3**, the heterocyclic derivatives **5** and **6** are formed by attack of the heterocyclic anion at the less hindered *exo* face of **1** to produce the *erythro* isomers. For all compounds, $^1$H-NMR spectra showed a coupling constant for $H_{3a}$ and $H_4$ of about 7.5−8.0 Hz, a value characteristic of *erythro* isomers.

In cases where more than one nitrogen is present in the nucleophile, the nitrogen that attaches to **1** is in accordance with the known[22−25] reactions of electrophiles with such nucleophiles; *viz.*, the nitrogen most distant from an electron-withdrawing substituent will attack the electrophile. Determination of isomeric identity was based on NMR results. For the compounds **5a**,**b**,**d**,**e**, $^3J$ coupling between the nonsubstituted carbon of the heterocyclic group and $H_4$ of the levoglucosenone moity was seen in the $^{13}$C-NMR spectra. For the other isomer this coupling would be observed for the substituted carbon atom, $C_5$. For the nitrotetrazole derivative **5g**, the chemical shift of the carbon atom in the tetrazole addend was observed at 167.8 ppm, which is characteristic for 2-N-substituted tetrazoles.[21] In the case of **5f**, the signals of the two carbons of the heterocycle as well as signals for the ester groups are identical, indicating 2-N substitution.

Only in reaction of 3-methylpyrazole, **4h**, were both isomers of the adduct **5h** observed. They are designated 1,3 and 1,5 indicating attachment at 1-N with methyl in the 3-position and attachment at 1-N with methyl in the 5-position respectively. For the 1,3-isomer, the $^{13}$C-NMR spectrum contains signals at 129.29 ppm ($C_5$) and 148.53 ppm ($C_3$) that are characteristic for a 1,3-substituted pyrazole. For the 1,5-isomer, the signals are at 138.17 ppm ($C_5$) and 138.36 ppm ($C_3$). The signals for the $CH_3$ group at 13.53 (1,3-isomer) and 10.78 ppm (1,5-isomer) are also characteristic for 1,3- and 1,5-substituted pyrazoles.[24] Moreover, there is additional coupling for one of the isomers on nonsubstituted carbon atom $C_5$ (see above). According to the NMR data the ratio of 1,3- and 1,5-isomers is 6:1 (see Scheme 6).

**Cathodically-Promoted Addition of Thiols to Levoglucosenone. New Stereoisomers of Alkyl- and Arylthio Derivatives of Levoglucosenone.**[26] As was shown above, a variety of derivatives of levoglucosenone can be obtained in high yield by the cathodic generation (*via* electrogenerated base) of anions of nitro and heterocyclic compounds that subsequently undergo Michael addition to **1**. The nitro and heterocyclic derivatives that were obtained arose from attack of the nitronate or heterocyclic anion at the less hindered *exo* face to produce the *erythro* isomers (*i.e.*, the added group occupied an axial position in the ketone-containing six-member ring, cf. Scheme 1). In fact, this is the only isomer that has been reported for the chemical version of the Michael addition of different CH-acids,[10,12] alcohols,[9a] and thiols[9b] to levoglucosenone.

There is apparently no energetic reason that the *threo* isomers should not be obtained. This notion was supported by AM1 calculations that showed, for a variety of addends, that the two isomers have very similar energies with calculated heats of formation differing by <3 kcal/mol. We now report that both *erythro* and *threo* isomers can be selectively prepared by addition of thiols to levoglucosenone under cathodic electrolysis conditions.

Electrolysis of thiols at a platinum cathode in the presence of an equimolar amount of levoglucosenone was conducted in a divided cell in a solution of 0.002 M $Bu_4$NBr in MeCN. Only a catalytic amount of electricity (0.02−0.12 F/mol) was required to give the addition products in almost quantitative yields (Table 1). The cathode compartment was purged with nitrogen to avoid air oxidation of thiolate anions. After removal of MeCN, the electrolysis products were isolated by column chromatography (silica gel, eluent: hexane/ethyl acetate).

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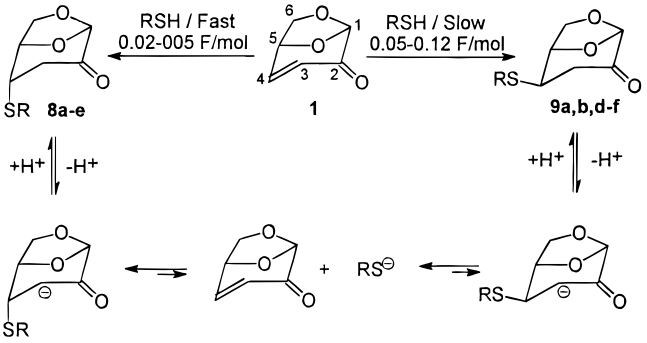
**Table 1. Electrochemical Michael Addition of Thiols to Cyclic Enones (Pt-Cathode; $Bu_4NBr$−MeCN)**

| thiol | enone | charge, F/mol | time, h | product | yield, % (isol) |
|---|---|---|---|---|---|
| *n*-$C_8H_{17}SH$ | **1** | 0.05 | 1 | **8a** | 86 |
| *n*-$C_8H_{17}SH$ | **1** | 0.10 | 4 | **9a** | 86 |
| *n*-$C_{10}H_{21}SH$ | **1** | 0.02 | 0.5 | **8b** | 93 |
| *n*-$C_{10}H_{21}SH$ | **1** | 0.10 | 6 | **9b** | 82 |
| 2-naphthalenethiol | **1** | 0.04 | 0.5 | **8c** | 95 |
| *p*-$ClC_6H_4SH$ | **1** | 0.05 | 1 | **8d**; 9d | 63; 29 |
| *p*-$ClC_6H_4SH$ | **1** | 0.11 | 5 | **8d**; 9d | 36; 54 |
| *p*-$MeOC_6H_4SH$ | **1** | 0.05 | 1 | **8e**; 9e | 70; 21 |
| *p*-$MeOC_6H_4SH$ | **1** | 0.10 | 6 | **8e**; 9e | 23; 68 |
| *p*-$MeOC_6H_4SH$ | **1** | 0.03 | 1 | **8e** | 93[a] |
| *p*-$O_2NC_6H_4SH$ | **1** | 0.05 | 14 days | **9f** | 60 |
| 2-naphthalenethiol | **10** | 0.04 | 1 | **11** | 95 |

[a] Undivided electrolysis: Pt-cathode and Mg-anode.

**Scheme 9**




R = $C_8H_{17}$ (**a**), $C_{10}H_{21}$ (**b**), 2-naphthyl (**c**)
*p*-Cl-$C_6H_4$ (**d**), *p*-MeO-$C_6H_4$ (**e**), *p*-$O_2N$-$C_6H_4$ (**f**)

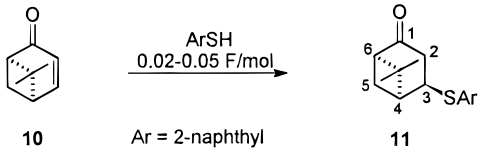
The key step of the reaction is the cathodic generation of thiolate anions by direct cleavage of the S−H bond with the formation of hydrogen. Because thiolate anions with tetraalkylammonium cations as counterions are such strong nucleophiles,[20] the addition proceeds rapidly and in high yield.

When *n*-octanethiol or *n*-decanethiol was reduced in the presence of **1** at normal current densities (*ca.* 0.2−0.3 mA/cm$^2$; 0.5−1 h), the *erythro* isomers, **8a**,**b**, were obtained in high yield. However, when the electrolysis was performed at 0.01−0.02 mA/cm$^2$ for a longer period of time (4−6 h), 90% (isolated yield) of the products found in the catholyte were the *threo* isomers **9a**,**b**. Slow electrolysis at low current density appears to be the key to obtaining the *threo* isomer. In fact, it was found that the isolated and purified *erythro* isomers **8a**,**b** could be converted to **9a**,**b** in excellent yield simply by subjecting a solution of **8a**,**b** to these same low current electrolysis conditions.

We propose that in these two cases the *threo* isomer is the thermodynamically favored product that is formed when the solution is maintained for a sufficient time under basic conditions where the retroaddition reaction[27] can occur. Multiple separation and readdition of the thiolate will eventually allow thermodynamics to prevail (Scheme 9).

Obviously, the stereochemistry of the addition is affected by the size of the incoming group. For example, addition of the more voluminous 2-naphthalenethiol produced the *erythro* isomer **8c** in >90% yield. Some *threo* isomer was detected in the crude product, but attempted isomerization of **8c** to **9c** was not successful.

**Scheme 10**




**10** Ar = 2-naphthyl **11**

Fast, high current electrolysis of the *p*-chloro- and *p*-methoxybenzenethiols produces mainly the expected *erythro* isomers **8d**,**e**, but under slow electrolysis conditions **9d** and **9e** are formed in larger amounts, *threo*/*erythro* being about 1.5 for the former and 3 for the latter. Electrolytic equilibration was achieved by electrolysis of pure isolated *threo* (**9d**) or *erythro* (**8d**) isomers of the *p*-chlorobenzenethiol derivative. The resulting *threo*/*erythro* (about 1.5; the same ratio was found starting with either isomer) was identical to that obtained above by addition at low current. So, in these two cases it appears that the two isomers have almost identical free energies.

It should be noted that when electrolysis of *p*-methoxybenzenethiol was carried out in an undivided electrolysis cell with a sacrificial Mg anode the *erythro*-isomer was formed exclusively. We suggest that the nucleophilic reactivity of the thiolate anions was decreased by $Mg^{2+}$ ions[20] generated at the anode. Thus, only the kinetic product (*erythro*) was formed and there was no opportunity for equilibration to occur by retro Michael addition.

The structures of new *threo*-isomer of the *p*-chlorobenzenethiol derivative of levoglucosenone as well as the *erythro*-isomer of the 3,4-dinitropyrazole adduct were confirmed by X-ray crystallography.[28]

Addition of *p*-nitrobenzenethiol proceeded very slowly and only after 2 weeks in carefully purged solution was a moderate yield of *threo* isomer **9f** obtained. The slower reaction is consistent with the fact that this thiol is a weaker nucleophile. The *erythro* isomer has not yet been detected.

For comparison, 2-naphthalenethiol was added under cathodic electrolysis conditions to (*R*)-(+)-apoverbenone (**10**) for which conjugative 1,4-addition *trans* to the geminal-dimethyl-bearing bridge has been reported.[29] Only one isomer (**11**) was isolated (Scheme 10), and isomerization was not observed apparently because the retro Michael reaction does not occur under the electrolysis conditions or because **11** is the thermodynamically more stable form. The structure of **11** was also confirmed by X-ray crystallography.[28]

In summary, a wide variety of derivatives of levoglucosenone have been synthesized by electrochemically promoted Michael additions as well as by purely chemical base catalysis. The electrochemical reaction proceeds under very mild conditions without using any base and in most cases gives superior yields. These studies illustrate the suitability of the electrochemical method for functionalization of **1**. We are presently investigating

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(28) Crystallography Laboratory of the University of Delaware. Stereoisomeric identity was established for **3e**, **5b**, **9d** and **11**. The author has deposited atomic coordinates for these structures with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(29) Tius, M.; Kannangara, G. S. K. *J. Org. Chem.* **1990**, *55*, 5711−5714.

the addition to levoglucosenone of other organic substances containing activated element−hydrogen bonds.

## Experimental Section

**Preparation of Levoglucosenone.** Cotton cellulose containing ~2% phosphoric acid was pyrolyzed in 300-g batches in an evacuable metal reaction vessel. Before addition of the phosphoric acid, the cellulose was treated with hot 1% HCl for 2.5 h in order to remove amorphous parts of the macromolecule, followed by washing with water and drying. The pyrolysis was carried out under vacuum (4 mmHg) at 350−400 °C for a period of 2−3 h, which was sufficient to complete the evolution of the pyrolysis gases. The tarry products were collected in a cooled condenser (−20 °C). Further isolation and purification of the product were carried out according to the procedure described in ref 1b. The yield of levoglucosenone after distillation was 5−8% (2% in ref 1b).

**Reagents.** Acetonitrile and chloroform were from Fisher. Triethylamine, piperidine, tetraethylammonium bromide, nitrocyclopentane, 2-nitropropane, all thiols, (*R*)-(−)-carvone, phthalimide, succinimide, and saccharin were obtained from Aldrich and were used as received. Ethyl nitroacetate (**2a**), ethyl 2-nitropropionate (**2b**), diethyl 2-nitroglutarate (**2c**), and the amide of nitroacetic acid (**2j**) were obtained from the Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Moscow. Dinitromethane[30] (**2g**), 5-nitro-2-phenacyltetrazole[22] (**2i**), ethyl 2-nitro-4-pentenoate[16a] (**2f**), the nitropyrazoles[31a,b] **4a**,**c**,**d**,32 nitrotetrazole[31c] (**4g**), 3-nitro-1,2,4-triazole[32a] (**4e**), 4,5-bis(methoxycarbonyl)-1,2,3-triazole[32b] (**4f**), 3,4-dinitropyrazole[32c] (**4b**), and (*R*)-(+)-apoverbenone[33] were prepared as described in the literature.

**Standard Procedure. Electrolysis with EGB for Addition of Nitro Compounds.** The electrolysis was carried out in a divided cell under galvanostatic conditions at a current density of 0.5−2 mA/cm$^2$ with vigorous stirring at room temperature. A platinum mesh cathode and platinum wire anode were used. Ten mL of 0.05−0.1 M $Bu_4NBr$ in absolute MeCN containing 0.25 g of **1** (0.002 M) and an equimolar amount of nitroalkane was used as catholyte. The cathode compartment was air-saturated. After passing 0.07−0.1 F/mol, the electrolysis was terminated. The solvent was evaporated, and a solution of the residue in a mixture of ethyl acetate and hexane (1:3) was filtered through a 2−3 cm layer of silica gel. After evaporation of the solvent, the analytically pure substances were obtained.

**Standard Procedure. Electrolysis for Addition of Thiols.** The procedure was the same as above except that the cathode compartment was purged with nitrogen to remove dissolved oxygen. $Bu_4NBr$ (0.002 M) was used, and the current densities were *ca.* 0.2−0.3 mA/cm$^2$ for rapid electrolysis (0.5−1 h) and 0.01−0.02 mA/cm$^2$ for slow electrolysis (4−6 h).

**Standard Procedure. Base-Catalyzed Addition of Nitro Compounds and Heterocycles.** A solution of **1** (5 mmol in 5 mL) in MeCN was added dropwise for 40 min to the preheated (40−50 °C) solution of **2a**−**c**,**i**,**j** or **4a**−**m** in 3 mL of $CHCl_3$ (for **2a**−**c**) or MeCN (for **2i**,**j** and **4a**−**m**) containing EtOH (25% vol.; only for **4k**) and 0.5 mmol of $Et_3N$ (for **2a**−**c**,**i**,**j** and **4a**−**g**,**k**−**m**) or piperidine (for **4h**−**j**). The reaction was continued for 2 days at the same temperature (for **4h**−**j**) or room temperature followed by removal of solvent. Compounds **3a**−**c**,**i** and **5f** were obtained as yellow oils while **3j** and **5a**−**e**,**g**,**j**−**m** were crystals or crystallizing oils. All heterocyclic derivatives of levoglucosenone except **5f** can be recrystallized from MeCN.

**6c.** Compound **5c** was dissolved in acetone and left in an NMR tube for 3 months. According to the NMR spectra, **6c** was formed. The ratio of **5c** to **6c** was 3:2.

**6i.** A brown oil was obtained after reaction that according to the NMR data is mostly **5i** with some impurities. After column chromatography, a yellow oil was obtained that solidified and according to the NMR spectrum was a 1:1 mixture of **5i** and **6i**.

**5j/6j.** A white precipitate separated during the reaction that according to NMR and IR data was a 3:1 mixture of **5j** and **6j**.

The product of the reaction of **1** with **4h** was purified by chromatography. A small amount of pure 1-N-addition isomer was isolated.

The assignment of the 4-axial (*erythro*) structure to the derivatives is based on comparison of $^1$H-NMR spectra (shifts and coupling constants for H$^4$ and H$^5$) with analogous compounds[8,9,11] as well as by comparison of physicochemical data for **3d**, **3h**, **7**, and **8b**, which have been previously reported.[8,9,11]

Selected NMR data (see the Supporting Information for remainder): $^1$H and $^{13}$C NMR (compounds **3a**−**c**,**f** are mixtures of diastereomers), ppm/TMS, $CDCl_3$, for **3a**−**g**, **8**, **9**, **11**; DMSO-$d_6$ for **5i**,**j**, **6i**,**j** and acetone-$d^6$ for all others.

***erythro*-Adduct of ethyl nitroacetate and levoglucosenone**, **3a.** $^1$H: 1.26t, 1.27t (3H, $J$ = 5.5 Hz); 2.25d, 2.30d (1H, $J$ = 17 Hz); 2.84dd, 2.91dd (1H, $J$ = 17, 4 Hz); 3.13dd, 3.15dd (1H, $J$ = 6, 4 Hz); 4.03dd (1H, $J$ = 8, 5 Hz); 4.10d (1H, $J$ = 8 Hz); 4.23q, 4.29q (2H, $J$ = 5.5 Hz); 4.54d, 4.88d (1H, $J$ = 5 Hz); 5.07s, 5.08s (1H Hz); 5.27d, 5.31d (1H, $J$ = 6 Hz). $^{13}$C: 13.73, 32.77, 33.50, 41.33, 41.43, 63.79, 67.68, 67.95, 73.15, 73.24, 87.88, 88.56,101.40,163.01, 163.22, 196.34, 196.66. Anal. Calcd for $C_{10}H_{13}NO_7$: C, 46.34; H, 5.05; N, 5.40. Found: C, 46.67; H, 5.08; N, 5.26.

**5a.** $^1$H: 2.91dm (1H; $J$ = 17.8 Hz); 3.45dd (1H; $J$ = 17.8, 7.8 Hz); 4.08dd (1H; $J$ = 5.6, 8.3 Hz); 4.43dd (1H; $J$ = 8.3; 1.0 Hz); 5.09bd (1H; $J$ = 5.6 Hz); 5.19s (1H Hz); 5.33d (1H; $J$ = 7.8 Hz); 7.03d (1H; $J$ = 2.6 Hz); 7.98d (1H; $J$ = 2.6 Hz). $^{13}$C: 36.47, 63.38, 66.84, 77.41, 102.40, 103.84, 132.88, 156.69, 197.45. Anal. Calcd for $C_9H_9N_3O_5$: C, 45.19; H, 3.79; N, 17.57. Found: C, 45.22; H, 3.90; N, 17.74.

**6c** (not isolated; small amount detected on storage of **5c**). $^1$H: 2.26dm (1H; $J$ = 15.6 Hz); 2.55dd (1H; $J$ = 15.6, 7.4 Hz); 3.89dd (1H; $J$ = 5.5, 8.0 Hz); 4.11dd (1H; $J$ = 8.0, 1.1 Hz); 4.75d (1H; $J$ = 7.4 Hz); 4.79bd (1H; $J$ = 5.5 Hz); 5.10s (1H); 5.95bs (1H); 6.20bs (1H); 8.09s (1H); 9.17s (1H). $^{13}$C: 35.07, 60.96, 66.45, 75.69, 90.93, 104.63, 131.31, 135.31, 138.02.

**9a.** $^1$H: 0.88t (3H); 1.15−1.65m (12H); 2.35dd (1H; $J$ = 16.2, 8.3 Hz); 2.57td (2H); 2.67dd (1H; $J$ = 16.2, 6.4 Hz); 3.36m (1H); 3.87dd (1H; $J$ = 8.0, 5.4 Hz); 4.30d (1H; $J$ = 8 Hz); 4.58bs (1H); 5.14s (1H). Anal. Calcd for $C_{14}H_{24}O_3S$: C, 61.78; H, 8.82; S, 11.78. Found: C, 61.34; H, 8.40; S, 12.17.

**11**. $^1$H: 0.87s (3H); 1.31s (3H); 1.90d (1H; $J$ = 11.0 Hz); 2.31bt (1H; $J$ = 4.7 Hz); 2.3−2.7m (3H); 2.84dd (1H; $J$ = 19.0, 8.1 Hz); 3.88t (1H; $J$ = 8.1 Hz); 7.4−7.9 m (7H). Anal. Calcd for $C_{19}H_{20}OS$: C, 77.05; H, 6.75; S, 10.82. Found: C, 77.18; H, 6.80; S, 10.09.

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**Supporting Information Available:** ORTEP representations and structure determination summaries for **5b**, **9d**, and **11** and NMR data and elemental analyses for **3b**−**j**, **5b**−**m**, **6i**,**j**, **8a**−**e**, and **9b**−**f** (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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