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LETTERS

Stereoselective Diels-Alder Reaction of Electrogenerated Quinones on a PTFE-fiber coated Electrode in Lithium Perchlorate / Nitromethane

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Abstract: Diels-Alder reaction of dienes and *in situ* generated quinones was accelerated on a PTFE-fiber in an electrolytic lithium perchlorate / nitromethane system. In the presence of PTFE-fiber on a glassy carbon electrode, unstable quinones were efficiently generated by electrooxidation and trapped by dienes maintained on the poly-fluorinated fiber to give the desired cycloadducts stereoselectively in excellent yields.
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A solvent system which possesses internal solvent pressure provides significant rate accelerations of the intermolecular cycloaddition process,[1)] and 5M lithium perchlorate in diethyl ether was shown to be a powerful medium for facilitating [4+2] cycloaddition reactions.[2)] In addition, the role of lithium perchlorate has been extensively investigated.[3)] Recently, we found that 1M lithium perchlorate in nitromethane also accelerated the Diels-Alder reaction, and the conductive medium could be further applied for electrolytic generation and cycloaddition of varied unstable compounds.[4)] The acceleration property through the agency of a polar medium seems, however, less effective for the compounds which are insoluble in these solvent systems. Moreover, dispersion of lipophilic or easily oxidizable compounds in the electrolytic conditions often prevents the electron transfer step by coating or oxidative decomposition on the electrodes. We therefore envisioned that the desired cycloaddition reaction should proceed at the interface of the polar solvent and a hydrophobic solid surface on which less polar compounds could be maintained. On the basis of this supposition, it can be further forecasted that, for example, polar hydroquinones are selectively oxidized to benzoquinones on the electrode even in the presence of lipophilic dinenes to accomplish the desired cycloaddition. We now report our findings, which show that a PTFE [poly-(tetrafluoroethylene)]-fiber coated electrode in lithium perchlorate / nitromethane realizes the oxidative generation of unstable benzoquinones and marked acceleration in their cycloaddition with easily oxidizabe dienes.

In a preliminary study, the effect of the PTFE-fiber for the acceleration of the Diels-Alder reaction in a lithium perchlorate / nitromethane system was examined (Table 1). In a mixture of 2,5-dimethy-*p*-benzoquinone **1** and isoprene **2**, yields of the cycloadducts of the Diels-Alder reaction markedly increased in the concentrated lithium perchlorate in nitromethane. In this highly polar solvent system, however, lipophilic dienes such as myrcene **3** scarcely dissolved, and the desired cycloaddition reaction with **1** was not effectively promoted. Accordingly, we introduced the PTFE-fiber in a polar solvent system. When compound **1** and **3** were dissolved in 3.0 M lithium perchlorate / nitromethane (10 ml) for 8hr, the desired cycloadducts **6** and **7**

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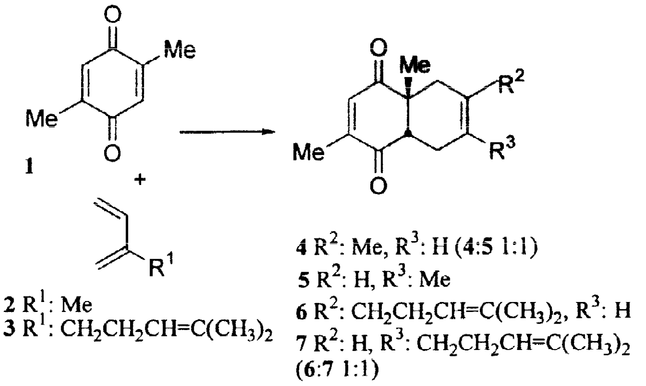
Table 1. **Reaction of 2,5-dimethyl-*p*-benzoquinone and dienes at ambient temperature in lithium perchlorate / nitromethane**

Diene	$LiClO_4$ (M)	PTFE (g)	Time (hr)	Products	Yield (%)
2	0	-	24	**4**+**5**	0
2	0.01	-	24	**4**+**5**	0
2	0.1	-	24	**4**+**5**	5.1
2	1.0	-	24	**4**+**5**	90.5
2	3.0	-	24	**4**+**5**	99.1
2	3.0	-	8	**4**+**5**	49.0
3	3.0	-	8	**6**+**7**	21.1
3	3.0	0.5	8	**6**+**7**	38.9
3	3.0	2.5	8	**6**+**7**	49.8
3	3.0	5.0	8	**6**+**7**	68.6

All reactions were performed with 0.1M in dienophile and 0.5 M in diene by using 10 ml of nitromethane. Yields were determined by ^{1}H-NMR.

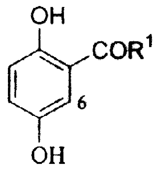


2 R^1: Me
3 R^1: $CH_2CH_2CH=C(CH_3)_2$

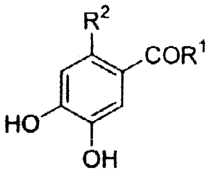
4 R^2: Me, R^3: H (4:5 1:1)
5 R^2: H, R^3: Me
6 R^2: $CH_2CH_2CH=C(CH_3)_2$, R^3: H
7 R^2: H, R^3: $CH_2CH_2CH=C(CH_3)_2$
(6:7 1:1)

were obtained in low yield(21.1%). In the presence of the PTFE-fiber in the reaction mixture, however, yields of the cycloadducts increased in proportion with the amount of the fiber, and the yield of the desired cycloadducts **6** and **7** increased to 68.6 % in 8 hr standing. Moreover, it was found that an electrolytic condition further promoted the Diels-Alder reaction of quinones and dienes. That is, from a solution of **1** and **3** in 0.5 M lithium perchlorate / nitromethane in the absence and presence of PTFE-fiber (2.5g in 10ml of CH_3NO_2, 24 hr at r.t.), the desired cycloadducts were obtained in 58.9% and 70.1% yield, respectively with the recovery of unreacted **1**. On the other hand, when the electric potential was applied to the reaction system(1.2V vs. cathode, 24hr at r.t. 2.5g of PTFE-fiber), the yield of the products increased to 80.2%. In this reaction condition, compounds **3**, **6** and **7** were maintained on the surface of the PTFE-fiber, and unreacted quinone was also recovered quantitatively.

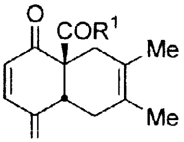
Accordingly, we expected that a PTFE-fiber coated electrode could realize the *in situ* generation of unstable quinones and their rapid trap by the easily oxidizable dienes on the fibers. The electrode was made up by coating a glassy carbon anode (60mm x 20mm) with PTFE-fibers (ca. 2.5 g of fiber, diameter ca. 20 μm), and was applied to the electrolysis of hydroquinones in 2M lithium perchlorate / nitromethane. Table 2 shows the results of cycloaddition reaction of easily oxidizable dienes and *in situ* generated quinones by the PTFE-fiber coated electrode. In this reaction system, most of the products were obtained in excellent yields, and they were confirmed to be maintained on the PTFE-fiber. On the other hand, in the absence of the PTFE-fiber, dienes were oxidized to decompose and the desired cycloadducts were obtained in less than 20% yield. In addition, stereoselective Diels-Alder reaction of electrogenerated chiral quinones was examined. Although *o*-cathechols **17**, **18** and (-)-menthyl, (+)-fenchyl 2,5-dihydroxyhydroquinones **11**, **12** gave the corresponding cycloadducts with dienes in low diastereomeric excess, it is remarkable and noteworthy that the essentially complete regio- and diastereoselectivity was achieved in the reaction of (-)-phenylmenthylesters **14** which gave the cycloadducts **29**, **33** in excellent yield. The fact that the hydrogen at C-6 of **14** is seen as a doublet at δ5.89



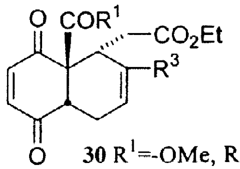
8 R^1= H
9 R^1= -OMe
10 R^1= $-OCH_2CH_2SiMe_3$
11 R^1= *A**
12 R^1= *B**
13 R^1= *C**
14 R^1= *D**



15 R^1, R^2 = Me
16 R^1= -OEt, R^2=H
17 R^1= *C**,R^2=H
18 R^1= *D**,R^2=H



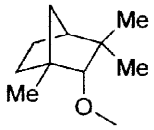
23 R^1=H
24 R^1= -OEt
25 R^1= $-OCH_2CH_2SiMe_3$
26 R^1= *A**
27 R^1= *B**
28 R^1= *C**
29 R^1= *D**



30 R^1=-OMe, R^3=Me
31 R^1= *A**, R^3=H
32 R^1= *B**, R^3=H
33 R^1= *D**, R^3=H

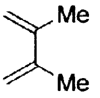
*A**=

*B**=



*C**=

*D**=



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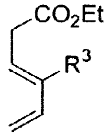
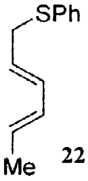


20 R^3=H
21 R^3=Me



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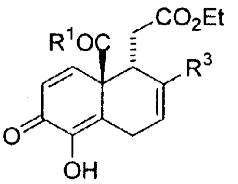
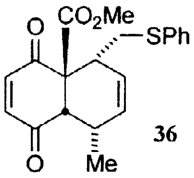


34 R^1=Et, R^3=Me
35 R^1=Et, R^3=H



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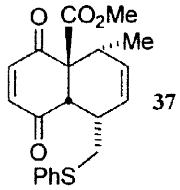

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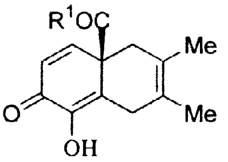

38 R^1= -OEt, R^2=H
39 R^1= *C**
40 R^1= *D**

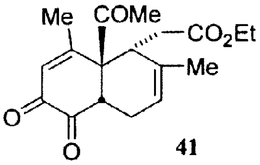

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Table 2 Cycloaddition reaction of electrogenerated quinones with dienes

Substrate	Diene	Products	Yield(%)[a]	d.e.(%)[b]
8	19	23	Quant.	
9	21	30	90	
9	22	36+37	98(1:2)	
10	19	25	94	
11	19	26	Quant.	17.0
11	20	31	96	21.4
12	19	27	Quant.	18.7
12	20	32	Quant.	30.9
13	19	28	Quant.	82.0
14	19	29	Quant.	>99
14	20	33	98	>99
15	21	41	98	
16	20	35	96	
16	21	34	97	
17	19	39	92	9.0
18	19	40	90	35.0

a)Yield refers to product after isolation.
b)Diastereomeric excess was determined by ^1H-NMR($CDCl_3$).Absolute configurations of cycloadducts have not been established.

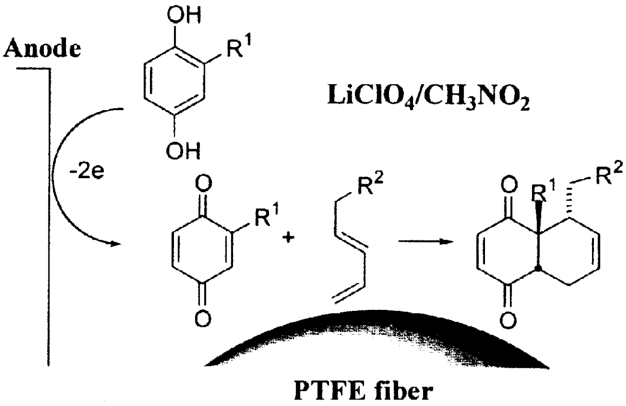

Fig. 1 Proposed mechanism of Diels-Alder reaction between electrogenerated quinones and dienes on the PTFE-fibers

and that of **11** lies at δ7.31 is the consequence of the aromatic shielding of the hydrogen at C-6 of **14** by the phenylmenthyl group. The effect suggests the interaction of the phenyl ring of the chiral auxiliary and hydroquinone moiety, which must also restrict the rotational freedom of the corresponding quinone intermediate generated by electrooxidation to give highly diastereoselective cycloaddition with dienes.

In this reaction system, it can be suggested that dienes and cycloadducts were maintained on the hydrophobic surface of the fiber, and just the polar hydroquinones could reach the glassy carbon electrode through the fibers (Fig.1). Electrochemically generated quinones should be immediately trapped by the dienes on the PTFE-fibers. The present electrochemical reaction system could be a promising system for the construction of varied functionalized skeletons, preparation of which has been difficult *via* conventional electrolytic means.

Acknowledgement

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5) *General procedure*: Anodic oxidation of **14** (0.5mmol) in 10 ml of $MeNO_2$ containing dry $LiClO_4$(500mg) as supporting electrolyte, AcOH(50mg), and 2,3-dimethylbutadiene **19** (49 mg, 0.6 mmol) was carried out at a constant potential (1200mV vs. SCE), using a PTFE-fiber coated glassy carbon plate (60 x 20 x 3 mm)as anode and a platinum plate (10 x 10 mm) as cathode, respectively, without separating the two electrodes under Ar. The reaction was quenched after 16 hr to afford cycloadduct 29 quantitatively. *Selected data of 29*: ^{1}H-NMR(δ, $CDCl_3$, 600MHz) 7.27(5H, m), 6.62(1H, d, *J* 10.2Hz), 6.60(1H, d, *J* 10.2Hz), 4.80 (1H, dt, *J* 10.8, 1.8Hz), 2.87(1H, t, *J* 6.0Hz), 2.34(1H, br.d, *J* 17.4Hz), 2.29(1H, d, *J* 15.0Hz), 2.27(1H, br.d, *J* 15.0), 1.97(1H, br.d, *J* 17.4Hz), 1.59(3H, br.s), 1.56(3H, br.s), 1.26(3H, s), 1.16(3H, s), 0.86(3H,d, *J* 6.2Hz); ^{13}C-NMR(δ, $CDCl_3$, 150MHz) 198.1, 195.4, 168.9, 151.4, 139.4, 137.8, 128.2, 125.4, 125.1, 123.1, 122.7, 77.8, 49.8, 48.1, 41.0, 39.7, 34.5, 33.8, 31.3, 29.4, 27.4, 26.9, 26.0, 25.4, 21.7, 18.8, 18.6.