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A New Selective Method for the Homolytic Alkylation and Carboxylation of Quinones by Monoesters of Oxalic Acid

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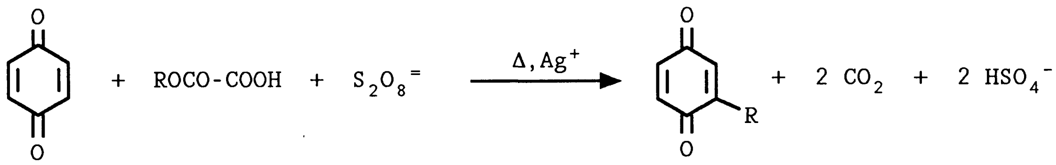
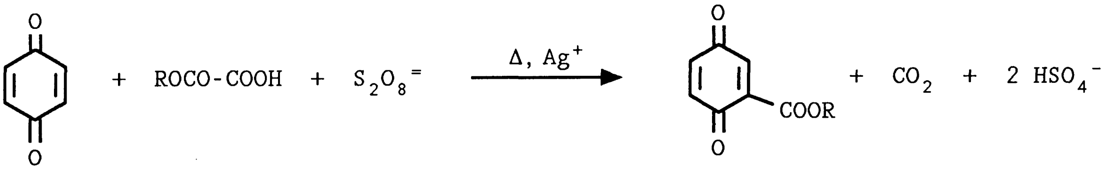
Alkyl and alkoxycarbonyl radicals were generated by oxidative decarboxylation of oxalic acid monoesters by persulfate; they were then utilized for the selective substitution of quinones.

The oxidative decarboxylation of oxalic acid monoesters proved to be a very effective source of alkoxycarbonyl and alkyl radicals, useful for selective syntheses. The alkylation of heteroaromatic bases was described in the preceding Letter$^{1)}$ and in a recent report$^{2)}$ of a more expensive and less effective procedure.

Now we report how this radical source can be successfully utilized for the selective alkylation (Eq.1) or carboxylation (Eq.2) of quinones in a two-phase system. The results are shown in Table 1. With esters of tertiary or secondary alcohols, alkylation (Eq.1) mainly occurs, whereas with primary alcohols carboxylation (Eq.2) becomes the main process. With esters of allylic alcohols only allylation occurs and we expect a similar behaviour with esters of benzylic alcohols.


(1)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Operating in a two-phase system, constituted by water and an organic solvent, such as CH_2Cl_2 or benzene, is particularly important for minimizing polysubstitution, because the reaction products are generally more lipophilic than the starting quinones and are therefore preferentially extracted by the organic solvent, whereas the substitution reaction takes place in the aqueous phase. With quinones of very low solubility in water, such as the naphthoquinone derivatives, using a two-phase system constituted by three solvents (CH_2Cl_2, CH_3CN, and H_2O) improves the effectiveness of the reaction.

Table 1. Alkylation (R) and Alkoxycarbonylation (COOR) of Quinones

Quinone	R	Solvent	Alkylation position	Ethoxy-carbonylation position	Conv. %	Yields[a] %
Benzoquinone	t-Bu	CH_2Cl_2	2	-	98	90
Benzoquinone	t-Am	CH_2Cl_2	2	-	40	98
Benzoquinone	1-Methyl-cyclohexyl	CH_2Cl_2	2	-	60	84
Benzoquinone	i-Pr	CH_2Cl_2	2(25%) 2,5(7.5%) 2,6 traces	2(22.4%) 2,6-Hydroquinone-(13.1%)	100	68
Benzoquinone	i-Pr	Benzene	2(43%) 2,5(29%) 2,6(6%)	traces	100	78
Benzoquinone	Et	Benzene	traces	2(69%) 2,6-Hydroquinone(14%)	81	83
Benzoquinone	Allyl	CH_2Cl_2	2	-	98	96
2-Me-benzoquinone	t-Bu	CH_2Cl_2	5	-	90	91
Naphthoquinone	t-Bu	CH_2Cl_2	2	-	53	94
Naphthoquinone	t-Bu	CH_2Cl_2:MeCN (1:1)	2	-	100	92
Naphthoquinone	t-Am	CH_2Cl_2:MeCN (1:1)	2	-	91	87
Naphthoquinone	t-Am	CH_2Cl_2	2	-	60	95
Naphthoquinone	i-Pr	CH_2Cl_2	2	traces	50	81
Naphthoquinone	i-Pr	CH_2Cl_2:MeCN (1:1)	2(96%)	2(4%)	100	89
Naphthoquinone	Cyclohexyl	CH_2Cl_2:MeCN (1:1)	2(94%)	2(6%)	100	93
Naphthoquinone	Allyl	CH_2Cl_2:MeCN (1:1)	2	-	66	93

a) Yields based on converted quinones.

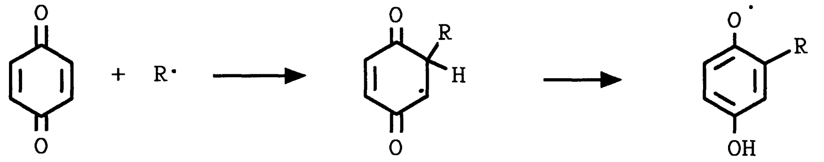
The mechanism of the reaction involves the following steps:
i) generation of the carbon-centered radicals (Eqs.3-5)

$$S_2O_8^{=} + 2\ Ag^{+} \longrightarrow 2\ SO_4^{=} + 2\ Ag^{2+} \qquad (3)$$

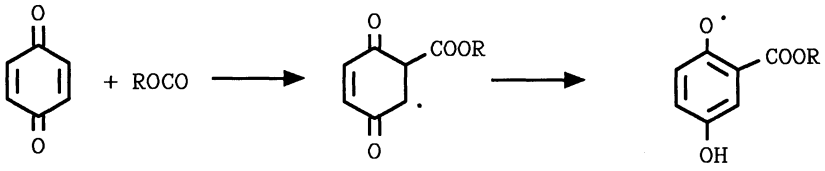
$$ROOC\text{-}COOH + Ag^{2+} \longrightarrow CO_2 + H^{+} + Ag^{+} + {\cdot}COOR \qquad (4)$$

$$RO\dot{C}O \longrightarrow R\cdot + CO_2 \qquad (5)$$

ii) addition to the quinone ring (Eq.6)

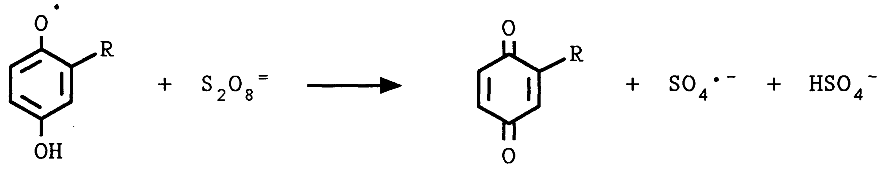


(6a)

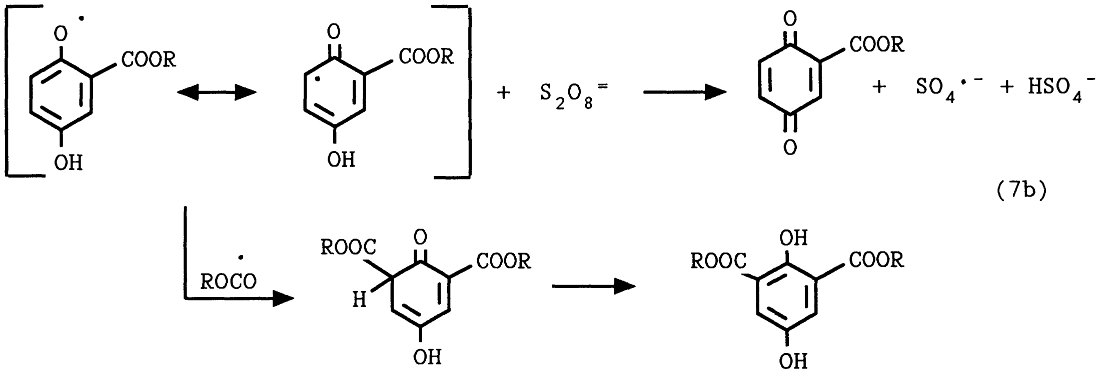


(6b)

iii) oxidation of the radical adduct in a redox chain (Eq.7)



(7a)



(7b)

It is noteworthy that when alkoxycarbonylation (Eq.2) is the prevailing reaction, as in the case of the reaction between benzoquinone and ethyl monoester, a minor amount of 2,6-diethoxycarbonylhydroquinone is formed. We explain this result by the fact that the introduction of an alkoxycarbonyl radical, instead of an alkyl radical, on the quinone ring increases the redox potential of the resulting phenoxy radical and makes its oxidation by persulfate slower (Eq.7). This allows to reach a stationary concentration of the phenoxy radical, suitable for acting as a scavenger towards another alkoxycarbonyl radical (Eq.7b).

Considering that the reaction takes place in the aqueous phase, in which the solubility of the quinone is generally very low, that the ethyl radical is not formed in significant amount and that the rate is given by the expression $r = k\,[\cdot COOR]\,[\text{quinone}]$, it follows that the rate constant for the addition of the ethoxycarbonyl radical to the quinone ring must be high ($>10^6\ M^{-1}s^{-1}$). The lower solubility of naphthoquinone explains its lower degree of alkoxycarbonylation compared to benzoquinone under identical reaction conditions.

A general experimental procedure is given: a solution of 10 mmol of monoester of oxalic acid and 5 mmol of quinone in 20 ml of the solvents reported in the Table was added to 20 ml of an aqueous solution containing 10 mmol of $Na_2S_2O_8$ and 0.5 mmol of $AgNO_3$. The mixture was refluxed for 2 h, then the organic layer was separated, dried and analyzed by GC and GC/MS. The reaction products were isolated by flash-chromatography on silica gel and identified by comparison with authentic samples.$^{3)}$ This is the first example, to the best of our knowledge, where the homolytic carboxylation of quinones is achieved. On the other hand, the above described alkylation represents the only procedure so far known for the radical alkylation of quinones by alcohols, whereas alkylation by carboxylic acids has been reported by several groups.$^{4)}$

References

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2) H. Togo, M. Aoki, and M. Yokoyama, *Chem.Lett.*, **1991**, 1691.
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