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THE REGIOCHEMISTRY OF TRAPPED RADICAL ANION-RADICAL CATION PAIRS FROM ARYL SUBSTITUTED PHTHALIMIDES

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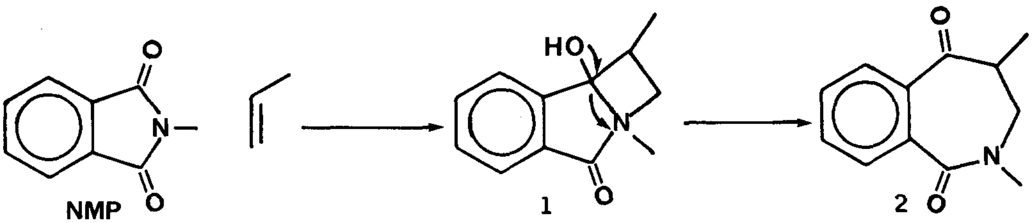
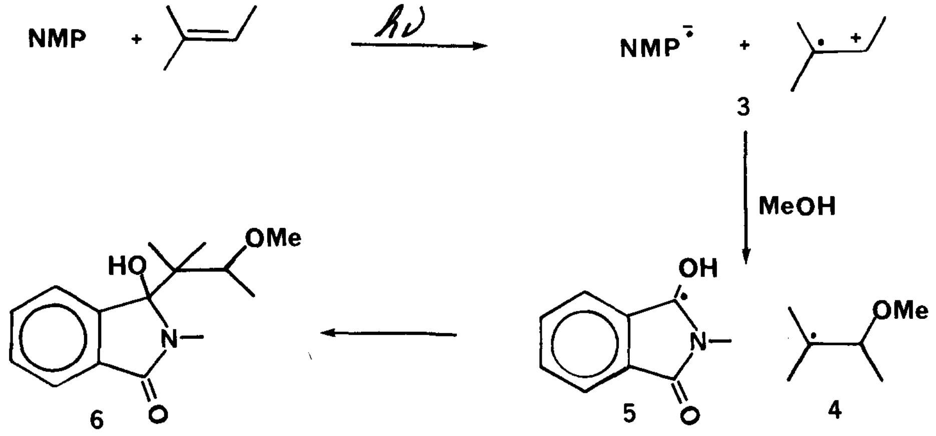
Abstract. A series of 4-substituted N-methyl phthalimides was irradiated in the presence of 2,3-dimethyl-2-butene in methanol and the product distributions of the trapped radical anion-radical cation analyzed on the basis of substituent effects on the radical anion.

Irradiation of N-methylphthalimide in the presence of alkenes results in two apparently competing processes. The addition of the alkene across the C(O)-N bond of NMP affords benzazepinediones 2[1,2] with the regiochemistry shown. This has been shown to be a concerted 2+2 addition process.[3,4] It has been proposed that when the oxidation potential of the alkene is low enough a competing electron transfer reaction apparently dominates the addition reaction and leads to the radical anion-radical cation pair 3. The nature of the solvent plays an important role on the direction of the reaction. For example, in non-reactive solvents such as acetonitrile, back electron transfer results in regeneration of the starting material, whereas in the presence of nucleophilic solvents such as methanol the ion pair is trapped in the form of ether 6. We have shown that the reaction correlates well with the Weller equation[5] and the structure of the trapped product is predictable from the expected radical pair 4+5.



In view of the complexity of this system, it was important for us to ascertain as much information as possible about the mechanisms of these competing reactions. Accordingly, we



proceeded to study the electron transfer chemistry of a series of aryl substituted N-methylphthalimides with the expectation that the regiochemistry of the products of these reactions would firmly establish the existence of the radical ion pair intermediate and might provide a mechanistic guide for further studies.

Irradiation of 7a (x=OMe) in methanol afforded a pair of products which were purified by hplc. The proton NMR of the major isomer showed doublets at δ7.43 (J=8Hz) and 7.31 (J=2Hz) and a doublet of doublets at δ6.81 (J=8Hz, J=2Hz) and was assigned structure 14a. The minor isomer showed doublets at δ7.66 (J=8Hz) and 6.99 (J=2Hz) and a doublet of doublets at 6.89 (J=8Hz, J=2Hz) and was assigned structure 13a.[6] Structure assignments (Table 1) for products from 7a-d were based on the relative peri deshielding effects of the ketone carbonyl vs the amide carbonyl.[7] Since ketone carbonyl groups should exert a greater anisotropic shift on the peri hydrogen than the amide carbonyl, we would expect Ha to be further downfield in 13a than in 14a and Hc to be further upfield in 13a than in 14a. This is what was observed.

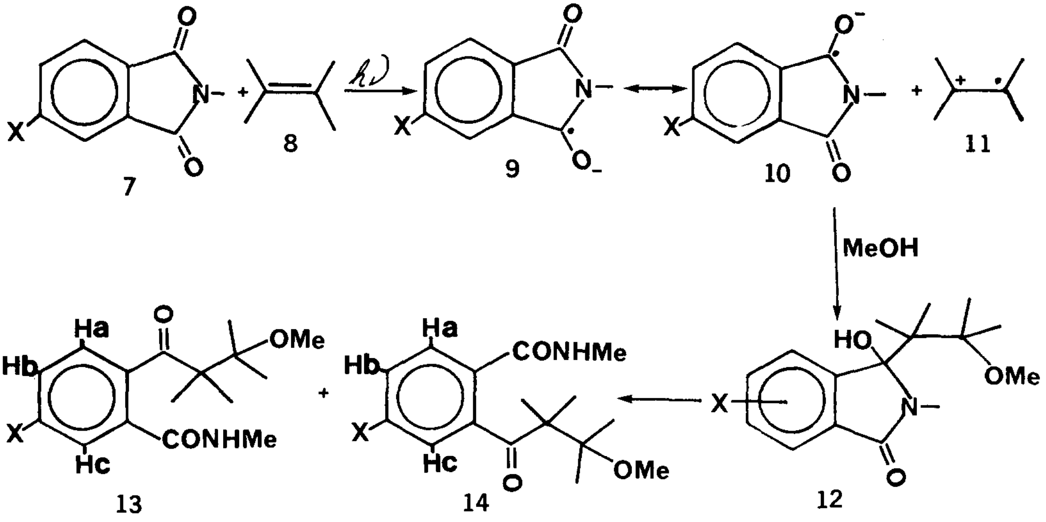


Table 1

Chemical Shifts of Aromatic Protons for **13** and **14**

	13			**14**		
	Ha	Hb	Hc	Ha	Hb	Hc
a(x=OCH_3)	7.66	6.89	6.99	7.43	6.81	7.31
b(x=CH_3)	7.56	7.18	7.29	7.14	7.38	7.46
c(x=Cl)	7.68	7.41	7.42	7.31	7.38	7.72
d(x=CO_2Me)	7.80	8.06	8.11	----	----	----

The **13**/**14** product distribution should give us information about the mechanism of the trapping process. For substituent effects on radical anion formation the best model is certainly electrochemical reduction. Although there are some data on substituted phthalimides available,[8] no studies are available that indicate which carbonyl in a substituted phthalimide is reduced. An appropriate model for the substituent effect on phthalimide carbonyl reductions is the corresponding electrochemical reductions in the benzaldehyde system. Studies indicate that benzaldehydes with *para* donors undergo electrochemical reduction with more difficulty than those with *para* acceptors,[9] thus we would expect preferential radical ion formation at the imide carbonyl *para* to acceptors and *meta* to donors (Fig. 1) and, if ground state radical anions are involved in this reaction, we would expect our trapping results to reflect this regiochemistry.

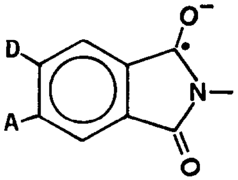


Figure 1

A series of aryl substituted phthalimides (**7a**-**d**) was irradiated in the presence of 2,3-dimethyl 2-butene in methanol and the products were separated by hplc.[10] The product distributions (Table 2) show a change in the regiochemistry of addition in going

Table 2

Product Mixtures from Trapping Experiments

Starting Material	Products	
7	**13**	**14**
a(OCH_3)	34%	66%
b(CH_3)	55%	45%
c(Cl)	56%	44%
d(CO_2Me)	100%	--

from a strong donor (OCH_3) to a strong acceptor (CO_2Me). Clearly these results are in accord with predictions from electrochemical studies and are consistent with the intermediacy of a ground state phthalimide radical anion-alkene radical cation in this reaction.

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6. All compounds gave acceptable C,H,N analyses. In addition to the NMR data reported, compounds **13**/**14** showed resonances at approximately: δ($CDCl_3$); 1.24 (s, 6H); 1.26 (s, 6H); 2.89 (d, 3H); 3.28 (s, 3H); 6.14 (b. 1H); IR ($CHCl_3$) 3440, 1660-1680 cm^{-1}.
7. Analysis of the NMR spectra of a series of models and aryl substituted benzazepinediones supports this conclusion.[4]
8. a) Zuman, P., "Substituent Effects in Polarography", Plenum Press, New York, 1967, pp. 43-129; b) $E_{1/2}$ values of -1.50V, -1.48V, -1.45V -1.30V, -1.14V were obtained for **7b**, **7a**, NMP. **7c** and **7d** respectively using a platinum electrode in DMF (H.Y. Cheng, unpublished results).
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10. A 10μ silica gel column with ether n-hexane as eluant was used. Response factors were used to determine values in Table 2.

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