CHEMISTRY LETTERS, pp. 1089-1092, 1978. Published by the Chemical Society of Japan

A DUALITY OF MECHANISM IN THE HOMOLYTIC SUBSTITUTION REACTION OF ANTHRONE WITH 1-CYANO-1-METHYLETHYL RADICALS

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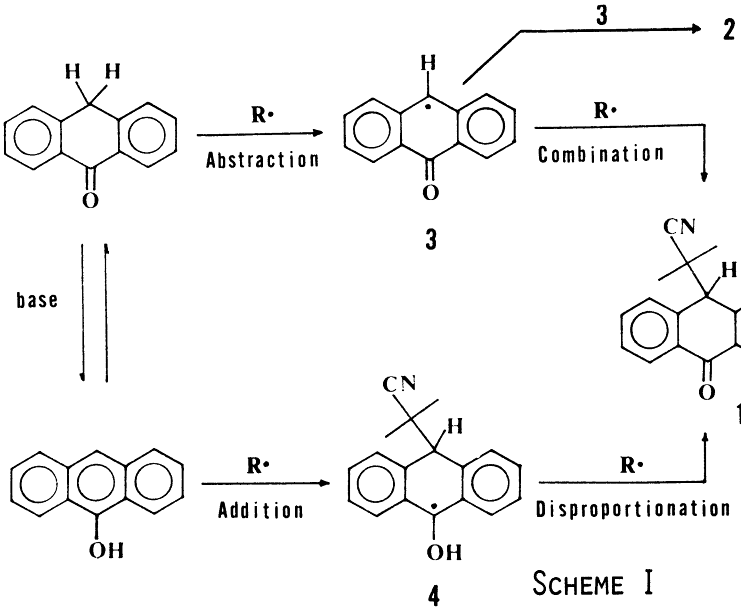
The mechanism of the homolytic substitution reaction of anthrone with 1-cyano-1-methylethyl radicals has been discussed on the basis of kinetic isotope effects as well as CIDNP. Under non-basic conditions the abstraction-combination mechanism is suggested, whereas the addition-disproportionation mechanism via anthranol prevails under basic conditions.

Recently we reported the title reaction to give the substitution product, 10-(1-cyano-1-methylethyl)anthrone, 1 which enabled us to avail ourselves of 9-(1-cyano-1-methylethyl)anthracene.[1] Although a great number of works have been published on the reactivity of 1-cyano-1-methylethyl radicals R·, little was known of their substitution reactions. Substitution at a saturated carbon might have been precluded by the extremely low capacity of the relatively stable radicals R· for abstracting hydrogen from aliphatic systems.[2] Only one example of homolytic aromatic substitution has been found in the action of R· on the heterocyclic nucleus of a benzisoxazole derivative;[3] however, substitution of this kind in the simple aromatic series appears difficult to occur, since the radicals are incapable of adding to benzene and naphthalene. While the radicals add to anthracenes, the initially formed radical intermediates undergo exclusive combination to 9,10-dihydroanthracenes as depicted by eq 1.[4] In this context, it seems of considerable interest to elucidate the mechanism of formation of 1. We wish to report here the results of our investigation providing definite evidence for a solvent dependent dual mechanism as illustrated in Scheme I.

The yield of 1 was markedly influenced by solvent basicity. The results obtained when anthrone (0.6 mmol) was treated with 2.4 equiv of azobisisobutyronitrile (AIBN) in various solvents (5 ml) at 80°C under nitrogen for 6 hr showed that the reactions in non-basic solvents, e.g., benzene and carbon tetrachloride (at reflux), gave 1 (ca. 30%) accompanied by minor amounts of bianthrone 2 (10 - 15%) and considerable amounts of anthrone remained unreacted (50 - 60%), whereas the use of basic solvents, e.g., pyridine and piperidine, greatly improved the yield of 1 (77 and 90%, respectively) with no detectable quantity of 2.[5] The enhanced effect of solvent basicity was disclosed when the relative rate of formation of 1 and 6_a, the radical adduct of 9-methoxyanthracene, produced through the process of eq 1 was measured by a competition method; k_1/k_{6_a} 0.22 in benzene, 1.5 in pyridine, and 27 in piperidine. It is well known that anthrone readily enolizes to anthranol in the presence of a base and anthranol dissociates in the strong base piperidine to give an orange solution charasteristic of the enolate ion

Distinct primary kinetic isotope effects, determined with anthrone and anthrone-10,10-d_2,[6] were observed in the non-basic solvents (k_H/k_D 3.9 in benzene at 80°C, 4.0 in carbon tetrachloride at 76°C), indicating that the hydrogen abstraction from the methylene group of anthrone is rate-determining.[7] In sharp contrast, no isotope effect was detected when the rates were compared for anthrone in a 4:1 mixture of pyridine-water and anthrone-10,10-d_2 in pyridine-heavy water of the same proportion (k_H/k_D = 1.0 at 80°C).[9] These results strongly suggest that there exist two pathways for the formation of 1. One is the abstraction-combination mechanism which involves the direct attack of R· on the methylene hydrogen of anthrone to generate anthronyl radicals 3 followed by combination of 3 and R·. The other formally resembles homolytic aromatic substitution, i.e., the addition-disproportionation mechanism via anthranol or its anion, and thus prevails under basic conditions (Scheme I). It should be noted that the intermediate radical 4 undergoes disproportionation rather than combination which would be expected from eq 1.

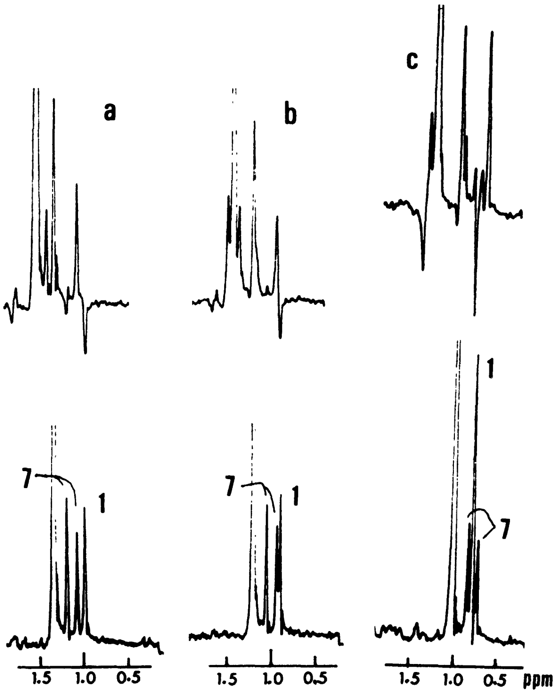
Additional evidence for a duality of mechanism was provided by CIDNP experiments. Because of higher temperatures required, another set of solvents were used for this purpose (1,1,2,2-tetrachloroethane and o-dichlorobenzene as non-basic solvents, and quinoline as a basic solvent). In FIG. 1 are shown the NMR spectra obtained during and after the reaction of 100 mg of anthrone with 20 mg



SCHEME I

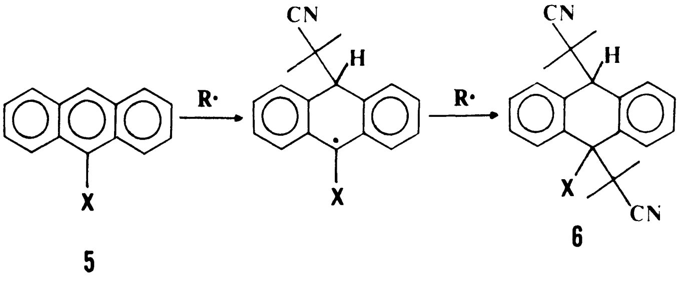
of AIBN in 0.4 ml of a solvent at 130°C. In the non-basic solvents an intense emission line appeared just at the position of the methyl proton signal of 1 (a and b in FIG.1). On the contrary, in the basic solvent quinoline, the reaction showed no emission from the methyl protons and the intensity of the proton signal increased smoothly while there was observed a typical doublet polarization due to isobutyronitrile 7 which was presumably produced by disproportionation of R· and 4 as well as that of a pair of R· (c in FIG.1).

FIG.1 The 60 MHz spectra in regions from 0.5 to 1.5 ppm (relative to hexamethyldisiloxane) during (top) and after (bottom) the reaction of anthrone with AIBN. For the reaction conditions, see text. Solvent: a, tetrachloroethane; b, o-dichlorobenzene; c, quinoline. The positions of methyl proton signals of 1 and 7 have been ascertained by measuring the NMR spectra of the authentic samples in the solvents used.



In the mode of introduction of a 1-cyano-1-methylethyl group, the initial step of the process proposed under basic conditions is identical with that of eq 1, and the final step of the process proposed under non-basic conditions has a close analogy with that of eq 1. As has already been reported with 9-bromoanthracene,[10] the group introduced in the initial step of eq 1 does not show polarization but does only the group introduced in the final step as theoretically predicted.

In the light of the addition-disproportionation mechanism, the high value of k_1/k_{6_a} observed in piperidine is anomalous, because the spread of relative



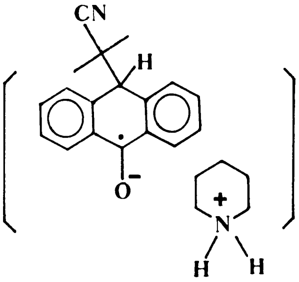
X

a, CH_3O

b, CH_3 (1)

c, CH_3CO

rates obtained from the reactions of R· with 9-substituted anthracenes 5_{a-c} was found to be very small; $k_{6_b}/k_{6_a} = 1.1$ and $k_{6_c}/k_{6_a} = 0.8$ (measured in benzene).[11] The most likely explanation is that the rate reflects the stability of the ketyl 8 formed by addition of R· to the enolate ion, since the efficient delocalization of both the unpaired electron and the negative charge is expected for ketyls.



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Acknowledgments: The authors are grateful to Professor H. Iwamura for helpful discussions. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education of Japan.

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2) The hydrogen abstraction from benzaldehyde has been proposed in order to explain the origin of a product obtained in a meager yield from thermal decomposition of AIBN in neat benzaldehyde: M. S. Kharasch, M. Zimmermann, W. Zimmt, and W. Nudenberg, J. Org. Chem., 18, 1045 (1953).
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5) All quantitative measurements were carried out by the NMR analyses of samples obtained after the reaction mixtures were subjected to steam distillation.
6) Prepared by dissolving 0.5 g of anthrone in a mixture of 2 ml each of pyridine and heavy water with warming. The resulting solution was diluted with 3 ml of carbon tetrachloride to give crystals (0.25 g).
7) This observation seems unusual, because attempts to achieve the substitution reactions of R· with fluorene, 9,10-dihydroanthracene, and xanthene which exhibit analogous reactivities toward phenyl radicals[8] were unsuccessful.
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9) The D_2O-pyridine system as a basic solvent was used to avoid isotopic exchange between anthrone-10,10-d_2 and a trace of water.
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(Received June 27, 1978)