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PHOTOREACTIONS OF AROMATIC COMPOUNDS—IV[1]

THE DIRECTING INFLUENCE OF THE METHOXY- AND THE NITRO- SUBSTITUENT IN THE PHOTODEUTERATION OF THE BENZENE NUCLEUS

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Abstract—Benzene derivatives undergo hydrogen–deuterium exchange when illuminated in acidic media such as CH_3COOD and/or CF_3COOD. The substitution pattern is very different from that observed in thermal exchange reactions. In the light reaction, anisole is preferentially substituted in *meta* and *ortho* positions while substitution in the *para* position is negligible. In nitrobenzene the order is *para* > *meta* ≫ *ortho*. In *p*-nitroanisole the two types of hydrogen are exchanged at equal rate in the light while the dark reaction effects substitution *ortho* to the methoxy group only. With anisole (phenol) and *p*-nitroanisole (*p*-nitrophenol) the calculated charge distribution rather than localization energies in the lowest $\pi \rightarrow \pi^*$ singlet gives a satisfactory description of the substitution pattern. With nitrobenzene the relations are more complicated. A short discussion is included.

INTRODUCTION

INITIATED by the observation[1] that nitrophenyl esters and nitrophenyl ethers undergo photo-induced reactions with nucleophilic reagents (water, methanol, hydroxide ion, methylamine) a long term study has been made in this laboratory of heterolytic photosubstitutions of aromatic compounds.[2] The *meta*-activation that was observed in all cases investigated,[3] is in marked contrast to the well known pattern of thermal substitution reactions. It, therefore, was deemed of primary interest to collect experimental data that would enable us to determine the relative reactivities (e.g. the electron availabilities in the case of electrophilic substitution) of the *ortho*, *meta* and *para* positions of substituted aromatic systems in the photo-excited state.

Hydrogen-deuterium exchange was selected as a suitable model reaction; it appeared to be easily induced by light.[4] This reaction has the advantage of being fairly symmetrical with respect to the substituting and the leaving groups. The investigation can be carried out in relatively simple media. In this paper, the results obtained with the (photo) deuteration in acidic media of anisole, nitrobenzene, *p*-nitroanisole and *m*-nitroanisole are reported.

EXPERIMENTAL

CF_3COOD and CH_3COOD (containing 5–10% of the non-deuterated compound) were used as deuterating agents in the H—D exchange reactions. Anisole and nitrobenzene are sufficiently soluble

[1] Preceding publications of this series: [a] R. O. de Jongh, W. Dorst and E. Havinga, *Rec. Trav. Chim.* **75**, 378 (1956); [b] E. Havinga, *Verslagen Kon. Ned. Akad. Wet. Afd. Natuurk.* **70**, 52 (1961); [c] E. Havinga and R. O. de Jongh, *Bull. Soc. Chim. Belg.* **71**, 803 (1962).

[2] A detailed account of part of the results is given in: R. O. de Jongh, thesis Leiden (1965).

[3] cf. also the results obtained by H. E. Zimmerman and V. R. Sandel, *J. Amer. Chem. Soc.* **85**, 915 (1963).

[4] cf. J. P. Colpa, C. MacLean and E. L. Mackor, *Tetrahedron* **19**, Suppl. 2, 65 (1963).

in these acids but the nitroanisoles were first dissolved in a small quantity of tetrahydrofuran in order to obtain a homogeneous system upon mixing with CF_3COOD. Portions of 10^{-2}–10^{-4} molar solutions (180 ml) were irradiated at room temp in a 250 ml vessel equipped with a magnetic stirrer. A Hanau Q 81 lamp was used as the light source. After illumination, the deuterating agent was removed together with the solvent by distillation under red. press. in case no exchange is effected by this procedure. Otherwise, samples of the reaction mixture were rapidly neutralized by addition of cooled conc. NaOH aq. The aromatic compounds were then isolated by extraction with an organic solvent and subsequent removal of the solvent by distillation.

The deuterium content of the aromatic compounds was determined by NMR. As the deuterium content of each position of the aromatic ring could not be calculated from the NMR spectra for anisole and nitrobenzene only, the derivatives 2,4-dibromoanisole and *m*-dinitrobenzene resp. were prepared and examined by NMR. H—D exchange between partly deuterated nitrobenzene and the mixture of nitric acid and sulphuric acid does not occur during the nitration reaction.[5]

The signal of the methoxy protons which are not exchanged, served as an internal standard for anisole and its derivatives. The spectra of nitrobenzene and *m*-dinitrobenzene were taken in the presence of an external standard (CH_3COOH). The NMR spectra were recorded on a Varian A-60 spectrometer using 10% solutions in either $CDCl_3$ or CCl_4 with tetramethylsilane as an internal reference. The following signals were identified and used in the analyses (δ-values in ppm)

Anisole:	$H_{arom} = 6{\cdot}7 - 7{\cdot}3$; $OCH_3 = 3{\cdot}6$
2,4-Dibromoanisole:	$H_3 = 7{\cdot}6$; $H_5 = 7{\cdot}3$; $H_6 = 6{\cdot}65$; $OCH_3 = 3{\cdot}8$
Nitrobenzene:	$H_2 = 8{\cdot}0$; $H_3 \simeq H_4 = 7{\cdot}4$
m-Dinitrobenzene:	$H_2 = 9{\cdot}0$; $H_4 = 8{\cdot}5$; $H_5 = 7{\cdot}7$
p-Nitroanisole:	$H_2 = 7{\cdot}9$; $H_3 = 6{\cdot}7$; $OCH_3 = 3{\cdot}75$

RESULTS

Anisole. The following deuterium distribution was found in four separate experiments, in which a solution of $6{\cdot}10^{-3}$ mole/l anisole in CH_3COOD was illuminated for 3–4 hr.

D_{ortho}: 7%, 6·5%, 8%, 8%, average 7·5%

D_{meta}: 9%, 8%, 8%, 7·5%; average 8%

D_{para}: less than 1%.

Using $CH_3COOD + CF_3COOD$ (mole ratio 8:1) as a deuterating medium and irradiating for 2 hr resulted in 11% D_{ortho} and 12% D_{meta}. Even under these conditions no photoinduced exchange at the *para* position could be detected. In the dark no exchange was observed between anisole and CH_3COOD upon refluxing for some hr. With CF_3COOD as a medium, heating for 2 hr at 70° resulted in 82% H → D exchange at the *ortho*, 0% D at the *meta* and 65% D at the *para*-position. The reaction constants of the dark reaction with CF_3COOD were determined at 20°:

$k_{H\to D}$*ortho*: 0·067 hr^{-1}

$k_{H\to D}$*para*: 0·052 hr^{-1}

Nitrobenzene. Irradiation for 4 hr of a $8{\cdot}10^{-3}$ molar solution of nitrobenzene in CF_3COOD/0·2 mole H_2SO_4/l resulted in the following deuterium uptake:

D_{ortho}: less than 1% in all experiments

D_{meta}: 4·5%, 5%, 5%, 5%, 6% average 5%

D_{para}: 8·5%, 9%, 8%, 9%, 9% average 8·6%

In an experiment with a greater H_2SO_4 content (0·35 mole/l) the D_{meta} and D_{para} were 10% and 13%, respectively, the deuterium content in the *ortho* position still not exceeding the experimental error. In the dark, nitrobenzene does not take up deuterium from CF_3COOD/0·2 mole H_2SO_4 in the course of several hr at room temp or even at 70°.

p-Nitroanisole. The two types of hydrogen (*ortho* and *meta*) were found to exchange at about equal rates when illuminated in CF_3COOD (~6% exchange upon irradiation for 4 hr). Exchange in the dark could be effected in a mixture of CF_3COOD and sulphuric acid; only the positions *ortho* to the methoxy group were found to react.

[5] cf. W. M. Lauer and W. G. Noland, *J. Amer. Chem. Soc.* **75**, 3689 (1953).

m-Nitroanisole. On illumination for ~4 hr, using CF_3COOD + 0·05 mole/l H_2SO_4 as deuterating medium, 9% of the hydrogen atoms at position 6 (*ortho* to the methoxy- and *para* to the nitro group) had been exchanged. The percentages deuterium at the other positions were much smaller and could not be determined accurately because of the complexity of the NMR spectrum of *m*-nitroanisole. In the dark the positions 2 + 4 showed the greatest tendency to react although the rates of exchange remained low even at elevated temperatures.

DISCUSSION

The first important conclusion to be derived from the experimental results is that in these photo-induced substitution reactions the differences in rate of reaction at the various positions are due to specific activation. The directive influence of a substituent in the excited state is in marked contrast to the well known aromatic substitution pattern in the ground state of the molecules.

There is a dramatic change in the activation of the *meta* position which e.g. in anisole under the experimental conditions does not react at all in the dark, but shows a high reaction rate in the light. A reverse relationship holds,—considering the *ortho*, *meta* and *para* positions in comparison to one another—for the *para* position. The least change in relative reactivity is observed with the *ortho* position which has a high order of reactivity in anisole both in the dark and in the light, whereas in nitrobenzene it is slow to react in the excited state as well as in the ground state. The same regularities seem to hold also in the case of the (photo) substitution of *meta*- and *para*-nitroanisole.

It appeared worthwhile to investigate with these rather simple systems as to how far the relative rates of photo-deuteration at *meta*,- *para*-(and *ortho*-) position can be theoretically understood.[6]

Starting from the assumption that the photodeuteration proceeds through a mechanism analogous to that generally accepted for electrophilic substitution at aromatic systems in the ground state, one might try as a first approximation to correlate the rates of photosubstitution to localization energies in the lowest excited (singlet) state. Although on closer inspection such a procedure seems questionable, localization energies in the ground state and in the lowest $\pi \rightarrow \pi^*$ excited singlet were calculated, using a selfconsistent field method of the kind described by Pople.[8–10] The calculations were completed by accounting for configuration interaction of the mono-excited singlets.

The results are summarized in Table 1. Since the data required for incorporating the methoxy group in the calculated systems seemed not yet sufficiently known, phenol was taken as a substitute for anisole. The "excited" localization energies appear to be much smaller than those of the ground state, thus accounting for the generally much higher reactivity of the excited molecules. However there is no striking parallelism between the localization energies at the various positions (*o*,*m*,*p*) in the excited

[6] For a discussion of the reaction pattern of aromatic molecules in the excited state, see also: Refs 1, 3, 7 and 2.

[7] R. Grinter, E. Heilbronner, M. Godfrey and J. N. Murrell, *Tetrahedron Letters* No. **21**, 771 (1961); R. Grinter and E. Heilbronner, *Helv. Chim. Acta.* **45**, 2496 (1962).

[8] J. A. Pople, *Trans. Far. Soc.* **49**, 1375 (1953).

[9] The authors wish to express their thankfulness to Drs. J. J. C. Mulder of the department of theoretical organic chemistry (head Prof. Dr. L. J. Oosterhoff) for performing the calculations and for valuable discussions.

[10] Since the available evidence[1,3] suggests that the reactions may occur in,—or at least start from—a singlet excited species we did not yet consider the electron distribution in triplet states.

TABLE 1. LOCALIZATION ENERGIES FOR ELECTROPHILIC ATTACK AT BENZENE, PHENOL AND NITROBENZENE IN THE GROUND STATE AND IN THE FIRST EXCITED ($\pi \rightarrow \pi^*$) SINGLET; $0{\cdot}1\ \beta = -0{\cdot}48$ eV $= -11$ Kcal

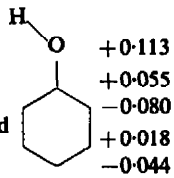
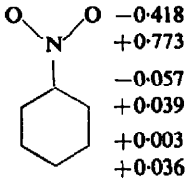
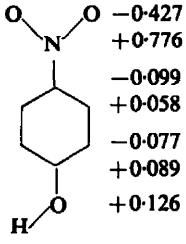
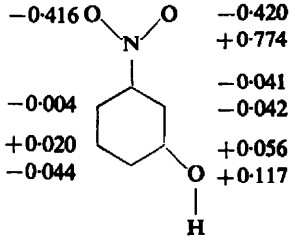
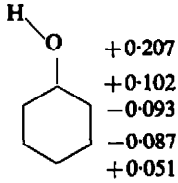
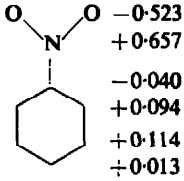
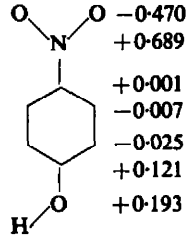
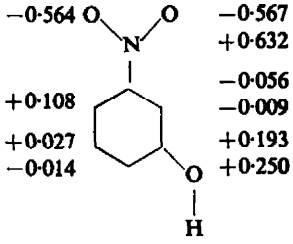
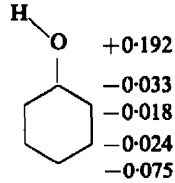
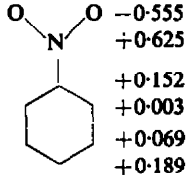
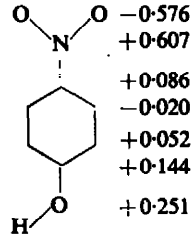
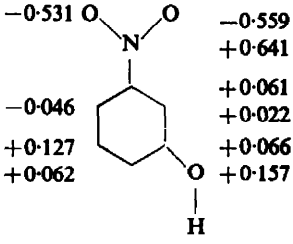
Compound	Position	Ground state	$\pi \rightarrow \pi^*$ singlet
Benzene		$-0{\cdot}517\ \beta$	$-0{\cdot}230\ \beta$
Phenol	*ortho*	$-0{\cdot}342$	$-0{\cdot}078$
	meta	$-0{\cdot}500$	$-0{\cdot}136$
	para	$-0{\cdot}353$	$-0{\cdot}182$
Nitro-	*ortho*	$-0{\cdot}634$	$-0{\cdot}180$
benzene	*meta*	$-0{\cdot}632$	$-0{\cdot}161$
	para	$-0{\cdot}653$	$-0{\cdot}213$

state and the relative rates of photoreaction at these positions. When viewed critically this is not surprising. Even if it is assumed that the calculated values are sufficiently accurate, it is doubtful whether the mechanism of the photosubstitution is analogous to that of the thermal reaction and whether it proceeds via a transition state leading to an electronically excited σ-complex. It seems likely that a vibrationally excited ground state complex will be formed and that this will cool down very rapidly, yielding the reaction product (or initial product) directly or via a normal ground state σ-complex. Another possible mechanism consists of electron transfer between the excited aromatic and the medium in the initial step of the reaction. In the case of anisole a positive radical ion can thus originate which will react with a deuterium atom formed in the surrounding acidic solvent. A comparable course, possibly the other way around, may be formulated for a compound such as nitrobenzene.

However this may be, it seems doubtful whether the photosubstitutions belong to the type of reaction the pattern of which can be satisfactorily deduced from localization energies. Theoretically, it looks more attractive to relate the relative rates of substitution of the various positions of such highly reactive species as these excited aromatic molecules certainly are, to their electron distribution. This charge distribution will attract and orientate the substituting agent (bound or solvated deuteron) in the first and decisive part of the extremely rapid process. From an alternative point of view the situation may also be described by saying that the electron distribution will indicate the positions where electron exchange with the reagent can proceed most readily. Table 2 represents the π-electron distribution for phenol, nitrobenzene, *m*- and *p*-nitrophenol in the ground state and in the two lowest excited singlets (Drs J. J. C. Mulder).

The calculations of the electron distribution were performed using the same method and data as for the localization energies. The agreement between the calculated charge distribution in the first excited singlet and the substitution pattern is satisfactory for anisole (phenol) and for *p*-nitroanisole (*p*-nitrophenol). This may be seen as a corroboration of the view that these photoreactions start from $\pi \rightarrow \pi^*$ singlet and proceed either as a direct electrophilic substitution or as an electron transfer followed by a substitution. With nitrobenzene and *m*-nitroanisole there is agreement between the electron densities in the S^1 state and the exchange pattern in so far as the positions that are calculated to be the most electron rich, react the fastest. However, in nitrobenzene the hydrogen in *meta* position is exchanged more rapidly than the calculated electron distribution would suggest. Possibly with nitrobenzene the

TABLE 2. CHARGE DISTRIBUTION IN THE GROUND STATE AND THE LOWEST EXCITED SINGLET STATES ORIGINATING FROM $\pi \rightarrow \pi^*$ TRANSITIONS†

	Phenol	Nitrobenzene	Nitrophenol	Nitrophenol
Ground state				
S^1				
	263 mμ $f_x = 0{\cdot}042$ $f_y = 0$	270 mμ $f_x = 0{\cdot}025$ $f_y = 0$	272 mμ $f_x = 0{\cdot}001$ $f_y = 0$	295 mμ $f_x = 0{\cdot}055$ $f_y = 0{\cdot}044$
S^2				
	221 mμ $f_x = 0$ $f_y = 0{\cdot}088$	242 mμ $f_x = 0$ $f_y = 0{\cdot}399$	263·5 mμ $f_x = 0$ $f_y = 0{\cdot}569$	245 mμ $f_x = 0{\cdot}003$ $f_y = 0{\cdot}217$

† f_x and f_y are taken in horizontal and vertical direction resp.

deuteration takes a somewhat different course compared with the reaction of molecules with a high electron density in the aromatic ring system. The investigation of other substituted benzenes may give information regarding such "anomalies" and whether they generally occur with molecules having substituents that deactivate the aromatic ring with respect to the substituting agent.