332. *Reactions of Aromatic Nitro-compounds in Alkaline Media. Part III.*[1] *The Behaviour of Picramide and of* NN-*Dimethylpicramide in Methanolic Sodium Methoxide.*

By V. GOLD and C. H. ROCHESTER.

Picramide and *NN*-dimethylpicramide both react with methanolic sodium methoxide solution at 25° to give coloured solutions.

With dimethylpicramide a 1 : 1 complex (equilibrium constant for formation at 25° = 7 l. mole^{-1}) is formed at low methoxide concentrations, whereas at higher methoxide concentrations a second complex, probably 1 : 2, is also formed. The solutions gradually change with formation of methyl picrate. The rate of this reaction parallels the proportion of dimethylpicramide present in solution as the 1 : 1 complex.

In the picramide solution there is evidence only of 1 : 1 interaction (equilibrium constant for formation at 25° = 38 l. mole^{-1}). The solutions decompose very slowly with liberation of nitrite ion and substitution of a nitro-group by a methoxyl group. The velocity of this reaction is also proportional to the concentration of the 1 : 1 complex.

The structural implications of the results are discussed.

PICRAMIDE is an aromatic amine containing potentially acidic hydrogen atoms. On this account, it is one of the indicators that have been used for establishing the H_- scale in basic media, on the assumption that its indicator behaviour is due to proton loss from the amino-group.[1] The *NN*-dimethyl derivative contains no such hydrogen atoms. Both compounds give intensely coloured solutions on addition of sodium methoxide to their solutions in methanol. Although the colour implies absorption of light in the same general spectral region as for the 1 : 1 methoxide complexes of 1,3,5-trinitrobenzene or methyl picrate, the similarity does not appear persuasive enough for a conclusion of structural similarity (see Figs. 1 and 2). The situation is complicated by the difference of the spectra of the two

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[1] Part II, preceding paper.

amines (without added base) in solution, both among themselves and from those of the other two trinitro-compounds. Steric effects may be important in this connection.

Picramide appears to be involved with methoxide in only one type of reversible interaction (1 : 1), as illustrated by the isosbestic points on the curves in Fig. 1. By contrast, the behaviour of dimethylpicramide is less simple (Fig. 2). A further difference between the two compounds lies in the nature of the irreversible reactions which succeed the establishment of equilibrium. Picramide, like trinitrobenzene [2] or 2,4,6-trinitrophenyl-*N*-methylnitramine (tetryl) [3] under similar conditions, loses a nitro-group which can be determined in solution as nitrite, whereas dimethylpicramide solvolyses with formation of methyl picrate and loss of the dimethylamino-group.

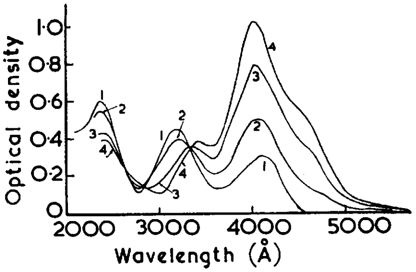

FIG. 1. Initial absorption spectra of picramide in methanolic sodium methoxide.

[OMe⁻] (M): 1, 0; 2, 0·0104; 3, 0·052; 4, 0·52. $[\text{Picramide}]_{\text{stoich}}$: $3{\cdot}58 \times 10^{-5}$M.

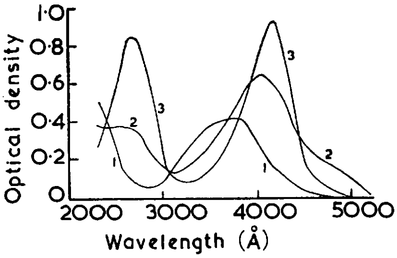

FIG. 2. Initial absorption spectra of *NN*-dimethylpicramide in methanolic sodium methoxide.

[OMe⁻] (M): 1, 0; 2, 0·186; 3, 0·935. $[\text{Dimethylpicramide}]_{\text{stoich}}$: $3{\cdot}69 \times 10^{-5}$M.

For picramide, the stoicheiometry of the equilibrium and the value of the equilibrium constant are established as follows. If the complex A is the result of 1 : 1 interaction, we have

$$\mathrm{P} + \mathrm{OMe}^- \rightleftharpoons \mathrm{A},$$

and

$$K_1 = [\mathrm{A}]/[\mathrm{P}][\mathrm{OMe}^-]. \tag{1}$$

For a 1-cm. cell, the optical density (D_0) at a single wavelength is given by

$$D_0 = \varepsilon_{\mathrm{A}}[\mathrm{A}] + \varepsilon_{\mathrm{P}}[\mathrm{P}]. \tag{2}$$

At 4000 Å, ε_{P} is evidently much smaller than ε_{A} (Fig. 1) but it is never negligible. Combining equations (1) and (2) with the material balance,

$$[\mathrm{P}]_{\text{stoich}} = [\mathrm{P}] + [\mathrm{A}],$$

we obtain

$$(D_0 - \varepsilon_{\mathrm{P}}[\mathrm{P}]_{\text{stoich}})^{-1} = \{K_1(\varepsilon_{\mathrm{A}} - \varepsilon_{\mathrm{P}})[\mathrm{OMe}][\mathrm{P}]_{\text{stoich}}\}^{-1} + \{(\varepsilon_{\mathrm{A}} - \varepsilon_{\mathrm{P}})[\mathrm{P}]_{\text{stoich}}\}^{-1}. \tag{3}$$

From the slope and intercept of the linear graph of the left-hand side of equation (3) against D_0 the following parameters (applying to 25°) were evaluated: $K_1 = 38$ l. mole^{-1}; ε_{A}(4000 Å) 29,300. Equation (4) of Part II [1] is the special case of this equation (3) when $\varepsilon_{\mathrm{P}} = 0$. An alternative form of (3), which also follows from equations (1) and (2), together with the material balance, is

$$(D_0 - \varepsilon_{\mathrm{P}}[\mathrm{P}]_{\text{stoich}})/[\mathrm{OMe}^-] = \varepsilon_{\mathrm{A}}K_1[\mathrm{P}]_{\text{stoich}} - K_1D_0. \tag{3a}$$

The validity of equation (3) and of the assumed 1 : 1 stoicheiometry and the deduced values

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[2] Schaal, *J. Chim. phys.*, 1955, **52**, 784; Stewart and O'Donnell, *J. Amer. Chem. Soc.*, 1962, **84**, 493.

[3] Farmer, *J.*, 1959, 3433.

of K_1 and ε_A is demonstrated by the agreement between experimental and calculated values of D_0 in Table 1.

TABLE 1.

Picramide. Variation of initial optical density with methoxide concentration.
$[\text{Picramide}]_{\text{stoich}} = 3{\cdot}58 \times 10^{-5}$M.

$[\text{OMe}^-]$ (M)	0·0104	0·052	0·156	0·520	1·040
D_0 (4000 Å)	0·497	0·789	0·947	1·018	1·042
D_0 (4000 Å) (calc.)	0·496	0·789	0·937	1·010	1·028

* Calc. from equation (3), with K_1 = 38 l. mole^{-1}; ε_A(4000 Å) = 29,300; ε_P(4000 Å) = 7770.

The subsequent reaction of picramide was followed by measurements of the concentration of nitrite in solution. It is very slow at 25°, and measurements extended over a period of many weeks. First-order rate constants were evaluated from straight-line plots of log ($[\text{P}]_0 - [\text{NO}_2^-]$) against time (where $[\text{P}]_0$ is the initial stoicheiometric concentration of picramide in solution) (Fig. 3). The absorption spectrum of a solution which had been allowed to react for 94 days at 25° (after which time the reaction was 76% complete according to the nitrite analyses) is given in Fig. 4.

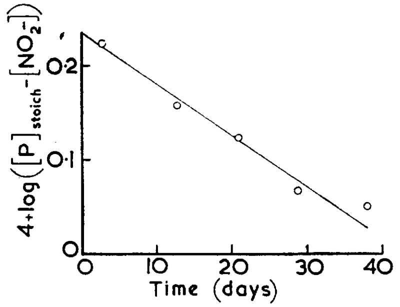

FIG. 3. Specimen reaction for picramide; $[\text{OMe}^-] = 0{\cdot}52$M.

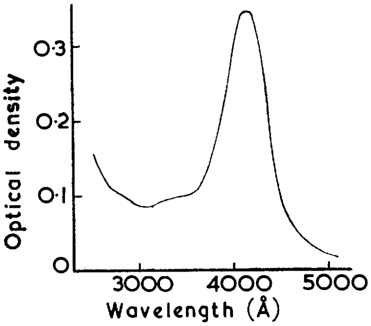

FIG. 4. Absorption spectrum of picramide solution after 76% reaction.

Conditions of reaction were: $[\text{Picramide}]_{\text{stoich}} = 1{\cdot}79 \times 10^{-5}$M, $[\text{OMe}^-] = 0{\cdot}52$M. Spectrum measured after tenfold dilution with methanol.

Velocity constants for the liberation of nitrite from solutions of picramide at different methoxide concentrations are given in Table 2. At all these concentrations the conversions of picramide into the coloured form is over 90% complete and the fact that the observed rate constant barely increases over this five-fold variation in the concentration of sodium methoxide strongly suggests that the transition state of this reaction, as that of the corresponding reaction of trinitrobenzene (Part II [1]), involves aromatic compound and methoxide ion to the same extent as the coloured species formed on addition of sodium methoxide to the nitro-compound. Equation (8) of Part II [1] should accordingly be applicable where k_2 is in the present case related to the measured rate of nitrite formation by the equation,

TABLE 2.

Picramide. Summary of first-order velocity constants for liberation of nitrite.

$[\text{OMe}^-]$ (M)	0·260	0·520	0·699	1·048	1·258
10^7k (sec.$^{-1}$)	1·49	1·49	1·57	1·60	1·68

$$k_2 = (1/[\text{A}])\text{d}[\text{NO}_2^-]/\text{d}t,$$

and when $[\text{A}] \longrightarrow [\text{P}]_{\text{stoich}}$, $k_2 \longrightarrow k$. From the results in Table 2, k_2 is found to be

$1{\cdot}64 \times 10^{-7}$ sec.$^{-1}$. Because of the extent of conversion into A, a reliable value of K_1 cannot be obtained from these results which, furthermore, relate to rather high methoxide concentrations in which the equilibrium would be governed by an acidity function rather than by the stoicheiometric concentration of methoxide ions.

With dimethylpicramide a coloured species was formed immediately after the addition of sodium methoxide to the solution in methanol. This was succeeded by a measurably slow change, indicated by intensification of the colour of the solution. This reaction was considerably more rapid than the secondary change in the case of picramide, but still sufficiently slow to allow the absorption spectrum of the first product to be recorded during the first few minutes after mixing. The speed of the subsequent reaction and the initial concentration of complex (obtained by extrapolation of the optical density to zero time; specimen run in Fig. 5) were determined by spectrophotometric measurements at 4800 Å. The spectrum of the secondary product coincided quantitatively with that of methyl picrate, at a corresponding methoxide concentration, and was stable, as required for methyl picrate.[4] The characteristic shape of this spectrum indicates that the final reaction product is formed by replacement of the dimethylamino-group of the starting material by methoxyl.

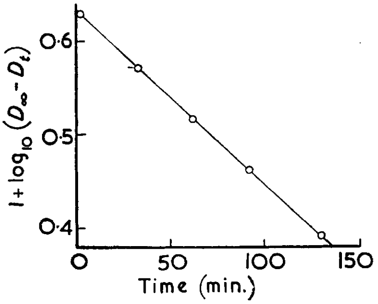

FIG. 5. Specimen reaction for *NN*-dimethylpicramide.

$[\text{OMe}^-] = 0{\cdot}140$M, $[\text{Dimethylpicramide}]_{\text{stoich}} = 3{\cdot}69 \times 10^{-5}$M.

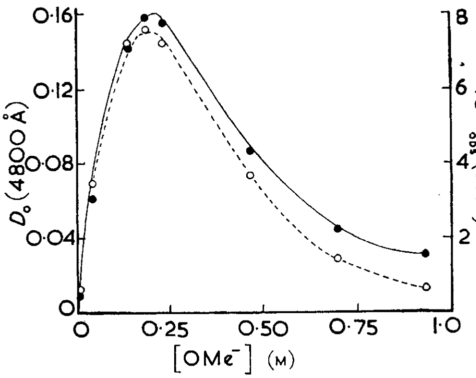

FIG. 6. Test of equations (8) and (9) for *NN*-dimethylpicramide.

● Experimental points for D_0; solid curve, prediction of D_0 from equation (9).

○ Experimental points for k; broken curve, prediction of k from equation (8).

The extrapolated initial optical density at 4800 Å increases with methoxide concentration up to a maximum value at 0·19M, and then decreases quite steeply. The rate constant for formation of methyl picrate ($k = -\text{d} \ln [\text{A}]/\text{d}t$) parallels this behaviour (Fig. 6). The results imply that the initial reaction between dimethylpicramide and sodium methoxide gives rise to equilibrium amounts of two different products. The product which predominates at low methoxide concentrations (E), and whose formation therefore involves a lower power of the methoxide concentration, has the higher absorption intensity at 4800 Å (see also Fig. 2). The correspondence between the curves in Fig. 6 further indicates that the stoicheiometric composition of the transition state for methanolysis is the same ($\pm n$ solvent molecules) as that of E, and that the product which predominates at high methoxide concentrations (F) does not decompose to methyl picrate at a significant rate. We interpret these results as indicating that methanolysis is a bimolecular reaction between dimethylpicramide and methoxide, and not a unimolecular decomposition of E (which would be equally compatible with these kinetics). Several points could be made in

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[4] Gold and Rochester, *J.*, 1964, 1687.

support of this conclusion. A strong argument is that if methanolysis proceeded by unimolecular loss of NMe_2^- from E or an isomer of E, then F, in which there are more OMe^- groups to provide negative charge for the leaving group, should decompose even more rapidly. The failure of F to react then argues against this hypothesis. On the other hand, if the methanolysis is a bimolecular nucleophilic replacement of NMe_2^- by OMe^-, the lowered reactivity of F is expected. By the same argument, since the attack of methoxide at the electron-depleted seat of substitution will not be furthered by electron donation elsewhere in the molecule, the lowest transition state will contain only one methoxide moiety per dimethylpicramide molecule. On this basis, E will likewise be a 1 : 1 complex.

The composition of complex F is also a problem. Not only is there no absolutely clear-cut division between the concentration regions in which E and F are found (as there is in the similar case of methyl picrate [4]), but the concentration range of chief interest for the second complex is one where the h_- acidity function diverges significantly from inverse proportionality to the concentration of sodium methoxide. However, measurements of H_- in methanolic sodium methoxide [5,6] are not available in sufficient detail to allow the conversion of methoxide concentrations into acidity function values and a discussion of our data on this basis. The equilibria are therefore expressed in terms of concentrations of methoxide, but we note that Ridd's measurements [5] suggest that h_- is inversely proportional to the methoxide concentration in the range below 0·25M and that it is roughly inversely proportional to the square of the methoxide concentration in the approximate range 0·5—1·4M.

The following model then describes the phenomena summarised in Fig. 6. Two complexes (E and F) are formed in rapidly established equilibria, the dependence of their equilibrium concentrations on the methoxide concentration being expressed by the equations

$$K_1 = [\mathrm{E}]/[\mathrm{PicNMe_2}][\mathrm{OMe^-}] \qquad (4)$$

$$K_2 = [\mathrm{F}]/[\mathrm{E}][\mathrm{OMe^-}]^3, \qquad (5)$$

and the rate of methanolysis by

$$\mathrm{d}[\mathrm{PicOMe}]/\mathrm{d}t = k[\mathrm{E}]. \qquad (6)$$

Since dimethylpicramide has no significant light-absorption at 4800 Å the extrapolated initial optical density (D_0) at that wavelength (for 1-cm. path-length) is given by

$$D_0 = \varepsilon_{\mathrm{E}}[\mathrm{E}] + \varepsilon_{\mathrm{F}}[\mathrm{F}]. \qquad (7)$$

Combination of equations (4)—(6) gives

$$k = k_3K_1[\mathrm{OMe^-}]/(1 + K_1[\mathrm{OMe^-}] + K_1K_2[\mathrm{OMe^-}]^4), \qquad (8)$$

and, similarly, equations (4), (5), and (7) lead to

$$D_0 = \frac{[\mathrm{PicNMe_2}]_{\mathrm{stoich}}(\varepsilon_{\mathrm{E}}K_1[\mathrm{OMe^-}] + \varepsilon_{\mathrm{E}}K_1K_2[\mathrm{OMe^-}]^4)}{1 + K_1[\mathrm{OMe^-}] + K_1K_2[\mathrm{OMe^-}]^4} \qquad (9)$$

Equations (8) and (9) satisfactorily reproduce the experimental points on both curves in Fig. 6, with the following fitted parameters: $K_1 = 7$ l. mole^{-1}; $K_2 = 26$ l.^{3} mole^{-3}; $k_3 = 1·45 \times 10^{-4}$ sec.$^{-1}$; $\varepsilon_{\mathrm{E}}(4800$ Å$) = 8300$; $\varepsilon_{\mathrm{F}}(4800$ Å$) = 500$. The curves drawn in Fig. 6 were calculated on this basis, the circles representing the experimental points. The value of K_1 and the dependence of [E] on the first power of the methoxide concentration are deduced mainly from the region of low methoxide concentrations where the neglect of activity coefficients is justifiable, and the results are therefore accepted at their face value. On the other hand, the determination of the value of K_2 and the dependence of [F] on the fourth power of methoxide concentration relies most heavily on experimental points for

[5] Ridd, *Chem. and Ind.*, 1957, 1268.

[6] Lambert and Schaal, *Compt. rend.*, 1962, **255**, 2256.

methoxide concentrations beyond 0·2M. The fourth-power dependence therefore probably implies an inverse-square dependence on h_-. The complex F is therefore probably formed by interaction of dimethylpicramide and two methoxide ions.

TABLE 3.

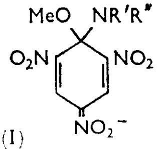
N-Dimethylpicramide. Comparison of predicted and experimental rate constants and initial optical densities.

	10^5k (sec.$^{-1}$)		D_0 (4800 Å)			10^5k (sec.$^{-1}$)		D_0 (4800 Å)	
[OMe$^-$] (M)	(exptl.)	(predicted *)	(exptl.)	(predicted †)	[OMe$^-$] (M)	(exptl.)	(predicted *)	(exptl.)	(predicted †)
0·0056	0·58	0·55	0·009	0·012	0·233	7·25	7·47	0·156	0·159
0·0466	3·50	3·57	0·062	0·074	0·466	3·70	3·68	0·087	0·090
0·140	7·22	6·92	0·142	0·145	0·699	1·45	1·43	0·045	0·046
0·186	7·63	7·48	0·159	0·158	0·932	0·68	0·65	0·031	0·031

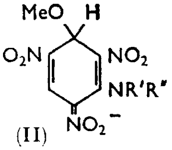
* Equation (8). † Equation (9).

The fact that the secondary reactions of picramide and dimethylpicramide lead to different products can be explained on the basis that replacement of the dimethylamino-groups occurs much more rapidly than replacement of the amino-group in the respective compounds. It is possible that the loss of the nitro-group occurs in both compounds at the same rate but, as this nitrite formation is much slower than the loss of the dimethylamino-group, it would escape detection. The enormous difference in the rate of loss of amino- and dimethylamino-groups with methanolic sodium methoxide is in contrast to the similarity of the values of K_1, and it is not paralleled in the reactions with aqueous sodium hydroxide.[7]

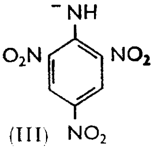
The possible structures of the 1 : 1 complexes in solution have to be discussed on the basis of less-direct evidence than in the cases of methyl picrate[4] and trinitrobenzene.[2] In view of the presence of potentially acidic hydrogen atoms only in picramide, it is evident that the same conclusions need not apply to the complexes of picramide and of dimethylpicramide. Farmer suggested the structure (I) (and the corresponding *ortho*-forms) for complexes of this kind.[3] The conclusion was based on his observation that both the reaction of methyl picrate with methylamine and that of *N*-methylpicramide with methanolic potassium hydroxide gave red products which, on decomposition with acid, gave only *N*-methylpicramide and no methyl picrate. Similar findings were obtained when other amines were used with methyl picrate. However, one may question this application of Meisenheimer's criterion for the attachment of an incoming group to the carbon atom already carrying a substituent.[8] Meisenheimer showed that the same mixture of products (PicOR and PicOR′) was formed on decomposition of a picrate complex, irrespective of whether it was formed from PicOR + OR′$^-$, or from PicOR′ + OR$^-$. The formation of a single product on acidification in Farmer's experiments, and always of the product in which the C–NR′R″ bond is preserved, leaves open the possibility that the addition of excess of amine to an alkyl picrate leads to immediate displacement of the alkoxide group, and that the colour reaction is interaction of the picramide derivative formed and a base.



(I)



(II)



(III)

In fact, there are several indirect pieces of evidence which argue against structure (I) in the case of dimethylpicramide. If (I) were the 1 : 1 complex formed, then the

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[7] Gold and Rochester, to be published.

[8] Meisenheimer, *Annalen*, 1902, **323**, 205; Jackson and Earle, *Amer. Chem. J.*, 1903, **29**, 89.

methanolysis reaction would be simply the unimolecular loss of NMe_2^- from (I) [*i.e.*, an S_N1 reaction of (I)]. Such a reaction would be assisted by addition of (or other reaction with) a further electron-supplying methoxide group, *i.e.*, the 1 : 2 complex should decompose to methyl picrate more rapidly than the 1 : 1 complex. However, the 1 : 2 complex has been shown to react much more slowly (if at all), and is therefore unlikely to contain the $>C(OMe)\cdot NMe_2$ grouping. (It is conceivable, but rather improbable, that this grouping is absent from the 1 : 2 complex and yet present in the 1 : 1 complex.) Of course, a configuration such as (I) must be passed through in the course of the methanolysis reaction, but this does not require a substantial equilibrium concentration of (I).

Structure (II) (and canonical forms involving location of the charge on other nitro-groups) appears more probable for dimethylpicramide. The attachment of the methoxyl group now resembles that postulated for trinitrobenzene.[2,9] If, as is expected, the effect of the *m*-dimethylamino-group on the stability is slight, one would then predict the value of K_1 for dimethylpicramide to be about 2/3 of the value for trinitrobenzene (the factor 2/3 being a statistical correction for the number of available positions in the two compounds). The experimental ratio of the two equilibrium constants is 7/15, in fair agreement with this qualitative prediction. These results suggest that the effect of the ***meta***-substituent is indeed small and, accordingly, the stability of (I) when $R' = R'' = H$ would be expected to be close to that when $R' = R'' = Me$. The fact that K_1 for picramide is about five times larger than K_1 for dimethylpicramide then suggests that another type of interaction can occur in picramide, and proton loss from the amino-group is an obvious possibility. However, the foregoing argument also suggests that about 20% of " the " 1 : 1 complex of picramide should exist as structure (II). It is remarkable that two possibilities of reaction for picramide appear to be so closely balanced. Since the ion (III) has the same stoicheiometry ($\pm n$ solvent molecules !) as a 1 : 1 addition complex, the relative proportions of these two species in solution would remain unaltered with changing methoxide concentration (so long as the activity of methanol stays sensibly constant, which it will in the dilute solutions in which the 1 : 1 complexes are formed), and the existence of isosbestic points is not at variance with the hypothesis. Orgel and Mulliken [10] pointed out that the existence of multiple equilibria of the same stoicheiometry is not directly demonstrable by the type of measurement usually carried out, although it may be possible to detect it by measurements at different temperatures.

EXPERIMENTAL

Picramide was recrystallised to constant melting point (192·5°) from acetic acid. *NN*-Dimethylpicramide was prepared from picryl chloride and dimethylamine,[11] crystallised from benzene, and dried in a vacuum desiccator (m. p. 139°). Sodium methoxide solutions were prepared as before.[4] All absorption measurements were made using a Unicam S.P. 500 spectrophotometer with 1-cm. matched silica cells.

Reactions were started by mixing thermostatted (25°) stock solutions of amine and sodium methoxide. Initial spectra were observed immediately after mixing. In the case of picramide the reaction was followed by removal of samples (2 ml.) of reaction solution, neutralisation by aqueous hydrochloric acid, and nitrite estimation according to Rider and Mellon's method,[12] a diluted sample of reaction medium being used in the black beam. In the case of *NN*-dimethylpicramide the progress of the reaction was observed by spectrophotometry, at 4800 Å, of samples withdrawn from the reaction flask. Both reactions were studied with rigorous exclusion of light.

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[*Received*, *July* 16*th*, 1963.]

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[9] Foster, *Nature*, 1959, **183**, 1042.
[10] Orgel and Mulliken, *J. Amer. Chem. Soc.*, 1957, **79**, 4839.
[11] Glazer, Hughes, Ingold, James, Jones, and Roberts, *J.*, 1950, 2674.
[12] Rider and Mellon, *Analyt. Chem.*, 1946, **18**, 96.