yield; m.p. 280° dec.; $\lambda_{max}$ 292 m$\mu$ ($\epsilon$ 4200) and 302 (4400); $\nu_{max}$ 3250, 1630, and 1600 cm.$^{-1}$. The structure VIII rather than VIIIa was assigned on the basis of the amide II band.
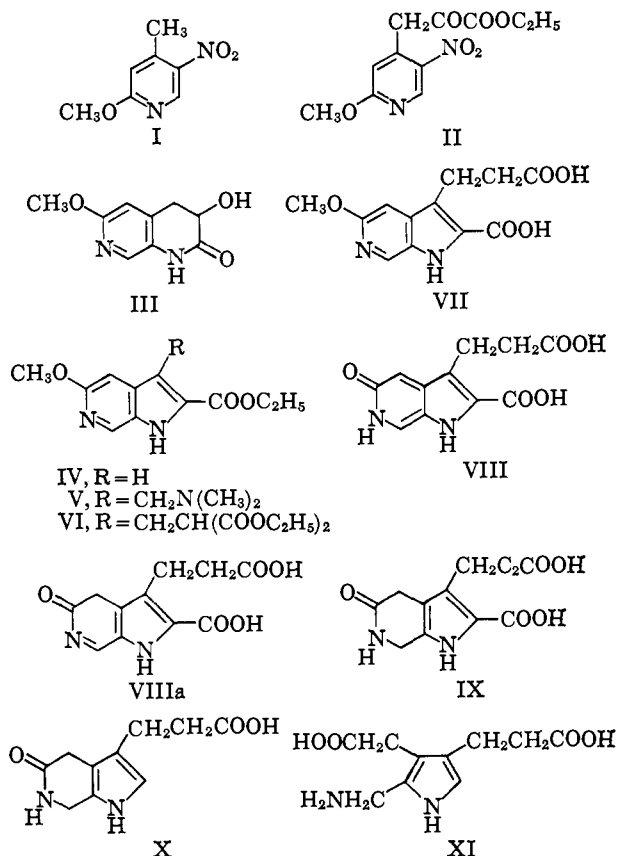


The pyridonepropionic acid VIII was hydrogenated in aqueous solution at pH 7 and 50 p.s.i. over palladium on carbon and, after adjustment of the pH to 4, 2-carboxyporphobilinogen lactam (IX) was obtained in 90% yield; m.p. 295° (lit.[3] m.p. 325°); $\lambda_{max}$ 276 m$\mu$ ($\epsilon$ 12,600). In boiling water, the carboxylactam IX was smoothly decarboxylated (80% yield) to porphobilinogen lactam (X), m.p. 295° dec. (lit.[3] m.p. 280–283°), which was then treated at 20° with 2 $N$ potassium hydroxide for 72 hr. When the pH was adjusted to 4, porphobilinogen (XI) was obtained as the monohydrate in 85% yield, m.p. 167° (lit.[3] m.p. 170–174°). It was identical with an authentic sample of porphobilinogen (from urine)[10] by paper chromatography, electrophoresis, and infrared absorption, and both gave identical lactams. Polymerization of our synthetic porphobilinogen, catalyzed by enzyme preparations from spinach and wheat germ,[11] gave quantitative yields of uroporphyrins.

The over-all yield of porphobilinogen (XI) starting from 2-methoxy-4-methyl-5-nitropyridine (I) is 19%, and an analogous series of compounds has been prepared from the 2-benzyloxy analog. By introducing different substituents at C-3 of the 6-azaindole IV, a series of azaindoles and pyrroles related to porphobilinogen has been obtained. These compounds and the

(10) We are indebted to Professor M. Grinstein (Buenos Aires) for samples of authentic porphobilinogen.
(11) L. Bogorad, *J. Biol Chem.*, **233**, 501, 510 (1958).

application of this synthesis to isomeric azaindoles will be described in our future publications.

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Received June 1, 1965

## Spontaneous Free-Radical Formation in the Pyrolysis of Nitroaromatic Compounds

*Sir:*

Nitroanilines, nitrotoluenes, nitrobenzaldehydes, nitrophenols, nitrophenyl disulfides, and numerous nitrobenzyl derivatives readily produce free radicals when heated above their melting points. This report gives our preliminary results on the effect of structure and temperature on this reaction.[1]

All nitroanilines studied gave free radicals upon heating (Table I), the *meta* derivatives giving rise to radicals at lower temperatures than the *ortho* or *para* derivatives. From a study of the concentration of radicals produced as a function of temperature, N,N-dimethyl-*m*-nitroaniline was found to behave very much like *m*-nitroaniline. These observations suggest that the radical formation in the case of the nitroanilines is the result of an electron-transfer reaction, since the ease of removal of an electron from the nitrogen unshared electron pair and the ease of reducing the substituted nitrobenzene would be expected to follow the order *meta* > *ortho* $\simeq$ *para*.[2]

$$2NO_2C_6H_4\ddot{N}R_2 \longrightarrow NO_2C_6H_4\dot{N}^+R_2 + NR_2C_6H_4NO_2\dot{}^-$$
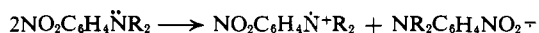
A hydrogen transfer mechanism seems unlikely since the ease of removal of hydrogen from *m*-nitroaniline would have to equal the ease of removal of an N-methyl hydrogen from N,N-dimethyl-*m*-nitroaniline.

The radicals indicated in the above reaction are considered the primary products of pyrolysis but not necessarily the radicals giving the e.s.r. spectrum observed. Heated nitroanilines gave broad triplets with relative intensities 1:1:1 (*e.g.*, *m*-nitroaniline) or quintets (*e.g.*, *o*- and *p*-nitroaniline) with splitting constants in reasonable agreement with expected values for nitrobenzene[3] or nitrosobenzene[4] radical anion derivatives. The broadness of the lines is probably due to rapid electron transfer with solvent (nitroaniline).

Although *p*-nitrotoluene did not give free radicals and *o*- and *m*-nitrotoluene only a trace at temperatures

(1) A Varian 4502 e.p.r. spectrometer was used to detect and monitor the formation of free radicals. Samples were heated in a flat quartz tube with preheated nitrogen inside a quartz dewar in the cavity of the spectrometer.
(2) Similar reactions are known to occur with carbanions: G. A. Russell and E. G. Janzen, *J. Am. Chem. Soc.*, **84**, 4153 (1962); G. A. Russell, E. G. Janzen, and E. T. Strom, *ibid.*, **86**, 1807 (1964).
(3) D. H. Geske, J. L. Ragle, M. A. Bambenek, and A. L. Balch, *ibid.*, **86**, 987 (1964).
(4) G. A. Russell and E. J. Geels, *ibid.*, **87**, 122 (1965).

**Table I.** Free-Radical Formation in the Pyrolysis of Nitroaromatic Compounds

| Nitroaromatic | Free-radical formation Temp., °C.[a] | Max. amt.[b] |
|---|---|---|
| o-Nitroaniline[c] | 250 | +++ |
| m-Nitroaniline[c] | 160 | +++++ |
| p-Nitroaniline | 260 | +++ |
| N,N-Dimethyl-m-nitroaniline[c] | 160 | ++++ |
| N,N-Dimethyl-p-nitroaniline | 250 | +++ |
| 2,4-Dinitroaniline[c] | 260 | ++++ |
| 2,4,6-Trinitroaniline[c] | 160 | ++ |
| 2,4-Dinitrodiphenylamine | 150 | + |
| o-Nitrotoluene | 180 | + |
| m-Nitrotoluene | 230 | + |
| 2,4-Dinitrotoluene | 260 | ++ |
| 2,4,6-Trinitrotoluene | 240 | +++ |
| 4'-Nitroacetophenone | 120 | ++ |
| Phenyl p-nitrobenzyl ether | 140 | +++ |
| Methyl (p-nitrophenyl)acetate | 80 | ++ |
| p-Nitrophenylacetonitrile | 240 | +++ |
| α-Bromo-p-nitrotoluene | 250 | ++++ |
| p-Nitrobenzyl alcohol | 100 | + |
| Bis(p-nitrophenyl)methane[c] | 240 | ++ |
| p-Nitrophenyldiphenylmethane | 120 | +++ |
| Tris(p-nitrophenyl)methane[c] | 120 | ++++ |
| o-Nitrobenzaldehyde | 80 | +++ |
| m-Nitrobenzaldehyde[c] | 200 | ++ |
| p-Nitrobenzaldehyde | 160 | +++ |
| 2,4,6-Trinitrobenzaldehyde | 100 | + |
| m-Nitrophenol | 240 | ++ |
| p-Nitrophenol | 140 | ++ |
| 2,4,6-Trinitrophenol | 130 | +++ |
| Bis(o-nitrophenyl) disulfide | 140 | ++++ |
| Bis(p-nitrophenyl) disulfide | 100 | ++++ |

[a] Lowest temperature for first detection of radicals or rapid increase of concentration of radicals if starting material contains free radicals. [b] Maximum concentration of radicals observed at any temperature up to 300° (highest temperature available); approximate concentrations: $+ = 10^{-6}\,M$, $++ = 10^{-5}\,M$, $+++ \, 10^{-4}\,M$, etc. [c] Readily detectable amounts of free radicals in commercially available or preparatively pure chemicals.

up to 300°, 2,4-dinitrotoluene and 2,4,6-trinitrotoluene produced radicals readily. Nitrobenzyl derivatives (e.g., methyl p-nitrophenylacetate, p-nitrobenzyl alcohol, phenyl p-nitrobenzyl ether, p-nitrophenyldiphenylmethane, and tris(p-nitrophenyl)methane) gave free radicals at relatively low temperatures. In the case of p-nitrophenyldiphenylmethane a triplet was first seen at lower temperatures (120°) which was dominated at higher temperatures by a single peak with hyperfine structure resembling the trityl radical. The intensity of this peak was reversibly dependent on temperature, as should be expected for a trityl–hexaarylethane equilibrium.

A hydrogen atom transfer mechanism seems most feasible for the free-radical formation for these nitroaromatic compounds where unpaired electrons are not available.[5,6]

$$2NO_2C_6H_4CH \longrightarrow NO_2C_6H_4C \cdot + H\dot{N}O_2C_6H_4CH$$
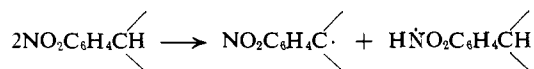
In the case of p-nitrophenyldiphenylmethane at 120° both products of the disproportionation can be seen, but in most other cases the radicals observed probably

(5) Evidence for this mechanism will be presented in a following paper; e.g., the hydrocarbon related to Koelsch's radical (C. F. Koelsch, *J. Am. Chem. Soc.*, 79, 4439 (1957)), 2-phenylbisbiphenylenepropene, gives the e.s.r. spectrum of Koelsch's radical in nitrobenzene at 80–190° under nitrogen.
(6) Photoinduced hydrogen atom transfer to nitrobenzene from THF has been reported: R. L. Ward, *J. Chem. Phys.*, 38, 2588 (1963).

are derived from the reduced nitrobenzene function. A hydrogen transfer mechanism can also explain the free-radical formation in the case of the nitrobenzaldehydes

$$2NO_2C_6H_4CHO \longrightarrow NO_2C_6H_4\dot{C}O + H\dot{N}O_2C_6CHO \longrightarrow ?$$

and nitrophenols

$$2NO_2C_6H_4OH \longrightarrow NO_2C_6H_4O \cdot + H\dot{N}O_2C_6H_4OH \longrightarrow ?$$

It is apparent from our experiments that nitrotoluenes, nitroanilines, nitrobenzaldehydes, and to some extent nitrophenols spontaneously react to produce free-radicals more readily (i.e., higher concentrations at lower temperatures) as the number of nitro groups increases: p-nitrotoluene < 2,4-dinitrotoluene < 2,4,6-trinitrotoluene; p-nitroaniline < 2,4-dinitroaniline < 2,4,6-trinitroaniline; p-nitrobenzaldehyde < 2,4,6-trinitrobenzaldehyde; p-nitrophenol < 2,4,6-trinitrophenol. This is consistent with the expected increased affinity of the polynitro aromatic nucleus for electron or hydrogen abstraction. Such reactions must be important in the initiation of the thermal decomposition of explosives.

In a number of cases spontaneous free-radical formation occurred in the solid state (e.g., p-nitrophenyldiphenylmethane, tris(p-nitrophenyl)methane, and the nitrophenyl disulfides), although the rate of radical formation was much more rapid at temperatures above the melting[f] points. As indicated in the table many solid nitroaromatic compounds contain free radicals as impurities.

Except for polynitroaromatic derivatives, little change in ease of radical formation or character of signal was found whether the sample was heated in an open tube or sealed under nitrogen. In a number of cases good resolution of the signal was obtained: 2,4-dinitrotoluene, 2,4,6-trinitrotoluene, p-nitroacetophenone, o- and p-nitrobenzaldehyde, and the nitrophenyl disulfides gave complex spectra sometimes indicating more than one radical species present; 2,4,6-trinitrobenzaldehyde, p-nitrophenol, and 2,4,6-trinitrophenol gave triplets. The interpretation of some of these spectra is not straightforward and will be described at a later date.

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**The Photoisomerization of α-Phellandrene. A Structural Reassignment[1]**

*Sir:*

In a recent publication, Crowley has reported that irradiation of an ethereal solution of α-phellandrene (I)

(1) The partial support of this research by National Science Foundation Grant No. G-22541 is acknowledged with pleasure.