Reaction of *ortho*-Nitro-substituted Benzene Derivatives with Ferrous Oxalate

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The reaction of ferrous oxalate with methyl 4-(*o*-nitrophenyl)butyrate, methyl *o*-nitrophenoxyacetate, *o*-nitrocumene, *o*-t-butylnitrobenzene, *NN*-dimethyl-*o*-nitroaniline, *o*-nitroanisole, and nitrocyclohexane at 215—260° gave a variety of compounds, including cyclisation products and primary amines. Most of the results may be interpreted in terms of the formation of nitrene intermediates, although other mechanisms such as the dehydration of *aci*-nitro-tautomers, where these are possible, may be operative.

SIMPLE aromatic nitro-compounds have been shown to react with transition-metal oxalates to give azo- and azoxy-benzenes and phenazines, and occasionally traces of primary aromatic amines.[1,2] This behaviour is similar to that of the corresponding aryl azides upon thermolysis and photolysis,[3,4] and has best been explained in terms of the formation of a nitrene intermediate bound to the surface of the metal derivative.[1,4]

The reaction of ferrous oxalate with some *o*-nitro-substituted benzene derivatives has led to a number of interesting cyclisations. For example, 2-nitrobiphenyl gave carbazole,[5] and 2-nitrodiphenylamines gave phenazines.[6] 2-*o*-Nitrophenylpyridine cyclised to pyrido-[1,2-*b*]indazole,[7] 2,4,6-trimethyl-2′-nitrobiphenyl gave 2′-amino-2,4,6-trimethylbiphenyl and 8,10-dimethylphenanthridine,[2] *o*-aminophenylcyclohexane and carbazole were obtained from 2-*o*-nitrophenylcyclohexane,[2] and indole-2-carboxylic acid and indole were formed from *o*-nitrophenylcinnamic acid.[2] Similar cyclisations have been effected from the appropriate azide,[7-10] from nitro-compounds and triethyl phosphite,[11,12] and, in instances where an *aci*-nitro-compound can be formed from a suitable nitrobenzene derivative,

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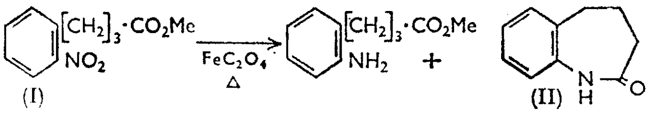
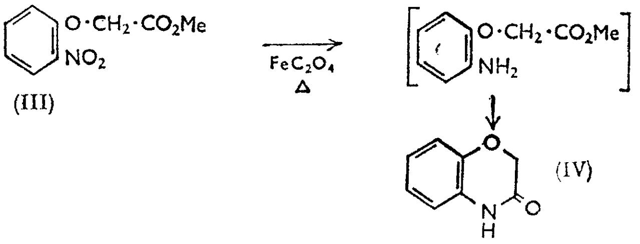
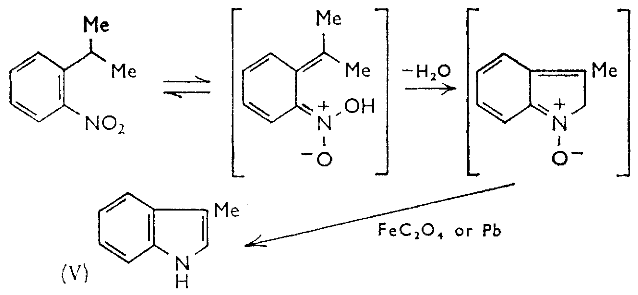
thermally in the absence of a reagent.[13] It has also been shown that the production of 2-phenylcarbazole from 2-nitro-*p*-terphenyl is induced by tars formed in the reaction mixture which deoxygenate the nitro-group.[14] It has been suggested that, in those cases where an *aci*-nitro-tautomer can be formed, the cyclisations proceed by two different mechanisms, particularly if a suitable deoxygenation agent is absent.[1] The present paper reports some further studies of the reaction of some *o*-nitrosubstituted benzene derivatives with ferrous oxalate, aimed at determining the scope and limitations of this cyclisation.

When methyl 4-(*o*-nitrophenyl)butyrate (I) was heated with ferrous oxalate only the corresponding primary amine and its cyclisation product, the tetrahydrobenzazepinone (II), were isolated; no quinoline or indole derivatives that could have resulted from the insertion of a nitrene into a methylene group of the side-chain were observed. Similarly, methyl *o*-nitrophenoxyacetate (III) gave only 2*H*-1,4-benzoxazine-3(4*H*)-one (IV), but no C–H insertion products. Compounds (II) and (IV) undoubtedly arise from the thermal cyclisation of the intermediate amino-esters.[15]

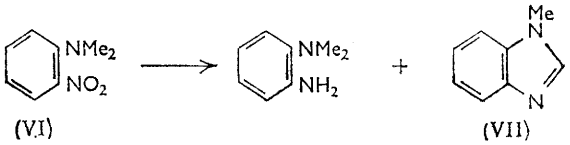




When heated with ferrous oxalate or with lead shot, *o*-nitrocumene gave 3-methylindole (V) in a very low yield, but no 3-methylindoline. Dehydrogenation is known to occur in the presence of ferrous oxalate.[2]

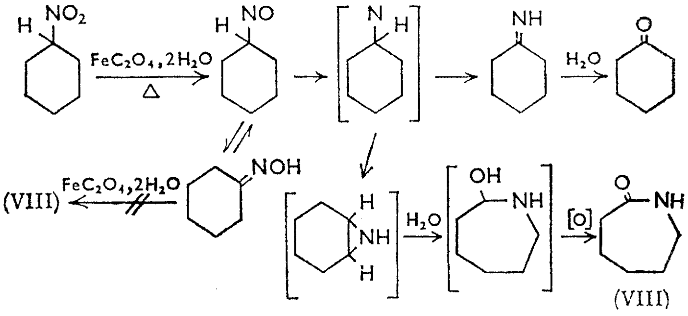


Alternatively, (V) could be formed by cyclisation of an *aci*-nitro-tautomer[3] followed by ferrous oxalate deoxygenation[16] of the resulting *N*-oxide. In support of this possibility is the fact that no 3,3-dimethylindoline[17] was obtained from *o*-t-butylnitrobenzene and ferrous oxalate; only *o*-amino-*t*-butylbenzene was formed, probably *via* a nitrene intermediate.[1] On the other hand, *NN*-dimethyl-*o*-nitroaniline (VI), which cannot form an *aci*-nitro-tautomer, did give a small amount of 1-methylbenzimidazole (VII), together with *NN*-dimethyl-*o*-phenylenediamine, when heated with ferrous oxalate.



The reaction of *o*-nitroanisole with ferrous oxalate was also examined. No benzoxazole or benzoxazoline could be detected, and the main products were *o*-anisidine and 2,2′-dimethoxyazobenzene. A very minor product was also formed in quantities too small to permit direct identification. The same product was obtained (10%) when *o*-anisidine was heated with ferrous oxalate. Its i.r. and u.v. spectra indicated that it was an *o*-anisidine derivative which still possessed a primary amino-group. The mass spectrum corresponded to that of a methyl *o*-anisidine ($C_8H_{11}NO$) and the new methyl group was clearly visible in the n.m.r. Fragment ions corresponding to ($M - CH_3$), (M − CHO), and ($M - CH_3$ − CO) were observed. The identity of the methylated *o*-anisidine was not established further.

Finally, the reaction of nitrocyclohexane with ferrous oxalate dihydrate at 230—250° gave cyclohexanone and hexahydroazepin-2-one (VIII). The formation of cyclohexanone can be accounted for by a 1,2-hydrogen shift in the intermediate nitrene followed by hydrolysis of the resulting imine. The azepine is not formed by a Beckmann-type rearrangement of cyclohexanone oxime: when the latter was heated with ferrous oxalate dihydrate under the same conditions it was recovered unchanged. A possible route is shown in the Scheme.



Scheme

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EXPERIMENTAL

Reaction of Methyl 4-(o-*Nitrophenyl)butyrate with Ferrous Oxalate Dihydrate*.—(*a*) A mixture of the butyrate (2·1 g.) and ferrous oxalate dihydrate (2·5 g.) was heated with granulated lead (10 g.) under reflux at 240—260° for 40 min. The cooled mixture was extracted repeatedly with hot benzene, the combined extracts were dried ($MgSO_4$), and the solvent was evaporated off to leave a dark brown oil (0·5 g.), which was chromatographed on a column of alumina. Elution with benzene–ether (2 : 1 v/v) gave 2,3,4,5-tetrahydro-1-benzazepin-2-one (0·12 g.), m.p. and mixed m.p.[18] 147—148° (from benzene). Elution with more polar solvents gave intractable tars. In some of the runs, methyl 4-(*o*-aminophenyl)butyrate, b.p. 186—191°/15 mm. was eluted with benzene–ether (2 : 1 v/v).

(*b*) When the reaction was carried out as in (*a*) with methyl 4-(*o*-nitrophenyl)butyrate (9·7 g.), *n*-dodecane (20 g.), and ferrous oxalate dihydrate (12 g.) at 220—230° for 60 min. only the benzazepinone (0·45 g.) was formed. Some starting ester (3·08 g.) and 4-(*o*-nitrophenyl)butyric acid (0·44 g.) were recovered.

Reaction of Methyl o-*Nitrophenoxyacetate with Ferrous Oxalate Dihydrate*.—A mixture of methyl *o*-nitrophenoxyacetate (10 g.), ferrous oxalate dihydrate (12 g.), and lead shot (20 g.) was heated under reflux at 230—260° for 45 min. The mixture was worked up and chromatographed as before. Elution with benzene–ether (2 : 1 v/v) gave a dark red solid (0·012 g.) which was not characterised, $\nu_{max.}$ 3400m, 3310w, 3180w, 3130w, 3060w, 2920m, 2850m, 1688s, 1585s, 1498s, 1400m, and 740s cm.$^{-1}$. Elution with benzene–ether (1 : 2 v/v) gave 2*H*-1,4-benzoxazin-3(4*H*)-one (0·64 g.), m.p. and mixed m.p.[19] 176·5—178° (from 95% ethanol). Elution with methanol gave a brown amorphous solid which was extracted with ether; the residue after evaporation of the ether gave a pale yellow solid, m.p. 179—181° (decomp.) (from ethanol), soluble in water, methanol, and benzene, $\nu_{max.}$ (KBr) 3450s, 3250s, 2980w, 2940w, 1620s, 1585w, 1525m, 1425m, 1350m, 1280m, 1022s, 945m, 865m, 830w, 768w, 735m, 720w, and 698w cm.$^{-1}$, not characterised further.

Reaction of o-*Nitrocumene with Ferrous Oxalate Dihydrate*.—(*a*) A mixture of *o*-nitrocumene (5·0 g.) and ferrous oxalate dihydrate (6·0 g.) was heated under reflux with granulated lead (15 g.) at 215—225° for 10 min., and the mixture was worked up and chromatographed as before. *o*-Nitrocumene (2·49 g.) was eluted by light petroleum (b.p. 40—60°). 3-Methylindole (0·018 g.), m.p. and mixed m.p. 97—98°, was eluted with light petroleum (b.p. 40—60°)–benzene (1 : 2 v/v).

(*b*) *o*-Nitrocumene (5·8 g.), ferrous oxalate dihydrate (7·0 g.), dodecane (10 g.), and lead shot (25 g.) were heated for 60 min. The only identifiable product was 3-methylindole (0·041 g.).

(*c*) *o*-Nitrocumene (0·5 g.) was placed in each of three identical Pyrex tubes (12 mm. × 1 ft.) sealed at one end. To one, ferrous oxalate dihydrate (0·5 g.) and granulated lead (5 g.) were added, to the second only granulated lead (5 g.), and to the third only glass beads. The three tubes were heated simultaneously at 240—250° for 45 min. and the products were extracted with ether. The solvent was evaporated off and the residues were analysed by g.l.c. on an ethyleneglycol succinate column (20% on Gas-Chrom P; 4 ft. × $\frac{1}{4}$ in.) at 182° (helium flow rate 65 ml./min.). Two peaks (retention times 3·0 and 18·8 min.) were shown to correspond to *o*-nitrocumene and 3-methylindole, respectively (yields of skatole 0·021, 0·016, and 7·4 × 10^{-4} g., respectively).

Reaction of o-t-*Butylnitrobenzene with Ferrous Oxalate*.—(*a*) A mixture of *o*-t-butylnitrobenzene (3·0 g.) and ferrous oxalate dihydrate (3·5 g.) was heated under reflux with granulated lead at 240—250° for 30 min. The mixture was extracted with ether, the extracts were dried ($MgSO_4$), and the ether was distilled off. The residue was analysed by g.l.c. on an Apiezon L (20% on Gas-Chrom P) column (8 ft. × $\frac{3}{8}$ in.) at 210° (helium flow rate 125 ml./min.). Three peaks (retention times of 15, 18·7, and 21·8 min.) were observed; the latter two were due to *o*-t-butylaniline (0·18 g.) and *o*-t-butylnitrobenzene (2·5 g.), respectively. 3,3-Dimethylindoline[17] had a retention time of 17·5 min. under these conditions and was not detected.

(*b*) In the absence of ferrous oxalate but with lead shot only a trace of *o*-t-butylaniline could be detected by g.l.c.

Reaction of NN-*Dimethyl*-o-*nitroaniline with Ferrous Oxalate*.—The nitro-compound (4·5 g.) and ferrous oxalate dihydrate (5 g.) were heated under reflux with lead shot (15 g.) at 200—230° for 40 min. The mixture was extracted with benzene, the benzene was evaporated off, and the residue was distilled at 250°/0·1 mm. The distillate was analysed by g.l.c. on an Apiezon L (25% on 100—140 mesh Gas-Chrom P) column (8 ft. × $\frac{1}{4}$ in.) at 200°. Only three of the nine peaks recorded were large enough to permit collection in sufficient quantities for identification. These were due to *o*-amino-*NN*-dimethylaniline (0·5 g.), b.p. 213—217° (lit.,[20] 218°), unchanged *NN*-dimethyl-*o*-nitroaniline, and *N*-methylbenzimidazole (0·1 g.), m.p. and mixed m.p. 60—61° (retention times 4·7, 10·0 and 13·2 min., respectively).

Reaction of o-*Nitroanisole with Ferrous Oxalate Dihydrate*.—A mixture of chromatographically pure *o*-nitroanisole (2·9 g.) and ferrous oxalate dihydrate (3·5 g.) was boiled under reflux at 230—260° for 40 min. The mixture was worked up and analysed as described for *NN*-dimethyl-*o*-nitroaniline. Five peaks were recorded (retention times 2·2, 3·2, 4·5, 5·8, and 13·0 min.; relative areas 1·5 : 40 : 1 : 200 : 2). The peaks at 3·2, 5·8, and 13·0 min. were due to *o*-anisidine (0·17 g.), *o*-nitroanisole, and 2,2′-dimethoxyazobenzene (0·005 g.), m.p. 153° (lit.[21] 153—153·5°), respectively (retention times and i.r. spectra). More 2,2′-dimethoxyazobenzene (0·015 g.) and tars (0·23 g.) were obtained by chromatography of the residue after distillation on alumina.

The compounds corresponding to the other two peaks could not be collected in sufficient quantities to permit identification. Neither was due to benzoxazole (retention time 4·2 min.), which, when added to the reaction mixture was resolved from the peak at 4·5 min.

A product apparently identical (i.r.) with that of retention time 4·5 min. was obtained (10%) by heating *o*-anisidine (2 ml.) with ferrous oxalate dihydrate (2·5 g.) at 190°. The cooled mixture was extracted with hot benzene (50 ml.), the solid was filtered off, and the solution was evaporated. The residue was analysed by g.l.c.; it was best resolved on a column (6 ft. × $\frac{3}{16}$ in.) packed with

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Apiezon M (25%) on Chromosorb W (60—80 mesh) at 150° (helium flow rate 100 ml./min.). The product was colourless when pure but slowly turned burgundy red. Mass spectrum: *m/e* 137 (M^+, $C_8H_{11}ON$), 123, 122, 108, 95, 94, 80, and 77. N.m.r. spectrum (CCl_4): τ 7·21 (Me), 6·24 (OMe), and 3·5 (ArH) (NH_2 hidden by peak at τ 6·24).

Reaction of Nitrocyclohexane with Ferrous Oxalate Dihydrate.—A mixture of nitrocyclohexane (5·0 g.) and ferrous oxalate dihydrate (8·0 g.) was heated under reflux with granulated lead (15 g.) at 230—250° for 45 min. The mixture was worked up in the usual way and analyzed by g.l.c. on an Apiezon L (25% on Gas Chrom P) column (16 ft. × $\frac{1}{4}$ in.) at 214° (helium flow rate 41 ml./min.). Three products were detected and identified: cyclohexanone (1·5 g.; retention time 5·6 min.), unchanged nitrocyclohexane (0·43 g.; 10·9 min.), and hexahydroazepin-2-one (0·09 g.; 19·0 min.; m.p. 68—69°).

When cyclohexanone oxime (1·0 g.), ferrous oxalate dihydrate (1·8 g.), and granulated lead (10 g.) were heated at 230—240° for 1 hr. no hexahydroazepinone was formed (g.l.c.).

We thank the National Research Council of Canada for a studentship (to B. A. D.), a bursary (to R. A. B.), and other financial support. We also thank Mrs. S. S. Singer for carrying out the reaction between *o*-anisidine and ferrous oxalate.

[8/1859 *Received, December* 16*th*, 1968]