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OXIDATION WITH METAL OXIDES—II[1]

OXIDATION OF CHALCONE PHENYLHYDRAZONES, PYRAZOLINES, o-AMINOBENZYLIDINE ANILS AND o-HYDROXY BENZYLIDINE ANILS WITH MANGANESE DIOXIDE

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Abstract—Several chalcone phenylhydrazones and pyrazolines have been oxidized with manganese dioxide to give pyrazoles in good yields. Oxidation of *p*-nitrobenzylidene-*o*-aminophenol and *m*-nitrobenzylidene-*o*-aminophenol gave the corresponding benzoxazoles, whereas, substituted benzylidene-*o*-phenylenediamines gave the corresponding benzimidazoles.

IN AN earlier communication,[1] the oxidation of several aldehyde and ketone phenylhydrazones with active manganese dioxide was reported. The oxidation of benzophenone phenylhydrazone, for example, gave a mixture of benzophenone and biphenyl. Under similar conditions, benzaldehyde phenylhydrazone gave a mixture of 1,2-(bisphenylazo)1,2-diphenylethane and N^{α},N^{β}-diphenyl-$N^{\beta'}$-benzalbenzhydrazidine. When heated under reflux in benzene, however, benzaldehyde phenylhydrazone gave products like biphenyl, benzil osazone, 2,4,5-triphenyl-1,2,3-triazole and 2,3-diphenyl-1,4-dibenzaltetrazene. A free-radical mechanism has been suggested for these oxidations. In continuation of this work we have examined the oxidation of several chalcone phenylhydrazones, pyrazolines, *o*-aminobenzylidene anils and *o*-hydroxybenzylidene anils employing active manganese dioxide.

The oxidation of chalcone phenylhydrazones with lead tetraacetate has been reported to give pyrazoles.[2] In our study, we find that chalcone phenylhydrazones can be conveniently oxidized to pyrazoles in excellent yields by manganese dioxide. Benzalacetophenone phenylhydrazone (I), for example, gave a 73% yield of 1,3,5-triphenylpyrazole (III) on treatment with manganese dioxide. In addition, a small amount of biphenyl (10%) could also be isolated from this reaction. Similarly, *m*-nitrobenzalacetophenone phenylhydrazone (II) gave a 61% yield of 1,3-diphenyl-5-(*m*-nitrophenyl)pyrazole (IV) and 6·5% yield of biphenyl. A probable route for the oxidation of these phenylhydrazones is shown in Chart I. Manganese dioxide can abstract a hydrogen atom from benzalacetophenone phenylhydrazone (I), for example, to give a radical intermediate Ia which can then cyclize giving rise to a new intermediate Ib. Further oxidation of Ib can be achieved by manganese dioxide to give the pyrazole (III). Similarly, the phenylhydrazone II will be converted to the pyrazole IV, through the intermediates IIa and IIb. The formation of small amounts of biphenyl in these oxidations may be due to the combination of phenyl radicals with the solvent (benzene) and the phenyl radicals themselves are probably formed

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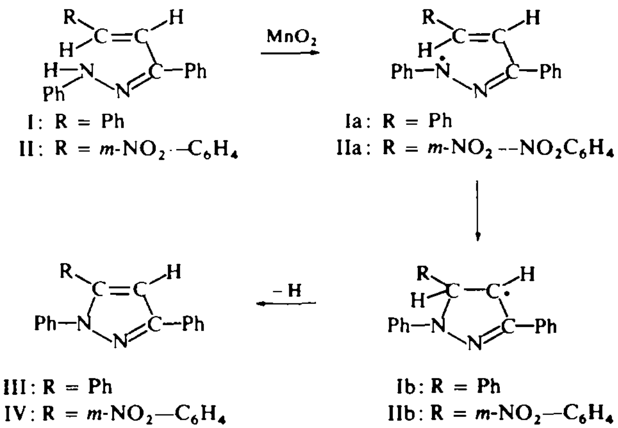
as fragmentation products of intermediates like Ia and IIa. In our earlier studies on the oxidation of aldehyde and ketone phenylhydrazones employing manganese dioxide, we have shown that such phenylation reactions do take place as evidenced by the formation of mixed biphenyls when solvents like toluene and cumene were employed.[1]

CHART I



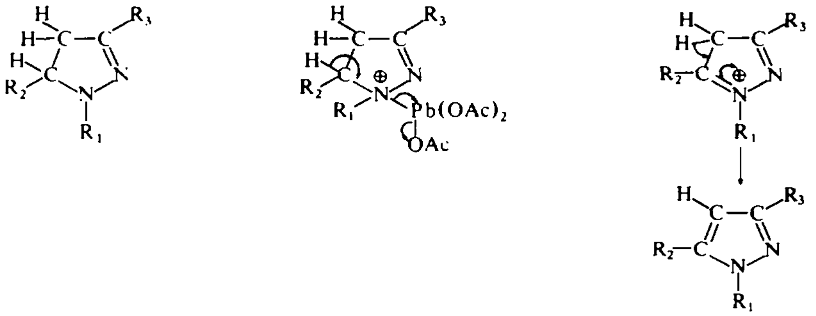
I: $R = Ph$
II: $R = m\text{-}NO_2\text{-}C_6H_4$

Ia: $R = Ph$
IIa: $R = m\text{-}NO_2\text{--}NO_2C_6H_4$

III: $R = Ph$
IV: $R = m\text{-}NO_2\text{—}C_6H_4$

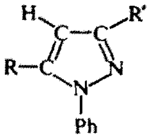
Ib: $R = Ph$
IIb: $R = m\text{-}NO_2\text{—}C_6H_4$

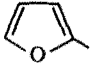
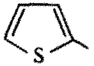
Pyrazolines have been oxidized by several reagents such as lead dioxide,[3] mercuric oxide,[3] bromine,[3,4] potassium permanganate,[4,5] chromic oxide,[3] and silver nitrate.[6] In a recent study, Gladstone and Norman,[2] have shown that pyrazolines can be oxidized to pyrazoles using lead tetraacetate. These workers have suggested an ionic mechanism for this reaction, which involves the initial attack of the tertiary nitrogen of the pyrazoline on lead tetraacetate to displace an acetate group, followed by successive loss of two protons.



During the course of the present investigation, several 1,3,5-trisubstituted pyrazolines were oxidized with active manganese dioxide. 1,3,5-Triphenyl-2-pyrazoline, for example, when treated with manganese dioxide in benzene at room temperature, gave a 93% yield of 1,3,5-triphenylpyrazole. Similarly, 1,3-diphenyl-5-(*p*-bromophenyl)pyrazoline, 1,3-diphenyl-5-furylpyrazoline, 1,3-diphenyl-5-thienylpyrazoline, 1,3-diphenyl-5-(*m*-chlorophenyl)pyrazoline, 1,5-diphenyl-3-(*p*-bromophenyl)pyrazoline, 1,5-diphenyl-3-styrylpyrazoline, 1,5-diphenyl-3-methylpyrazoline were oxidized

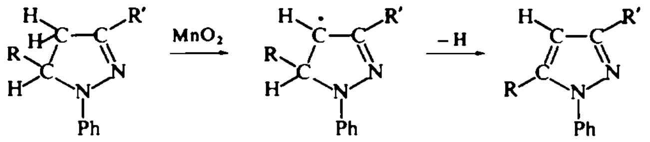
TABLE 1. IR SPECTRAL CHARACTERISTICS OF 1,3,5-TRIARYLPYRAZOLES



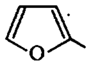
Pyrazole	R'	R	Skeletal vibrations (cm^{-1})					C—H in-plane	C—H out-of-plane	Mono-substituted benzene
III	Ph	Ph	1595 (s)	1535 (w)	1495 (vs)	1450 (vs)	1415 (m)	1350 (s)	922 (s)	770 (vvs)
IV	Ph	m-NO_2—C_6H_4	1595 (s)	1538 (w)	1498 (vs)	1450 (s)	1420 (m)	1348 (s)	915 (s)	780 (vvs)
V	Ph	p-Br—C_6H_4	1595 (s)	1538 (w)	1499 (vs)	1450 (vs)	1420 (m)	1348 (s)	920 (s)	770 (vvs)
VI	Ph		1594 (s)	1525 (w)	1491 (vs)	1450 (vs)	1415 (m)	1350 (s)	920 (s)	770 (vvs)
VII	Ph		1593 (2)	1535 (w)	1499 (vs)	1450 (vs)	1418 (m)	1351 (s)	930 (s)	765 (vvs)
VIII	p-Br—C_6H_4	Ph	1598 (s)	1538 (w)	1499 (vs)	1450 (vs)	1420 (m)	1348 (s)	920 (s)	770 (vvs)
IX	Ph	m-Cl—C_6H_4	1598 (s)	1536 (w)	1499 (vs)	1448 (vs)	1418 (m)	1350 (s)	916 (m)	770 (vvs)

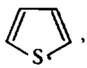
to the corresponding pyrazoles (V–XI) by manganese dioxide in yields ranging between 75–95%. Manganese dioxide is a better reagent for the oxidation of pyrazolines than either lead tetraacetate or any other reagent tried earlier. A probable path for this reaction is shown in Chart II.

CHART II



V: R = p-Br—C_6H_4, R′ = Ph

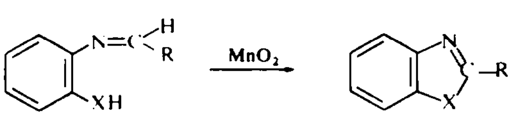
VI: R =  , R′ = Ph

VII: R =  , R′ = Ph

VIII: R = m-Cl—C_6H_4, R′ = Ph
IX: R = Ph, R′ = p-Br—C_6H_4
X: R = Ph, R′ = Ph—CH=CH—
XI: R = Ph, R′ = Me

The IR spectra of several 1,3,5-triphenylpyrazoles have been examined and the results are shown in Table 1. The bands in the region 1595, 1535, 1495 and 1415 cm^{-1} are probably due to skeletal vibrations of phenyl rings. Only one band around 1450 cm^{-1} can be unequivocally assigned to the skeletal vibrations of the heterocyclic ring; it is, however, possible that skeletal vibration of the heterocyclic ring are hidden under intense phenyl vibrations. The band around 1350 cm^{-1} is possibly due to Ar–N stretching frequency or —C—H in-plane deformation of the heterocyclic ring. Since the intensity is too high, it is not possible to confirm the assignment. The 920 cm^{-1} band characteristic of 1,3,5-triarylpyrazole could arise from the ring vibration or C—H out-of-plane deformation of pyrazoles. All the pyrazoles examined show a band at 760 cm^{-1}, characteristic of monosubstituted benzenes.

The oxidation of *o*-aminobenzylidene anils and *o*-hydroxybenzylidene anils are reported to give benzimidazoles and benzoxazoles, respectively.[7] Recently, nickel peroxide has also been used in oxidizing *o*-hydroxybenzylidene anils to benzoxazoles.[8] We have tried the oxidation of few *o*-amino- and *o*-hydroxybenzylidene anils employing manganese dioxide at room temperature. Thus, the oxidation of *p*-nitrobenzylidene-*o*-phenylenediamine and *m*-nitrobenzylidene-*o*-phenylenediamine



XII: R = p-NO_2—C_6H_4, X = NH
XIII: R = m-NO_2—C_6H_4, X = NH
XIV: R = p-NO_2—C_6H_4, X = O
XV: R = m-NO_2—C_6H_4, X = 0

gave 15% and 25% yield of *p*- and *m*-nitrophenylbenzimidazoles (XII and XIII), respectively. Under similar conditions, *p*-nitrobenzylidene-*o*-aminophenol and *m*-nitrobenzylidene-*o*-aminophenol gave 75% and 72% yields of 2-(*p*-nitrophenyl)-benzimidazole (XIV) and 2-(*m*-nitrophenyl) benzoxazole (XV), respectively.

EXPERIMENTAL

All m.ps are uncorrected and were determined in a Thomas Hoover m.p. apparatus. IR spectra were determined on a Perkin-Elmer Infracord spectrometer and UV spectra on a Cary 14-R spectrophotometer.

Starting materials. Active MnO_2 (85 g) was prepared by using $MnSO_4 \cdot 2H_2O$ (140 g) and $KMnO_4$ (160 g) as reported.[9] Chalcone phenylhydrazones, pyrazolines, *o*-aminobenzylidine anils and *o*-hydroxybenzylidene anils were prepared by standard procedures. 1,3-diphenyl-5-(*m*-chlorophenyl)pyrazoline, not been reported in the literature, was prepared in an 82% yield (4·8 g) by boiling a mixture of *m*-chlorobenzalacetophenone (4 g, 0·016 mole) and phenylhydrazine (1·7 g, 0·016 mole) in boiling AcOH (150 ml) for 15 min. The pure product after recrystallization from EtOH melted at 103°. (Found: C, 75·48; H, 5·3; N, 8·3. $C_{21}H_{17}N_2Cl$ required: C, 75·7; H, 5·1; N, 8·4%.) UV spectrum (EtOH): 200 (ε, 26,800), 230 (19,700), 298 (10,300) and 350 mμ (21,700). IR spectrum (KBr): ν_{max} 1600 (C=N), 1440 (CH_2), 1345 (Ar—N), 1130 cm^{-1} (C—N).

Oxidation of benzalacetophenone phenylhydrazone. A mixture of benzalacetophenone phenylhydrazone (2 g, 0·0006 mole) and MnO_2 (10 g) was stirred in dry benzene (150 ml) for 5 hr at room temp. Removal of the inorganic material and solvent gave a product which was recrystallized from EtOH to give 1·45 g (73%) of III, m.p. 137° (mixture m.p.). UV spectrum (EtOH): 248 mμ (ε, 30,500).

From the mother liquor 0·1 g (10%) of biphenyl, m.p. 70° (mixture m.p.) could be isolated.

Oxidation of m-*nitrobenzalacetophenone phenylhydrazone.* Treatment of *m*-nitrobenzalacetophenone phenylhydrazone (2 g, 0·006 mole) with MnO_2 (10 g) in dry benzene (150 ml) for 5 hr at room temp and work-up as in the previous case gave a product which was chromatographed on alumina. Elution with pet. ether (b.p. 60–80°) gave 0·06 g (6·5%) of biphenyl, m.p. 70° (mixture m.p.). Further elution of the alumina column with a mixture (1:1) of benzene and pet. ether (b.p. 60–80° gave a yellow solid which was recrystallized from EtOH to give 1·26 g (61%) of IV, m.p. 130°. There was no depression in the m.p. when mixed with an authentic sample of IV.[10] UV spectrum (cyclohexane): 221 (ε, 24,100) and 248 mμ (46,000).

Oxidation of pyrazolines. In a typical run, a mixture of 2 g (0·006 mole) of the pyrazoline and 10 g of active MnO_2 was stirred in dry benzene for 5 hr at room temp. The inorganic material was removed by filtration and the solvent was removed under vacuum. The products were recrystallized from suitable solvents.

1,3,5-Triphenylpyrazoline (2 g) gave 93% (1·85 g) yield of III, m.p. 137° (mixture m.p.).

Oxidation of 1,3-diphenyl-5-(*p*-bromophenyl)pyrazoline (2 g) gave 1·8 g (94%) of V, which melted at 131°, after recrystallization from EtOH. (Found: C, 67·05; H, 3·9; N, 7·57. $C_{21}H_{15}Br$ requires: C, 67·4; H, 4·02; N, 7·84%); UV spectrum (EtOH): 250 mμ (ε, 40,500).

Oxidation of 1,3-diphenyl-5-furylpyrazoline (2 g) gave 1·75 g (89%) of VI, m.p. 64°, after recrystallization from EtOH. (Found: C, 79·54; H, 5·0; N, 9·7. $C_{19}H_{14}N_2O$ requires: C, 79·7; H, 4·89; N, 9·79%); UV spectrum (EtOH): 248 mμ (ε, 28,300).

1,3-Diphenyl-5-thienylpyrazoline (2 g) gave 1·8 g (91%) of VII, m.p. 112° (lit.[11] m.p. 108°). (Found: C, 75·2; H, 4·8; N, 9·0. $C_{19}H_{14}N_2S$ requires: C, 75·6; H, 4·6; N, 9·2%); UV spectrum (EtOH): 251 mμ (ε, 36,000).

1,3-Diphenyl-5-(*m*-chlorophenyl)pyrazoline (1 g) gave 0·75 g (76%) of VIII, m.p. 91°. (Found: C, 76·0; H, 4·6; N, 8·38. $C_{21}H_{15}N_2Cl$ requires: C, 76·2; H, 4·53; N, 8·4%); UV spectrum (EtOH): 251 mμ (ε, 30,800).

Compound IX, m.p. 159° was obtained in 94% yield. (Found: C, 67·41; H, 4·3; N, 8·0. $C_{21}H_{15}N_2Br$ requires: C, 67·3; H, 4·0; N, 7·84%); UV spectrum (EtOH): 251 mμ (ε, 41,000).

Compound X m.p. 139° (mixture m.p.) was obtained in 92% yield.

Compound XI m.p. 62°, was obtained in a 75% yield. The identity of this compound was confirmed by comparison of its IR spectrum with that of an authentic sample;[12] UV spectrum (EtOH): 241 mμ (ε, 18,000).

Oxidation of p-*nitrobenzylidene*-o-*phenylenediamine.* Treatment of *p*-nitrobenzylidene-*o*-phenylenediamine (2 g, 0·008 mole) with MnO_2 (8 g) in benzene at 10° for 2 hr gave 0·29 g (15%) of XII, m.p. 329° (mixture m.p.).

Oxidation of m-*nitrobenzylidene*-o-*phenylenediamine*. A mixture of *m*-nitrobenzylidene-*o*-phenylenediamine (2 g, 0·008 mole) and MnO_2 (7 g) in benzene (150 ml) was stirred at 10° for 2 hr, yielding a product which was chromatographed on alumina. Elution with pet. ether and benzene mixture gave a 0·48 g (25%) of XIII, m.p. 208° (mixture m.p.).

Oxidation of p-*nitrobenzylidene*-o-*aminophenol*. Treatment of a mixture of *p*-nitrobenzylidene-*o*-aminophenol (2 g, 0·008 mole) in benzene (150 ml) at 10° for 2 hr gave 1·48 g (75%) of XIV, m.p. 268° (mixture m.p.).

In a repeat run, when the reaction was carried out at room temp using the same amount of materials, a 40% yield of benzoxazole was obtained.

Oxidation of m-*nitrobenzylidene*-o-*aminophenol*. *m*-Nitrobenzylidene-*o*-aminophenol (2 g, 0·008 mole) and MnO_2 (8 g) in dry benzene (150 ml) were stirred at 10° for 2 hr, yielding 1·2 g (72%) of XV, m.p. 210–211° (mixture m.p.), on recrystallization from EtOH.

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