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Nitration of Aromatic Heterocycles with Palladium(II) Acetate and Sodium Nitrite

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(Received August 9, 1982)

Synopsis. Treatments of 1,3-dimethyluracil, 1-methyl-2-pyridone, and thiophene with palladium(II) acetate and sodium nitrite gave the corresponding nitro-substituted products.

The treatment of benzene with palladium(II) salts and sodium nitrite in acetic acid was reported to give nitrobenzene.[1] We have studied the oxidation of aromatic heterocycles with palladium(II) acetate.[2] In the course of the studies, we have found that the treatments of 1,3-dimethyluracil (**1a**), 1-methyl-2-pyridone (**2a**), and thiophene (**4a**) with palladium acetate and sodium nitrite gave the corresponding nitro-substituted products in good yields.

The treatment of **1a** with palladium acetate and sodium nitrite in acetic acid at the reflux temperature gave 1,3-dimethyl-5-nitrouracil (**1b**) in a good yield. In the absence of palladium acetate, the treatment of **1a** with sodium nitrite gave only a small amount of **1b**, although it was reported that the reaction of **1a** with nitronium tetrafluoroborate gave **1b**.[3] These results are summarized in Table 1. Previously it was reported that the oxidation of **1a** with palladium acetate in acetonitrile gave a mixture of dimeric compounds.[4] However, under the present conditions no dimeric compounds were obtained. The attempted nitration of **1a** with other metal acetates and sodium nitrite were unsuccessful, as listed in Table 1.

The treatments of 1-methyl-2-pyridone (**2a**) and of thiophene (**4a**) with palladium acetate and sodium nitrite also resulted in the nitration, although it is known that the treatment of **2a** with nitric acid gives 1-methyl-3-nitro-2-pyridone, 1-methyl-5-nitro-2-pyridone (**2b**), and 3,5-dinitro-1-methyl-2-pyridone (**3b**),[5] and a similar treatment of **4a** gives 2-nitrothiophene, 2,5-dinitrothiophene, and 2,4-dinitrothiophene (**4b**).[6] When **2a** was treated with palladium acetate and sodium nitrite, **3b** was obtained in the yield of 49% together with a small amount of **2b**. The treatment of **4a** under similar conditions also gave **4b**, but no mononitrothiophenes were obtained. It was previously reported that the nitration of 3-nitrothiophene gave

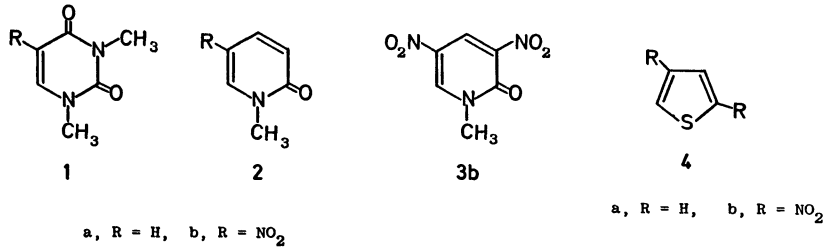

Fig. 1.

Table 1. Nitration of **1a**, **2a**, and **4a** with metal acetates and sodium nitrite[a]

Substrate	Metal acetate (mmol)	$NaNO_2$ (mmol)	Reaction time/h	Conversion / %	Products Isolated (yield/%)
1a (1 mmol)	$Pd(OAc)_2$ (1)	2	7	63	**1b** (81)[b]
1a (1 mmol)	$Pd(OAc)_2$ (1)	2	18	82	**1b** (74)[b]
1a (1 mmol)		2	7	15	**1b** (77)[b]
1a (1 mmol)	$Cu(OAc)_2$ (1)	2	7	24	**1b** (50)[b]
1a (1 mmol)	AgOAc (1)	2	7	20	**1b** (55)[b]
1a (1 mmol)	$Ni(OAc)_2 4H_2O$ (1)	2	7	17	**1b** (70)[b]
1a (1 mmol)	$Co(OAc)_2 4H_2O$ (1)	2	7	7	**1b** (trace)
1a (1 mmol)	$Mn(OAc)_2 4H_2O$ (1)	2	7	8	**1b** (trace)
2a (1 mmol)	$Pd(OAc)_2$ (1)	3	7	55	**2b** (7)[b]; **3b**(49)[b]
2a (1 mmol)		3	7	14	**2b** (10)[b]; **3b**(50)[b]
4a (2 mmol)	$Pd(OAc)_2$ (1)	3	7		**4b** (22)[c–e]
4a (20 ml)	$Pd(OAc)_2$ (1)	10	10		**4b** (66)[c,d,f]
4a (20 ml)		20	10		**4b** (trace)[d,f]

a) The reactions were carried out in acetic acid (30 ml) at the reflux temperature under nitrogen unless otherwise noted. b) Yields based on the substrate **1a** or **2a** consumed. c) Yields (mol/mol%) based on $Pd(OAc)_2$ used. d) The amount of **4a** recovered was not determined. e) The reaction was carried out at 80 °C. f) The reactions were carried out in AcOH (40 ml) at 80 °C in air.

only **4b**, while 2-nitrothiophene gave a mixture of 2,5-dinitrothiophene and **4b**,[6] suggesting that the formation of **4b** from **4a** proceeded *via* 3-nitrothiophene. The attempted nitration reactions of pyrroles such as 1-methyl-, 1-acetyl-, and 1-benzoylpyrroles, 1-acetylindole, and furan with palladium acetate and sodium nitrite in acetic acid were unsuccessful.

Experimental

*1,3-Dimethyl-5-nitrouracil (**1b**).* A solution of 1,3-dimethyluracil **1a** (1 mmol), $Pd(OAc)_2$ (1 mmol), and $NaNO_2$ (2 mmol) in acetic acid (30 ml) was heated at the reflux temperature under nitrogen for 18 h. The reaction mixture was evaporated to give a brown residue which was then chromatographed on a silica-gel plate with ethyl acetate as the developer to give **1a** (0.18 mmol), and **1b** (0.61 mmol), the latter being identical with the sample prepared by the method of Huang and Torrence.[3]

*1-Methyl-5-nitro-2-pyridone (**2b**) and 1-Methyl-3,5-dinitro-2-pyridone (**3b**).* A solution of 1-methyl-2-pyridone (**2a**) (1 mmol), $Pd(OAc)_2$ (1 mmol), and $NaNO_2$ (3 mmol) in acetic acid (30 ml) was heated at the reflux temperature under nitrogen for 7 h. The reaction mixture was evaporated and chromatographed on a silica-gel plate with ethyl acetate as the developer to give **2a** (0.45 mmol), **2b** (0.04 mmol; mp 173—174 °C, lit,[7] 173—174 °C), and **3b** (0.27 mmol) which was identical with the sample prepared by the method of Matsumura *et al.*[5] The structure of **2b** was further confirmed by comparing its ^{1}H-NMR spectrum with that of the compound reported by Mohrle and Weber.[7]

*2,4-Dinitrothiophene (**4b**).* A solution of $Pd(OAc)_2$ (1 mmol) and $NaNO_2$ (10 mmol) in a mixture of thiophene **4a** (20 ml) and acetic acid (40 ml) was heated at 80 °C in air for 10 h. The reaction mixture was evaporated and chromatographed on a silica-gel plate with benzene as the developer to give **4b** (0.66 mmol); mp 54—56 °C (lit,[6] 56 °C); IR (Nujol) 1540, 1510, 1340 cm^{-1}; NMR ($CDCl_3$) $\delta=8.43$—8.66(m); Mass: *m/e* (relative intensity) 174 (M^+, 100), 144(12), 82(49), 81(36), 70(22), 69(44).

The authors wish to thank Professor Tsunao Hase and Professor Tsutomu Sakakibara of Kagoshima University for their encouragement throughout the study.

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