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THE REARRANGEMENT OF SUBSTITUTED O-ARYL OXIMES TO 5- AND 7-SUBSTITUTED BENZOFURANS

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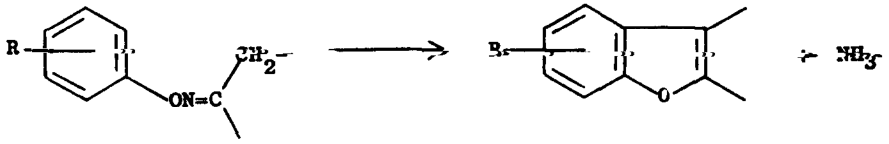
The recent appearance of Sheradsky's[1] paper dealing with the preparation of benzofurans prompts us to submit some of our own work dealing with this rearrangement reaction, which we have found has a formal analogy to the Fischer indole synthesis. In our work 0-(*o*- and *p*-substituted)aryl



oximes are converted to 5- or 7-substituted benzofurans. R is an electron-withdrawing group such as nitro in a position ortho or para to the oxygen. The presence of this group in our synthesis is necessary to permit formation of the desired intermediate oxime by the reaction of an activated aryl halide and the salt of an oxime. Other groups such as trifluoromethyl and carbalkoxy work equally well.

The production of 0-aryl oximes is carried out generally in a polar solvent such as dimethylformamide or dimethylsulfoxide. The metal salt of the oxime is best treated with an activated halide such as *p*-halonitrobenzene. Quenching the reaction mixture in water gives the 0-aryl oxime. By this method, 0-(*p*-nitrophenyl)acetone oxime (mp 104-106°) results in 80-90% yield, found for $C_9H_{10}N_2O_3$: C, 55.83; H, 5.34; N, 14.27. 0-(2,4-Dinitrophenyl)-acetone oxime (mp 89-91°) results in 61% yield, found for $C_9H_9N_3O_5$: C, 45.21;

H, 3.85; N, 17.28. O-(*o*-Nitrophenyl)acetone oxime (mp 56-59°) results in 66% yield, found for $C_9H_{10}N_2O_3$: C, 55.50; H, 5.09: N, 13.73. O-(*p*-Nitrophenyl)-2-butanone oxime (mp 41-42°) results in 60% yield, found for $C_{10}H_{12}N_2O_3$: C, 57.61; H, 5.79; N, 13.48. O-(*p*-Trifluoromethylphenyl)-acetone oxime (mp 46-49°) results in 70% yield, found for $C_{10}H_{10}F_3NO$: C, 54.91: H, 4.60: N, 6.32. O-(*p*-Nitrophenyl)cyclohexanone oxime (mp 99-101°) results in 87% yield, found for $C_{12}H_{14}N_2O_3$: C, 61.75; H, 6.17; N, 11.61.

The rearrangement of the O-oximes was done with alcoholic hydrogen chloride under reflux. The above oximes readily gave the expected 2-methyl-5-nitrobenzofuran[2] (90%); 5,7-dinitro-2-methylbenzofuran[3] (20%); 2-methyl-7-nitrobenzofuran (50%) found for $C_9H_7NO_3$: C, 60.98; H, 3.94; N, 7.79; 2,3-dimethyl-5-nitrobenzofuran (39%) found for $C_{10}H_9NO_3$: C, 62.98; H, 4.82; N, 7.30; 2-methyl-5-(trifluoromethyl)benzofuran (79%) found for $C_{10}H_7F_3O$: C, 59.76; H, 3.45; 1,2,3,4-tetrahydro-8-nitrobenzofuran (86%) found for $C_{12}H_{11}NO_3$: C, 66.30; H, 5.03: N, 6.50.

It is of interest to note that when the oxime of 2-butanone is used, as would be expected in the Fischer indole synthesis, the product is predominantly (3 to 1) 2,3-dimethyl-5-nitrobenzofuran. Pure 3-ethyl-5-nitrobenzofuran was not isolated but nmr on the crude left no doubt as to its presence. Furthermore in this cyclization it is interesting that even two nitro groups did not stop cyclization even though the yield of pure material was low (20%). Further work has shown the generality of the reaction, a further description of which will be forthcoming.

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