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AN UNUSUAL EXAMPLE OF NUCLEOPHILIC SUBSTITUTION WEAKLY ACTIVATED BY A *meta*-METHYL GROUP

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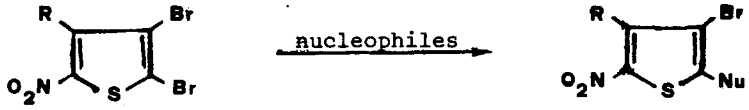
A *meta*-methyl group usually lowers nucleophilic reactivity of a leaving nitro-activated halogen atom due to its electron-repelling effect[1] (factor 2-5), or in special cases by secondary steric effects[2] (factor 1000).

We now report an example of nucleophilic substitution reactions weakly activated by a *meta*-methyl group.

2,3-Dibromo-5-nitrothiophene (I)[3] and 2,3-dibromo-4-methyl-5-nitrothiophene (II) (obtained by mercuration and bromination of 2-nitro-3-methylthiophene,m.p.72°, from light petroleum) react with piperidine and sodium benzenethiolate to give the corresponding piperidyl derivatives (III, m.p.77°, orange from methanol, λ_{max} 428 nm, logε 4.1; IV, m.p.110°, orange from ethanol, λ_{max}425 nm, logε 4.1) and sulphides (V, m.p.112°, yellow from ethanol, λ_{max}386 nm, logε 3.9; VI,m.p.99°, yellow from methanol/dioxan, λ_{max} 388 nm, logε 4.0).



III;R=H ,Nu=NC_5H_{10}
IV ;R=CH_3,Nu=NC_5H_{10}
V ;R=H ,Nu=SC_6H_5
VI ;R=CH_3,Nu=SC_6H_5

By measurement of the rate of piperidino- and benzenethiolate-debromination, we have observed that, within the explored temperature range, $k_I/k_{II} \approx 0.6 \div 0.8$ (see Table). The expected value should be at least 2 - 5,[†] which is the value previously reported by us[1f] in 5-membered heterocycles and known in many other cases in derivatives of 6-membered rings (benzene,[1b] pyridine,[1c] pyrimidine,[1d] quinoline,[1e] etc.).

This peculiar behaviour can be related to the effect by the 4-methyl group which increases the Reinheimer and Bunnett effect[5] of the 3-bromine on the activated 2-bromine.

[†] If the 3-bromine could exert a buttressing effect on the methyl group (making evident interactions between $-CH_3$ and NO_2) there would be a stronger kinetic effect present (k_I/k_{II} > 10).

TABLE
KINETIC DATA[a] AND THERMODYNAMIC PARAMETERS FOR NUCLEOPHILIC SUBSTITUTIONS IN METHANOL

Substrate	Nucleophile	k at 20.00°C (l $mol^{-1}sec^{-1}$)[b]	$\Delta H^{\neq}$ (kcal/mol)[c]	$\Delta S^{\neq}$ (u.e.)[c]
I[d]	piperidine	$0.765 \cdot 10^{-4}$	13.5	31.3
II[d]	piperidine	$1.08 \cdot 10^{-4}$	13.8	29.5
I[e]	sodium benzenethiolate	6.23	12.7	11.6
II[e]	sodium benzenethiolate	7.66	11.1	16.4

[a] The kinetics were followed spectrophotometrically as previously described.[4]

[b] The rate constants are accurate to within ± 3%.

[c] At 20°C, calculated from kinetic data in the range 20-40° and 0-20° respectively for reactions with piperidine and sodium benzenethiolate.

[d] Concentrations of reagents: substrate = $1 \cdot 10^{-3}$M; piperidine = $2 \cdot 10^{-2}$M.

[e] Concentrations of reagents: substrate = benzenethiol = $2.5 \cdot 10^{-4}$M; sodium methoxide about $1 \cdot 10^{-3}$M.

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