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# SELECTIVE NICKEL-CATALYSED HYDROGEN EXCHANGE OF PHENOL, ANILINE AND PYRIDINE DERIVATIVES

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GROUP VIII metal catalysed exchange with deuterium oxide of the $\alpha$-hydrogen atoms of pyridine[1,2] and $\alpha$-picoline[3] has been reported to be faster than that of the $\beta$- or $\gamma$- hydrogen atoms, and when aniline was heated with deuterium oxide, sodium deuteroxide, and Raney alloy, the hydrogen ortho- to the amino group exchanged faster than that meta- or para- to it[4].

We have found that nickel on kieselguhr is a substantially more selective catalyst for these exchange reactions, and its use permits the convenient preparation of pyridine and aniline derivatives deuterium-labelled $\alpha$- or ortho- to the nitrogen. Further, the pattern of selectivity is analogous with phenols, and with isoquinoline, but with quinoline not only H(2) but also H(7) and H(8) are selectively exchanged.

Typical results are given in the table. The p.m.r. spectrum shows that the exchange of aniline was limited to the ortho- and para- positions,

| Substrate | Re-action Time (hr.)* | Average Number of Deuterium Atoms per Molecule in† | Whole mole-cule | Relative Abundances of Molecules‡ with the Number of Deuterium Atoms per Molecule Shown | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| p-Cresol | 4.0 | Methyl, 2.72, 3; H(2) + H(6), 1.77, 2; H(3) + H(5), 0.01, 2 | 4.50 | - | 0.003 | 0.016 | 0.096 | 0.299 | 0.540 | 0.046 | - | | |
| 3,5-Dimethyl-phenol | 24.0 | Methyl, 5.31, 6; H(2) + H(6), 1.80, 2; H(4), 0.03, 1 | 7.14 | - | - | - | - | 0.008 | 0.047 | 0.174 | 0.370 | 0.376 | 0.026 |
| Aniline | 1.0 | H(2) + H(4) + H(6), 1.66, 3; H(3) + H(5), 0.01, 2 | 1.67 | 0.038 | 0.285 | 0.648 | 0.029 | - | - | | | | |
| p-Toluidine | 1.5 | Methyl, 2.70, 3; H(2) + H(6), 1.77, 2; H(3) + H(5), 0.09, 2 | 4.56 | - | - | 0.007 | 0.065 | 0.307 | 0.612 | 0.008 | - | | |
| Pyridine | 1.0 | H(2) + H(6), 1.88, 2; H(3) + H(5), 0.07, 2; H(4), 0.00, 1 | 1.95 | - | 0.085 | 0.872 | 0.043 | - | - | | | | |
| isoQuinoline | 1.0 | H(1), 0.91, 1; H(3), 0.88, 1; other H, 0.09, 5 | 1.88 | 0.025 | 0.174 | 0.698 | 0.104 | - | - | - | - | | |
| Quinoline | 2.0 | H(2), 0.89, 1; H(3), 0.04, 1; H(4), 0.02, 1; H(5) + H(6) + H(7), 0.69, 3; H(8), 0.89, 1 | 2.53 | 0.002 | 0.060 | 0.390 | 0.506 | 0.041 | 0.001 | - | - | | |

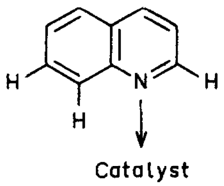
* The substrate (0.7 g), deuterium oxide (2 ml), and 20% nickel on kieselguhr (0.1 g) were agitated in an evacuated sealed tube at 99° for the time specified.

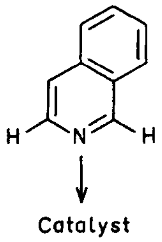
† Calculated from the peak areas due to residual protium in the p.m.r. spectrum and the average deuterium content of the whole molecule determined mass spectrometrically. Results are listed in the order: group, average number of D atoms, total number of hydrogen ($H^1$ + D) atoms in the group.

‡ Determined mass spectrometrically on samples treated, if necessary, with water to convert active deuterium to protium. Correction has been made for naturally occurring $C^{13}$.

while the cut-off after $-d_2$ in the deuterium distribution shows that exchange was largely limited to two positions, which must therefore have been the ortho- positions. Though H(5), H(6), and H(7) of quinoline are bracketed together in the table, it is clear from the p.m.r. spectrum that H(5) and H(6) are little, and H(7) extensively, exchanged. As with alkylbenzenes under similar conditions[5,6], there was extensive exchange of the benzylic hydrogen of those compounds which contained it. No exchange occurred in experiments in which the nickel on kieselguhr was replaced by kieselguhr alone.

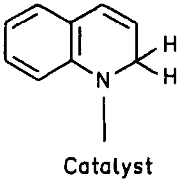
The location of the aromatic hydrogen atoms which are exchanged suggests that for all these compounds under the conditions used the mechanism is one in which the substrate is adsorbed by means of hetero atom - catalyst bonds, and the aromatic hydrogen atoms nearest the catalyst in the adsorbed species are the most readily exchanged. The same mechanism has previously been proposed[4] for the Raney-nickel catalysed exchange of aniline. The phenomenon is particularly well exemplified with quinoline and isoquinoline, for which the corresponding adsorbed species together with the selectively exchanged hydrogen atoms are shown below.



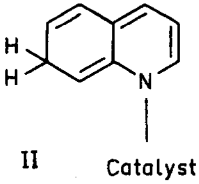


Exchange by way of structures similar to I and II is rendered unlikely by the impossibility of writing an analogous structure for the exchange of H(8) in quinoline.

I



II



Operation here of the dissociative $\pi$-complex substitution mechanism recently proposed[7] for the platinum-catalysed exchange of aromatic hydrogen is also unlikely as it predicts slower exchange of hydrogen atoms ortho to substituent groups, which is the opposite of the effects observed here with phenol and aniline derivatives.

A full and detailed account of this work will be published elsewhere.

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