Cobalt as a Catalyst for Specific Isotopic Hydrogen Labelling in Heterocyclic Compounds

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THE ability to label molecules in specific positions with either deuterium or tritium in a one-step process is useful for the study of reaction mechanisms and molecular structure. We have now used cobalt for the first time as a heterogeneous catalyst for the exchange of organic hydrogen with deuterium oxide and studied the selectivity of this catalyst in the exchange of the α-positions in heterocyclic compounds. The results should also be of significance in fundamental heterogeneous catalysis where evidence is accumulating to show that a relationship exists between the manner of bond formation on catalyst surfaces and the chemistry of inorganic co-ordination compounds

The data (Table) for the exchange reactions with D_2O and cobalt show exclusive α-specificity in pyridine, 2- and 3- picolines (methylpyridines), 2,5-lutidine (dimethylpyridine), and pyridazine. In 4-picoline and 2,4-lutidine, besides exchange in the α-position, significant isotope incorporation has also occurred in the 4-methyl group. The cut-off in the low-voltage mass spectrum of the deuterated compounds confirms this orientation obtained by n.m.r. Quinoline and isoquinoline are less reactive with deuterium; however the method is still suitable for specific α-labelling with tritium. It will also be observed that the active catalyst is prepared by sodium borohydride reduction of an

TABLE

Exchange[a] *of heterocycles with* D_2O *on cobalt*

Compound	Catalyst[b]	Atom %D[c]	Isotope orientation[d] (α)	(β)	(γ)	Methyl	Isotope distribution[e] d_0	d_1	d_2	d_3	d_4	d_5
Pyridine	$CoCl_2$	22·3	1·09	0·04	0·00		20·2	48·5	31·2	0·1		
	$NiCl_2$	20·1	0·78	0·25	0·02		32·7	39·9	22·0	4·9	0·5	
	$RuCl_3$	25·5	1·13	0·03	0·12		19·3	42·0	31·5	6·3	0·8	0·1
	$RhCl_3$	32·8	0·86	0·46	0·32		15·1	31·7	32·2	16·3	4·3	0·4
	K_2PdCl_4	35·5	0·75	0·69	0·33		14·5	32·2	35·4	20·6	6·5	0·8
	$(NH_4)_2IrCl_6$	2·7					89·4	8·5	1·8	0·2	0·1	
	H_2PtCl_6	27·4	1·06	0·17	0·14		17·8	39·8	31·7	8·9	1·6	0·2
2-Picoline	$CoCl_2$	10·6	0·79	0·01	0·00	0·05	40·1	47·0	11·7	1·1	0·1	
3-Picoline	$CoCl_2$	14·4	0·97	0·00	0·02	0·03	25·8	48·4	25·1	0·5	0·2	
4-Picoline	$CoCl_2$	17·7	1·07	0·03		0·21	21·2	42·5	29·7	5·9	0·5	0·1
2,4-Lutidine	$CoCl_2$	8·8	0·56	0·04		0·14(4)[f]	37·8	47·5	12·7	1·8	0·2	
2,5-Lutidine	$CoCl_2$	5·7	0·47	0·02	0·02	0·00	53·2	43·3	3·0	0·4	0·1	
2,6-Lutidine	$CoCl_2$	1·3					89·3	10·1	0·5	0·1		
	$PtO_2,2H_2O$	17·8		0·71	0·46	0·43(2,6)[f]	32·8	22·3	19·9	13·7	5·2	2·9
Pyridazine	$CoCl_2$	7·2	0·29	0·00			73·9	23·7	2·2	0·2		
Quinoline	$CoCl_2$	2·6					83·2	15·5	1·2	0·1		
Isoquinoline	$CoCl_2$	3·9	02·7(1)[f]	0·13(3)[f]	0·00(4,5,6,7,8)[f]		75·6	21·6	2·7	0·1		

[a] All reactions performed at 130° for 48 hr. without shaking

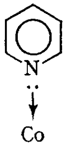
[b] Catalyst prepared by $NaBH_4$ reduction; Co_2O_3 gave 1·8 atom %D with pyridine

[c] Statistical equilibrium; pyridine and quinolines (50·0); picolines (41·7); lutidines (35·7); pyridazine (71·4).

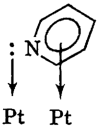
[d] Average number of deuterium atoms in positions shown (from n.m.r.)

[e] From low-voltage mass spectrometry

[f] Position of substituent (H or CH_3)



(I)



(II)

aqueous solution of cobalt chloride; Co_2O_3, even after reduction with hydrogen or borohydride, being relatively inactive.

The present technique is simple and applicable to both deuterium and tritium. Mechanistically the results are important since, with cobalt, charge-transfer adsorption of pyridine presumably involves only the nitrogen lone-pair and the molecule is initially adsorbed in a vertical position on the surface (species I) whereas in crossing the Periodic Table from nickel to platinum as catalysts for the exchange (Table) there is an increasing additional participation of the π-electrons of the ring in the adsorption process so that the molecule is now tilted (species II). Thus, with these other catalysts, the β- and γ-positions are now favourably placed for σ-bond formation on the catalyst surface and hence undergo exchange presumably by the dissociative π-complex mechanism already suggested.[1,2]

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[1] J. L. Garnett and W. A. Sollich-Baumgartner, *Adv. Catalysis*, 1966, **16**, 95.
[2] R. R. Fraser and R. N. Renaud, *J. Amer. Chem. Soc.*, 1966, **88**, 4365.