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ISOMERISATION OF DIHYDROPYRIDINES

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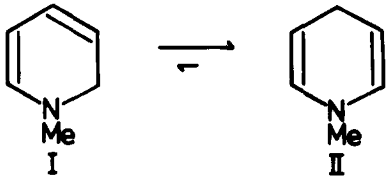
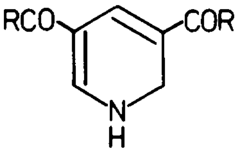
Little work has been done on the isomerisation of dihydropyridines[3]. A few scattered experiments indicate that in general 1,2-dihydropyridines are converted into 1,4-dihydropyridines, although in the case of photoisomerisation[4] the reverse takes place. After the inception of this work Fowler[5] showed that in the presence of KOBu^t/DMSO at 91.6° 1-methyl-1,2-dihydropyridine (I) and the 1,4-isomer (II) formed an equilibrium mixture containing 92.3% of (II). The recently discovered[6] isomerisation involving hydride transfer was shown to convert dimethyl 1,2,6-trimethyl-1,4-dihydropyridine-3,5-carboxylate quantitatively and irreversibly into the 1,2-isomer in the presence of the corresponding pyridinium salt in methanol; however, N-substituted dihydronicotinamides in acetonitrile produced an equilibrium mixture containing 91% of the 1,4-isomer under these conditions[7].

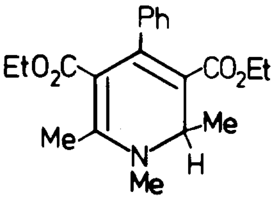
Transition metal complexes of Ru, Ir, Pt and Rh are known[8] to isomerise double bonds in carbocyclic compounds. The action of chromium hexacarbonyl on 1,3,4-trimethyl-1,2-dihydropyridine was reported[9] to afford a mixture of chromium complexes derived from the corresponding 1,2- and 1,6-dihydropyridines; the pure complexes on heating reverted to a mixture of these isomers. Surprisingly, it was claimed[9] that treatment of 1,4-dihydropyridines with $Cr(CO)_6$ yielded the chromium complexes of the corresponding 1,2-dihydropyridines.



We have investigated the action on dihydropyridines of the following transition metal complexes: $Cr(CO)_6$, $IrCl(CO)(PPh_3)_2$, $IrH(CO)PPh_3)_3$, $RhCl_3.3H_2O$, $RhCl(CO)(PPh_3)_2$, and $RhCl(PPh_3)_3$. Only the latter complex was active and converted the 1,2-dihydropyridines (III) - (VI) into their 1,4-isomers. The corresponding pyridine always accompanied the product; this is presumably due to traces of oxygen since pyridines (but not 1,4-dihydropyridines) were also formed in control experiments without the catalyst. The 1,4-isomers of (III) - (VI) were unchanged by $RhCl(PPh_3)_3$. Reactions were monitored by TLC and the products identified by UV spectroscopy; the results of typical experiments are listed in Table 1.



III; R=OMe
IV; R=Me



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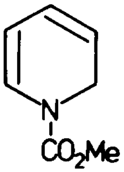

VI

TABLE 1

Isomerisation of 1,2-Dihydropyridines with $RhCl(PPh_3)_3$ [a]

Dihydropyridine (m moles)		Catalyst (m moles)	Time[b]
III[10,11]	(0.014)	0.004	6 hours
IV[11]	(0.033)	0.003	16 hours
V[12]	(0.019)	0.006	3 days
VI[13]	(0.040)	0.003	> 5 days[c]

[a] The dihydropyridine (3-8 mg) and catalyst (3-6 mg) in benzene (2 ml) were heated at 100° in a sealed ampoule under nitrogen. Two runs and a control experiment were carried out for each compound.

[b] Time for complete reaction as determined by TLC.

[c] Reaction incomplete after 5 days.

Preparative experiments were carried out for the dihydropyridines (III) and (IV), the products being isolated by thick layer or column chromatography and identified by UV and NMR spectroscopy. The results are summarised in Table 2.

TABLE 2

Preparative Isomerisations[a]

Dihydropyridine (m moles)	Catalyst (m moles)	Time	Products % 1,4-DHP	% py
III (0.25)	0.03	24 hr	64	36
(0.3)[b]	0.04	24 hr	75	25
IV (0.4)[c]	0.05	24 hr	44	34
(0.3)	0.03	36 hr	59	41
(0.3)[d]	-	36 hr	-	43

[a] In benzene (20 ml) at 100° in sealed ampoule under nitrogen.

[b] In sealed ampoule under vacuum.

[c] Some unchanged starting material recovered.

[d] Control experiment; starting material (57%) was also isolated.

These results are in line with other[3,5,7] experiments which indicate that the more stable 1,4-dihydropyridines are formed on isomerisation.

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