α-Chlorination with Carbon Tetrachloride and α-^{1}H/^{2}H Exchange with [^{2}H]Chloroform of Amidines

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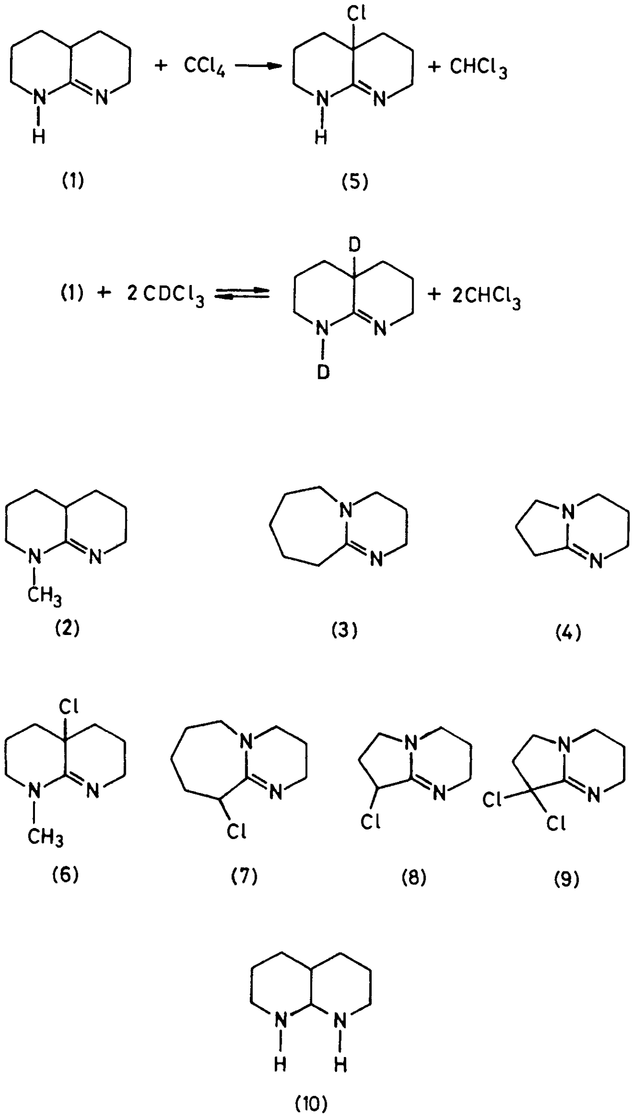
Summary The bicyclic amidines (**1**)—(**4**) have been found to be α-chlorinated with carbon tetrachloride at room temperature in darkness under nitrogen, (**1**) and (**3**) also undergo ^{1}H–^{2}H exchange in the α-position with [^{2}H]-chloroform.

The bicyclic amidine 2,10-diazabicyclo[4.4.0]dec-1-ene (1,2,3,4,4a,5,6,7-octahydro-1,8-naphthyridine) (**1**)[1] which is used in studies of multiple catalysis[2] is found to undergo reactions with carbon tetrachloride, yielding the α-chlorinated amidine 6-chloro-2,10-diazabicyclo[4.4.0]dec-1-ene (**5**) and chloroform (Scheme 1).



Scheme 1

A 0·05 M solution of (**1**) in carbon tetrachloride in a 5 mm n.m.r. tube was degassed. The tube was filled with nitrogen, sealed, and kept in the dark at room temperature for 14 days. In the ^{13}C n.m.r. spectrum, the signals from (**1**) [δ† 24·2 (CH$_2$), 29·1 (CH$_2$), 35·4 (CH), 45·0 (CH$_2$), and 161·6 (C) p.p.m.] were replaced by six new signals at δ 19·7 (CH$_2$), 38·0 (CH$_2$), 44·7 (CH$_2$), 60·7 (C), 77·0 (CHCl$_3$), and 156·7 (C) p.p.m., indicating quantitative conversion of (**1**) into the product. The signals at δ 60·7 and 156·7 were easily saturated, as would be expected for the quaternary 1- and 6-carbons in (**5**). ^{13}C N.m.r. data reported by us earlier for compound (**1**) are partially incorrect owing to ^{1}H–^{2}H exchange reported below.[1] The ^{1}H n.m.r. spectrum [δ† 2·2 (m, 8H), 3·4 (m, 4H), and 5·7 (s, br, 1H, NH)], the mass spectrum [*m/e* 172 and 174 (M^+), ratio 3 : 1], i.r. data [ν_{max}(CHCl$_3$) 1650 cm^{-1} (C=N)], and elemental analysis confirmed that the product was (**5**).

When a solution of (**1**) in carbon tetrachloride was kept in daylight at room temperature the same product was obtained and no substantial difference in reaction rate was observed.

The tertiary amidines 10-methyl-2,10-diazabicyclo[4.4.0]-dec-1-ene (**2**), DBU (1,5-diazabicyclo[5.4.0]undec-5-ene) (**3**), and DBN (1,5-diazabicyclo[4.3.0]non-5-ene) (**4**) are also α-chlorinated, yielding (**6**)—(**9**), with carbon tetrachloride at 45 °C, under N$_2$ and in darkness. DBU is monochlorinated, but DBN gives a mixture of mono- and di-α-chlorinated products (**8**) and (**9**). The introduction of the second chlorine in DBN is a slower process than the introduction of the first.

Reactions of amines with carbon tetrachloride are relatively well known, giving mainly amine hydrochlorides, imines, and chloroform as primary products. Most investigations have used light, oxygen, or metal salts, and both ionic and free-radical mechanisms have been suggested.[3] In the work on the 'uncatalysed' reaction,[4] a mechanism was proposed which proceeded through an electron transfer from the amine to carbon tetrachloride in an initially formed weak charge-transfer complex, followed by decomposition into a chloride ion and a trichloromethyl radical. The radical then abstracted an α-hydrogen within the solvent cage, yielding chloroform and an iminium salt. This then reacted further. Thermal energy is assumed to be the initiator for the electron transfer step.

A similar mechanism can be envisaged for our reactions. An initial *N*-chlorination, followed by α-hydrogen abstraction, and subsequent rearrangement of the chlorine to the α-position would form the product in either an ionic or a radical non-chain mechanism.

On the other hand, the synthetic precursor of (**1**), 2,10-diazabicyclo[4.4.0]decane (**10**), underwent no reaction detectable by ^{1}H n.m.r. spectroscopy when kept in a carbon tetrachloride solution in a sealed n.m.r. tube and exposed to daylight at room temperature for one month. The different

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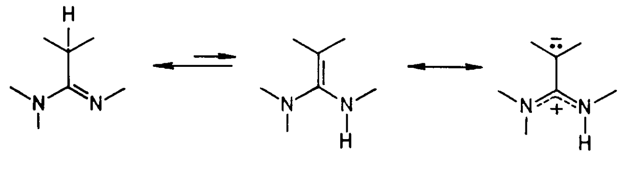
† The ^{13}C n.m.r. data are given with CCl$_4$, δ 96·0 p.p.m., as internal reference. The assignments were made in an off-resonance decoupling experiment. ^{1}H N.m.r. data are given with CHCl$_3$, δ 7·2, as internal reference.



(11)

Scheme 2

products and the relative ease with which (**1**) reacts, and the slow uncatalysed reactions between amines and carbon tetrachloride, show that the reactivity of (**1**) is unusual, and the possibility of some other mechanism.

Alternatively, the tautomeric keten aminal (**11**) could be the reactive form in the reactions (Scheme 2). However, known reactions of keten aminals, and the analogous enamines, with carbon tetrachloride result in trichloromethyl radical addition to the α-carbon,[5] in contrast to α-chlorination.

The α-chlorinations with carbon tetrachloride in the basic amidine medium make it conceivable that there is a resemblance between this reaction and the chlorinations of ketones, sulphones, nitriles, and amides studied by Meyers and others.[6] In these reactions, the α-carbanions formed in the KOH–Bu^{t}OH medium react with carbon tetrachloride in a radical anion–radical pair mechanism giving α-chlorinated products.

A fast ^{1}H–^{2}H exchange at the NH position and a slower exchange at the α-position in (**1**) was observed when a solution of (**1**) in [^{2}H]chloroform was studied by ^{1}H and ^{13}C n.m.r. spectroscopy (Scheme 1). In the ^{1}H n.m.r. spectrum, the NH signal almost completely disappeared and, in the ^{13}C n.m.r. spectrum, the signal at δ 35·4 p.p.m. corresponding to the α-carbon was replaced by a small triplet from the C^{2}H signal with almost the same shift. DBU was also deuteriated at the α-position, as indicated by the disappearance of the α-C^{1}H$_2$ multiplet at δ 2·1, and the increase in the chloroform singlet. This exchange is slower than the exchange of (**1**).

^{1}H–^{2}H exchange with [^{2}H]chloroform has been observed for NH protons in amidines because of the strong basicity of amidines.[7] The α-exchange indicates that the keten aminal form (**11**) is an intermediate in the reaction (Scheme 2).

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