Imidazoquinolinethiones from quinolines: a new molecular rearrangement

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8-Aminoquinolines and the dithiazolium salt 1 give *N*-(8-quinolinyl)iminodithiazoles 4 which undergo an unusual type of thermal rearrangement to give the new imidazo[5,4,1-*ij*]quinoline-4-thiones 6; it appears that the thione sulfur is delivered intramolecularly (9 → 10).

Whilst investigating the application in synthesis of the reagent 4,5-dichloro-1,2,3-dithiazolium chloride ('Appel salt')[1] **1** we found, amongst several useful transformations,[2] that thermolysis of the imines **2**, readily made from **1** and primary aromatic amines, gave 2-cyanobenzothiazoles **3** (Scheme 1).[3] This provides a general and attractive route to 2-cyanobenzothiazoles from substituted anilines in two simple steps.[4] Furthermore, the 2-cyano group can be removed in high yield by hydrolysis and decarboxylation with hot concentrated hydrochloric acid.

We therefore decided to apply this new route to fused thiazoles to the synthesis of a family of strongly cytotoxic thiazolopyridoacridine alkaloids, such as kuanoniamine A **7**.[5] One step in the synthesis involved heating the imino-1,2,3-dithiazole **4a**, made from 8-amino-6-methoxy-4-phenylquinoline and Appel salt **1** (Scheme 2). We expected to produce the thiazole **5a**, by analogy with the conversion of several such imines **2** into the corresponding benzothiazoles **3**. Thermolysis of neat **4a** at 200 °C was complete in less than 1 min but it did not produce the expected thiazole **5a**. Instead the burgundy red, isomeric structure **6a**† (49%) was formed in a new type of molecular rearrangement in which one of the dithiazole sulfur atoms has been transferred to the quinoline 2-position.

It first became apparent that the product was not the fused thiazole **5a** when attempted nitration [$Cu(NO_3)_2$, Ac_2O or HNO_3, AcOH] or bromination (Br_2, AcOH) was rapid and virtually quantitative at room temperature, to give the *same* product in which the one sulfur atom had been replaced by one oxygen atom. The spectroscopic data of the sulfur and the oxygen compounds were remarkably similar and apparently the sulfur had simply been replaced by oxygen with no other structural change. This suggested the possible oxidation of a thiocarbonyl compound to a carbonyl compound, which had a $\nu_{C=O}$ at 1692 cm^{-1} in accord with a 2-quinolinone structure. All spectroscopic data fitted well for **8a**† as the oxidation product; notably the characteristic ^1H NMR signal for the quinoline 2-H and its coupling, $J_{2,3}$, with the 3-H, had disappeared in both compounds. Thus in the conversion of **4a** into **6a** we had uncovered a new decomposition pathway for arylimino-1,2,3-dithiazoles in an unexpected rearrangement, and a potentially useful (if general) route to the unknown imidazo[5,4,1-*ij*]quinolin-4-ones and imidazo[5,4,1-*ij*]quinoline-4-thiones from readily available 8-aminoquinolines.

We synthesised a number of 8-aminoquinolines and converted them with Appel salt **1** into the imines **4**, bearing or not bearing a 'blocking' group (Me, Cl) in the 2 or 7 position. In all cases (**4a–d**) where the quinoline 2-position was unsubstituted, the rearrangement occurred to give the brown red imidazoquinoline-4-thiones **6** (Scheme 3),† though the yields are modest and need to be improved. Neat thermolyses at 200 °C are very fast but complex; in boiling toluene or chlorobenzene the reactions are clean, but very much slower.

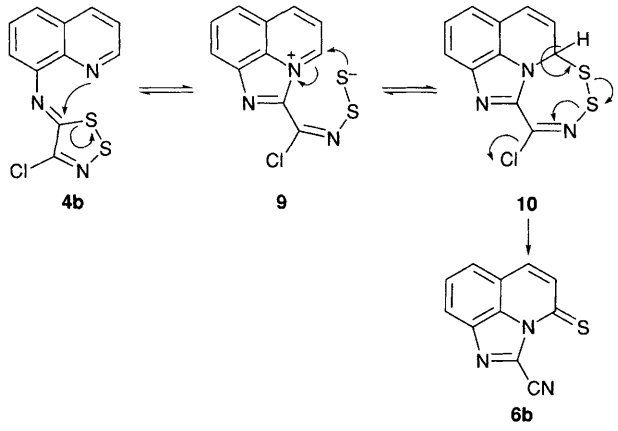
Scheme 1

Scheme 2

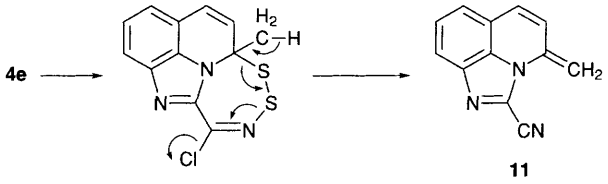
Scheme 3

	4				6
	R^2	R^4	R^6	R^7	Yield (%)
a	H	Ph	MeO	H	49
b	H	H	H	H	33
c	H	Ph	H	H	38
d	H	H	H	Me	25
e	Me	H	H	H	No thiones detected
f	Cl	H	H	H	No thiones detected

A possible mechanism is proposed, for the simplest case, in Scheme 4. Rather than the 'normal' cyclization[2–4] of the iminodithiazole ring onto the adjacent benzo position, the quinoline nitrogen has participated as a neighbouring nucleophile (see **4b**) to give the imidazoquinoline **9** which can then collapse to the tetracyclic species **10**. Elimination of HCl and loss of one sulfur atom from the 7-membered ring in **10**, possibly *via* the nitrile sulfide, would yield **6b**. Thus the 4-thione sulfur in the product is delivered intramolecularly; this is suggested since no 6-thiones were observed, even when the quinoline 2-position was blocked (**4e–f**), making the intermolecular delivery of sulfur much less likely. In agreement with this mechanism was the isolation from the methyl compound **4e** of a very minor product, tentatively assigned structure **11**, resulting from the elimination of HCl and S_2, as shown in Scheme 5.



Scheme 4



Scheme 5

This new thermal rearrangement of *N*-(8-quinolinyl)iminodithiazoles provides a route to the unknown imidazo[5,4,1-*ij*]quinoline-4-thiones and to this rare ring system.[6]

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Footnote

† All new compounds were characterized by spectroscopy and elemental analysis.

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