Synthesis and spectroscopic study of aminals derived from 8-aminoquinoline

JUANA BELLANATO

Instituto de Optica, C.S.I.C. Serrano, 121. Madrid-6. Spain

ENRIQUE GALVEZ

Department of Organic and Pharmaceutical Chemistry, School of Pharmacy, Universidad Complutense, Madrid-3, Spain

AND

ROSARIO ESCOBAR AND JOSE MANUEL CANO-PAVON

Department of Analytical Chemistry, Faculty of Chemistry, The University, Sevilla-4, Spain

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Treating 8-aminoquinoline with di-2-pyridyl ketone, pyridine-2-carboxaldehyde, or 6-methylpyridine-2-carboxaldehyde leads to the formation of the corresponding aminal instead of the expected Schiff base. The ir, 'H nmr, and mass spectra of these compounds are described and discussed.

Infrared and ¹H nmr analyses indicate that these aminals enjoy intramolecular hydrogen bonding. This effect is considered to contribute significantly to their unusual stability.

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L'amino-8 quinoléine réagit avec la di-pyridyl-2 cétone, la pyridinecarboxaldéhyde-2 ou la méthyl-6 pyridinecarboxaldéhyde-2 en donnant les composés aminés correspondants au lieu des bases de Schiff attendues. On décrit les spectres de rmn, les spectres de masse et les spectres ir de ces composés et on en discute. L'analyse des spectres ir et de rmn indique que ces composés aminés possèdent des liaisons hydrogènes intramoléculaires. On pense que cet effet contribue grandement à leur stabilité inusitée.

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Introduction

There are few data in the literature concerning formation of aminals from the reaction of primary amines with aldehydes (1-4). Lions *et al.* reported that 8-aminoquinoline (1) reacts readily with pyridine-2-carboxaldehyde (5, 6) and 6-methylpyridine-2-carboxaldehyde (7) to give the Schiff bases. However, under the working conditions described in the present paper, the corresponding aminals were obtained instead of the Schiff bases.

In a previous paper (8) we described the synthesis and some analytical properties of the compound di(2-pyridyl)-N,N-di((8-quinolyl)amino)methane (DPQAM, 2), which was obtained by reaction of 1 with di-2-pyridyl ketone. We describe here the preparation and spectroscopic features of the aminals formed by condensation of 1 with pyridine-



2-carboxaldehyde (PQAM, 3) and 6-methylpyridine-2-carboxaldehyde (6M-PQAM, 4). The structures of 2-4 are also discussed.

Experimental

Synthesis

DPQAM(2)

Compound 2 was prepared as previously described (8). POAM(3)

Pyridine-2-carboxaldehyde (0.56 g) was added to a solution of 8-aminoquinoline (1.5 g) in absolute ethanol (1.2 mL) and the mixture was warmed at 40°C for 5 min. After cooling to room temperature, ether (50 mL) was added, and the collected product (yellow needles) was recrystallized from ethanol (mp 109-112°C, yield 25%). A change in the reactant ratio did not affect the yield. Anal. calcd. for $C_{24}H_{19}N_5$: C 76.37, H 5.07, N 18.56; found: C 76.70, H 4.79, N 18.90.

6M-PQAM (4)

6-Methylpyridine-2-carboxaldehyde (0.66 g) was added to a solution of 8-aminoquinoline (1.5 g) in absolute ethanol (1.5 mL) and the mixture was heated at 60°C for 10 min and then cooled to room temperature. After addition of ether, the yellow-brownish needles were collected and recrystallized from ethanol (mp 119–121°C, yield 30%). As in the case of 2 and 3, modification of the reactant ratio did not affect the yield. *Anal.* calcd. for $C_{25}H_{21}N_5$: C 76.70, H 5.40, N 17.88; found: C 76.69, H 5.33, N 17.65.

Methods

Infrared spectra were recorded on a Perkin-Elmer 457 spectrophotometer. Indene and polystyrene were used for instrument calibration. All compounds were compressed into KBr pellets. Spectra in deuterated chloroform and carbon tetrachloride solutions at different dilutions were also recorded.

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FIG. 2. Infrared spectrum of 3 in the solid state (KBr).

¹H nmr spectra were obtained in DMSO- d_6 or deuterated chloroform at 90 MHz with a Varian EM 390 spectrometer using tetramethylsilane as internal reference.

The ¹³C nmr spectrum of **2** was recorded at 20 MHz with a Varian FT-80A spectrometer in the Fourier transform mode; the spectrum was obtained under moderate heating; DMSO- d_6 (39.6 downfield relative to tetramethylsilane) was used as reference.

The mass spectra were measured at 70 eV on an AEI Model MS-30 instrument. Spectra of solid samples were obtained by direct injection into the source at 250°C with the probe at a temperature 20°C below the melting points.

Results and discussion

Infrared spectra

The KBr-infrared spectra of compounds 2-4 are given in Figs. 1-3, and the N—H stretching frequencies determined from their solid and solution spectra, including data for 1 in Table 1.

Some infrared characteristics of 8-aminoquinoline have been discussed by Jensen and Nielsen (9).

It can be expected that in the molecule of 8-aminoquinoline one of the hydrogen atoms of the amino group takes part in intramolecular hydrogen bonding with the heterocyclic nitrogen, and consequently the two infrared bands at 3450 and 3350 cm⁻¹ in the spectrum of the solid are assigned to the "free" and bonded N—H, respectively. In CDCl₃ solution these bands shift towards 3500 and 3990 cm⁻¹ respectively. On deuteration both bands disappear and four bands are observed in the 2650–2450 cm⁻¹ region corresponding to monoand di-deuterated species. As remarked by Jensen and Nielsen, the bands at 1617 and 1598 cm⁻¹ are sensitive to deuteration which is implicative of a contribution of the δ (N—H) mode to both bands.

The infrared spectrum of 2 in KBr shows a band at 3340 cm^{-1} which is commensurate with the presence of secondary NH group ruling out a Schiff base structure for this compound. In some solid samples another band or shoulder at 3305 cm^{-1} appeared in the spectrum indicating differences in the surroundings of both N—H groups in the crystal. Characteristic bands of the 8-quinolyl group appear at 1592, 1579, 1508, 1477, 1429, 1377, 1337, 1098, 820, and 795 cm⁻¹. The bands due to the

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FIG. 3. Infrared spectrum of 4 in the solid state (KBr).

TABLE 1. Infrared frequencies (cm^{-1}) of compounds 1-4 in the NH stretching region

Medium	Infrared frequency ^e								
	1		2		3		4		
	Free	Bonded	Free	Bonded	Free	Bonded	Free	Bonded	
KBr	3450s	3350s	_	3340m 3305w		3405m 3370m		3395s	
CDCl ₃ ^a	3495w	3465sh 3390w	3495vw	3465sh 3355w	3495w	3465sh 3390m	3495vw	3465sh 3395m	
$\operatorname{CCl}_4{}^b$			3500vw	3345w	3495vw	3390w	3498vw	3390w	

°0.05 *M.* ^b<0.01 *M.* ^cAbbreviations: s, strong; m, medium; w, weak; sh, shoulder; v, very.

di-2-pyridyl group are obscured in the spectrum probably due to overlapping by the predominant quinoline bands. The band at 1616 cm⁻¹ of 8-aminoquinoline (partly δNH_2) is shifted towards 1611 cm⁻¹ and its intensity decreases. This new band is not sensitive to deuteration. The spectra in CCl₄ and CDCl₃ showed only minor changes. The v(N—H) band appears nearly at the same frequency in KBr as it does in solution (Table 1) and is consistent with the chelate structure. However, a new band at 3500 cm⁻¹ indicates the coexistence of free NH groups and a shoulder at 3385 cm⁻¹ can be attributed to the existence of other chelated species. All these bands disappear on deuteration, confirming the presence of N—H character.

In the case of 3 several crystalline forms were obtained giving slightly different spectra. Changes were observed in the N-H stretching region which revealed different types of hydrogen bonding. The spectrum given in Fig. 2 shows two v(N-H) bands at 3405 and 3370 cm⁻¹, suggesting that one NH group is single bonded whilst the other takes part in a bifurcated hydrogen bond. In this spectrum the quinoline characteristic bands are

observed at 1592, 1579, 1569, 1502, 1470, 1420, 1375, 1337, 1104, 816, 787, and 743 cm⁻¹. In very dilute CCl₄ solutions two bands at 3495 and 3390 cm⁻¹ are observed and support the existence of free NH groups as in compound 2. The CDCl₃ solution spectra are similar and also reveal the presence of chelated species. In both solvents results are best interpretated if only single bonded NH groups exist.

Contrary to the case of compound 3, only a crystalline form was obtained for 4. Its KBrspectrum (Fig. 3) shows a sharp v(N-H) band at $3395 \,\mathrm{cm}^{-1}$ and bands due to the quinoline rings at 1591, 1580, 1571, 1517, 1508, 1473, 1423, 1380, 1337, 1131, 820, 797, 791, 758, and $750 \,\mathrm{cm}^{-1}$. Results in CCl₄ and CDCl₃ are comparable to those obtained for 3 and are interpreted in the same way.

Nuclear magnetic resonance spectra

The most significant features of the 'H nmr spectra of 2–4 are listed in Table 2.

The spectrum of **3** shows a triplet at $\delta 6.30$ which converts into a singlet on deuteration. This signal is assigned to the methine proton coupled to the

TABLE 2. ¹H nmr chemical shifts and multiplicities^{a,b} for 2-4

Compound	С _α Н	NH	Me
2		9.90s	
		9.92 ^c	
3	$6.25t^{3}J \sim 5$	d	
4	6.24t, ³ J 6	d	2.6s
	6.52t, ^{c3} J 7	đ	2.5s

^aSpectra recorded at 90 MHz in CDCl₃ with internal TMS unless otherwise stated.
^bAbbreviations: s, singlet; t, triplet.
^cIn DMSO-d₆.
^dNot identified. See text.

amine protons. The existence of this coupling suggests that the amine hydrogens are bonded. Moreover, the triplet shape indicates that the amine signal appears at lower field than the signal of the methine proton and therefore must be overlapped by the heterocyclic proton signals. The data for compound 4 are similar to those found for 3 (see Table 2).

In the case of compound 2, the signal at $\delta 9.90$ which disappears on deuteration is attributed to the amine protons. The high δ -value of this signal is attributed to the strong chelated hydrogen bonds in this compound.

Finally, the proton noise-decoupled ¹³C nmr spectrum of 2 which shows a signal at δ 73.95 corresponding to a tetrahedral carbon unequivocally proves the aminal structure for compound 2.

Mass spectra

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The mean features of the mass spectrum of 2 are: a very weak M⁺ peak at m/e 454, an intense peak at m/e 144, and a weak peak at m/e 310 which are originated from M⁺ through a C—N cleavage with a simultaneous hydrogen rearrangement. The loss of a pyridinium radical ion (m/e 78) from the ion m/e 310 explains the base peak at m/e 232. Moreover, a metastable peak at m/e 173.3 confirms the transition $310\rightarrow 232$. This fragmentation is in agreement with literature data (10). The peak at m/e 144 is attributed to an aminoquinolinium radical ion which originates the peaks at m/e 117, 116, 90, 89, 63, and 39 in accordance with the literature (11). The above data suggest the fragmentation pattern depicted by Scheme 1.

The mass spectra of compounds 3 and 4 presented similar features to those of compound 2. In addition, an intense peak at m/e 129 and less abundant peaks at m/e 102, 76, 75, 51, and 50 were also observed. The ion of m/e 129 is due to quinolinium ion-radical $C_9H_7N^+$ which is originated from the molecular ion and/or from the amine ion through a cleavage with hydrogen rearrangement (see Scheme 1). Furthermore, in the mass spectra of 3 and 4 weak peaks at m/e 249 and 263 were respectively observed and are attributed to $(M - C_9H_6N)$.

Summarizing, the obtained results show that from the reaction of 8-aminoquinoline with pyridine-2-carboxaldehyde, 6-methyl-pyridine-2-carboxaldehyde, and di-2-pyridyl ketone aminals are obtained. The stability of these aminals is due to the occurrence of intramolecular hydrogen bonding which is also present even in polar solvents as was deduced from spectroscopic data. In this context it may be noted that when l-naphtylamine reacts with benzaldehyde the Schiff base is formed very easily (8).

The mechanism proposed for the formation of



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the aminals studied is given in Scheme 2 for compound 2. The immonium cation 6 is stabilized by intramolecular hydrogen bonding; thus the nucleophilic addition of a second molecule of 8aminoquinoline to 6 leads to 7 and finally to the aminal 2 by the loss of a proton.

The aminals 2-4 are good analytical reagents for transition metals, specially Fe(II), originating stable chelates (8). They can also be applied for the indirect determination of voluminous anions such as perchlorate, iodide, and others which form ionic pairs with the chelates allowing the extraction of these chelates.

Throughout the present work the complexes of the reagents with Fe(II), Ni(II), Co(II), and Cu(I) in the form of perchlorates or iodides have been isolated. The study of the relation between spectroscopic properties and structures of these complexes will be the subject of a future paper.

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