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THE STRUCTURE DETERMINATION OF LEUCOANTHRAQUINONES BY PROTON AND CARBON-13 NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

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SUMMARY

Leucoquinizarin reacts with amines to give mono- and diaminoanthraquinones. Since contamination by diaminoanthraquinones greatly influences the quality of monoaminoanthraquinones as dyestuffs (and vice versa), it is important to elucidate the structure of leucoanthraquinones in connection with the reactivity and selectivity of the reaction with amines. The structure of the leuco compound of 1,4-bis(butylamino)anthraquinone was assigned to be 1,4-dibutylamino-2,3-dihydroanthracene-9,10-dione by p.m.r. However, the structure of the leuco compounds of 1,4-dihydroxyanthraquinone(quinizarin) and 1-butylamino-4-hydroxyanthraquinone could not be determined definitely by p.m.r. alone. An examination of ^{13}C-n.m.r. spectra of anthraquinones and leucoanthraquinones afforded convincing data. The structures of the leuco compounds of quinizarin and 1-butylamino-4-hydroxyanthraquinone were concluded to be 9,10-dihydroxy-2,3-dihydroanthracene-1,4-dione and 1-butylamino-10-hydroxy-2,3-dihydroanthracene-4,9-dione respectively. The reactive species of leuco-quinizarin are discussed on the basis of the results.

1. INTRODUCTION

Leucoquinizarin (**7**) reacts with amines much more rapidly than the parent quinizarin (**3**) to give two products, monoamino and diaminoanthraquinone derivatives. The proportion of these amination products changes with the reaction conditions. Since contamination of diaminoanthraquinones tends to dull the colour of monoaminoanthraquinones (and vice versa), the selectivity of

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the reaction will largely influence the quality of the dyestuff. The structures of leucoquinizarin and its amino-substituted derivatives are important in connection with selective amination, and have concerned several authors.[1–6] However, no method sufficient to demonstrate decisively their structures has been described. In this paper the structures of 1,4-disubstituted anthraquinones and their leuco compounds, as suggested by p.m.r. and ^{13}C-n.m.r. spectroscopy are reported.

2. RESULTS AND DISCUSSION

Proton magnetic resonance data of 1,4-disubstituted anthraquinones and their leuco compounds are compared in Table 1. 1,4-Disubstituted anthraquinones (**1–4**), (summarised in Table 1) were shown to possess aromatic protons(4H) of A_2B_2 type, and other aromatic proton signals (2H) of A_2 or AB type at their 2 and 3 positions. Resonance lines of amino and hydroxyl protons were observed at lower field.

Leuco-1,4-dimethoxyanthraquinone (**8**) was shown to possess hydroxyl protons(2H) in singlet and aromatic protons of both A_2B_2 and A_2 type similar to **4**. Consequently the structure of **8** can be definitely assigned to 1,4-dimethoxy-9,10-dihydroxyanthracene.

On the other hand, leuco-1,4-bis(butylamino)anthraquinone (**5**) lacks the singlet aromatic protons of A_2 type observed in 1,4-bis(butylamino)-anthraquinone (**1**) at its 2 and 3 positions but has a new sharp methylene proton signal(4H) in singlet at 2·70 ppm, and it has aromatic proton signals in a symmetrical A_2B_2 pattern at 7·58(2H) and 8·42(2H) ppm and a broad signal of amino protons(2H) at 14·32 ppm. Protons of the butyl amino group appeared

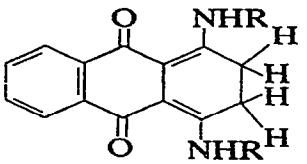
TABLE 1

CHEMICAL SHIFTS IN PMR SPECTRA OF ANTHRAQUINONES AND THEIR LEUCO COMPOUNDS ($CDCl_3$)

Anthraquinones		*Aromatic C-5,8*[a]	*Aromatic C-6,7*[a]	*Methylene*	*Amino*	*Hydroxyl*
1,4-bis(butylamino)	**1**	8·16	7·50	—	10·73	—
1-butylamino-4-hydroxy	**2**	8·16	7·63	—	10·18	13·60
1,4-dihydroxy	**3**	8·26	7·76	—	—	12·85
1,4-dimethoxy[b]	**4**	8·07	7·61	—	—	—
leuco compound of **1**,	**5**	8·42	7·58	2·70(s)	14·32	—
leuco compound of **2**,	**6**	8·36	7·62	2·88(t)	14·90	13·95
leuco compound of **3**,	**7**	8·42	7·77	3·05(s)	—	13·50
leuco compound of **4**[c]	**8**	8·30	7·40	—	—	9·78

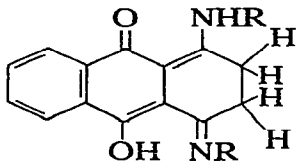
[a] The signals of the aromatic ring protons indicated A_2B_2 type patterns except the leuco compound (**6**).
[b] The methoxy protons at 3·90 ppm.
[c] The methoxy protons at 3·93 ppm.
(s) singlet
(t) triplet

at 1·00(3H), 1·55(4H), and 3·35(2H) ppm. These p.m.r. data indicated that the ring substituted by butylamino groups was not aromatic, but the other ring was a symmetrically substituted benzene ring. Therefore the most probable structure of **5** can be assigned to **5a** ($R = C_4H_9$), and other forms (**5b–5d**) should be excluded.

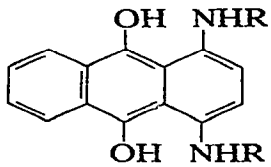


5a

5b

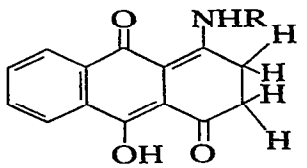


5c

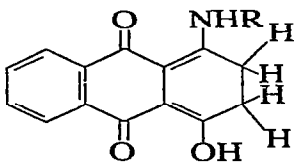


5d

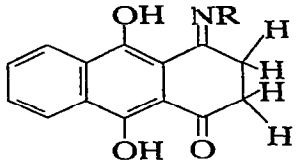
The possible structures of leuco-1-butylamino-4-hydroxy-anthraquinone (**6**; $R = C_4H_9$) are the following,



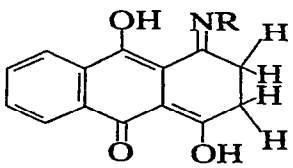
6a



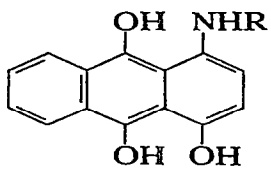
6b



6c



6d



6e

The p.m.r. spectrum of **6** shows methylene protons(4H) as triplet at 2·88 ppm, one hydroxyl proton(1H) as a sharp singlet at 13·95 ppm and one amino proton(1H) as a broad signal at 14·90 ppm. This result permits the assignment of **6** to **6a** or **6b**. As shown in Fig. 1, aromatic protons(4H) appeared in a more

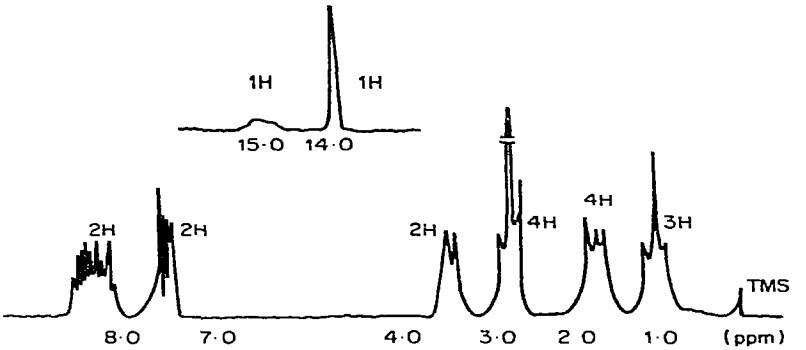
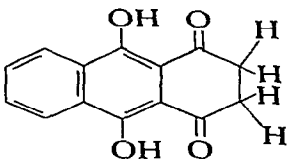


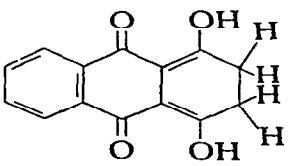
Fig. 1. The p.m.r. spectrum of leuco-1-butylamino-4-hydroxyanthraquinone(**6**).

spread out multiplet, as distinct from the other leucoanthraquinone derivatives (**5**, **7**, and **8**), all of which showed the presence of aromatic protons in a symmetrical A_2B_2 type. This p.m.r. spectrum seems to demand an unsymmetrical 4,9-diketo form for **6**, such as **6a**. The presence of an amino group may exclude the possibility of **6d**.

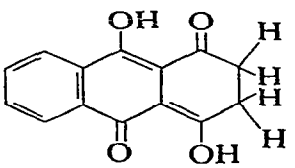
With respect to leucoquinizarin (**7**), the four possible structures (**7a–7d**) can be written.



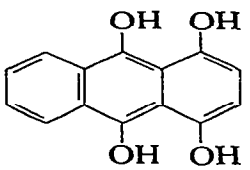
7a



7b



7c



7d

The presence of a symmetrical aromatic ring and methylene and hydroxyl protons may suggest the possibilities of the structures **7a** or **7b**. The chemical shift of methylene protons will be moved downfield by the presence of an adjacent carbonyl group. A comparison of the chemical shift of methylene protons of **7** with those of leuconaphthazarin and leuconaphthoquinone seems to show that this is indeed the case. Bloom and his co-workers have proposed

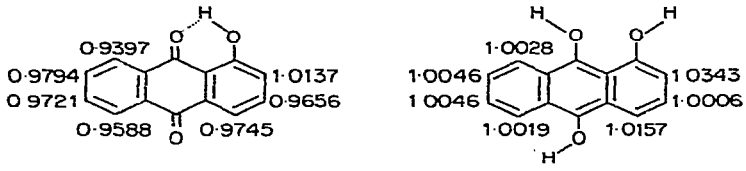


Fig. 2. The calculated π-electron densities.

the structure of **7** in solution to be **7a** by comparing the chemical shift of methylene protons with those of leuconaphthazarin (3·05 ppm) and leuconaphthoquinone (3·08 ppm).[7] Egerton and his co-workers[8] and Greenhalgh[9] have claimed that the consideration of u.v. spectra and reactivity of **7** could not exclude the possibility of an equilibrium mixture of **7a** and **7b**. Ultraviolet spectra and reactivity, however, cannot give clear evidence of the structure of **7** and n.m.r. observations may be the best approach to the elucidation of its structure. A p.m.r. index of the active methylene and methyl is the coupling constant between ^{13}C and proton, $J_{^{13}C-H}$, which is determined from their satellite bands, and depends on their hybridization stage. However, the satellite bands of the methylene signal could not be observed due to low solubility in the solvent and an overlap with the signal of the butylamino group. The chemical shift of the aromatic protons will depend on the type of the ring, since the π-electron densities of the ring vary with its substituents. In Fig. 2 the π-electron densities, calculated by the PPP method, of 1-hydroxyanthraquinone and 1,9,10-trihydroxyanthracene are shown.

The differences in the chemical shifts of the α and β protons between anthraquinones and their leuco compounds may therefore be expected to give some evidence towards elucidation of the structure of the leuco compounds. However, contrary to expectation, any regularity in the differences in the chemical shifts of α and β protons could not be found. The considerations mentioned above seem to show that the alternative of **6a** or **6b** for leuco-1-butylamino-4-hydroxyanthraquinone and of **7a** or **7b** for leucoquinizarin cannot be determined unequivocally by the use of p.m.r. alone.

An examination of ^{13}C-n.m.r. spectra of the anthraquinone derivatives (**1–4**) and their leuco compounds (**5–8**) was expected to afford definitive data enough to elucidate the structures of **6** and **7**. The chemical shift data are shown in Table 2. The resonance peaks of carbonyl carbons (C-9, 10) of anthraquinones were characteristically observed at about 180 ppm.[10] Signals of 1,4-naphthoquinone and 1,4-benzoquinone carbonyl carbons appear also at about 185 ppm.[11] On the other hand, the chemical shifts of carbonyl carbons adjacent to a methylene or methyl carbon are at about 200 ppm; *o*-hydroxyacetophenone, 200·4 ppm; *o*-methoxyacetophenone, 200·1 ppm;[12] and acetylacetone, 201·9 ppm.[11]

TABLE 2

CHEMICAL SHIFTS IN C-13 NMR SPECTRA OF ANTHRAQUINONES AND THEIR LEUCO COMPOUNDS. ($CDCl_3$)

Compound	*C*-1	*C*-2	*C*-3	*C*-4	*C*-5	*C*-6	*C*-7	*C*-8	*C*-9	*C*-10	*C*-11	*C*-12	*C*-13	*C*-14
1	146·1	123·3	123·3	146·1	125·9	131·7	131·7	125·9	182·0	182·0	109·6	109·6	134·6	134·6
2	147·3	123·6[a]	128·4	156·4	126·4[a]	133·8	132·1	126·0	181·3	186·9	107·9	113·4	132·3	135·1
3	157·8	129·3	129·3	157·8	127·0	134·4	134·4	127·0	186·8	186·8	126·8	126·8	133·4	133·4
4	153·9	126·1	126·1	153·9	120·1	133·1	133·1	120·1	183·0	183·0	122·6	122·6	134·0	134·0
5	162·1	22·9	22·9	162·1	125·7	129·9	129·9	125·7	172·2	172·2	102·2	102·2	135·7	135·7
6	165·1	23·8	34·5	199·9	124·4	130·1	129·6	125·7	153·0	172·2	107·3	101·8	129·9	135·2
7	200·8	35·7	35·7	200·8	124·4	130·4	130·4	124·4	154·9	154·9	107·3	107·3	129·1	129·1

The butyl group was observed as follows: (**1**) 13·9, 20·4, 31·8, 42·6; (**2**) 13·9, 20·3, 31·4, 42·5; (**5**) 13·9, 20·3, 31·9, 43·2; (**6**) 13·6, 20·1, 31·6, 43·6.

The spectrum of leuco-1,4-dimethoxyanthraquinone could not be obtained due to its rapid oxidation under measurement.

[a] These assignments were tentative, the reverse was also possible.

The chemical shift of the carbonyl carbon of **7** was 200·8 ppm and assigned the 1,4-diketo form **7a** for **7**. In the case of leuco-1-butylamino-4-hydroxyanthraquinone (**6**), the chemical shifts of carbonyl carbons were 199·9 and 177·2 ppm. The former value indicates a carbonyl carbon adjacent to the methylene carbon. The latter value corresponds to the chemical shift of the carbonyl carbon of leuco-1,4-bis(butylamino)anthraquinone (**5**). Furthermore, the methylene carbons of **6** showed signals at 34·5 and 23·8 ppm. These values resemble those from **7** and **5**, respectively and the results permit a conclusion that **6** exists exclusively as an unsymmetrical 4,9-diketo form (**6a**) in solution. All the n.m.r. data from **7** indicated that it existed predominantly in the form **7a** in the solution, as suggested by Bloom.[7] The kinetic study of the reaction between leucoquinizarin (**7**) and butylamine revealed that both the energy of activation and the pre-exponential term for this reaction were extraordinarily small.[a] This fact can be interpreted by supposing that the most active species among the tautomeric isomers (**7a–7d**) for the amination reaction was **7a**, and the low energy and entropy of activation were characteristic of the reaction, or that the tautomeric isomer in a small amount in solution, such as the unsymmetric 1,10-diketo form (**7c**), was the most active species. Leuco compound (**6**) in an unsymmetric 4,9-diketo form (**6a**) was found to be much less reactive to amines than leucoquinizarin (**7**). This excludes the possibility that the 1,10-diketo form can play an important role as an active species, even if present in solution.

3. EXPERIMENTAL

Quinizarin from Sumitomo Chemical Ltd was purified by column chromatography on silica gel (using benzene as the developing solvent), followed by recrystallisation from ethanol. m.p. 200·4–201·4°C (corrected). (Found: C, 70·24; H, 3·20. $C_{14}H_8O_4$ requires C, 70·00; H, 3·36.)

The 1-butylamino-4-hydroxyanthraquinone was prepared by the reaction of leucoquinizarin with butylamine in ethanol and purified by column chromatography on silica gel (benzene), followed by recrystallisation from hexane. m.p. 127·1–127·6°C (corrected). (Found: C, 73·17; H, 5·95; N, 4·87. $C_{18}H_{17}O_3N$ requires C, 73·20; H, 5·80; N, 4·74.) The 1,4-bis(butylamino)anthraquinone was prepared and purified similarly to the case of 1-butylamino-4-hydroxyanthraquinone, followed by recrystallisation from hexane. m.p. 121·2–121·5°C (corrected) (Found: C, 75·42; H, 7·55; N, 8·11. $C_{22}H_{26}O_2N_2$ requires C, 75·40; H, 7·48; N, 8·00.)

The 1,4-dimethoxyanthraquinone was prepared by the reaction of quinizarin with methyl iodide in DMF–KOH system and purified by recrystallisation from

[a] Unpublished data: $\Delta E = 6{\cdot}6$ cal mol^{-1}, $A = 1{\cdot}30 \times 10^4$ litre mol^{-1} min^{-1}, determined in ethanol.

ethanol. m.p. 177·4–178·9°C (corrected). (Found: C, 71·41; H, 4·40. $C_{16}H_{12}O_4$ requires C, 71·64; H, 4·51.)

Leucoquinizarin was prepared as has been reported by Banshou[3] and recrystallised from ethanol under nitrogen atmosphere to give orange needles, m.p. 157·2–157·5°C (ref. 3: 154·7–155·2°C). (Found: C, 69·75; H, 4·06. $C_{14}H_{10}O_4$ requires C, 69·42; H, 4·16.) Thin-layer chromatography of leucoquinizarin on silica gel plate showed only one spot with a characteristic blue fluorescence ascribed to leucoquinizarin.

Leuco-1-butylamino-4-hydroxyanthraquinone was prepared by the reduction of 1-butylamino-4-hydroxyanthraquinone by the use of sodium carbonate and sodium dithionite in water. The mixture was stirred for 6 h at 80°C under nitrogen atmosphere. The brown precipitate was filtered, washed with degassed water, and recrystallised from ethanol. All procedures were carried out under nitrogen atmosphere. m.p. 150·0–150·4°C (corrected). (Found: C, 72·25; H, 6·40; N, 4·86. $C_{18}H_{19}O_3N$ requires C, 72·71; H, 6·44; N, 4·71.) Thin-layer chromatography of this compound on silica gel plate showed only one spot with yellowish green fluorescence. It was confirmed to be identical with the compound obtained by the reaction of leucoquinizarin with butylamine by comparison of both t.l.c. and visible spectra.

Leuco-1,4-bis(butylamino)anthraquinone was prepared by the reaction with an excess of butylamine in ethanol. The crude compound was recrystallised several times from ethanol to give pure leuco-1,4-bis(butylamino)-anthraquinone, dark brown in colour. All stages were carried out under nitrogen.) m.p. 168·6–169·6°C (corrected). (Found: C, 75·07; H, 8·01; N, 7·80. $C_{22}H_{28}O_2N_2$ requires C, 74·97; H, 8·01; N, 7·95.) This compound was oxidised in solution to give blue 1,4-bis(butylamino)anthraquinone.

Leuco-1,4-dimethoxyanthraquinone was prepared by the reduction of 1,4-dimethoxyanthraquinone by sodium carbonate and sodium dithionite in water and treated similarly to the case of leuco-1-butylamino-4-hydroxyanthraquinone. m.p. 172·5–173·5°C (corrected). (Found: C, 70·75; H, 4·97. $C_{16}H_{14}O_4$ requires C, 71·10; H, 5·22.) This compound in solution was also oxidised to yellow 1,4-dimethoxyanthraquinone.

3.1. *N.m.r. measurements*

The p.m.r. spectra were recorded in $CDCl_3$ solution at 35°C with a Hitachi R-24 spectrometer using tetramethylsilane as an internal standard. The structure of leucoquinizarin was also observed to be 1,4-diketo form (**7a**) in $CDCl_3$–C_2D_5OD (1 : 1) solution.

The ^{13}C-n.m.r. spectra were recorded in $CDCl_3$ solution containing tetramethylsilane as an internal standard with a JEOL FX-60 spectrometer. Leuco-compounds were measured under nitrogen atmosphere.

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