

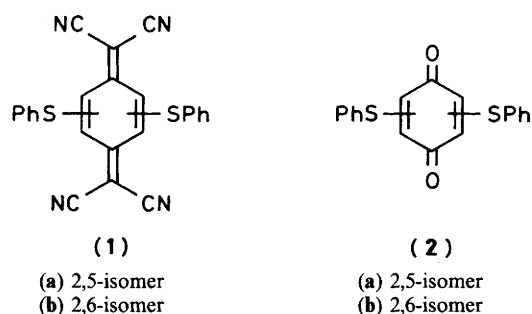
On the Inapplicability of the Lehnert Reagent for 1,2-Dicyanomethylation of 2,5- and 2,6-Diphenylthiobenzoquinones: Synthesis and Structure of Isomeric 2-Amino-5-hydroxy-4,6- and 2-Amino-5-hydroxy-4,7-diphenylthiobenzo[*b*]furan-3-carbonitriles

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The Lehnert reagent (TiCl_4 -pyridine) has been shown not to activate the carbonyl groups of dithiophenyl-substituted benzoquinone isomers in nucleophilic attack by dicyanomalonate. Instead, 1,4-addition to the quinone ring results in the title benzofuran derivatives. The reaction mechanism is shown to be unlike those where carbon atoms are attached to the quinone ring or when the sulphur atom is part of an aromatic system. The crystal data of 2-amino-5-hydroxy-4,6-diphenylthiobenzo[*b*]furan-3-carbonitrile are: triclinic, $P1$, $a = 10.092(6)$, $b = 10.828(7)$, $c = 9.976(6)$ Å, $\alpha = 73.35(5)$, $\beta = 100.13(4)$, $\gamma = 116.13(4)^\circ$, $V = 936.2(9)$ Å³, $Z = 2$. The proposed reaction mechanism and the crystal structure of the title compound are presented and discussed.

In the last few years it has been established that 1,4-quinones can be efficiently transformed into the appropriate tetracyanoquinodimethane (TCNQ) derivatives through dicyanomethylation using the Lehnert reagent (TiCl_4 -pyridine).¹ The synthetic usefulness of this method was proved by the facile preparation of tetracyanoanthraquinodimethane,² tetramethyl-TCNQ,³ and other TCNQ derivatives.⁴ It is assumed that TiCl_4 promotes the nucleophilic addition specifically to the carbonyl carbones and inhibits 1,4-additions.

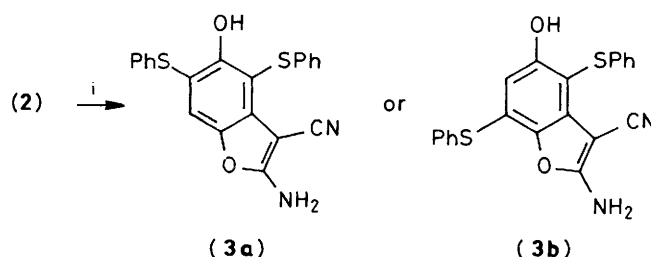
In the course of our work on D_2A -type molecules⁵ (two donors attached chemically to one acceptor), we were interested in the preparation of the bis(phenylthio)-TCNQ derivatives (1). A tempting route involved, naturally, the direct condensation of the appropriately substituted *p*-benzoquinones (2) with malononitrile, using the Lehnert reagent.



Surprisingly, we discovered that this method is apparently not applicable to the phenylthio-substituted benzoquinones. Thus, the reaction of either 2,5-diphenylthio-1,4-benzoquinone (2a) or 2,6-diphenylthio-1,4-benzoquinone (2b) with malononitrile in the presence of Lehnert reagent proceeded by 1,4-addition followed by cyclization to yield the 2-amino-5-hydroxy-4,6-bis(phenylthio)benzo[*b*]furan-3-carbonitriles (3a) and (3b) (Scheme 1).

A possible mechanism is presented in Scheme 2.

Similar benzofuran derivatives are sometimes obtained when unsubstituted (and certain substituted) 1,4-benzoquinones react with malononitrile in the presence of simple bases.^{6,7} It is generally accepted that TiCl_4 activates 1,2-additions to quin-

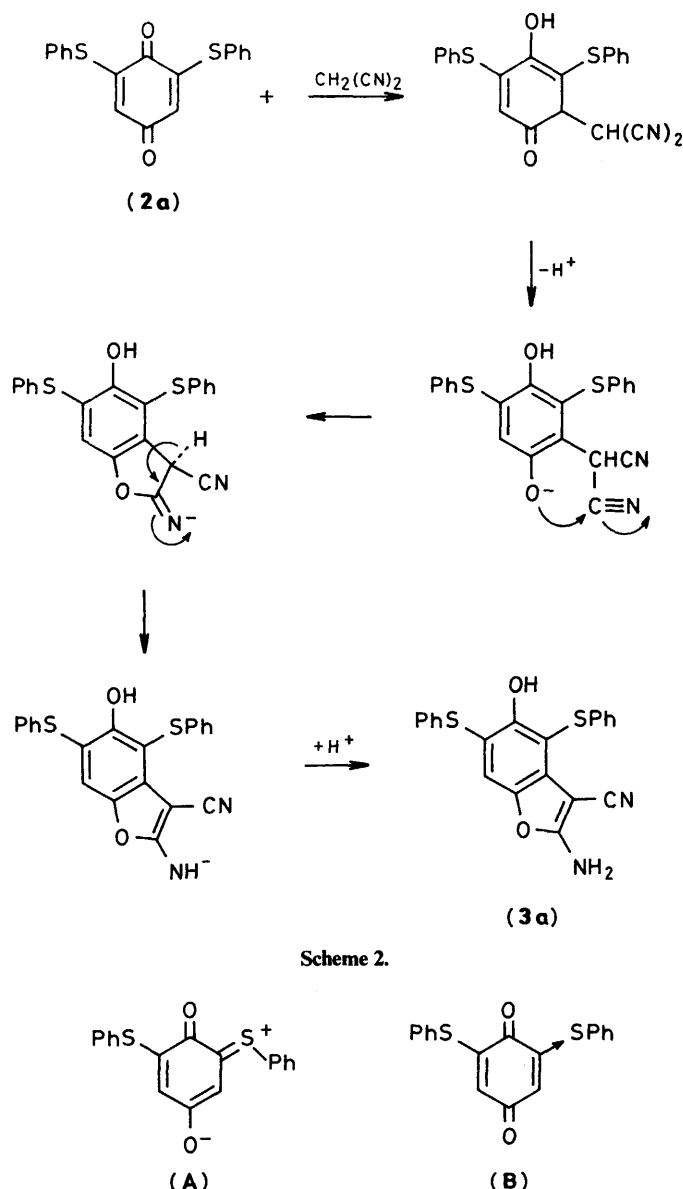


Scheme 1. Reagents: i, $\text{CH}_2(\text{CN})_2$, TiCl_4/py .

ones by complexation with the quinonic oxygens; this prevails over the usual 1,4-addition to α,β -unsaturated systems.

The exclusive 1,4-addition reaction (rather than the expected 1,2-addition) could be rationalized by at least two factors. The two bulky phenylthio groups may exert steric hindrance which inhibits a nucleophilic attack on the adjacent carbonyl group. Furthermore, such an attack on the second carbonyl group is disfavoured due to resonance effects, as represented by form (A). The favoured nucleophilic attack on the β -carbon atoms (the non-substituted carbons) may stem from an inductive effect exerted by the phenylthio group, as represented by form (B). These effects do not seem to be valid when the sulphur atoms are part of an aromatic system. For example, dithiophenobenzoquinone does react in the normal mode with the Lehnert reagent yielding the corresponding TCNQ.⁸ It is noteworthy that the failure of the Lehnert reagent to condense directly with the carbonylic groups of the thio-substituted benzoquinones (2a) and (2b), or to facilitate a nucleophilic attack on the β -carbon atoms, may indicate that it does not play any role in the reaction mechanism.

The spectral data (^1H and ^{13}C n.m.r., i.r., and m.s.), summarized in Tables 1 and 2, strongly support structures (3) as the best representation of these compounds. The i.r. solid state spectrum is unusual as it shows five N-H stretching bands in the region 3450–3185 cm^{-1} . These five bands appear when spectra are recorded in the solid (KBr or Nujol mull), while in solution (CHCl_3) only the usual two (symmetric and asymmetric) N-H stretching bonds are observed. A different chemical environment for the two amino-hydrogen atoms in the crystal could be responsible for this non-equivalence (see



below). This difference in behaviour of the N-H frequencies will be discussed in the molecular structure section. A strong cyano-absorption also appears at 2212 cm^{-1} for both isomers. ^1H N.m.r. spectroscopy reflects a profound difference between (3a) and (3b). Thus, the lone aromatic hydrogen atom of the benzofuran system in (3a) shows a chemical shift of δ 7.22, while the corresponding hydrogen atom in (3b) appears at much higher field (δ 6.48). Also, the hydroxylic hydrogen of (3a) shows a sharp signal at δ 7.11 and in (3b) it appears at δ 6.63. ^{13}C N.m.r. spectroscopy, as described in Table 2, is found to be in good agreement with structure (3). The exact assignment of the carbon atoms was based on comparison with other closely related systems, as well as pertinent literature.⁹

Molecular and Crystal Structures of (3a).—The atomic numbering of (3a) is shown in Figure 1 and the crystallographic structure in Figure 2. Positional parameters, bond lengths, and bond angles are presented in Tables 3 and 4. The whole molecule, except the two phenyl rings and the amino hydrogen atoms, is almost planar and the maximum deviation from planarity is by the hydroxy hydrogen atom [by $0.28(5)\text{ \AA}$]. This hydrogen atom appears to interact with S(2) in a fashion

Table 1. ^1H N.m.r., i.r., and m.s. data for (3a) and (3b) (recrystallized from CHCl_3).

(3a) ^a		
ν/cm^{-1} ^b	$\delta_{\text{H}}/\text{ppm}$ ^c	m/z ^d
3 440, 3 390,	5.40 (2 H, bs, NH_2)	390 (M^+ , 100)
3 310, 3 250,	7.11 (1 H, s, OH)	313 ($M^+ - \text{Ph}$, 5.4)
3 190, 2 212	7.22–7.27 (10 H, m)	248 (10.2)
1 650, 740	7.36 (1 H, s)	203 ($M^+ - \text{Ph}_2\text{SH}$, 7.6)
		173 ($M^+ - 2\text{PhS}$, 9.2)
		109 (PhS, 1.5)
		77 (Ph, 7.2)
(3b) ^e		
		390 (M^+ , 100)
		313 ($M^+ - \text{Ph}$, 6.8)
3 445, 3 435,	5.32 (2 H, bs, NH_2)	281 ($M^+ - \text{PhS}$, 26.6)
3 315, 3 240,	6.48 (1 H, s)	248 (9.5)
3 185, 2 212	6.63 (1 H, s, OH)	224 (6.3)
1 663, 750	7.2–7.4 (10 H, m)	109 (PhS, 2.0)
		77 (Ph, 5.6)

^a M.p. 185°C . ^b KBr pellets. ^c Relative to Me_4Si . ^d % Relative abundance. ^e M.p. 175°C .

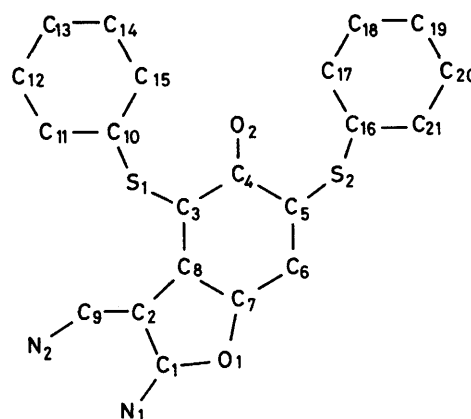


Figure 1. Atom numbering for 2-amino-5-hydroxy-4,6-diphenylthio-benzo[b]furan-3-carbonitrile (3a). Hydrogen atoms have been deleted for clarity.

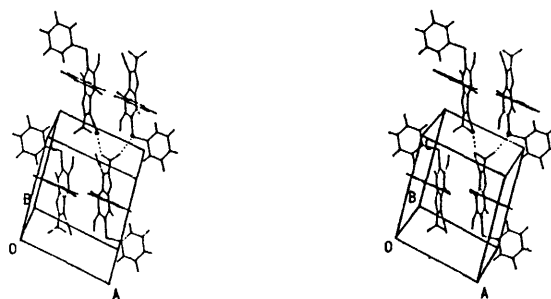


Figure 2. Packing diagram of molecule (3a) showing the inverse related two molecules in the unit cell and the amino hydrogen atoms which are hydrogen bonded to N(2) ($1 - x, 1 - y, 2 - z$) by $2.54(1)\text{ \AA}$ and S(2) ($x, y, 1 + z$) by $2.74(6)\text{ \AA}$.

reminiscent of a hydrogen bond $\text{H} \cdots \text{S}$, the distance being $2.44(5)\text{ \AA}$ which is less than the sum of their van der Waals radii by nearly 0.6 \AA . Even though the dihedral angles between the benzofuran moiety and the two phenyl rings differ considerably (65.8° and 98.2°) they are almost perpendicular to each other (96.9°).

Table 2. ^{13}C N.m.r. chemical shifts of (3a) and (3b).

Compound	δ_{C} for carbon atoms indicated ^a					
	1	2	3	Aromatic ^b	4, 5	6, 7
(3a)	112.8	114.1	117.9	126.5, 126.6, 127.0 128.7, 129.2	133.0 135.4	155.4, 166.4
(3b)	109.8	114.0	117.9	126.6, 126.7, 127.6 128.0, 128.6, 128.8 129.2, 129.3, 129.6 129.8	130.7 132.9	155.5, 165.8

^a In ppm relative to Me_4Si . ^b See Figure 1 for numbering scheme.**Table 3.** Fractional co-ordinates ($\times 10^4$) of (3a). E.s.d.s in terms of the least-significance digit are given in parentheses.

Atom	x	y	z
S(1)	5 639(2)	7 829(2)	4 653(2)
S(2)	8 446(2)	6 060(2)	1 845(2)
O(1)	7 623(4)	4 178(4)	7 217(4)
O(2)	6 795(5)	7 632(5)	2 221(5)
N(1)	6 890(6)	3 703(6)	9 425(6)
N(2)	5 154(7)	6 383(6)	8 608(6)
C(1)	6 966(6)	4 468(6)	8 103(7)
C(2)	6 501(6)	5 534(6)	7 385(6)
C(3)	6 593(6)	6 796(6)	4 697(6)
C(4)	7 078(6)	6 802(6)	3 458(7)
C(5)	7 845(7)	5 959(6)	3 429(6)
C(6)	8 059(7)	5 053(7)	4 725(6)
C(7)	7 537(6)	5 035(6)	5 881(5)
C(8)	6 836(6)	5 891(6)	5 914(7)
C(9)	5 756(7)	6 067(6)	8 028(7)
C(10)	6 907(6)	9 610(6)	3 999(6)
C(11)	6 339(8)	10 623(7)	3 568(7)
C(12)	7 254(9)	12 035(8)	3 128(7)
C(13)	8 739(8)	12 465(8)	3 032(7)
C(14)	9 296(8)	11 455(7)	3 437(7)
C(15)	8 397(7)	10 027(7)	3 924(6)
C(16)	10 113(7)	7 631(7)	1 612(7)
C(17)	10 829(8)	8 394(8)	2 610(8)
C(18)	12 110(9)	9 606(9)	2 307(9)
C(19)	12 707(9)	10 035(9)	1 039(8)
C(20)	12 038(10)	9 285(9)	37(9)
C(21)	10 723(10)	8 088(8)	316(8)

Two molecules constitute a unit cell and they are related to each other by an inversion centre as shown in Figure 2. Thus the planes of the two benzofuran rings of these centrosymmetric molecules are parallel to each other, with an interplanar distance of 3.48 Å. The intermolecular short contact in these two molecules is between N(2) (nitrilic nitrogen) and S(2) [3.470(5) Å]. Although this distance is slightly greater than the sum of their van der Waals radii (3.35 Å) the directionality of this interaction satisfies the condition proposed by Rosenfield *et al.*,¹⁰ that the nucleophilic group should approach the sulphur oppositely along one of its covalent bonds. No other intermolecular contacts between these two molecules are observed and the sole interaction is probably of dipole-dipole nature.

One of the amino hydrogen atoms points towards S(2) of the neighbouring molecule ($x, y, 1 + z$) with a distance of 2.74(6) Å while the second amino hydrogen points towards the nitrilic nitrogen [N(2)] of a molecule related by $(1 - x, 1 - y, 2 - z)$ with an interatomic distance of 2.54(1) Å. This non-equivalency of the two amino hydrogens is responsible for the differences in the i.r. spectra of (3a) in the solid state and in solution. Thus, a KBr pellet spectrum of (3a) shows five bands in the 3 185–3 450 cm^{-1} region which correspond to two symmetric and two asymmetric stretching vibrations of the two different N–H

Table 4. Bond lengths and bond angles for molecule (3a).

Bond lengths/Å			
C(1)–N(1)	1.336	C(1)–C(10)	1.383
C(1)–O(1)	1.367	C(11)–C(12)	1.378
C(2)–C(9)	1.408	C(12)–C(13)	1.372
C(9)–N(2)	1.145	C(14)–C(15)	1.393
O(1)–C(7)	1.402	C(10)–C(15)	1.376
C(7)–C(8)	1.401	S(2)–C(5)	1.748
C(3)–C(4)	1.405	S(2)–C(16)	1.780
C(3)–C(8)	1.386	C(16)–C(17)	1.374
C(4)–O(2)	1.371	C(17)–C(18)	1.379
C(4)–C(5)	1.442	C(18)–C(19)	1.365
C(5)–C(6)	1.429	C(19)–C(20)	1.364
C(6)–C(7)	1.341	C(20)–C(21)	1.388
S(1)–C(3)	1.757	C(16)–C(21)	1.393

Bond angles/°			
O(1)–C(1)–N(1)	116.0	C(3)–S(10)–C(11)	117.0
N(1)–C(1)–C(2)	133.8	S(1)–C(10)–C(15)	124.1
C(1)–C(2)–C(8)	107.1	C(10)–C(1)–C(12)	120.8
C(1)–C(2)–C(9)	122.7	C(11)–C(1)–C(13)	119.0
C(8)–C(2)–C(9)	130.0	C(12)–C(13)–C(14)	118.1
C(2)–C(9)–N(2)	176.8	C(13)–C(14)–C(15)	121.8
C(2)–C(8)–C(7)	104.6	C(10)–C(15)–C(14)	119.3
O(1)–C(7)–C(8)	110.6	C(11)–C(10)–C(15)	118.9
O(1)–C(7)–C(6)	125.3	C(5)–S(2)–C(16)	104.0
C(6)–C(7)–C(8)	124.1	S(2)–C(16)–C(17)	125.0
C(3)–C(8)–C(7)	120.5	S(2)–C(16)–C(21)	116.2
C(2)–C(8)–C(3)	134.9	C(17)–C(16)–C(21)	118.8
C(4)–C(3)–C(8)	116.8	C(16)–C(17)–C(18)	119.9
S(1)–C(3)–C(8)	122.7	C(17)–C(18)–C(19)	120.7
S(1)–C(3)–C(4)	120.4	C(18)–C(19)–C(20)	120.7
C(3)–C(4)–C(5)	122.8	C(19)–C(20)–C(21)	119.0
O(2)–C(4)–C(3)	118.6	C(16)–C(21)–C(20)	120.8
O(2)–C(4)–C(5)	118.6	C(5)–C(6)–C(7)	118.5
C(4)–C(5)–C(6)	117.2	S(2)–C(5)–C(4)	119.8
S(2)–C(5)–C(6)	123.0		

bonds while the broad fifth band is due to the intramolecular N–H...OH hydrogen bond.

The solution i.r. spectrum (dichloromethane, 0.1 mm NaCl cell) shows only two bands on a weak broad band at 3 391 and 3 493 cm^{-1} . Similar effects have been observed in the frequency of acetylenic hydrogen stretching due to C–H...O intermolecular contacts in a variety of crystal environments.¹¹

Experimental

General Methods.—M.p.s were determined on a Mettler FP5 single crystal apparatus and are uncorrected. I.r. spectra were recorded on Perkin-Elmer 781 and on Nicolet DX FT-IR i.r. spectrophotometers. The ^1H n.m.r. spectra were recorded on a Bruker WP 200 SY spectrometer in CDCl_3 and chemical shifts are reported in ppm (δ) downfield from Me_4Si . ^{13}C N.m.r. spectra were recorded on the same instrument in 12 mm tubes with proton-noise decoupling. Mass spectra (70 eV) were determined with a Finnigan 4021 spectrometer. A Chromatotron (2 mm circular plates) prepared from Kieselgel 60 PF-254 was used for preparative separations. All commercial grade solvents were distilled prior to use. 2,5- and 2,6-Bis(phenylthio)benzoquinones were prepared as described earlier.¹² Light petroleum refers to the fraction boiling 60–80 °C.

2-Amino-5-hydroxy-4,6-bis(phenylthio)benzo[b]furan-3-carbonitrile (3a).—A mixture of 2,6-bis(phenylthio)-1,4-benzoquinone (0.324 g, 1.0 mmol) and dicyanomalonate (0.238 g, 3.6 mmol) in dichloromethane (25 cm^3) was stirred at room temperature under an atmosphere of argon. To the cooled (0 °C)

mixture, pyridine (18 cm³, 0.23 mol) and freshly distilled TiCl₄ (1.28 g, 6.67 mmol) were added dropwise over 20 min. An exothermic reaction took place and the resulting black solution was stirred at room temperature for an additional 2 h. Dichloromethane (50 cm³) was added and the mixture extracted with 5% HCl solution (3 × 35 cm³) and then with water (3 × 35 cm³). The organic layer was dried (MgSO₄) and the solvent evaporated under reduced pressure. T.l.c. (CH₂Cl₂–light petroleum, 1:1) at this stage revealed several spots of which the major one turned green upon exposure to iodine vapour. The product (0.135 g, 35%) was isolated by column chromatography on silica gel (70–230) using CH₂Cl₂–light petroleum (1:1) as the eluant; m.p. 180 °C (CHCl₃) (Found: C, 64.25; H, 3.9; N, 6.9; S, 16.0. C₂₁H₁₄N₂S₂O₂ requires C, 64.62; H, 3.60; N, 7.18; S, 16.41%). Higher yields of the same product could be obtained by carrying out the reaction with pyridine only, omitting the titanium(IV) tetrachloride.

2-Amino-5-hydroxy-4,7-bis(phenylthio)benzo[b]furan-3-carbonitrile (3b).—The same procedure described above with 2,5-bis(phenylthio)-1,4-benzoquinone (0.324 g, 1.0 mmol) gave the 4,7-diphenylthio analogue (0.12 g, 32%); m.p. 174–175 °C (CHCl₃) (Found: C, 64.6; H, 3.5; N, 7.1; S, 16.1. C₂₁H₁₄N₂S₂O₂ requires C, 64.62; H, 3.60; N, 7.18; S, 16.41%).

Crystal Data for Molecule (3a).—Formula C₂₁H₁₄N₂S₂O₂, *M* = 390, triclinic, space-group *P*1, *a* = 10.092(6), *b* = 10.828(7), *c* = 9.976(6) Å, α = 73.35(5), β = 100.13(5), γ = 116.13(4)°, *V* = 936.2(9) Å³, *F*(000) = 404, *Z* = 2, *D*_c = 1.36 g cm^{−3}. *X*-Ray single crystal data were collected on a Syntex *P*1 diffractometer (λMo-*K*_α) = 0.710 69 Å, graphite monochromator. Unit-cell parameters were determined by a least-squares fit of 15 accurately centred reflections (4 < 2θ < 15°). 1 706 reflections were considered to be non-zero at the 3σ significance level of the 2 439 unique reflections in the range 0 < 2θ < 50°. No absorption corrections were applied and there was no evidence for crystal decomposition during the data collection. Scattering factors for all elements were taken from the International Tables for *X*-ray Crystallography.¹³

The structure was solved by direct methods using SHELX 86¹⁴ which yielded the positions of all non-hydrogen atoms. Least-squares refinement using SHELX 76¹⁴ converged at an *R* value of 0.068 for positional parameters and an isotropic thermal parameters for all non-hydrogen atoms. The *R*_w value is 0.065. Geometric calculations were carried out by GEOM¹⁵ and illus-

trations were prepared using PLUTO¹⁶ and ORTEP.¹⁷ Hydrogen atom co-ordinates, thermal parameters, and torsion angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC).*

Acknowledgements

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* Supplementary data. See 'Instructions for Authors' (1989), *J. Chem. Soc., Perkin Trans. 2*, in the January issue.