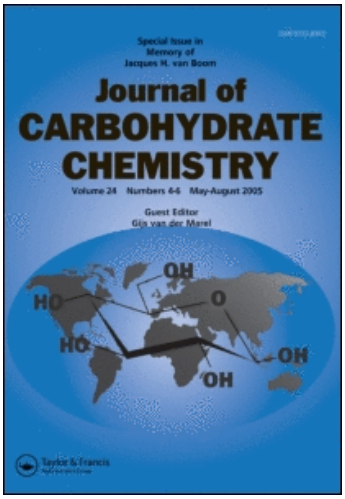

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REGIOCONTROLLED INCORPORATION AND ANNULATION OF GLUCOSE INTO SPIROTHIAZOLE AND SPIROTHIAZOLOXAZOLE DERIVATIVES

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ABSTRACT

Cyclic ketones **1a-f** reacted with mercaptoacetic acid in benzene and/or toluene in the presence of *p*-toluenesulfonic acid afforded the corresponding spiro-1,3-oxathialanone derivatives (**2a-f**). Compounds **2a-f** reacted with glucosamine hydrochloride in a mixture of pyridine and ethanol to yield 3-(2'-glucosyl)-2-spiro[1'-cycloalkyl]thiazolidin-4-one derivatives **4a-f**. Reaction of **4a-f** with fused sodium acetate in a mixture of acetic anhydride and acetic acid gave annulated spirothiazoloxazologlucose derivatives **6a-f**. All the synthesized spiro derivatives were identified by conventional methods (IR, ^{1}H NMR spectroscopy and elemental analyses).

INTRODUCTION

Spiroheterocyclic derivatives have considerable importance as drugs and a wide scope of applications.[1-15] Pharmacological activities of thiazolidinone derivatives have been extensively studied,[16-18] while thiazoloxazoles showed diverse biological activities.[19-23] The incorporation of heterocyclic moieties with carbohydrates have gained some importance.[24-27]

The antimicrobial properties of glucosamine derivatives containing alkyl chains have been of major interest in the last few years.[28] From all the foregoing facts, and as a continuation of our previous work,[29-36] we report herein the synthesis of some new spirothiazologlucose and spirothiazoloxazole derivatives.

RESULTS AND DISCUSSION

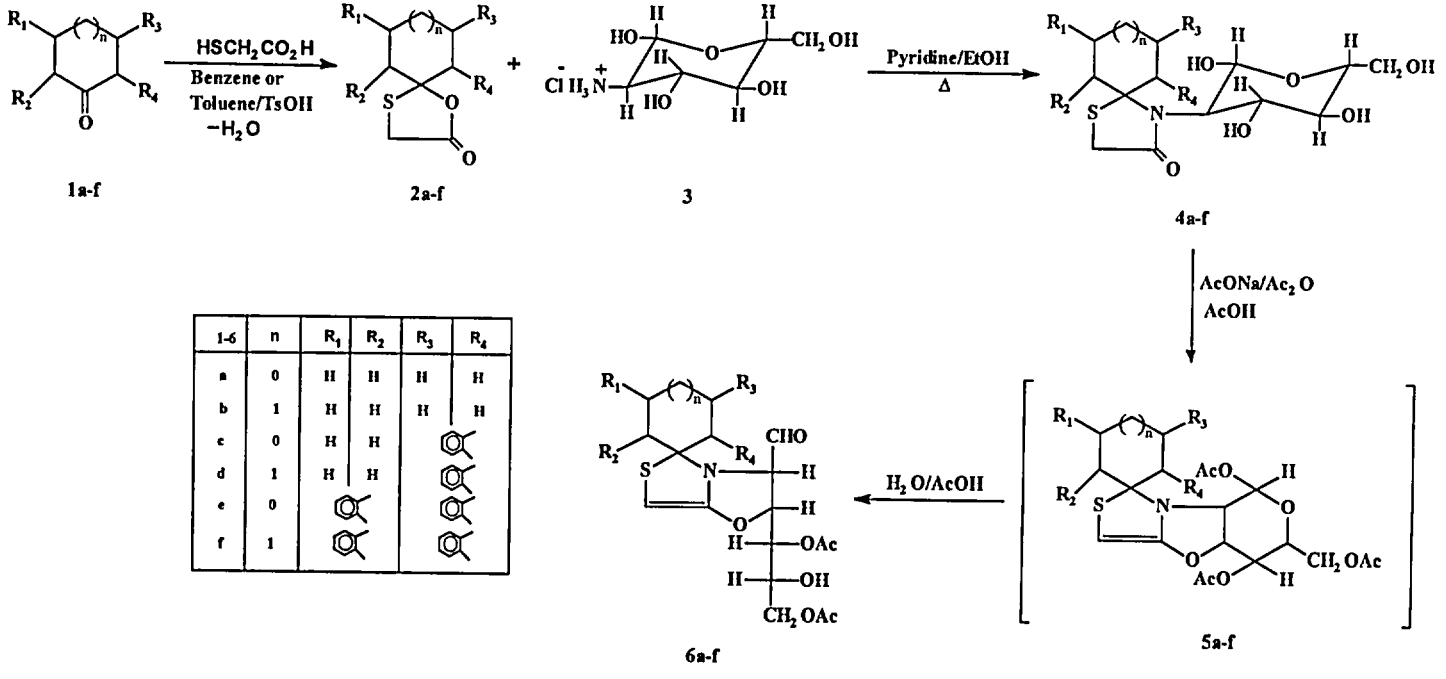
Our syntheses were started with the reaction of cyclopentanone **(1a)**, cyclohexanone **(1b)**, 1-indanone **(1c)**, 1-tetralone **(1d)**, fluorenone **(1e)** and anthrone **(1f)** with mercaptoacetic acid in benzene and/or toluene in the presence of *p*-toluenesulfonic acid to give 1-oxa-4-thiaspiro[4.4]nonan-2-one **(2a)**, 1-oxa-4-thiaspiro[4.5]decan-2-one **(2b)**, spiro[indan-1,2'-[1',3']oxathialan]-5'-one **(2c)**, spiro[tetrahydronaphthalene-1,2'-[1',3']oxathialan]-5'-one **(2d)**, spiro[fluoren-9,2'-[1',3']oxathialan]-5'-one **(2e)** and spiro[anthracene-9(10)-2'-[1',3']oxathialan]-5'-one **(2f)** respectively (Scheme). The structures of compounds **2a-f** were elucidated by the comparison of their physical properties, elemental analyses and spectroscopic data with the reported literature data.[37,38]

Compounds **2a-f** reacted with glucosamine hydrochloride in a mixture of pyridine and ethanol to afford 1-thia-4-(2'-glucosyl)-4-azaspiro[4.4]nonan-3-one **(4a)**, 1-thia-4-(2'-glucosyl)-4-azaspiro[4.5]decan-3-one **(4b)**, 3-(2'-glucosyl)-2-spiro[1'-indanyl]thiazolidin-4-one **(4c)**, 3-(2'-glucosyl)-2-spiro[1'-tetrahydronaphthalenyl]thiazolidin-4-one **(4d)**, 3-(2'-glucosyl)-2-spiro[9'-flourenyl]thiazolidin-4-one **(4e)** and 3-(2'-glucosyl)-2-spiro[9'(10)anthracenyl]thiazolidin-4-one **(4f)** respectively in fairly good yield (65-77%, Table) (Scheme). The structures of compounds **4a-f** were established from their elemental analyses and spectroscopic data (Table). For example, the IR spectrum of compound **4d** showed the following absorption bands: 3650-3600 cm^{-1} for the hydroxyl group of the glucose moiety, 3060 cm^{-1} for aromatic CH stretching, 2860 cm^{-1} for aliphatic CH stretching, 1720 cm^{-1} for the carbonyl group and 720 cm^{-1} for C-S stretching. The ^1H NMR spectrum of **4d** (DMSO-d_6/TMS) showed the following signals: δ 2.00-2.50 (6 H, m) for the three methylene groups of the tetralin ring, 2.75-3.00 (4 H, m) for the protons at C_1, C_2, C_3, C_4, C_5 of the glucose moiety, 3.40 (2 H, s) for the methylene protons of the thiazolidinone ring, 4.00-4.20 (5 H, m) for the four hydroxyl protons at C_1, C_3, C_4, C_6 and the C_2 proton of the

glucose moiety, 4.55 (2 H, m) for the methylene protons of C_6 of glucose unit and 7.00-7.80 (4 H, m) for the aromatic protons of the tetralin ring. Also, low resolution mass spectrometry of compound **4d** showed a fragment of *m/z* (% relative intensity) 218 (66%) which indicated the incorporation of the glucose molecule with compounds **2a-f** (Scheme). Reaction of compounds **4a-f** with fused sodium acetate in a mixture of acetic anhydride and acetic acid at reflux followed by pouring the reaction mixture into cold water yielded the incorporated acetylated glucose moiety with spirothiazoloxazoles **(6a-f)** in excellent yield (73%-80% Table) (Scheme). The elucidation of the structures of compounds **6a-f** were based on their elemental analyses and spectroscopic data (Table). For example, the IR spectrum of compound **6f** showed characteristic absorption bands at 3630-3600 cm^{-1} for the OH group of the glucose moiety, 3050 cm^{-1} for the aromatic CH stretching, 2860 cm^{-1} for the aliphatic CH stretching, 1800, 1720 cm^{-1} for the carbonyl groups of the acetyl group at C_4 and C_6 of the glucose unit, 850 cm^{-1} for the double bond in the thiazole ring and 720 cm^{-1} for C-S stretching. The ^1H NMR spectrum of **6f** (DMSO-d_6/TMS) showed the following signals: δ 2.45 (6 H, s) for the two methyl groups of the acetoxy groups at C_4 and C_6 of glucose moiety, 3.30 (2 H, s) for the methylene protons at C_{10} of the anthracene ring, 2.90 (1 H, d) for the hydroxyl proton at C_5 of glucose residue, 4.10 (2 H, d) for the two protons at C_2 and C_3 of oxazole ring, 4.20 (2 H, d) for the two protons at C_4 and C_5 of the glucose molecule, 4.30 (2 H, s) for the methylene protons at C_6 of glucose, 4.60 (1 H, s) for the proton of the thiazole ring (C_5 at that ring), 7.00-8.20 (8 H, m) for the aromatic protons of the anthracene ring and 9.75 (1 H, s) for the proton of the aldehyde group of C_1 of the glucose molecule.

EXPERIMENTAL

General methods. The time required for completion of the reaction was monitored by thin-layer chromatography (TLC), melting points were determined in open glass capillaries and are uncorrected. IR spectra were recorded on a Pye-Unicam SP 200 G spectrophotometer. ^1H NMR spectra were measured using an EM 360 90 MHz NMR spectrophotometer. Microanalyses were determined on a Perkin Elmer 240 C microanalyser. Mass spectra were performed on a Finnigan 4023 quadrupole system equipped with a Model 4500 source upgrade.



1-6	n	R_1	R_2	R_3	R_4
a	0	H	H	H	H
b	1	H	H	H	H
c	0	H	H		
d	1	H	H		
e	0				
f	1				

Scheme

TABLE. Physical data of Spirothiazolo-3-(2'-glucosyl)-4-one derivatives (**4a-f**) and Spirothiazoloxazolylglucose derivatives (**6a-f**)

Compd. No.	Yield (%)	MP (°C)	Molecular Formula (solvent of crystallization)	Anal.Calcd/(Found) %				IR (KBr), cm^{-1}	^1H NMR (DMSO-d_6), δ (TMS)ppm
				C	H	N	S		
4a	70	125-127	$C_{13}H_{21}NO_6S$ (ethanol)	48.90 (48.70)	6.58 (6.40)	4.38 (4.25)	10.03 (10.00)	3650-3600 (OH), 2850 (CH aliph), 1720 (C=O), 720 (C-S).	1.30-1.70 (4 H, m), 1.90-2.20 (4 H, m), 2.70-3.00 (4 H, m), 3.38 (2 H, s), 4.00-4.20 (5 H, m), 4.50 (2 H, m).
4b	77	145-147	$C_{14}H_{23}NO_6S$ (ethanol)	50.45 (50.25)	6.90 (6.80)	4.20 (4.10)	9.60 (9.50)	3640-3600 (OH), 2850 (CH aliph), 1720 (C=O), 720 (C-S).	1.32-1.75 (6 H, m), 1.90-2.20 (4 H, m), 2.70-3.00 (4 H, m), 3.36 (2 H, s), 4.00-4.20 (5 H, m), 4.50 (2 H, m).
4c	76	160-162	$C_{17}H_{21}NO_6S$ (methanol)	55.58 (55.40)	5.72 (5.60)	3.81 (3.65)	8.71 (8.60)	3650-3600 (OH), 3050 (CH arom), 2860 (CH aliph), 1720 (C=O), 730 (C-S).	2.00-2.40 (4 H, m), 2.70-3.00 (4 H, m), 3.38 (2 H, s), 4.00-4.20 (5H, m), 4.50 (2 H, m), 7.00-7.80 (4 H, m).
4d	69	215-217	$C_{18}H_{23}NO_6S$ (methanol)	56.69 (56.60)	6.03 (6.00)	3.67 (3.65)	8.39 (8.30)	3650-3600 (OH), 3060 (CH arom), 2860 (CH aliph), 1720 (C=O), 720 (C-S).	2.00-2.50 (6 H, m), 2.75-3.00 (4 H, m), 3.40 (2 H, s), 4.00-4.20 (5 H, m), 4.55 (2 H, m), 7.00-7.80 (4 H, m).
4e	66	220-222	$C_{21}H_{21}NO_6S$ (ethanol)	60.72 (60.60)	5.06 (5.00)	3.37 (3.25)	7.71 (7.65)	3640-3600 (OH), 3050 (CH arom), 2870 (CH aliph), 1720 (C=O), 730 (C-S).	2.70-3.00 (4 H, m), 3.50 (2 H, s), 4.00-4.20 (5 H, m), 4.55 (2 H, m), 7.00-7.80 (8 H, m).
4f	65	280-282	$C_{22}H_{23}NO_6S$ (ethanol)	61.53 (61.40)	5.36 (5.25)	3.26 (3.20)	7.45 (7.40)	3630-3600 (OH), 3050 (CH arom), 2860 (CH aliph), 1720 (C=O), 730 (C-S).	2.70-3.00 (4 H, m), 3.40 (2 H, s), 3.30 (2 H, s), 4.00-4.20 (5 H, m), 4.55 (2 H, m), 7.00-7.80 (8 H, m).
6a	80	190-192	$C_{17}H_{23}NO_7S$ (ethanol)	52.90 (52.80)	5.97 (5.90)	3.63 (3.60)	8.31 (8.25)	3650-3600 (OH), 2860 (CH aliph), 1800,1720 (C=O), 850 (C=C), 730 (C-S).	1.30-1.70 (4 H, m), 1.90-2.20 (4 H, m), 2.40 (6 H, s), 2.90 (1 H, d), 4.10 (2 H, d), 4.20 (2 H, d), 4.30 (2 H, s), 4.60 (1 H, s), 9.70 (1 H, s).

(Continued)

TABLE. *Continued*

Compd. No.	Yield (%)	MP (°C)	Molecular Formula (solvent of crystallization)	Anal.Calcd/(Found) %				IR (KBr), cm^{-1}	^1H NMR (DMSO-d_6), δ (TMS)ppm
				C	H	N	S		
6b	77	160-162	$C_{18}H_{25}NO_7S$ (methanol)	54.13 (54.00)	6.26 (6.10)	3.50 (3.40)	8.02 (8.00)	3650-3600 (OH), 2890 (CH aliph), 1800,1720 (C=O), 840 (C=C), 720 (C-S).	1.32-1.75 (6 H, m), 1.90-2.20 (4 H, m), 2.40 (6 H, s), 2.90 (1 H, d), 4.10 (2 H, d), 4.20 (2 H, d), 4.30 (2 H, s), 4.60 (1 H, s), 9.70 (1 H, s).
6c	78	170-172	$C_{21}H_{23}NO_7S$ (ethanol)	58.19 (58.00)	5.31 (5.20)	3.23 (3.15)	7.39 (7.30)	3650-3600 (OH), 3060 (CH arom), 2870 (CH aliph), 1800,1720 (C=O), 850 (C=C), 730 (C-S).	2.00-2.40 (4 H, m), 2.40 (6 H, s), 2.90 (1 H, d), 4.10 (2 H, d), 4.20 (2 H, d), 4.30 (2 H, s), 4.60 (1 H, s), 7.00-7.80 (4 H, m).
6d	76	180-182	$C_{23}H_{25}NO_7S$ (methanol)	60.13 (60.00)	5.44 (5.40)	3.05 (3.00)	6.97 (6.85)	3640-3610 (OH), 3060 (CH arom), 2850 (CH aliph), 1800,1720 (C=O), 850 (C=C), 720 (C-S).	2.00-2.50 (6 H, m), 2.45 (6 H, s), 2.90 (1 H, d), 4.10 (2 H, d), 4.20 (2 H, d), 4.30 (2 H, s), 4.60 (1 H, s), 7.00-7.80 (4 H, m), 9.80 (1 H, s).
6e	75	200-202	$C_{25}H_{23}NO_7S$ (ethanol)	62.37 (62.30)	4.78 (4.75)	2.91 (2.85)	6.65 (6.60)	3640-3600 (OH), 3060 (CH arom), 2860 (CH aliph), 1800,1720 (C=O), 850 (C=C), 730 (C-S).	2.45 (6 H, s), 2.90 (1 H, d), 4.10 (2 H, d), 4.20 (2 H, d), 4.30 (2 H, s), 4.60 (1 H, s), 7.00-8.20 (8 H, m), 9.75 (1 H, s).
6f	73	210-212	$C_{26}H_{25}NO_7S$ (ethanol)	63.03 (63.00)	5.05 (5.00)	2.82 (2.80)	6.46 (6.40)	3630-3600 (OH), 3050 (CH arom), 2860 (CH aliph), 1800,1720 (C=O), 850 (C=C), 720 (C-S).	2.45 (6 H, s), 2.90 (1 H, d), 3.30 (2 H, s), 4.10 (2 H, d), 4.20 (2 H, d), 4.30 (2 H, s), 4.60 (1 H, s), 7.00-8.20 (8 H, m), 9.75 (1 H, s).

Preparation of spiro[cycloalkyl and/or polycyclic-2'-[1',3']oxathialan]-5'-one derivatives (2a-f). These compounds were prepared according to the reported procedure.[37,38]

Synthesis of 3-(2'-glucosyl)-2-spiro[1'-cycloalkyl]thiazolidin-4-one derivatives (4a-f). General procedure. Each compound **2a-f** (10 mmol) was dissolved in a mixture of pyridine/ethanol (50 mL, 1:4). To this solution glucosamine hydrochloride (2.16 g, 10 mmol) was added, and the reaction mixture was refluxed for 12 h. At the end of the reflux time, the reaction mixture was cooled to room temperature, poured into cold 10% hydrochloric acid solution (50 mL) whereby the target products **4a-f** precipitated, were removed by filtration, dried and crystallized from appropriate solvents: **4a**, ethanol; **4b**, ethanol; **4c**, methanol; **4d**, methanol; **4e**, ethanol; **4f**, ethanol. Yields, melting points, elemental and spectral analyses are depicted in the Table.

Synthesis of the annulated spirothiazoloxazologlucose derivatives (6a-f). General procedure. Each compound **4a-f** (1 mmol) was fused with fused sodium acetate (5 mmol), then dissolved in a mixture of acetic anhydride and acetic acid (25 mL, 2:1). The reaction mixture was refluxed for 6 h, then cooled to room temperature and poured into cold water (50 mL) whereby the desired products **6a-f** were precipitated, filtered off, dried and crystallized from appropriate solvents: **6a**, ethanol; **6b**, methanol; **6c**, ethanol; **6d**, methanol; **6e**, ethanol; **6f**, ethanol. Yields, melting points, elemental and spectral analyses are depicted in the Table.

REFERENCES AND NOTES

1. M. T. Crimmins, D. G. Washburn, J. D. Katz and F. J. Zawacki, *Tetrahedron Lett.*, **39**, 3439 (1998).
2. K. Mogilaiah and R. B. Rao, *Indian J. Chem., Sect. B*, **37B**, 139 (1998).
3. J. L. Bullington and J. H. Dodd, *J. Heterocycl. Chem.*, **35**, 397 (1998).
4. A. M. El-Sayed, A. M. M. El-Saghier, M. A. A. Mohamed and A. K. El-Shafei, *Gazz. Chim. Ital.*, **127**, 605 (1997).
5. H. Abdel Ghany, *Phosphorus, Sulfur and Silicon*, **122**, 173 (1997).
6. B. Kokel, B. Bachet and A. Cousson, *Bull. Soc. Chim. Belg.*, **106**, 293 (1997).
7. M. Ibrahim-Quali, M. Sinibaldi, Y. Train, D. Guillaume and J. C. Gramain, *Tetrahedron*, **53**, 16083 (1997).
8. T. Nagasaka, H. Sato and S. I. Saeki, *Tetrahedron Asymmetry*, **8**, 191 (1997).
9. H. Pellissier, P. Y. Michellys and M. Santelli, *J. Org. Chem.*, **62**, 5588 (1995).
10. T. V. Lee and J. R. Porter, *Org. Synth.*, **72**, 189 (1995).
11. L. Fisers, F. Sauter, J. Froehlich, Y. Feng and K. Mereiter, *Monatsh. Chem.*, **125**, 909 (1994).

12. M. S. Malamas, *J. Heterocycl. Chem.*, **31**, 565 (1994).
13. J. Frohlich, F. Sauter and K. Blasl, *Heterocycles,* **37**, 1879 (1994).
14. J. A. Wendt, P. J. Gauvreau and R. D. Bach, *J. Am. Chem. Soc.*, **116**, 992 (1994).
15. P. A. Wender, A. W. White and F. E. McDonald, *Org. Synth.*, **70**, 204 (1992).
16. L. Somogyi, G. Batta and A. L. Tokes, *Liebigs Ann. Chem.*, **11**, 1209 (1992).
17. M. Zoghbi and J. Warkentin, *Tetrahedron,* **49**, 10229 (1993).
18. S. P. Singh, S. S. Parmar, K. Roman and C. I. Stenberg, *Chem. Rev.*, **81**, 175 (1981) and references cited.
19. R. Raghunathan, M. Shanmugasundaram, S. Bhanumathi and E. J. P. Malar, *Heteroatom Chemistry,* **9**, 327 (1998).
20. K. H. Park, M. M. Olmstead and M. J. Kurth, *J. Org. Chem.*, **63**, 113 (1998).
21. G. Zvilichovsky, V. Gurvich and S. Cohen, *J. Chem. Res. Synop.*, **9**, 335 (1994).
22. M. Zoghbi and J. Warkentin, *Can. J. Chem.*, **71**, 912 (1993).
23. J. Wrobel and A. Dietrich, *Heterocycles*, **38**, 1823 (1994).
24. M. A. E. Sheban, *Adv. Heterocycl. Chem.*, **70**, 163 (1998).
25. J. Gervay, T. M. Flaherty and D. Holmes, *Tetrahedron,* **53**, 16355 (1997).
26. E. H. El Ashry and Y. El Kilany, *Adv. Heterocycl. Chem.*, **69**, 129 (1998).
27. A. I. Khodair, E. S. I. Ibrahim, A. M. Diab, M. M. Abd-El Aziz, B. M. T. Omar and E. S. H. El Ashry, *Pharmazie,* **53**, 294 (1998).
28. S. Matsumura, Y. Kawamura, S. Yoshikawa, K. Kawada and T. Uchibori, *J. Am. Oil Chem. Soc.*, **70**, 17 (1993).
29. M. S. Al-Thebeiti and M. F. El-Zohry, *Phosphorus, Sulfur and Silicon,* **88**, 251 (1994).
30. M. S. Al-Thebeiti, *Heteroatom Chemistry,* **5**, 571 (1994).
31. M. S. Al-Thebeiti and M. F. El-Zohry, *Heteroatom Chemistry,* **6**, 567 (1995).
32. M. S. Al-Thebeiti and M. F. El-Zohry, *Heterocycles,* **41**, 2475 (1995).
33. M. S. Al-Thebeiti, *Heterocycles,* **48**, 145 (1998).
34. M. S. Al-Thebeiti and M. F. El-Zohry, *Indian J. Chem.*, **37**, 804 (1998).
35. M. S. Al-Thebeiti and M. F. El-Zohry et al., *Bull. Pol. Acad. Sci. Chem.*, **46**, 353 (1998).
36. M. S. Al-Thebeiti, *Phosphorus, Sulfur and Silicon,* (proof), (1998).
37. M. F. El-Zohry, I. M. A. Awad and A. A. Abdel-Hafez, *Arch. Pharm.* (Weinheim), **326**, 115 (1993).
38. A. A. Al-Ahmadi and M. F. El-Zohry, *Heteroatom Chemistry,* **7**, 171 (1996).