Acta Cryst. (1989). C45, 1566–1568

Structure of a Potentially Heptadentate Tripodal Ligand, Tris[4-(2-thienyl)-3-aza-3-butenyl]amine

BY ELMER C. ALYEA*

Department of Chemistry and Biochemistry, University of Guelph, Guelph, Ontario, Canada N1G 2W1

SHIXIONG LIU

Institute of Structural Chemistry, Fuzhou University, Fuzhou, People's Republic of China

AND BAOLONG LI, ZHENG XU AND XIAOZENG YOU

Coordination Chemistry Institute, Nanjing University, Nanjing, People's Republic of China

(*Received* 28 *December* 1988; *accepted* 15 *February* 1989)

Abstract. $C_{21}H_{24}N_4S_3$, $N(C_7H_8NS)_3$, $M_r = 428{\cdot}6$, monoclinic, $C2/c$, $a = 29{\cdot}341\ (1)$, $b = 9{\cdot}250\ (2)$, $c = 16{\cdot}622\ (3)$ Å, $\beta = 97{\cdot}27\ (2)°$, $V = 4475\ (2)$ Å^3, $Z = 8$, $D_x = 1{\cdot}27$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 3{\cdot}31$ cm^{-1}, $F(000) = 1808$, $T = 298$ K, $R = 0{\cdot}044$ for 2781 observed reflections. The three pendant arms, each containing an azomethine and a thiophene moiety and linked by the central sp^3-hybridized tertiary amine atom, N(4), form a potentially heptadentate ligand pocket. Principal bond lengths are C=N 1·254 (4) (av.), C—N(4) 1·462 (4) (av.), C—S 1·709 (4) (av.), C—C between the apical N(4) and azomethine C=N 1·509 and C—C between the azomethine C=N and thiophene moiety 1·449 Å.

Introduction. Some chemical and physical properties of the potentially heptadentate ligand tris[4-(2-pyridyl)-3-aza-3-butenyl]amine, abbreviated as py_3tren, in the series of $[M(py_3tren)]^{2+}.BF_4^-$ and PF_6^- salts ($M = 3d^{5-10}$ transition-metal ions) were recently reviewed (Kirchner, Mealli, Bailey, Howe, Torre, Wilson, Andrews, Rose & Lingafelter, 1987). The nature of the interaction between the transition-metal ion and the bridging tertiary amine atom of py_3tren was of central interest since the ligand was designed to give monocapped trigonal antiprismatic coordination polyhedra. Multidentate ligands with pendant arms are also of current interest to coordination chemists, especially in the synthesis of metalloprotein model compounds (XXVI International Conference on Coordination Chemistry, 1988; Meade & Busch, 1985). As part of metal complexation studies of potentially heptadentate Schiff-base ligands derived from tris(2-aminoethyl)-amine (tren) (Alyea, Li, Xu & You, 1989) we have determined in this work the molecular structure of the new tripodal ligand tris[4-(2-thienyl)-3-aza-3-butenyl]amine, which is abbreviated as S_3tren.

Experimental. Colourless transparent crystals grown from acetone solution. Accurate cell dimensions and crystal orientation matrix determined on an AFC-5R diffractometer by a least-squares treatment of the setting angles of 20 reflections in the range $10 < \theta < 15°$. Crystal dimensions $0{\cdot}24 \times 0{\cdot}34 \times 0{\cdot}32$ mm; intensities of reflections with indices h 0 to 34, k 0 to 11, l −20 to 20 with $2 < 2\theta < 50°$ measured; ω–2θ scans; ω-scan width $(1{\cdot}260 + 0{\cdot}400\text{tg}\theta)°$, graphite-monochromatized Mo $K\alpha$ radiation. Intensities of three reflections measured every 2 h showed no evidence of crystal decay. 4330 reflections measured. 4236 unique. 2720 with $I > 3\sigma(I)$ labelled observed and used in structure solution and refinement; $R_{int} = 0{\cdot}018$. Data corrected for Lorentz–polarization and absorption effects (max. and min. transmission factors 1·095 and 0·8430). Gaussian integration, grid $6 \times 6 \times 6$. Space group $C2/c$ or Cc from systematic absences hkl, $h + k = 2n + 1$ and $h0l$, $l = 2n + 1$. $C2/c$ chosen and confirmed by the analysis.

The crystal structure was solved by direct methods. Refinement was by full-matrix least-squares calculations, initially with isotropic and then with anisotropic thermal parameters. At an intermediate stage in the refinement, difference maps showed maxima in positions consistent with the expected locations of the H atoms; in the final rounds of calculations the H atoms were positioned on geometrical grounds (C—H 0·95 Å) and included (as riding atoms) in the structure-factor calculations. The final cycle of refinement (on F) included 253 variable parameters, $R = 0{\cdot}044$, $wR = 0{\cdot}055$, goodness-of-fit 1·48, $w = 1/\sigma^2(F_o)$. Max. shift/e.s.d. = 0·01, density in final difference map $\pm 0{\cdot}24$ e Å^{-3}; no

* To whom correspondence should be addressed.

0108-2701/89/101566-03$03.00

Table 1. *Atomic coordinates and equivalent isotropic thermal parameters*

Anisotropically refined atoms are given in the form of the equivalent isotropic thermal parameter defined as: $\frac{4}{3}[a^2B_{11} + b^2B_{22} + c^2B_{33} + ab(\cos\gamma)B_{12} + ac(\cos\beta)B_{13} + bc(\cos\alpha)B_{23}]$.

	x	y	z	B_{eq}(Å^2)
S(1)	0·33174 (3)	0·05840 (8)	0·57619 (5)	4·30 (4)
S(2)	0·28388 (3)	−0·4858 (1)	0·36881 (5)	4·48 (4)
S(3)	0·46477 (3)	−0·1541 (1)	0·34212 (5)	5·21 (4)
N(1)	0·34784 (8)	−0·2437 (3)	0·6442 (1)	3·9 (1)
N(2)	0·37477 (8)	−0·5715 (3)	0·4614 (2)	4·4 (1)
N(3)	0·47572 (8)	−0·2234 (3)	0·5228 (1)	4·2 (1)
N(4)	0·42638 (7)	−0·4493 (2)	0·6187 (1)	3·4 (1)
C(1)	0·3039 (1)	0·1512 (4)	0·4962 (2)	5·3 (2)
C(2)	0·2831 (1)	0·0628 (5)	0·4392 (2)	5·6 (2)
C(3)	0·2893 (1)	−0·0845 (4)	0·4589 (2)	4·3 (1)
C(4)	0·31529 (9)	−0·1044 (3)	0·5319 (2)	3·2 (1)
C(5)	0·32714 (9)	−0·2396 (3)	0·5730 (2)	3·4 (1)
C(6)	0·3570 (1)	−0·3853 (4)	0·6812 (2)	4·9 (1)
C(7)	0·4081 (1)	−0·4140 (3)	0·6943 (2)	4·3 (1)
C(11)	0·2591 (1)	−0·3728 (4)	0·2951 (2)	5·0 (2)
C(12)	0·2901 (1)	−0·2857 (4)	0·2667 (2)	5·2 (2)
C(13)	0·3350 (1)	−0·3090 (3)	0·3044 (2)	4·4 (1)
C(14)	0·3372 (1)	−0·4151 (3)	0·3614 (2)	3·6 (1)
C(15)	0·3774 (1)	−0·4718 (3)	0·4108 (2)	3·9 (1)
C(16)	0·4170 (1)	−0·6256 (4)	0·5066 (2)	5·0 (2)
C(17)	0·4181 (1)	−0·6002 (3)	0·5965 (2)	4·4 (1)
C(21)	0·4331 (1)	−0·0553 (4)	0·2693 (2)	5·4 (2)
C(22)	0·4014 (1)	0·0259 (4)	0·2998 (2)	5·2 (2)
C(23)	0·4024 (1)	0·0084 (3)	0·3843 (2)	4·4 (1)
C(24)	0·4350 (1)	−0·0861 (3)	0·4163 (2)	3·7 (1)
C(25)	0·4461 (1)	−0·1307 (3)	0·5003 (2)	4·0 (1)
C(26)	0·4847 (1)	−0·2575 (4)	0·6090 (2)	4·7 (1)
C(27)	0·4755 (1)	−0·4147 (4)	0·6247 (2)	4·1 (1)

Table 2. *Bond lengths* (Å) *and angles* (°) *for* $N(C_7H_8NS)_3$

S(1)—C(1)	1·702 (4)	S(1)—C(4)	1·719 (3)	S(2)—C(11)	1·702 (4)
S(2)—C(14)	1·715 (3)	S(3)—C(21)	1·697 (4)	S(3)—C(24)	1·717 (3)
N(1)—C(5)	1·261 (3)	N(1)—C(6)	1·457 (4)	N(2)—C(15)	1·257 (4)
N(2)—C(16)	1·455 (4)	N(3)—C(25)	1·244 (4)	N(3)—C(26)	1·459 (4)
N(4)—C(17)	1·457 (4)	N(4)—C(7)	1·465 (4)	N(4)—C(27)	1·467 (3)
C(1)—C(2)	1·339 (5)	C(2)—C(3)	1·407 (5)	C(3)—C(4)	1·361 (4)
C(4)—C(5)	1·446 (4)	C(6)—C(7)	1·510 (4)	C(11)—C(12)	1·344 (5)
C(12)—C(13)	1·403 (5)	C(13)—C(14)	1·360 (4)	C(14)—C(15)	1·446 (4)
C(16)—C(17)	1·510 (4)	C(21)—C(22)	1·343 (5)	C(22)—C(23)	1·410 (5)
C(23)—C(24)	1·355 (4)	C(24)—C(25)	1·454 (4)	C(26)—C(27)	1·507 (5)

C(7)—N(4)—C(17)	111·3 (2)	C(7)—N(4)—C(27)	110·9 (2)
C(17)—N(4)—C(27)	111·0 (2)	N(4)—C(7)—C(6)	112·3 (2)
C(7)—C(6)—N(1)	110·3 (3)	C(6)—N(1)—C(5)	117·7 (3)
N(1)—C(5)—C(4)	121·9 (3)	C(5)—C(4)—S(1)	121·1 (2)
C(5)—C(4)—C(3)	127·8 (3)	C(3)—C(4)—S(1)	111·0 (2)
C(4)—S(1)—C(1)	91·5 (2)	S(1)—C(1)—C(2)	112·0 (3)
C(1)—C(2)—C(3)	113·1 (3)	C(2)—C(3)—C(4)	112·3 (3)
C(15)—N(2)—C(16)	118·5 (3)	C(25)—N(3)—C(26)	118·4 (3)
N(2)—C(15)—C(14)	122·1 (3)	N(3)—C(25)—C(24)	123·1 (3)
N(4)—C(17)—C(16)	112·4 (3)	N(4)—C(27)—C(26)	113·2 (2)
C(11)—S(2)—C(14)	91·4 (2)	C(21)—S(3)—C(24)	91·9 (2)

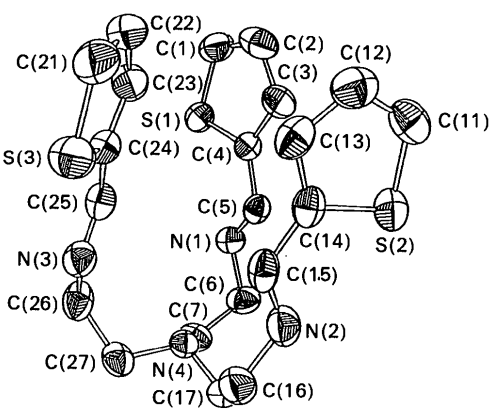

Fig. 1. View of the molecule with atom numbering.

chemically significant features. Scattering factors and anomalous-dispersion corrections from *International Tables for X-ray Crystallography* (1974). All calculations were performed on a MicroVAXII computer using *TEXSAN* (Molecular Structure Corporation, 1985). Atomic coordinates and details of molecular geometry are given in Tables 1 and 2.* Fig. 1 is a view of the molecule prepared using *TEXSAN*.

Discussion. The crystal structure contains discrete molecules separated by normal van der Waals distances. Within the S_3tren molecules, the three pendant arms of the new ligand which are bridged by the tertiary amine atom, N(4), form a pocket within which one might envisage one or two metal atoms being coordinated. Potential donor atoms are N(4), the three azomethine N atoms [N(1), N(2) and N(3)] and the three S atoms of the thiophene moieties [S(1), S(2) and S(3)]. In the free S_3tren molecules, the dihedral angles between the S(1), S(2) and S(3) plane and the plane of each thiophene ring are 91·4, 88·3 and 93·7°, respectively; this nearly perpendicular orientation of the thienyl group doubtless minimizes repulsions between the three pendant rings.

The central N(4) atom lies 0·448 Å above the triangular plane through C atoms C(7), C(17) and C(27). The N(4)—C(7), N(4)—C(17) and N(4)—C(27) bond lengths [1·462 (4) Å av.] are normal single-bond distances. The three C—N(4)—C bond angles range from 110·9 (2) to 111·3 (2)°, signifying near tetrahedral sp^3 hybridization for the N(4) atom. The N(1)—C(5), N(2)—C(15) and N(3)—C(25) bond lengths within each ligand arm are between 1·244 (4) and 1·261 (3) Å, corresponding to normal double-bond distances for these azomethine linkages. In contrast, the average of N(1)—C(6), N(2)—C(16) and N(3)—C(26) bond lengths [1·457 (4) Å] is typical for a single-bond distance. Similarly, the C(6)—C(7), C(16)—C(17) and

* Lists of structure factors, thermal parameters, calculated hydrogen coordinates and mean-plane data have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51963 (24 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

C(26)—C(27) bond distances [1·509 (5) Å av.] are normal single bonds. The C—C bonds linking the thiophene groups to the C=N bonds, *e.g.* C(4)—C(5), are shorter [1·449 (4) Å av.], indicating that conjugation occurs between the C=N and thiophene moieties. Bond distances and angles within the thiophene group are unexceptional, *e.g.* C—S 1·709 (4) Å av., C—S—C 91·6 (2)° av. Complexation studies of S_3tren are underway.

This research was initiated under an operating grant to ECA by the Natural Sciences and Engineering Research Council of Canada.

References

ALYEA, E. C., LI, B. L., XU, Z. & YOU, X. Z. (1989). In preparation.
XXVI International Conference on Coordination Chemistry (1988). *Book of Abstracts*. Porto, Portugal.
International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)
KIRCHNER, R. M., MEALLI, C., BAILEY, M., HOWE, N., TORRE, L. P., WILSON, L. J., ANDREWS, L. C., ROSE, N. J. & LINGAFELTER, E. C. (1987). *Coord. Chem. Rev.* **77**, 89–163.
MEADE, T. J. & BUSCH, D. H. (1985). *Prog. Inorg. Chem.* **33**, 59–126.
Molecular Structure Corporation (1985). *TEXSAN Structure Analysis Package*. MSC, 304 Longmire Drive, College Station, TX 77840, USA.

Acta Cryst. (1989). C**45**, 1568–1571

Anticancer Agent Development. 3. X-ray Structure of Dimethyl 1-Methoxy-6,7-methylenedioxy-4-(3,4,5-trimethoxyphenyl)-*trans*-3,4-dihydronaphthalene-2,3-dicarboxylate

BY JOHN R. PETERSON,*† HOANG D. DO AND ROBIN D. ROGERS*

The Michael Faraday Laboratories, Department of Chemistry, Northern Illinois University, DeKalb, IL 60115, *USA*

(*Received* 28 *December* 1988; *accepted* 14 *February* 1989)

Abstract. $C_{25}H_{26}O_{10}$, $M_r = 486{\cdot}48$, monoclinic, $P2_1/n$, $a = 13{\cdot}708$ (6), $b = 11{\cdot}755$ (4), $c = 15{\cdot}491$ (5) Å, $\beta = 108{\cdot}92$ (3)°, $V = 2361{\cdot}3$ Å^3, $Z = 4$, $D_x = 1{\cdot}37$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71073 Å, $\mu = 0{\cdot}66$ cm^{-1}, $F(000) = 1024$, $T = 293$ K, final $R = 0{\cdot}051$ for 1884 observed [$F_o \geq 5\sigma(F_o)$] reflections. The 3-methoxycarbonyl group and the 4-aryl ring occupy quasiaxial positions in the observed structure. There is no crystallographically imposed symmetry. Several intermolecular van der Waals interactions of note occur in this compound.

Introduction. Synthetic congeners of the American mayapple constituent podophyllotoxin have sparked much interest in recent years as anticancer agents (Beers, Imakura, Dai, Li, Cheng & Lee, 1988; Jardine, 1980). The epipodophyllotoxin derivatives etoposide and teniposide are two such therapeutically useful preparations (Kaneko & Wong, 1987; Keller-Juslen, Kuhn, Wartburg & Stahelin, 1971). The natural products and the synthetic modifications elicit their antineoplastic effect by strikingly different mechanisms, however. The natural lignans induce metaphase arrest in dividing cells by reversible binding to tubulin, which in turn disrupts mitotic spindle formation and microtubule assembly (Jardine, 1980; Loike & Horwitz, 1976). In contrast, etoposide and teniposide neither bind nor inhibit tubulin or prevent microtubule assembly at relevant concentrations. These compounds instead exert their anticancer activity by arresting cell division at the S or G_2 phase of the cell cycle through an interaction with DNA topoisomerase II (Chow, MacDonald & Ross, 1988; Kohn, 1987). The latter interaction leads to an inhibition of DNA catenation activity and the production of DNA single- and double-strand breaks. In conjunction with our synthetic investigations on the podophyllotoxins (Peterson, Winter, Do & Rogers, 1989; Peterson, Do & Rogers, 1988), we are interested in ascertaining the molecular requirements associated with the specific manifestation of each of the above biological *modus operandi*. Such knowledge is anticipated to permit the scientifically sound design of new anticancer drugs that are based upon natural product models. Herein we describe the X-ray crystal structure and an analysis of the closest contacts between neighboring molecules in the crystal lattice for dimethyl 1-methoxy-6,7-methylene-

*Authors to whom correspondence should be addressed.
†Current address: Department of Pharmacognosy, School of Pharmacy, The University of Mississippi, University, MS 38677, USA.

0108-2701/89/101568-04$03.00