$\beta = 95.1\ (1)°$; $V = 1349.7$ Å^3, $M_P = 217.87$, $d_{calcd} = 1.068$ g cm^{-3}, $d_{obsd} = 1.07$ g cm^{-3}, $Z = 4$. The measurements could be taken at room temperature, although a time-dependent decay of the intensities, which amounted to ~25% at the end of data collection, was observed, and corrected for. Of the 2662 measured reflections, 1758 were used for the refinement of the structure ($R = 8.7\%$).

The structure (Figure 1) unambiguously shows the location of the two B atoms on P and N. It is noteworthy that the N–B bond length [1.655 (8) Å] is comparable to that found in the only normal amine–borane adduct whose structure has been determined to our knowledge, namely, $Me_3N{\cdot}BH_3$ (1.638 ± 0.010 Å by microwave spectroscopy[12]). The P–B bond length [1.873 (7) Å] is short but comparable to those found in other adducts in which phosphorus has electronegative substituents.[2] The P–N bond [1.757 (4) Å] is as expected in the absence of π bonding.[13]

When BF_3 is allowed to react with **3a**, the first equivalent of BF_3 is probably coordinated to the nitrogen atom, as suggested by the low, $J_{BP} = 4.5$ Hz and $J_{PF} = 27$ Hz, couplings. This is further evidence for the strong donor character of the N atom.

In summary, all these observations indicate that the phosphorus and nitrogen atoms of these aminophosphanes behave as independent donors of comparable strengths. The behavior of these ligands with relation to transition-metal derivatives is under investigation.

Supplementary Material Available: Tables of atomic and thermal parameters and bond lengths and angles (2 pages). Ordering information is given on any current masthead page.

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[12] Cassoux, P.; Kuczkowski, R. L.; Bryan, P. S.; Taylor, R. C. *Inorg. Chem.* **1975**, *14* 126.

[13] Corbridge, D. E. C., Ed. "The Structural Chemistry of Phosphorus", Elsevier: Amsterdam, 1974.

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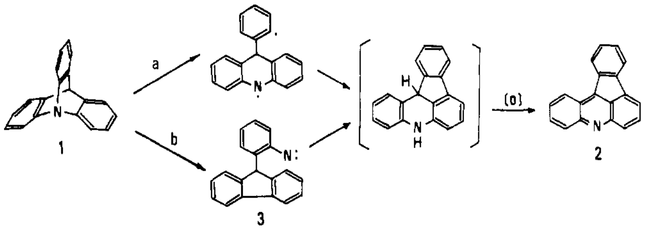
Formation of *o*-(9-Fluorenyl)phenylnitrene in the Photoisomerization of 1-Azatriptycene

Sir:

In view of the recent interest in the polar effects of substituents on the di-π-methane rearrangement[1] and the intriguing diversion therefrom of the the photorearrangement of triptycenes to give carbene intermediates,[2] it seemed to be high time to investigate the photochemical behavior of 1-azatriptycene (**1**), the first example of the di-π-methane system carrying the heteroatom at the methane position. An intriguing question about **1** is which end of the *o*-benzeno moieties will take part in the bridging: in other words, is a carbene or nitrene species formed from the bridgehead atom?

In 1964, **1** was prepared via the internal nucleophilic addition to a benzyne and subjected to UV irradiation by Wittig and Steinhoff.[3] Indenoacridine (**2**) was obtained inefficiently in acetic acid and interpreted as arising from C–N bond cleavage followed by free-radical phenylation (route a in Scheme I). We have investigated the photoreaction under various conditions, found a number of new products due to nitrene **3** in these reactions, and therefore suggest route b for **2** as well. The results are summarized in Table I.

Scheme I



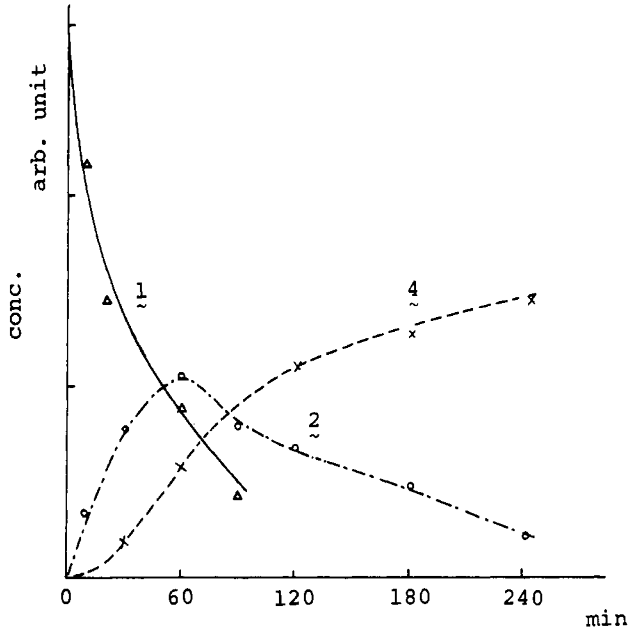


Figure 1. The appearance of products and disappearance of the starting material during the irradiation of **1** in acetic acid (0.51 mM) vs. time.

The irradiation of **1** in acetic acid with a low-pressure mercury lamp in an immersion apparatus was monitored by high-performance LC to give the results shown in Figure 1. Formation of **2** as described in the literature[3] was reproduced except that **2** was photolabile under these conditions, giving 12b-methyl-5,12b-dihydro derivative **4**, mp 151–153 °C, as a secondary product: IR (Nujol) 3370, 1580, 1290, and 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.40 (3 H, s), 6.30 (1 H, br s), and 6.8–8.0 (11 H, m). Apparently, Wittig and Steinhoff stopped the reaction at low conversion. According to the known photochemical behavior of acridines,[4] **4** can be reasoned as being formed from the ion pair consisting of the conjugate acid of **2** and acetate anion produced from the photoexcited state of **2**. Electron transfer followed by decarboxylation and recombination would give **4**.

In dilute methanolic sodium methoxide, azepine derivative **5** was isolated as orange needles, mp 162–164 °C dec, in 69% yield. In acetonitrile in the presence of TCNE, adduct **6**, colorless plates, mp 183–185 °C dec, was obtained. Structures **5** and **6** were unequivocally established by spectral data. The mass spectra of **5** and **6** showed parent peaks at *m/e* 255 and 383 [base peak at *m/e* 255 = M$^+$ – 128 (TCNE)], respectively. The 100-MHz ^{1}H NMR of **5** showed three olefinic protons, A, B, and C, at δ 4.7 (m, 10 and 4.5 Hz coupling with the C and D signals, respectively), 6.3 (t, 4.2 Hz coupling with D), and 6.7 (d, 10 Hz coupling with

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[1] For leading references see: Santiago, C.; McAlduff, E. J.; Houk, K. N.; Snow, R. A.; Paquette, L. A. *J. Am. Chem. Soc.* **1978**, *100*, 6149. Zimmerman, H. E.; Armesto, D.; Amezua, M. G.; Gannett, T. P.; Johnson, R. P. *Ibid.* **1979**, *101*, 6367.

[2] Iwamura, H.; Yoshimura, K. *J. Am. Chem. Soc.* **1974**, *96*, 2652. Iwamura, H.; Tukada, H. *Tetrahedron Lett.* **1978**, 3451.

[3] Wittig, G.; Steinhoff, G. *Liebigs Ann. Chem.* **1964**, *676*, 21.

[4] Kira, A.; Kato, S.; Koizumi, M. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1221. Castellano, A.; Catteau, J. P.; Lablache-Combier, A.; Allan, G. *Can. J. Chem.* **1973**, *51*, 3508. Vermeersch, G.; Febvay-Garot, N.; Caplain, S.; Lablache-Combier, A. *Tetrahedron* **1975**, *31*, 867.

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Table I. Conditions and Products for Irradiations of 1 and 9

run	substrate	concn, mM	solvent	addendum	conversion, %	percentage 2	4	5	6	10
1	**1**	0.51	AcOH		24	60	7	0		6
2	**1**	0.51	AcOH		>95	8	48	0		10
3	**1**	1.40	CH_3OH	CH_3ONa^a	66	0		69		0
4	**9**	0.40	CH_3OH	CH_3ONa^a	72	0		34		0
5	**1**	1.34	CH_3CN	TCNE[b]	73	5		0	74	0
6	**9**	1.31	CH_3CN	TCNE[c]	91	0.5	0	0	48	0
7	**1**·HCl	0.51	CH_3CN		64	49				
8[d]	**1**	0.067	$C_2H_5OH-CH_3OH$		47	8		≤1		41
9[d]	**9**	0.063	$C_2H_5OH-CH_3OH$	CH_3ONa	79	3.5		≤1		27

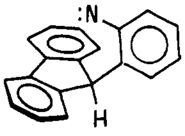
[a] 4.35 mM. [b] 2.67 mM. [c] 2.70 mM. [d] 77 K (others were at ambient temperatures).

Table II. ^1H Chemical Shifts and Coupling Data for the TCNE Adducts of 1*H*-Azepine Derivatives

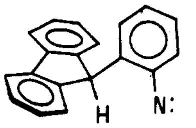
	δ H_3	$H_4{}^a$	H_5	H_6	*J*, Hz J_{45}	J_{34}	J_{56}	J_{35}
6	6.76	5.04	3.92	7.02	8.5	8.2	6.6	3.0
6a[6]	7.1	5.22	3.92	6.55	8.8	8.8	8.1	
6b[6]	6.63		3.16	6.33			7.7	1.1
6c[6]	6.93	5.22	3.80		9.0	9.2		

[a] The β-H of the enamines characteristically at high field.

A), respectively, and two methylene protons, D, at δ 3.8 (triplet-like, 4.5 and 4.2 Hz coupling with signals A and B, respectively) in addition to the aromatic multiplets at δ 7.0–7.8. The coupling pattern is consistent with the partial structure $N{-}CH^{C}{=}CH^{A}{-}CH_2^{D}{-}CH^{B}{=}$.[5] The marked similarity of the ^1H NMR of **6** to **6a–c**[6] as well as the coupling patterns leaves little doubt that the assigned structure is correct (Table II).



3a



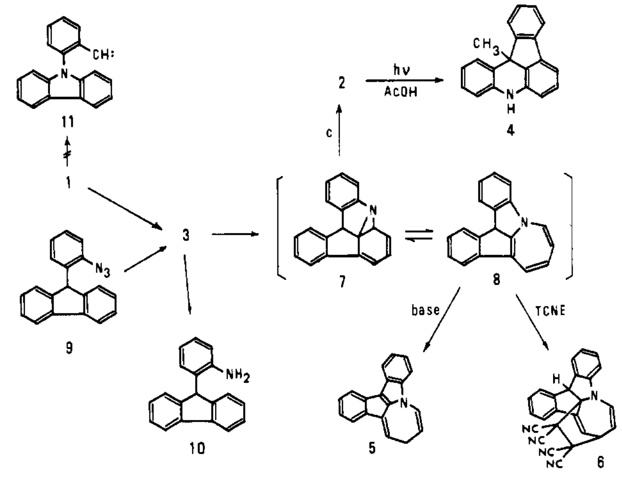
3b

The results are fully indicative of the formation of nitrene **3**. Azanorcaradiene (**7**) will be in equilibrium with 1*H*-azepine (**8**). Under acidic conditions, isomerization to the corresponding aniline will lead to the formation of the dihydroacridine (route c in Scheme II),[7] while **8** may be isolated as its tautomer **5**[5] under base catalysis and can be trapped as such in the presence of TCNE to give **6**.

Nitrene **3** was generated unambiguously by the photolysis of azide **9**[8] to give the same results but with slightly different product ratios (see Table I). The last point could be attributed to different spin states and/or conformations of nitrene **3** generated from **1** and **9** (vide infra).

Irradiation of **1** with a low-pressure mercury lamp in methylcyclohexane glass at 4.2 K produced the characteristic intense X, Y transition[9] of the triplet arylnitrene **3** (D ~1.0 cm^{-1}, E 0.0 cm^{-1}) as shown in Figure 2.[10] The observed field positions for **3** generated from **1** and **9** were 6820 and 6837 G, respectively. This slight but meaningful difference could be due to different

Scheme II



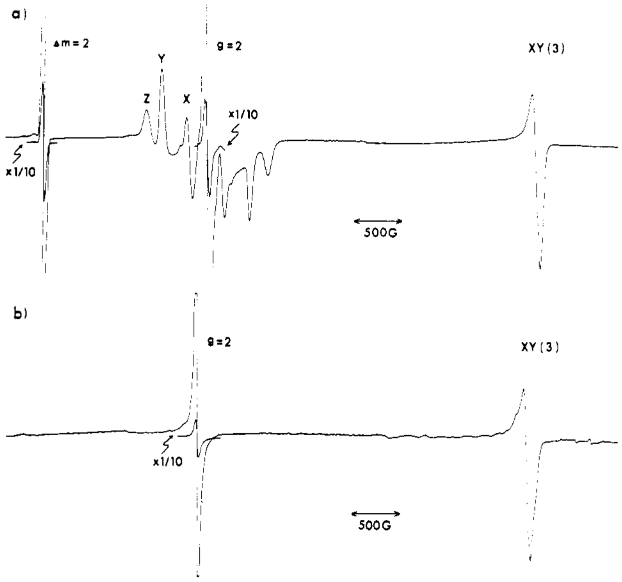


Figure 2. EPR spectra obtained on irradiating (a) **1** and (b) **9** in methylcyclohexane glass at 4.2 K. In both cases the klystron frequency was 9.30 GHz and the $g = 2$ region of the spectra showed a strong signal due to the adventitious formation of free radicals. For additional signals in (a) see note 10.

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[5] The 2,3-dihydro-2-methylene-1*H*-azepine structure obtained in the ring closure of *o*-benzylphenylnitrene (Cliff, G. R.; Collington, E. W.; Jones, G. *J. Chem. Soc. C* **1970**, 1490) is not compatible with the present NMR data.

[6] Baldwin, J. E.; Smith, R. A. *J. Am. Chem. Soc.* **1965**, *87*, 4819. Paquette, L. A.; Kuhla, D. E.; Barrett, J. H.; Leichter, L. M. *J. Org. Chem.* **1969**, *34*, 2888.

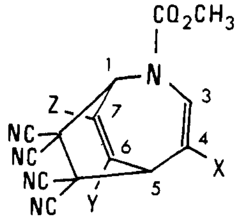
[7] For the aromatization of azepines and/or azanorcardienes to anilines under the influence of acids, see: Stohrer, W. D.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 825

[8] *o*-(9-Fluorenyl)aniline (**10**), mp 158–159.5 °C, was prepared by $AlCl_3$-catalyzed isomerization of *N*-(9-fluorenyl)aniline, colorless needles, mp 159–161 °C, which in turn was obtained by the $LiAlH_4$ reduction of fluorenone anil. Diazotization of the hydrochloride of **10** in concentrated HCl followed by treatment with sodium azide gave **9**, colorless needles, mp 140.5–141 °C. Satisfactory elemental analyses were obtained for all new compounds.

[9] For leading references see: Dürr, H.; Kober, H. *Top. Curr. Chem.* **1976**, *66*, 89. Hall, J. H.; Fargher, J. M.; Gisler, M. R. *J. Am. Chem. Soc.* **1978**, *100*, 2029. Chapman, O. L.; Sheridan, R. S.; LeRoux, J. P. *Ibid.* **1978**, *100*, 6245.

[10] Measured on a Varian E-112 EPR spectrometer (9.30 GHz) equipped with an optical transmission cavity accessory and an Oxford cryostat, the latter being connected with a helium reservoir through transfer tubing. The EPR signal of **3** from **1** was accompanied by the multiplet in the $g = 2$ region characteristic of the diradical species: D 0.060, E 0.0083 cm^{-1} and $\Delta m = 2$ at 1670 G. The resonance was not observed when **3** was generated from **9** nor when irradiation was carried out at temperatures higher than 36 K. Identification of the diradical species responsible for the signal is under way.

conformations. Nitrene **3** from **1** should be formed in the sp conformation **3a** by the least motion principle, whereas **9** is in the *ap* conformation as shown by NMR[11] and conformation **3b** should be generated at the cryogenic temperature of the glass.



6a, X = Y = Z = H
6b, X = Z = CH$_3$; Y = H
6c, X = Z = H, Y = CH$_3$

By analogy with the photochemistry of triptycenes,[2] most of the reactions at ambient temperatures are considered to be those of singlet nitrene **3** from the excited singlet state of **1**. Support for this interpretation was obtained by the finding that, when the ground-state triplet of the nitrene was populated at low temperature (runs 8 and 9 in Table I), the products were rich in the aniline derivative **10**[8] characteristic of the triplet species.

We were not able to detect any photoproducts due to a carbene species. Thus the formation of nitrene **3** in preference to carbene **11** is to be noted. There are several possible explanations for the observed high bridging regioselectivity, and they can occur at several points along the reaction coordinate of the di-π-methane rearrangement. The first point would be the geometrical nonequivalence of the two ends of the *o*-benzeno moieties in this rather rigid molecule. The C–N bond distance is expected to be somewhere between 1.42 (observed for triphenylamine) and 1.45 Å (for trimethylamine) and should be decidedly shorter than the 1.53 Å observed for the bridgehead-to-benzene C–C bond in many triptycenes.[12] Therefore, the distance between the two benzene rings for π–π overlap can be more effective at the end near the nitrogen bridgehead. Higher electronegativity of nitrogen vs. carbon may be employed to rationalize the higher stability of the initially formed aziridine-2,3-dicarbinyl diradical as compared to cyclopropyldicarbinyl diradical.[13] Rationalization for this argument is based on the inductive effect of a heteroatom on strengthening the opposite C–C bond of the three-membered ring and is supported by the findings on the effect of heteroatom on the equilibrium of the tropylidine–norcaradiene valence tautomerization. The norcaradiene structure gets more stabilized as we go from CH$_2$ through NH to O at position 7.[14] If the next step of rearrangement of the initially formed diradicals can be product controlling or the second step takes place concertedly with the first bridging, the weaker C–N bond energy relative to the C–C would be invoked. Conclusions on these points must be postponed until a more systematic study on the effect of substituents at the "methane" position on the bridging regioselectivity is completed.

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(11) The ^{1}H NMR spectrum characteristic of the *ap* conformation was observed for **9**.[2] Since the spectrum did not change in the temperature range −50–70 °C, **9** was considered to be present in the *ap* form only. Amine **10** was found to be in two forms in a ratio of *ap*:*sp* = 4:1. From the coalescence point (−11 °C) of the two singlet lines due to the 9-H of the fluorene ring, a rough estimate of the rate and the activation free energy was given as 25 s^{-1} and 13.6 kcal mol^{-1}, respectively. These values may approximate those for **3**.

(12) Anzenhofer, K; de Bohr, J. J. *Z. Kristallogr.* **1970**, *131*, 103.

(13) We thank a referee for pointing out this possibility. This explanation might, however, get into trouble if we note the finding of Zimmerman (Zimmerman, H. E.; Welter, T. R. *J. Am. Chem. Soc.* **1978**, *100*, 4131) that the methane carbon becomes electron deficient as bridging occurs to form the S_1 cyclopropyldicarbinyl diradical. An electron-deficient nitrogen will be less favored than a similar carbon.

(14) Stohrer, W.-D *Chem. Ber.* **1973**, *106*, 970. Günther, H.; Pawliczek, J. B.; Tunggal, B. D.; Prinzbach, H.; Levin, R. H. *Ibid.* **1973**, *106*, 984.

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2-(Hydroxymethyl)aspartic Acid: Synthesis, Crystal Structure, and Reaction with a Transaminase

Sir:

The interaction of transaminases with analogues of the natural substrates has been the subject of numerous investigations. Thus, dicarboxylic acids are effective inhibitors of the well-known transaminase, aspartate aminotransferase.[1-4] Of special interest is 2-methylaspartate which inhibits but appears to undergo "transimination", the initial stage in the normal enzymatic reaction.[3,5] In this paper we describe the synthesis and X-ray crystal structure of 2-(hydroxymethyl)aspartic acid and the preliminary evaluation of its interaction with cytosolic aspartate aminotransferase of pig heart. This compound is of interest both as an inhibitor and because of the possibility of attaching it through the hydroxyl group to a suitable polymeric matrix to form a material suitable for affinity chromatography of proteins that bind aspartate. Although several variations of the Strecker synthesis were attempted, as was synthesis via the hydantoin, we were able to prepare the compound only in a 3% yield by the following procedure.

To a solution of 7.50 g (73 mmol) of sodium bisulfite in 16 mL of water was added 10 g (53 mmol) of ethyl 4-acetoxyacetoacetate prepared as described by DeGraw.[6] The resulting solution was treated with 2.60 g (73 mmol) of sodium cyanide in 7.0 mL of water. After 10 min in an ice bath, the upper organic phase was separated, dried over sodium sulfite, and filtered. The colorless liquid was placed in a glass-lined pressure vessel and 100 mL of liquid ammonia was added. The mixture was allowed to stand for 24 h in the sealed reaction vessel at room temperature. After the pressure was released, the contents of the vessel were transferred to a flask with a small amount of water and were concentrated to dryness. The residue was treated with 50 mL of cold, concentrated hydrochloric acid and was allowed to warm to room temperature overnight. The solution was refluxed for 2.5 h, filtered through a small bed of Norit A charcoal, and concentrated to dryness. The residue was triturated with 20 mL of absolute ethanol and the precipitated inorganic salts were filtered off and washed with two 7-mL portions of absolute ethanol. Ethyl ether (15 mL) was added to the filtrate and the supernatant was concentrated to dryness. The residue was dissolved in 50 μL of water. The solution was neutralized with silver carbonate, filtered through Norit A, and treated with gaseous H$_2$S. The precipitated silver sulfide was removed by filtration through Norit A and the filtrate was concentrated to 10 mL. The pH was adjusted to 3.0 by addition of Dowex 50W-8X in the hydrogen form, and the final product was crystallized by addition of ethanol. The amino acid was recrystallized three times from methanol–water mixtures. The colorless needles (0.25 g, 3% yield) of racemic 2-(hydroxymethyl)aspartic acid decomposed at 188 °C; NMR (H$_2$O; NaOD) δ 2.28 (d, J = 16 Hz, 1 H), 2.65 (d, J = 16 Hz, 1 H), 3.44 (d, J = 12 Hz, 1 H), 3.66 (d, J = 12 Hz, 1 H).

The α subform of the cytosolic isoenzyme of aspartate aminotransferase was isolated from pig hearts by previously described methods.[7] Other chemicals were of reagent grade.

A rectangularly shaped, colorless crystal of approximate dimensions 0.2 × 0.2 × 0.4 mm was chosen for data collection. The positions of ten reflections which were obtained from four preliminary ω-oscillation photographs taken at various ϕ settings on a four-circle diffractometer were put into an automatic indexing program.[8] The resulting reduced cell and reduced-cell scalars indicated an orthorhombic system which was subsequently confirmed by axial photographs. Lattice constants (a = 8.921 (2), b = 9.608 (1), and c = 7.937 (1) Å) were determined by a least-squares fit to $\pm 2\theta$ measurements of 11 high-angle reflections

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(1) Jenkins, W. T.; D'Ari, L. *J. Biol. Chem.* **1966**, *241*, 5667.

(2) Michuda, C. M.; Martinez-Carrion, M. *J. Biol. Chem.* **1970**, *245*, 262.

(3) Braunstein, A. E. *Enzymes, 3rd. Ed.* **1973**, *9*, 379.

(4) Blayley, P. M.; Harris, H. E. *Eur. J. Biochem.* **1975**, *56*, 455.

(5) Fasello, D.; Giartosio, A.; Hammes, G. G. *Biochemistry*, **1966**, *5*, 197.

(6) DeGraw, J. I. *Tetrahedron* **1972**, *28*, 967.

(7) Yang, B. I.; Metzler, D. E., *Methods Enzymol.* **1979**, *62D*, 528.

(8) Jacobson, R. A. *J. Appl. Crystallogr.* **1976**, *9*, 115.

0002-7863/80/1502-7136$01.00/0