

## References

- ARNOTT, S. & DOVER, S. D. (1968). *Acta Cryst.* **B24**, 599–605.
- BURGESS, A. W. & SCHERAGA, H. A. (1975). *Proc. Natl Acad. Sci. US*, **72**, 1221–1225.
- CHOU, Y. & FASMAN, G. D. (1977). *J. Mol. Biol.* **115**, 135–175.
- COOK, W. J., EINSPAHR, H., TRAPANE, T. L., URRY, D. W. & BUGG, C. E. (1980). *J. Am. Chem. Soc.* **102**, 5502–5506.
- COTRAIT, M., GEOFFRE, S., HOSPITAL, M. & PRÉCIGOUX, G. (1979). *Acta Cryst.* **B35**, 114–118.
- DE WIED, D. (1977). *Ann. NY Acad. Sci.* **297**, 263–274.
- DE WIED, D., WITTER, A. & GREVEN, H. M. (1975). *Biochemical Pharmacology*, Vol. 24, pp. 1463–1468. Oxford: Pergamon Press.
- GARNIER, J., OSGUTHORPE, D. J. & ROBSON, B. (1978). *J. Mol. Biol.* **120**, 97–103.
- International Tables for X-ray Crystallography* (1974). Vol. IV. Birmingham: Kynoch Press.
- IUPAC-IUB COMMISSION ON BIOCHEMICAL NOMENCLATURE (1970). *Biochemistry*, **9**, 3471–3478.
- JIBSON, M. D. & LI, C. N. (1979). *Int. J. Pept. Protein Res.* **14**, 113–122.
- KARLE, I. L. (1978). *J. Am. Chem. Soc.* **100**, 1286–1289.
- KARLE, I. L. (1979). *J. Am. Chem. Soc.* **101**, 181–184.
- KOSTANSEK, E. C., THIESSEN, W. E., SCHOMBURG, D. & LIPSCOMB, W. N. (1979). *J. Am. Chem. Soc.* **101**, 5811–5815.
- MAIN, P., WOOLFSON, M. M., LESSINGER, L., GERMAIN, G. & DECLERCQ, J.-P. (1978). *MULTAN. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
- MUTTER, H., MUTTER, M. & BAYER, E. (1979). *Z. Naturforsch. Teil B*, **34**, 874–885.
- RAMACHANDRAN, J. (1973). *Hormonal Proteins and Peptides*, edited by C. H. LI, Vol. 2 pp. 1–28. New York: Academic Press.
- STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
- TOMA, F., FERMANDJIAN, S., LÖW, M. & KISFALUDY, L. (1978). *Biochim. Biophys. Acta*, **534**, 112–122.

*Acta Cryst.* (1982). **B38**, 2176–2181

**Structures of the Nitrosamides: (I) *N*-Methyl-*N*-nitroso-urea, (II) *N,N'*-Dimethyl-*N*-nitroso-urea, (III) 2-Nitroso-2-azabicyclo[2.2.2]octan-3-one and (IV) *N*-Methyl-*N*-nitroso-*p*-nitrobenzamide**

BY KEITH PROUT,\* JOHN FAIL, SANTIAGO HERNANDEZ-CASSOU† AND FANG MING MIAO‡

*Chemical Crystallography Laboratory, Oxford University, 9 Parks Road, Oxford OX1 3PD, England*

(Received 6 October 1981; accepted 15 February 1982)

**Abstract**

The crystal and molecular structures of the title compounds have been determined by X-ray methods. (I)  $C_2H_5N_3O_2$ ,  $M_r = 103.08$ , is monoclinic, with  $a = 5.302$  (1),  $b = 5.617$  (1),  $c = 15.442$  (2) Å,  $\beta = 90.09$  (1)°,  $U = 459.9$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.49$  Mg m<sup>-3</sup>, space group  $P2_1/n$ ; 725 reflections,  $R_w = 0.057$ ; (II)  $C_3H_7N_3O_2$ ,  $M_r = 117.11$ , is monoclinic, with  $a = 8.412$  (1),  $b = 9.953$  (1),  $c = 7.435$  (1) Å,  $\beta = 115.09$  (1)°,  $U = 563.8$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.37$  Mg m<sup>-3</sup>, space group  $P2_1/a$ ; 809 reflections,  $R_w = 0.057$ ; (III)  $C_7H_{10}N_2O_2$ ,  $M_r = 154.17$ , is orthorhombic, with  $a =$

$15.634$  (2),  $b = 6.966$  (2),  $c = 6.698$  (6) Å,  $U = 729.5$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.40$  Mg m<sup>-3</sup>, space group  $Pnam$ ; 540 reflections,  $R_w = 0.064$ ; (IV)  $C_8H_7N_3O_4$ ,  $M_r = 209.16$ , is triclinic, with  $a = 7.116$  (3),  $b = 8.414$  (2),  $c = 8.462$  (4) Å,  $\alpha = 103.24$  (3),  $\beta = 103.11$  (6),  $\gamma = 97.98$  (4)°,  $U = 470.5$  Å<sup>3</sup>,  $Z = 2$ ,  $D_c = 1.48$  Mg m<sup>-3</sup>, space group  $P\bar{1}$ ; 679 reflections,  $R_w = 0.052$ . The nitrosamide residue  $R-C(O)-N(NO)-R'$  is best regarded as a planar group in all four compounds. Cohesion of the crystal structures is effected by hydrogen-bonding networks in (I) and (II) and van der Waals packing forces in (III) and (IV).

\* To whom correspondence should be addressed.

† Permanent address: Universidad Autonoma de Barcelona, Departamento de Química Analítica, Spain.

‡ Permanent address: Department of Chemistry, Tianjin Teachers College, Tianjin, China.

**Introduction**

*N*-Nitroso compounds are an important group of chemical carcinogens which may represent a con-

siderable potential health hazard from their inadvertent formation from the interaction of nitrogenous food-stuffs and drugs with inorganic nitrites either added as preservatives or formed by the reduction of nitrates. Of the *N*-nitroso compounds the nitrosamides are a particularly potent group of compounds whose structural parameters appear not to have been reported, although two clearly related structures 1-(2-chloroethyl)-3-(*trans*-4-methylcyclohexyl)-1-nitrosourea (V) (Smith, Camerman & Camerman, 1978) and 2-(*N*-nitrosomethylamino)acetamide (VI) (Templeton, Templeton & Zalkin, 1973) have been determined.

### Experimental

The compounds were prepared and crystallized by Dr B. R. Brown and co-workers in the Dyson Perrins Laboratory, Oxford. The crystals were handled at all times as potent toxic agents and those for X-ray work were sealed in glass capillaries. The X-ray data were collected on an Enraf-Nonius CAD4-F diffractometer with Mo  $K\alpha$  radiation from a graphite monochromator. In each case, the unit cell and orientation matrix were determined from the least-squares best fit to the setting angles of 25 reflections.

#### Additional crystal data and data-collection parameters

(I) Space group  $P2_1/n$  [ $C_{2h}^5$ , No. 14, non-standard setting,  $\pm(x, y, z; \frac{1}{2} + x, \frac{1}{2} - y, \frac{1}{2} + z)$ ], systematic absences  $h0l, h + l = 2n + 1; 0k0, k = 2n + 1$ , Mo  $K\alpha$  radiation,  $\mu = 0.12 \text{ mm}^{-1}$ , crystal size  $0.5 \times 0.4 \times 0.3 \text{ mm}$ . Scan  $\omega/2\theta$ , scan angle  $(1.2 + 0.35 \tan \theta)^\circ$ ,  $\theta \leq 28^\circ$ , 1170 independent reflections, 725 reflections with  $I \geq 3\sigma(I)$ .

(II) Space group  $P2_1/a$  [ $C_{2h}^5$ , No. 14, non-standard setting,  $\pm(x, y, z; \frac{1}{2} + x, \frac{1}{2} - y, z)$ ], systematic absences  $h0l, h = 2n + 1; 0k0, k = 2n + 1$ , Mo  $K\alpha$  radiation,  $\mu = 0.11 \text{ mm}^{-1}$ , crystal size  $0.5 \times 0.3 \times 0.3 \text{ mm}$ . Scan  $\omega/2\theta$ , scan angle  $(1.2 + 0.35 \tan \theta)^\circ$ ,  $\theta \leq 28^\circ$ , 1360 independent reflections, 809 reflections with  $I \geq 3\sigma(I)$ .

(III) Space group  $Pnam$  [ $D_{2h}^{16}$ , No. 62, setting as for No. 33,  $\pm(x, y, z; -x, -y, \frac{1}{2} + z; \frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} + z; \frac{1}{2} + x, \frac{1}{2} - y, z)$ ] from structure analysis, systematic absences  $0kl, k + l = 2n + 1; h0l, h = 2n + 1$ . Mo  $K\alpha$  radiation,  $\mu = 0.113 \text{ mm}^{-1}$ , crystal size  $0.2 \times 0.2 \times 0.3 \text{ mm}$ . Scan  $\omega/2\theta$ , scan angle  $(1.7 + 0.35 \tan \theta)^\circ$ ,  $\theta \leq 25^\circ$ , 700 independent reflections, 540 with  $I \geq 3\sigma(I)$ .

(IV) Space group  $P1$  ( $C_1^1$ , No. 2) from structure analysis, no systematic absences. Mo  $K\alpha$  radiation,  $\mu = 0.13 \text{ mm}^{-1}$ , crystal size  $0.2 \times 0.2 \times 0.3 \text{ mm}$ . Scan  $\omega/2\theta$ , scan angle  $(1.0 + 0.35 \tan \theta)^\circ$ ,  $\theta \leq 25^\circ$ , 1651 independent reflections, 679 reflections with  $I \geq 3\sigma(I)$ .

The data were corrected for Lorentz and polarization effects but not for absorption. In each case, the structure was determined by direct methods (Main,

Lessinger, Woolfson, Germain & Declercq, 1977) [(I) 65 reflections  $1.56 < E < 3.09$ , (II) 72 reflections  $1.61 < E < 3.55$ , (III) 100 reflections  $1.18 < E < 2.79$ , (IV) 120 reflections  $1.83 < E < 3.76$ ] and refined by full-matrix least-squares analysis. H atoms were located from difference syntheses and refined with slack constraints (Waser, 1963; Rollett, 1969). In each case the H atoms were refined with isotropic thermal parameters and other atoms with anisotropic thermal parameters. The final values of  $R$  and  $R_w$  were (I) 0.041, 0.057; (II) 0.042, 0.057; (III) 0.071, 0.064 and (IV) 0.042, 0.052. In each case a Chebyshev weighting scheme (Carruthers & Watkin, 1979) was used with coefficients (I) 486, 643, 159; (II) 138, 185, 52; (III) 180, 253, 79 and (IV) 30, 40, 12. The compound (III) had been expected to have the non-centrosymmetric space group  $Pna2_1$  but the structure analysis left no doubt that the molecule has a symmetry plane and used the crystallographic mirror plane of  $Pnam$ . The Oxford CRYSTALS system (Carruthers & Watkin, 1980) was used for all calculations. Complex neutral-atom scattering factors were taken from *International Tables for X-ray Crystallography* (1974). The final atomic positions and equivalent isotropic temperature factors are given in Tables 1, 2, 3 and 4,\* and interatomic distances and inter-bond angles with e.s.d.'s calculated from the full variance-covariance matrix in Tables 5, 6, 7 and 8.

\* Lists of structure factors and anisotropic thermal parameters for all four compounds have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36786 (34 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Positional parameters ( $\times 10^4$ ) and isotropic temperature factors ( $\times 10^4$ ) for (I), with e.s.d.'s in parentheses

$U_{\text{eq}}$  values have a mean e.s.d. of  $0.0009 \text{ \AA}^2$ .

	$x$	$y$	$z$	$U_{\text{eq}}^*/U$ ( $\text{\AA}^2$ )
O(1)	3013 (3)	7503 (3)	184 (1)	457
O(2)	4706 (3)	11707 (3)	2533.2 (9)	466
N(1)	6364 (3)	6532 (3)	1018 (1)	408
N(2)	3814 (3)	9785 (3)	1368.2 (9)	316
N(3)	5305 (3)	10057 (3)	2051 (1)	375
C(1)	4374 (3)	7832 (3)	806 (1)	340
C(2)	1632 (4)	11309 (4)	1218 (1)	416
H(11)	7244 (41)	6804 (44)	1449 (13)	192 (40)
H(12)	6720 (42)	5465 (37)	651 (13)	192 (40)
H(21)	517 (49)	11286 (64)	1702 (14)	467 (46)
H(22)	845 (54)	10864 (60)	704 (14)	467 (46)
H(23)	2145 (58)	12949 (34)	1148 (19)	467 (46)

\* In Tables 1, 2, 3 and 4, for the non-hydrogen atoms,  $U_{\text{eq}} = (U_1 U_2 U_3)^{1/3}$ , where  $U_1$ ,  $U_2$  and  $U_3$  are the mean square displacements ( $\text{\AA}^2$ ) along each of the principal axes of the thermal ellipsoid.

Table 2. Positional parameters ( $\times 10^4$ ) and isotropic temperature factors ( $\times 10^4$ ) for (II), with e.s.d.'s in parentheses

$U_{eq}$  values have a mean e.s.d. of  $0.001 \text{ \AA}^2$ .

	x	y	z	$U_{eq}/U$ ( $\text{\AA}^2$ )
O(1)	6749 (2)	281 (1)	9194 (3)	491
O(2)	3518 (2)	-3207 (2)	6066 (3)	667
N(1)	7712 (2)	-1824 (2)	10241 (3)	413
N(2)	5006 (2)	-1470 (1)	7556 (2)	402
N(3)	4896 (2)	-2803 (2)	7390 (3)	499
C(1)	6573 (2)	-935 (2)	9077 (3)	386
C(2)	3588 (3)	-611 (3)	6250 (4)	562
C(3)	9396 (3)	-1411 (2)	11783 (4)	530
H(11)	7464 (34)	-2651 (22)	10020 (39)	413
H(21)	3977 (40)	286 (24)	6682 (47)	572 (50)
H(22)	2508 (32)	-834 (31)	6255 (44)	572 (50)
H(23)	3261 (39)	-819 (32)	4920 (34)	572 (50)
H(31)	10086 (43)	-2115 (30)	12561 (48)	828 (67)
H(32)	9318 (47)	-770 (33)	12663 (47)	828 (67)
H(33)	10097 (41)	-933 (34)	11296 (49)	828 (67)

Table 3. Positional parameters ( $\times 10^4$ ) and isotropic temperature factors ( $\times 10^4$ ) for (III), with e.s.d.'s in parentheses

$U_{eq}$  values have a mean e.s.d. of  $0.002 \text{ \AA}^2$ .

	x	y	z	$U_{eq}/U$ ( $\text{\AA}^2$ )
C(1)	4049 (2)	148 (5)	2500	322
C(2)	3174 (2)	-764 (4)	2500	273
C(3)	3107 (2)	-2062 (3)	637 (4)	358
C(4)	3835 (2)	-3535 (4)	619 (4)	415
C(5)	4373 (2)	-3302 (5)	2500	354
N(1)	4678 (2)	-1284 (4)	2500	341
N(2)	5508 (2)	-737 (5)	2500	489
O(1)	4213 (2)	1833 (3)	2500	522
O(2)	6010 (2)	-2090 (6)	2500	636
H(11)	2719 (22)	322 (45)	2500	242 (33)
H(12)	2544 (14)	-2722 (25)	670 (29)	408 (31)
H(13)	3136 (11)	-1303 (25)	-514 (32)	348 (31)
H(14)	3591 (11)	-4856 (34)	574 (27)	407 (32)
H(15)	4203 (12)	-3307 (29)	-555 (32)	462 (33)
H(16)	4884 (21)	-4197 (51)	2500	292 (35)

### Results and discussion

Fig. 1, 2, 3 and 4 are perspective drawings (Davies, 1981) of (I), (II), (III) and (IV) with the numbering scheme. The nitrosamide residue  $R-C(O)-N(NO)-R'$  in the title compounds is best regarded as a planar group with the dihedral angle between the  $-C(O)N-$  and  $-N(NO)$  planes varying between  $0$  (III) and  $13.4^\circ$  (IV). The relevant torsion angles are given in Table 9. In (III) the nitrosamide group lies in a crystallographic mirror plane so is necessarily planar. The nitroso  $N-O$  bonds in (I) to (IV) vary from  $1.218$  to  $1.231 \text{ \AA}$  but the

Table 4. Positional parameters ( $\times 10^4$ ) and isotropic temperature factors ( $\times 10^4$ ) for (IV), with e.s.d.'s in parentheses

$U_{eq}$  values have a mean e.s.d. of  $0.003 \text{ \AA}^2$ .

	x	y	z	$U_{eq}/U$ ( $\text{\AA}^2$ )
C(1)	1204 (6)	-5486 (5)	2653 (6)	344
C(2)	-599 (6)	-5945 (6)	1425 (6)	408
C(3)	-1950 (7)	-4929 (5)	1454 (6)	378
C(4)	-1500 (7)	-3491 (6)	2750 (6)	388
C(5)	243 (7)	-3014 (6)	3986 (6)	426
C(6)	1612 (7)	-4000 (6)	3911 (7)	414
C(7)	2802 (7)	-6429 (6)	2616 (6)	422
C(8)	3893 (11)	-9127 (8)	1881 (10)	684
N(1)	-2945 (6)	-2399 (5)	2804 (6)	501
N(2)	2354 (6)	-8179 (5)	2135 (5)	451
N(3)	533 (6)	-8918 (5)	2118 (5)	496
O(11)	-4229 (5)	-2587 (4)	1508 (5)	610
O(12)	-2786 (6)	-1363 (5)	4111 (5)	699
O(31)	265 (6)	-10433 (4)	1767 (5)	649
O(71)	4499 (5)	-5734 (4)	2970 (5)	573
H(21)	-911 (69)	-7050 (62)	489 (67)	318 (88)
H(31)	-3301 (77)	-5250 (57)	654 (64)	246 (83)
H(51)	518 (74)	-2008 (66)	4697 (66)	271 (89)
H(61)	2735 (80)	-3726 (61)	4702 (68)	337 (92)
H(81)	7661 (106)	-8272 (86)	3810 (94)	1079 (104)
H(82)	3576 (101)	-9885 (82)	971 (90)	651 (114)
H(83)	3857 (120)	-9751 (96)	2504 (106)	874 (123)

Table 5. Bond distances ( $\text{\AA}$ ) and bond angles ( $^\circ$ ) for (I), with e.s.d.'s

O(1)-C(1)	1.215 (2)	N(2)-C(2)	1.457 (2)
C(1)-N(1)	1.324 (2)	N(2)-N(3)	1.326 (2)
C(1)-N(2)	1.431 (2)	N(3)-O(2)	1.231 (2)
N(1)-C(1)-O(1)	125.8 (2)	C(1)-N(2)-N(3)	116.6 (2)
N(1)-C(1)-N(2)	116.0 (2)	N(3)-N(2)-C(2)	122.1 (2)
O(1)-C(1)-N(2)	118.3 (2)	N(2)-N(3)-O(2)	114.4 (2)
C(1)-N(2)-C(2)	121.3 (2)		

Table 6. Bond distances ( $\text{\AA}$ ) and bond angles ( $^\circ$ ) for (II), with e.s.d.'s

C(3)-N(1)	1.453 (3)	N(2)-C(2)	1.454 (3)
N(1)-C(1)	1.321 (2)	N(2)-N(3)	1.332 (2)
C(1)-O(1)	1.218 (2)	N(3)-O(2)	1.227 (2)
C(1)-N(2)	1.427 (2)		
C(3)-N(1)-C(1)	121.4 (2)	C(1)-N(2)-C(2)	122.0 (2)
N(1)-C(1)-N(2)	116.1 (2)	C(1)-N(2)-N(3)	116.7 (2)
N(1)-C(1)-O(1)	125.9 (2)	C(2)-N(2)-N(3)	121.3 (2)
O(1)-C(1)-N(2)	118.1 (2)	N(2)-N(3)-O(2)	113.9 (2)

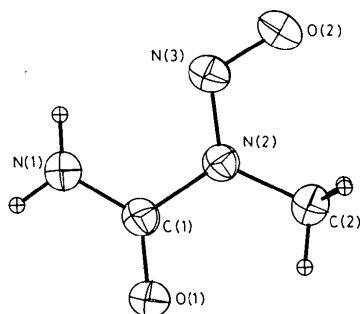
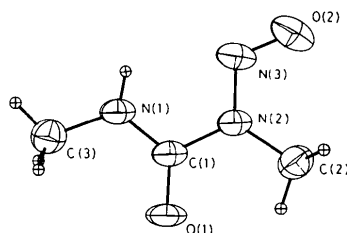
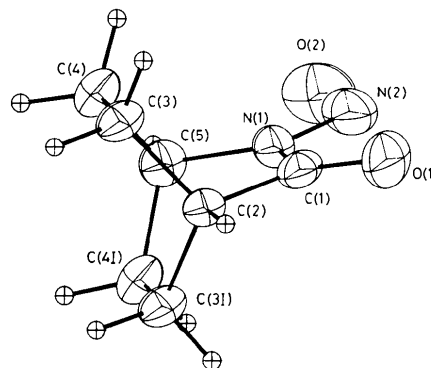
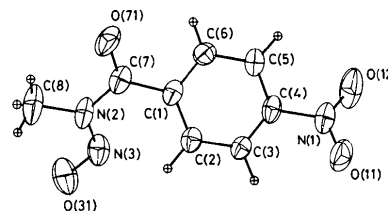
differences are probably not significant. The  $N-O$  bond length in the nitrosourea (V),  $1.218 \text{ \AA}$  (Smith *et al.*, 1978), is shorter than in (I) and (II),  $1.231$  and  $1.227 \text{ \AA}$ , but again not significantly so. In (VI) where *E* and *Z* conformers of the nitrosamine are found in the same asymmetric unit the  $N-O$  bond lengths are  $1.237$  and  $1.223 \text{ \AA}$  and may be different from each other (Templeton *et al.*, 1973) and the longer may also differ

Table 7. Bond distances (Å) and bond angles (°) for (III), with e.s.d.'s

C(1)–C(2)	1.508 (4)	C(1)–N(1)	1.401 (5)
C(2)–C(3)	1.545 (3)	N(1)–N(2)	1.353 (4)
C(3)–C(4)	1.532 (4)	N(2)–O(2)	1.227 (5)
C(4)–C(5)	1.524 (3)	C(1)–O(1)	1.201 (4)
C(5)–N(1)	1.485 (4)		
C(1)–C(2)–C(3)	107.9 (2)	C(5)–N(1)–C(1)	116.7 (3)
C(3)–C(2)–C(31)	107.8 (3)	C(1)–N(1)–N(2)	118.2 (3)
C(2)–C(3)–C(4)	110.4 (2)	N(1)–C(1)–O(1)	123.1 (4)
C(3)–C(4)–C(5)	109.4 (2)	N(1)–C(1)–C(2)	109.7 (3)
C(4)–C(5)–N(1)	106.2 (2)	C(2)–C(1)–O(1)	127.3 (4)
C(4)–C(5)–C(41)	111.6 (3)	N(1)–N(2)–O(2)	113.4 (4)
C(5)–N(1)–N(2)	125.1 (3)		

Table 8. Bond distances (Å) and bond angles (°) for (IV), with e.s.d.'s

C(1)–C(2)	1.396 (6)	N(1)–O(12)	1.212 (5)
C(2)–C(3)	1.373 (6)	C(1)–C(7)	1.476 (6)
C(3)–C(4)	1.377 (6)	C(7)–O(71)	1.204 (5)
C(4)–C(5)	1.369 (6)	C(7)–N(2)	1.405 (6)
C(5)–C(6)	1.368 (6)	N(2)–C(8)	1.467 (7)
C(6)–C(1)	1.389 (6)	N(2)–N(3)	1.352 (5)
C(4)–N(1)	1.472 (6)	N(3)–O(31)	1.218 (4)
N(1)–O(11)	1.220 (5)		
C(1)–C(2)–C(3)	120.2 (5)	O(11)–N(1)–O(12)	123.9 (5)
C(2)–C(3)–C(4)	118.2 (5)	C(6)–C(1)–C(7)	117.0 (4)
C(3)–C(4)–C(5)	123.1 (5)	C(2)–C(1)–C(7)	123.4 (5)
C(4)–C(5)–C(6)	118.3 (5)	C(1)–C(7)–O(71)	121.6 (5)
C(5)–C(6)–C(1)	120.6 (5)	C(1)–C(7)–N(2)	119.9 (4)
C(6)–C(1)–C(2)	119.5 (5)	O(71)–C(7)–N(2)	118.5 (5)
C(5)–C(4)–N(1)	118.2 (5)	C(7)–N(2)–C(8)	120.3 (5)
C(3)–C(4)–N(1)	118.7 (5)	C(7)–N(2)–N(3)	116.9 (4)
C(4)–N(1)–O(11)	117.3 (5)	C(8)–N(2)–N(3)	122.4 (5)
C(4)–N(1)–O(12)	118.8 (5)	N(2)–N(3)–O(31)	113.8 (4)

Fig. 1. Perspective view of *N*-methyl-*N*-nitroso-urea (I). In all the Figs. 1, 2, 3 and 4, thermal ellipsoids are drawn at the 50% probability level. H atoms are shown as spheres of arbitrary radius.Fig. 2. Perspective view of *N,N'*-dimethyl-*N*-nitroso-urea (II).Fig. 3. Perspective view of 2-nitroso-2-azabicyclo[2.2.2]octan-3-one (III). Symmetry code: (I)  $x, y, \frac{1}{2} - z$ .Fig. 4. Perspective view of *N*-methyl-*N*-nitroso-*p*-nitrobenzamide (IV).

significantly from the N–O of the nitrosamides (III) and (IV). In (I) to (IV) the N–N bond lengths fall into two groups. The shorter bond lengths (I) 1.326 and (II) 1.332 Å in the nitroso-ureas are in very good agreement with that of 1.333 Å found in (V) and perhaps longer than those in the nitrosamine (VI), 1.328 and 1.308 Å. The longer bond lengths are found in the nitrosamides (III) 1.353 and (IV) 1.352 Å. For the C–N(NO) bonds the nitroso-ureas have the longer bonds (I) 1.431 and (II) 1.427 Å and the nitrosamides the shorter bonds (III) 1.401 and (IV) 1.404 Å and a similar grouping is found in the carbonyl C=O bond lengths (I) 1.215 and (II) 1.218 Å in the nitroso-ureas and (III) 1.201 and (IV) 1.204 Å for the nitrosamides. The former are shorter than the C=O bonds in urea, 1.257 Å (Mullen & Hellner, 1978), and the latter shorter than in acetamide, 1.244 Å (Ottersen, 1975), and are comparable in length with ketonic carbonyl bonds. The N–C(alkyl) bond lengths are almost exactly equal at 1.455 Å for the N–C(methyl) bonds in (I), (II) and (IV) and slightly longer than in *N*-methylurea (Huiszoon & Tiemessen, 1976), but the N–C(alkyl) bond in (III), 1.485 Å, is longer, perhaps due to strain in the bicyclic system. The N–C(O)–N group of the nitroso-ureas is asymmetric with the C–N(NO) bond longer (1.43 Å mean) than in *N*-methylurea, 1.336 Å, (Huiszoon & Tiemessen, 1976) and the other C–N bonds slightly shorter (1.32 Å mean) than in *N*-methylurea, 1.340 Å. In the nitrosamides the (O)C–N(NO) bonds are longer than the corresponding bonds in acetamides (Ottersen,

Table 9. Selected torsion angles ( $^{\circ}$ )E.s.d.'s lie in the range 0.5–1.0 $^{\circ}$ .

(I)			
O(2)–N(3)–N(2)–C(2)	–0.9	N(1)–C(1)–N(2)–C(2)	–178.3
O(2)–N(3)–N(2)–C(1)	–117.7	O(1)–C(1)–N(2)–C(2)	1.7
N(1)–C(1)–N(2)–N(3)	–1.4	O(1)–C(1)–N(2)–N(3)	178.5
(II)			
O(2)–N(3)–N(2)–C(2)	0.1	C(2)–N(2)–C(1)–N(1)	–175.9
O(2)–N(3)–N(2)–C(1)	–179.6	C(3)–N(1)–C(1)–O(1)	3.1
C(2)–N(2)–C(1)–O(1)	4.1	C(3)–N(1)–C(1)–N(2)	–176.9
(III)			
N(2)–N(1)–C(5)–C(4)	–120.58	O(1)–C(1)–C(2)–C(3)	121.87
(IV)			
O(31)–N(3)–N(2)–C(7)	–176.8	N(3)–N(2)–C(7)–C(1)	–15.5
O(31)–N(3)–N(2)–C(8)	–4.5	O(71)–C(7)–C(1)–C(2)	138.5
N(3)–N(2)–C(7)–O(71)	165.4	O(71)–C(7)–C(1)–C(6)	–36.2

1975). The changes in bond lengths when ureas or amides are nitrosated represent a redistribution of the delocalized  $\pi$  electrons and are consistent with the higher Hammett  $\sigma^-$  values associated with the nitroso group [1.57 (Rae & Dyll, 1966), 1.46 (Habraken, 1968)] and the lower values associated with amides  $\text{H}_2\text{NCO}$  [0.62 (Hoefnagel & Wepster, 1973)] and ketones  $\text{Me}_2\text{CO}$  [0.82 (Hine, 1975)]. Moreover, the differences in bond lengths between the nitrosoureas and nitrosamides reflected the difference in the  $\sigma^-$  values for amide and keto groups.

The variation of bond angles in nitrosourea and nitrosamide systems tends to reflect the expected distortions of the rather overcrowded planar system. The angle at the nitroso N departs very little from  $114^{\circ}$  in these compounds and in a wide range of nitroso systems (Talberg, 1979). The amide N and the carbonyl C are strictly trigonal planar in coordination. The angles at the carbonyl C deviate substantially from  $120^{\circ}$  with, in the nitrosoureas (I) and (II), the C=O bond bending away from the N not carrying the nitroso group.

In (I), (II) and (IV) the C=O group is *trans* to the N–N bond. The molecule (III) was chosen to be constrained to a *cis* conformation. There are no significant differences in dimensions between the *cis* and *trans* conformers other than those directly attributable to the constraints of the bicyclo[2.2.2]octane system. The relatively long C–N(NO) bonds in nitrosoureas

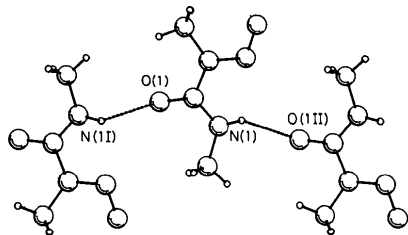


Fig. 5. The hydrogen-bonding scheme for *N,N'*-dimethyl-*N*-nitrosourea. Symmetry code: (I)  $\frac{1}{2} - x, \frac{1}{2} + y, 2 - z$ ; (II)  $\frac{1}{2} - x, -\frac{1}{2} + y, 2 - z$ .

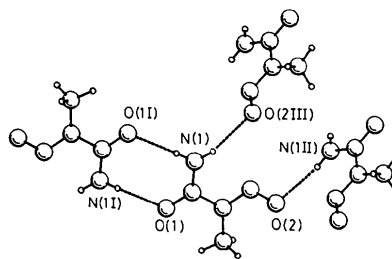


Fig. 6. The hydrogen-bonding scheme for *N*-methyl-*N*-nitrosourea. Symmetry code: (I)  $1 - x, 1 - y, -z$ ; (II)  $\frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$ ; (III)  $\frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$ .

and nitrosamides with conventionally determined (Lofthus, 1959)  $\pi$  bond orders of 0.2 and 0.3 suggest that the energy barriers between the *cis* and *trans* rotational conformers may be low. Consideration of the electrical dipolar value of the C=O and N–N(O) bonds points to the *trans* form as the more stable, that is the form found in (I), (II), (IV) and (VI) where there are no other constraints.

The dimensions of other parts of molecules (I) to (IV) are unexceptional.

Consideration of the shortest intermolecular contacts points to van der Waals packing forces for (III) and (IV), and hydrogen-bonding networks occurring in the nitrosoureas (I) and (II). In (II) weak hydrogen bonds are formed between the NH group and carbonyl group with the N...O distance 2.920 (2) Å; the hydrogen-bonding scheme is shown in Fig. 5. Each molecule is linked to two others, and this results in hydrogen-bonded chains parallel to **b**. In (I) weak hydrogen bonds are formed between the  $\text{NH}_2$  group and both the carbonyl and the nitroso oxygen atoms with  $(\text{NH}_2)\text{N}\cdots\text{O}(\text{CO})$  2.949 (2) and  $(\text{NH}_2)\text{N}\cdots\text{O}(\text{NO})$  3.057 (2) Å (Fig. 6). Each molecule is linked to three others, two hydrogen bonds to one molecule and one each to the other two. This results in a two-dimensional hydrogen-bonded network.

## References

- CARRUTHERS, J. R. & WATKIN, D. J. (1979). *Acta Cryst.* **A35**, 698–699.
- CARRUTHERS, J. R. & WATKIN, D. J. (1980). *CRYSTALS User Manual*, Oxford Univ. Computing Laboratory, Oxford.
- DAVIES, E. K. (1981). *CHEMGRAF User Manual*, Oxford Univ. Chemical Crystallography Laboratory, Oxford.
- HABRAKEN, C. L. (1968). *Recl Trav. Chim. Pays-Bas*, **87**, 1241–1242.
- HINE, J. (1975). *Structural Effects on Equilibria in Organic Chemistry*. New York: John Wiley.
- HOEFNAGEL, A. J. & WEPSTER, B. M. (1973). *J. Am. Chem. Soc.* **95**, 5357–5366.
- HUISZON, C. & TIEMESSEN, G. W. M. (1976). *Acta Cryst.* **B32**, 1604–1606.

- International Tables for X-ray Crystallography* (1974). Vol. IV. Birmingham: Kynoch Press.
- LOFTHUS, A. (1959). *Mol. Phys.* **2**, 367–371.
- MAIN, P., LESSINGER, L., WOOLFSON, M. M., GERMAIN, G. & DECLERCQ, J.-P. (1977). *MULTAN 77. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
- MULLEN, D. & HELLNER, E. (1978). *Acta Cryst.* **B34**, 1624–1627.
- OTTERSEN, T. (1975). *Acta Chem. Scand. Ser. A*, **29**, 934–944.
- RAE, I. D. & DYALL, L. K. (1966). *Aust. J. Chem.* **19**, 835–839.
- ROLLETT, J. S. (1969). *Crystallographic Computing*, edited by F. R. AHMED, pp. 169–172. Copenhagen: Munksgaard.
- SMITH, H. W., CAMERMAN, A. & CAMERMAN, N. (1978). *J. Med. Chem.* **21**, 468–471.
- TALBERG, H. J. (1979). *Structural Aspects of Nitrosobenzenes*, Department of Chemistry, Oslo Univ., Oslo.
- TEMPLETON, L. K., TEMPLETON, D. H. & ZALKIN, A. (1973). *Acta Cryst.* **B29**, 50–54.
- WASER, J. (1963). *Acta Cryst.* **16**, 1091–1095.

*Acta Cryst.* (1982). **B38**, 2181–2184

## A Photographic Method for Reconstructing Three-Dimensional Information

BY YUICHI IGA, MASAMI KUSUNOKI, NORITAKE YASUOKA AND MASAO KAKUDO

*Institute for Protein Research, Osaka University, Yamadaoka 3-2, Suita, Osaka 565, Japan*

(Received 23 December 1981; accepted 18 February 1982)

### Abstract

A photographic method for obtaining the three-dimensional coordinates of atoms constituting a Kendrew-type molecular model is described. The method is based on the fact that a photograph is a perspective projection. The method needs two photographs taken from arbitrary directions. The two-dimensional coordinates of any atom are measured on these photographs with the aid of computer graphics. The coordinates of several standard points are measured by another method, say a plumb bob and thread, and used to obtain the transformation matrix from the two-dimensional coordinates on the photographs to the three-dimensional coordinates. An accuracy of 0.3 Å is easily achieved, and the method was successfully applied to the structure analysis of cytochrome  $c_3$ .

---

At the final stage of an X-ray structure analysis of a protein crystal, model-building is usually carried out, fitting the polypeptide models of standard bond lengths and angles into the electron density map. Computer graphics systems are increasingly used for such a purpose and it is not necessary to build a structure model. Nevertheless, a protein crystallographer tends to build a model, perhaps because such a model represents the secondary and tertiary structures better, and it is easy to explain the biochemical importance of

his work. In other words, a structure model better visualizes the significance of his results.

It then becomes an important process to read out the atomic coordinates from a structure model. Some devices which do this have been described in the literature (Richards, 1968; Salemme & Frehr, 1972; Mitsui, 1979), but there may well be other methods used by protein crystallographers. It can be said that each laboratory has its own method for measuring the atomic coordinates, and any such method must be rapid as well as precise.

Here we wish to describe a photographic method to be used for such a purpose. This method uses the following procedure. Two photographs of a model are taken from any direction; it is desirable that these directions are perpendicular to each other, but information about the spatial relationship between them is not necessary. The optical density of every unit area on the photographs is converted to a digital value using a high-speed rotating drum scanner. Several standard points or atoms in the model (at least six) are read out from the model by any method. The transformation matrix can then be calculated. The two-dimensional coordinates from a set of photographs are then combined to reconstruct the three-dimensional coordinates. The method is quite general and is also applicable to other purposes. A remarkable feature of this method is the need for information on only a few points; this number is far less than the number of points to be measured.