330.32), C, 54.54; H, 3.97. Found: C, 54.48; H, 4.06.

1-(*p*-Bromophenyl)-2,2,2-trifluoroethyl tosylate (12d): mp 92–92.5 °C; NMR (CCl_4) δ 2.45 (s, 3, $ArCH_3$), 5.60 (q, 1, J = 6 Hz, $CHCF_3$), 7.5 (m, 8, Ar).

The triflates **12e**, **12f**, and **12g** were oils whose NMR spectra (CCl_4) showed the $CHCF_3$ quartet at δ 5.80, 5.74, and 5.90, respectively, and aromatic signals around δ 7.5. A correct C, H analysis was obtained for **12g**.

Products were examined by placing approximately 30 mg of tosylate or triflate in an NMR tube in 0.5 mL of the appropriate solvent and heating for 10 half-lives for solvolysis. Distinctive shifts of the $CHCF_3$ quartet (J = 6 Hz) were observed, with the following chemical shift ranges: tosylates δ 5.8–6.1, triflates δ 6.0–6.1, ethyl ethers δ 4.6–4.8, acetates δ 6.1–6.2, and trifluoroacetates δ 6.3–6.4.

The products $PhCH(OCH_2CH_3)CF_3$ (**17a**) and $PhCH(O_2CCF_3)CF_3$ (**17b**) were isolated after aqueous workup and purification by VPC (3 m × 12 mm IV-17 at 150 °C) and gave consistent NMR spectra in CCl_4 (see above) and elemental analyses: Anal. Calcd for $C_{10}H_{11}F_3O$ (**17a**; mol wt 204.20): C, 58.82; H, 5.43. Found: C, 59.14; H, 5.56. Anal. Calcd for $C_{10}H_6F_6O_2$ (**17b**; mol wt 272.16): C, 44.13; H, 2.22. Found: C, 44.03; H, 2.36. The acetate $PhCH(O_2CCH_3)CF_3$ (**17c**) has been reported previously.[22a]

Kinetics were typically measured by injecting 1.5 μL of a 0.6 M solution of the sulfonate into 1.2 mL of solvent in a 1-cm path length UV cell thermostated in the cell compartment of a Cary 118 or 210 spectrophotometer. The reactions were monitored by observing the change in the UV absorption at a position near 260 nm, which gave a maximum absorbance change for the particular sulfonate and solvent.

For runs at higher temperatures aliquots were sealed in glass ampules and withdrawn from a constant temperature bath at appropriate intervals and stored in the freezer. When all the samples had been withdrawn, the absorbances of each of the solutions were measured. An acetolysis rate for **12b** was also measured by titration and gave the same rate constant as the spectrophotometric method.

Polarimetric rates were monitored by using a Perkin-Elmer 141 polarimeter with a 1-mL water-jacketed cell with a 10.0-cm path length, which was maintained at 25.0 °C as measured with a thermocouple. The substrate (*R*)-(−)-**12e** was unstable in an isolated state so freshly prepared material was dissolved in ether to give a 0.073 M stock solution that could be stored in the freezer for months without apparent decomposition. For kinetic runs 1 mL of the stock solution was evaporated on the rotary evaporator. For rate measurements in EtOH the solvent was added to the flask, and the solution transferred to a volumetric flask that was made up to 5 mL. Rates in other solvents were more rapid so the dry triflate was quickly dissolved in 2 mL of the temperature equilibrated solvent by drawing in and out of a pipet, and the solution was promptly transferred to the cell. Mixing and transfer required 70 s, and the first reading could be made 20 s later. Typically 10–20 readings were made over at least 2 half-lives, and excellent first-order kinetics (correlation coefficients always at least 0.999) were obtained. Rates were monitored at 365, 436, and 546 nm, with no difference in measured rate constants.

Runs in TFA and HFIP were conducted in which the reaction was quenched after 1 or 2 half-lives for the UV rates by pipetting the solution into pentane and ice water and separating the pentane layer, which was washed with $NaHCO_3$ and NaCl solutions and evaporated. The product was dissolved in CCl_4 and the NMR spectrum recorded to determine the relative amounts of reactant and product from the integrals of the $PhCH(OS)CF_3$ resonances. The solution from the NMR measurement was diluted with more CCl_4 and the optical rotation measured. Control experiments in which the reactant was subjected to the workup procedure without exposure to the TFA or HFIP solvent showed that with rapid handling no change in the NMR or optical rotation was observed. The results of these experiments are given in Table III.

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Registry No. 12a, 84877-43-0; **12b**, 84877-44-1; **12c**, 13652-13-6; **12d**, 84877-45-2; **12e**, 84877-46-3; (*R*)-(−)-**12e**, 84877-47-4; **12f**, 84877-48-5; **12g**, 84877-49-6; **13c**, 434-45-7; **14c**, 340-04-5; **17a**, 65432-43-1; **17b**, 84877-50-9; **17c**, 17659-26-6; D, 7782-39-0.

Stereochemistry of Conformationally Restricted Analogues of the Antitumor Agent ICRF-159. 2.[1] Structures of Antimetastatically Active and Inactive Isomers of a Tricyclic Analogue

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Abstract: Crystal structure determinations of antimetastatically active and inactive isomers (*cis*- and *trans*-tetrahydrodipyrazino[1,2-*a*:2′,1′-*c*]pyrazine-1,3,10,12(2*H*,4*H*,9*H*,11*H*)-tetrone) of a tricyclic analogue of the antitumor agent ICRF-159 have been carried out. Comparisons of stereochemical parameters with those of the active cis cyclopropyl derivative of ICRF-159 have allowed conclusions to be reached regarding the molecular basis for the difference in activity in the tricyclic compounds. The trans-anti-trans isomer crystallizes in two solvated forms: crystals of the trans isomer in H_2O are triclinic, space group $P\bar{1}$ with cell constants a = 11.686 Å, b = 8.168 Å, c = 6.836 Å, α = 103.63°, β = 90.23°, γ = 112.83°, and two molecules per cell; crystals of the trans isomer in $(CH_3)_2SO$ are orthorhombic, space group *Pbcn*, a = 17.80 Å, b = 8.99 Å, c = 18.20 Å, with eight molecules per cell. Both structures were elucidated; the molecular conformations in the two crystals are virtually identical. Crystals of the cis-syn-trans tricyclic isomer are triclinic, space group $P\bar{1}$, with a = 6.33 Å, b = 7.35 Å, c = 13.70 Å, α = 116.61°, β = 94.95°, γ = 105.48°, and two molecules per unit cell.

The physiological and biochemical mechanisms underlying the processes of metastasis and the sites of action and effects of antineoplastic agents on metastatic tumor development are far from being well understood. Both for development of clinically useful drugs and for mechanistic studies, production of potent antimetastatic agents with defined stereochemistries is highly desirable.

Experiments with conformationally restricted cyclopropane analogues of the cytostatic agent ICRF-159 (**1**) have indicated that the cis isomer (**3**) has antimetastatic activity while the trans

(1) For part 1, see: Hempel, A.; Camerman, N.; Camerman, A. *J. Am. Chem. Soc.* **1982**, *104*, 3456–3458.

(2) (a) University of Toronto. (b) University of Washington.

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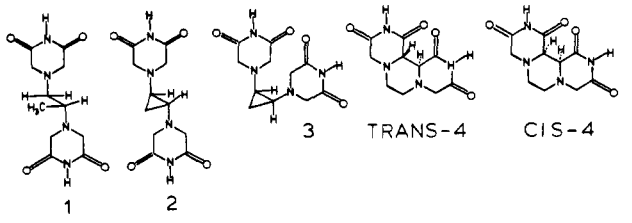

(**2**) stimulates metastasis in hamster lung adenocarcinoma[3] and murine B16 melanoma[4] models. To try to achieve greater potency and to overcome synthetic and solubility problems that limit the usefulness of the cyclopropyl analogues as mechanistic probes, Witiak et al.[5] synthesized tricyclic congeners (**4**) of the antimetastatic cis cyclopropane analogue and tested them in the B16 melanoma model. Although both tricyclic isomers ostensibly retain the "cisoid" relationship of dioxopiperazine rings characteristic of *cis*-**3**, and both exhibit similar solubility properties, only the trans-anti-trans (*trans*-**4**) stereoisomer displayed antimetastatic activity. We have crystallized and elucidated the three-dimensional structures of both tricyclic analogues in order to establish their conformational features, to compare them with the previously determined structures of ICRF-159[6] and the cis cyclopropyl analogue,[1] and to seek stereochemical bases for their differing activities. The *trans*-**4** compound crystallizes in two polymorphic forms, depending on the solvent; we report the structures of both forms here.

Experimental Section

Samples of *trans*-**4** and *cis*-**4** were supplied by D. T. Witiak and B. K. Trivedi. Two different crystal forms of *trans*-**4** were obtained by solvent evaporation from aqueous ethanol (shown by the structure determination to be the monohydrate) and from $(CH_3)_2SO$ (*trans*-**4**·$(CH_3)_2SO$ solvate); crystal data are given in Table I.

A. *trans*-4·H_2O. Intensity data were collected from a colorless prism of dimensions 0.2 × 0.3 × 0.5 mm on an automated diffractometer using Cu Kα radiation and $\theta/2\theta$ scan. Of 1977 independent reflections in the range $0 < 2\theta < 130°$, 1592 had $I > 3\sigma(I)$ and were used in the structure refinement. The intensities were corrected for background, an empirical ϕ correction for absorption was applied, and structure amplitudes were derived in the usual manner.

The solution of the crystal structure was achieved by using the direct phasing program MULTAN80. Input were 322 reflections with $|E| > 1.38$, and the E map based on the best set of phases allowed identification of all nonhydrogen atoms, including the oxygen atom of the water molecule. Refinement by anisotropic full-matrix least-squares followed by difference electron density calculations led to positions for all hydrogen atoms and to a final discrepancy index $R = 0.047$ for the observed reflections (in the course of the refinement procedure, nine low-index reflections exhibiting severe secondary extinction ($|F_c| \gg |F_o|$) were excluded). All parameters were refined except hydrogen atom temperature factors, which were held constant at $B = 2.14$ Å^2 (the mean of the isotropic values of the atoms to which they are bonded). Scattering factors were as cited for the heavy[7] and hydrogen atoms.[8] Table II lists the fractional coordinates for the non-hydrogen atoms; anisotropic thermal parameters, hydrogen atom coordinates, and tables of observed and calculated structure factors are deposited as supplementary material.

B. *trans*-4·$(CH_3)_2SO$ Solvate. The X-ray diffraction intensities deteriorated markedly when collected in air, so a needle of dimensions 0.10 × 0.15 × 0.5 mm was stabilized by sealing it in a capillary together with mother liquor, and data collection was carried out by the procedures described above. A total of 2504 independent data were measured, of which 1745 were classified as observed. The solution and refinement of the structure was performed as outlined for *trans*-4·H_2O. Refinement of all parameters except hydrogen atom temperature factors (fixed at $B = 2.8$ Å^2) converged at $R = 0.047$ for the observed data. Heavy-atom coordinates are presented in Table II; other parameters and structure factors are listed in the supplementary material.[9]

C. *cis*-4. A colorless prism (from aqueous ethanol) of dimensions 0.2 × 0.2 × 0.4 mm was used for data collection as described above. Of 1629 independent reflections in the range $0 < 2\theta < 110°$, 1474 were considered

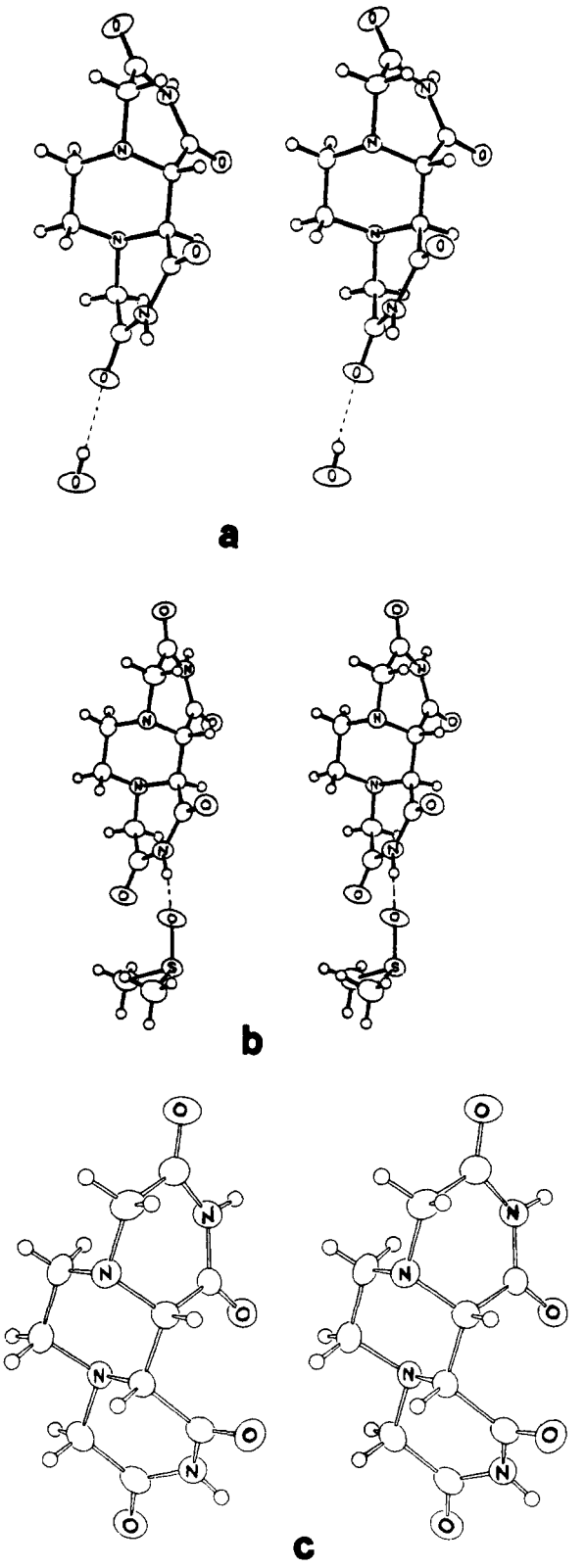

Figure 1. Stereoscopic drawings of the structures of (a) *trans*-4·H_2O, (b) *trans*-4·Me_2SO, (c) *cis*-**4**.

(3) Witiak, D. T.; Lee, H. J.; Goldman, H. D.; Zwilling, B. S. *J. Med. Chem.* **1978**, *21*, 1194–1197.
(4) Zwilling, B. S.; Campolito, L. B.; Reiches, N. A.; George, T. J.; Witiak, D. T. *Br. J. Cancer* **1981**, *44*, 578–583.
(5) Witiak, D. T.; Trivedi, B. K.; Campolito, L. B.; Zwilling, B. S.; Reiches, N. A. *J. Med. Chem.* **1981**, *24*, 1329–1332.
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(9) See paragraph at end of paper regarding supplementary material.

Table I. Crystal Data

	trans-4·H_2O	*trans*-4·$(CH_3)_2SO$	*cis*-4
formula	$C_{10}H_{12}N_4O_4 \cdot H_2O$	$C_{10}H_{12}N_4O_4 \cdot (CH_3)_2SO$	$C_{10}H_{12}N_4O_4$
M_r	270.24	330.36	252.15
crystal system	triclinic	orthorhombic	triclinic
space group	$P\bar{1}$	*Pbcn*	$P\bar{1}$
a, Å	11.686 (5)	17.802 (7)	6.330 (5)
b, Å	8.168 (4)	8.986 (4)	7.354 (5)
c, Å	6.838 (4)	18.195 (7)	13.702 (7)
α, deg	103.63 (8)	90	116.61 (8)
β, deg	90.23 (8)	90	94.95 (8)
γ, deg	112.83 (8)	90	105.48 (8)
no. of molecules in unit cell	2	8	2
density (calcd), g cm^{-3}	1.53	1.47	1.52
linear absorption coeff, cm^{-1}	10.75	21.66	10.34

to be observed. The solution and refinement (all parameters except hydrogen atom temperature factors, which were fixed at $B = 2.14$ Å^2) of the structure was accomplished by procedures similar to those used for the *trans*-4 crystals. The final residual was $R = 0.046$ for the observed data, except for eight omitted low-index reflections that demonstrated severe secondary extinction. Heavy-atom coordinates are listed in Table II; structure factor tables and other atomic parameters are listed in the supplementary material.[9]

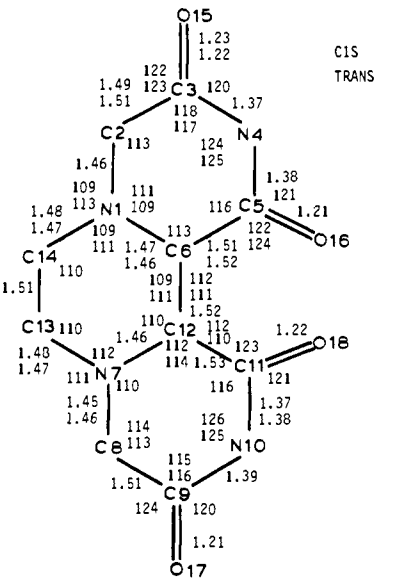

Figure 2. Atomic numbering scheme and bond distances and angles in *cis*-4 (upper numbers) and *trans*-4 (lower numbers, averaged values over the two *trans*-4 structures). Estimated standard deviations are 0.003–0.004 Å and 0.2–0.3°. A single number indicates identical values for both isomers.

Results and Discussion

Stereoscopic views of the molecular conformations in all three of the crystal structures are shown in Figure 1, and the atomic numbering scheme and bond parameters are given in Figure 2. The results confirm the geometries of the isomers: (1) the C14–N1 and C13–N7 bonds are cis to each other with N1–C14–C13–N7 torsion angles of 59°, 61°, and 56° in *trans*-4 hydrate, *trans*-4 solvate, and *cis*4, respectively (cf. with 0° and 138° in the crystal structures of the cis and trans cyclopropyl analogues[1] and 56° in racemic ICRF-159[6]), resulting in a "cisoid" relationship of the piperazinedione rings in both isomers; (2) the C5–C6–C12–C11 torsion angles are 157°, 159°, and 61° in the three structures, confirming the tricyclic trans-anti-trans and cis-syn-trans natures of *trans*-4 and *cis*-4.

The conformations of *trans*-4 in the hydrated and $(CH_3)_2SO$-solvated crystal structures are virtually identical. Bond lengths and angles, torsion angles within the molecules, and ring conformations do not differ significantly in the two structures (maximum deviation from mean = 3σ). The only effect of the different solvation molecules appears to be on the crystal packing arrangement.

The ring conformations in both isomers are similar. The piperazinedione rings form slightly bowed half-chairs, with the tetrahedral nitrogen atoms (N1, N7) lying 0.61–0.64 Å out of the plane of the carbon atoms and the trigonal nitrogen atoms being 0.0–0.1 Å from the plane in the same direction; the same conformational characteristics are present in these rings in the structures of both racemic and enantiomeric ICRF-159[6] and in the cis and trans cyclopropyl analogues.[1] The central rings have chair conformations in the two molecules. The corresponding bond distances and angles in *trans*-4 and *cis*-4 are in close agreement with each other (maximum deviation from mean = 3σ) and with accepted values.

Both tricyclic isomers were designed as relatively rigid structural analogues of the cis cyclopropane derivative of ICRF-159 in which the "cisoid" relationship of the piperazinedione rings, correlated with antimetastatic activity,[3] was retained. Only the *trans*-4 isomer demonstrated antimetastatic activity;[5] *cis*-4 was inactive.[5] For

Table II. Fractional Atomic Coordinates (×10^4)

	trans-4·$(CH_3)_2SO$			*trans*-4·H_2O			*cis*-4		
atom	*x*	*y*	*z*	*x*	*y*	*z*	*x*	*y*	*z*
N1	5769 (2)	3171 (3)	4549 (1)	7133 (2)	3792 (2)	4958 (3)	8393 (3)	1561 (3)	2921 (1)
C2	5799 (2)	1639 (4)	4809 (2)	7318 (2)	2175 (3)	3851 (3)	6682 (4)	2786 (3)	3787 (2)
C3	6504 (2)	804 (4)	4597 (2)	8314 (2)	1818 (3)	4859 (3)	5943 (3)	1473 (3)	4189 (2)
N4	6895 (2)	1348 (3)	4004 (2)	8592 (2)	2563 (3)	6897 (3)	7313 (3)	−455 (3)	3995 (1)
C5	6650 (2)	2464 (4)	3551 (2)	7954 (2)	3440 (3)	8128 (3)	9492 (3)	−1064 (3)	3672 (2)
C6	5909 (2)	3200 (4)	3764 (2)	6908 (2)	3669 (3)	7049 (3)	10214 (3)	284 (3)	3263 (2)
N7	6384 (1)	5763 (3)	3891 (1)	7635 (2)	7055 (2)	8121 (3)	12751 (3)	363 (3)	2051 (1)
C8	6354 (2)	7265 (4)	3589 (2)	7264 (2)	8546 (3)	9095 (3)	14416 (3)	−862 (4)	1175 (2)
C9	5577 (2)	7892 (4)	3519 (2)	6053 (2)	8357 (3)	8113 (4)	13688 (3)	−2528 (3)	174 (2)
N10	4996 (2)	6883 (3)	3440 (2)	5158 (2)	6567 (3)	7499 (3)	11960 (3)	−3191 (3)	350 (1)
C11	5081 (2)	5354 (4)	3416 (2)	5341 (2)	5029 (3)	7648 (3)	11037 (3)	−2640 (3)	1344 (2)
C12	5888 (2)	4789 (4)	3471 (2)	6665 (2)	5295 (3)	8254 (3)	11922 (3)	−1024 (3)	2330 (2)
C13	6200 (2)	5725 (4)	4675 (2)	7905 (2)	7125 (3)	6014 (3)	10967 (4)	1796 (3)	1773 (2)
C14	6287 (2)	4147 (4)	4946 (2)	8206 (2)	5527 (3)	4966 (3)	9237 (4)	3019 (3)	2684 (2)
O15	6720 (2)	−309 (3)	4911 (1)	8852 (2)	916 (3)	3932 (3)	4201 (2)	2109 (2)	4712 (1)
O16	6996 (1)	2773 (3)	3002 (1)	8209 (2)	3942 (2)	9939 (2)	10773 (3)	−2500 (2)	3789 (1)
O17	5447 (1)	9230 (3)	3507 (2)	5829 (2)	9620 (2)	7858 (3)	14533 (3)	−3292 (3)	−730 (1)
O18	4542 (1)	4558 (3)	3318 (1)	4467 (1)	3545 (2)	7341 (3)	9626 (2)	−3428 (2)	1418 (1)
O19	6427 (1)	1803 (1)	6727 (1)	9661 (2)	−1645 (3)	1406 (3)			
S20	6692 (1)	356 (3)	7053 (2)						
C21	7546 (2)	−77 (5)	6602 (2)						
C22	6120 (2)	−1064 (4)	6667 (2)						

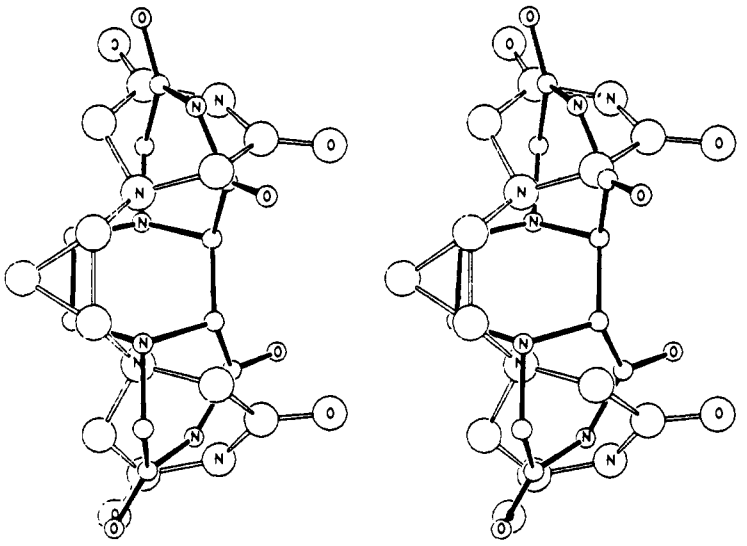

Figure 3. Stereoscopic superposition of *cis*-**3** (large circles, light bonds) and *trans*-**4**. Hydrogen atoms are omitted.

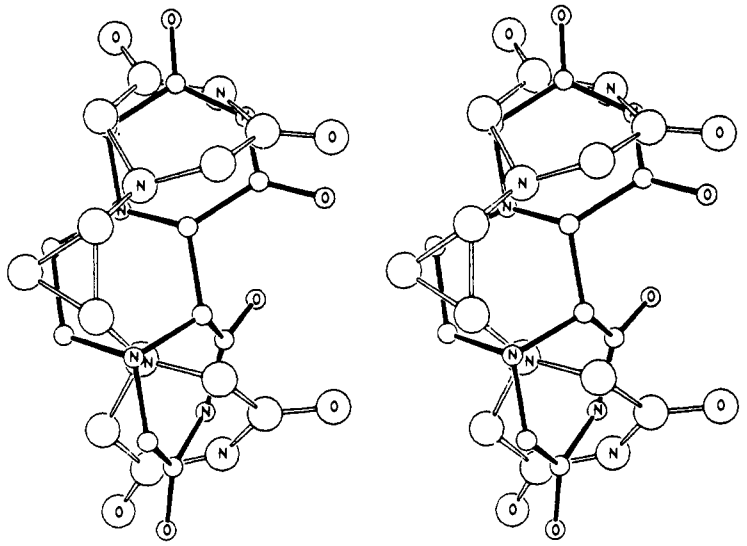

Figure 4. Stereoscopic superposition of *cis*-**3** (large circles, light bonds) and *cis*-**4**. Hydrogen atoms are omitted.

the development both of chemotherapeutic agents and of probes for a better understanding of the mechanisms of the metastatic process, it is of paramount importance to try to correlate the differing activities of the tricyclic isomers with differences in their stereochemical features. Figures 3 and 4 are stereoscopic superpositions of the structures of *trans*-**4** and *cis*-**4**, respectively, with the observed[1] crystal structure conformation of the cytostatic cis cyclopropane ICRF-159 analogue; the 12 atoms of the piperazine rings in each were maximally fitted in the superpositions. Several observations are noteworthy. Although the relationship of the piperazine rings in the tricyclic compounds is "cisoid", the rings are no longer oriented in a "face-to-face" manner with respect to each other as is the case for the cis cyclopropyl derivative (*cis*-**3**) or for the observed[6] cis conformation of ICRF-159; the C6–C12 bond prevents this and imposes a more nearly perpendicular arrangement of the rings in both isomers. Nevertheless, as may be seen in Figure 3, the spatial positions of the functional groups (oxygen and nitrogen atoms) in *cis*-**3** and *trans*-**4**, and their intramolecular separations, are roughly similar; this is shown quantitatively in Table III. Figure 4, on the other hand, shows that while spatial relationships among many of the functional groups in *cis*-**3** and *cis*-**4** are also similar, they differ significantly for one of the oxygen atoms (O18 in the *cis*-**4** structure). Thus (Table III) the inter-ring separation between O16 and O18, the "proximal" oxygen atoms attached to the piperazine rings, is only 3.07 Å in *cis*-**4**, compared to 4.59 and 4.68 Å in *trans*-**4** and the cis cyclopropyl analogue, respectively. Similarly, intramolecular distances between O18 and other functional atoms in *cis*-**4** are also constrained to be smaller than in the antimetastatically active compounds (Table III).

Table III. Selected Intramolecular Separations (Å) between Functional Groups

	compound		
distance	cis cyclopropyl	*trans*-4	*cis*-4
N1–N7	2.97	2.87	2.85
N4–N10	6.41	6.04	5.29
distal O15–O17	8.57	8.98	9.07
proximal O16–O18	4.68	4.59	3.07
N4–O18	5.92	5.18	3.41
O15–O18	7.77	6.51	5.24

Although the cis cyclopropyl compound possesses conformational mobility with respect to the orientations of the piperazine rings, it is reasonable to conclude from the differing activities and stereochemistries of the more rigid tricyclic isomers that antimetastatic activity in the ICRF-159 class of compounds is conferred by a conformation not very dissimilar from the one observed in the crystal structure of *cis*-**3**, i.e., one that results in the spatial relationships present in *cis*-**3** (or *trans*-**4**) for some or all of the functional groups. Further, it is not unreasonable to

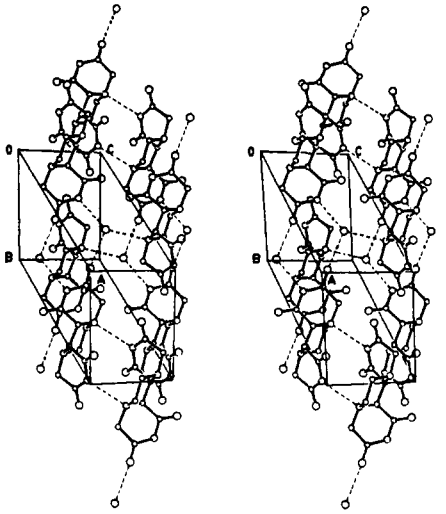

Figure 5. Stereoscopic representation of the molecular packing in the crystal of *trans*-**4**·H_2O.

speculate that one of the important stereochemical features for cytostatic action is an inter-ring separation of "proximal" oxygen atoms of about 4.5 Å; C6–C12 bond formation results in an interatomic O···O distance in *trans*-**4** compatible with that in *cis*-**3** and with activity, but in *cis*-**4** it results in a conformation in which the separation of "proximal" oxygens is constrained to be too short and therefore presumably incapable of interacting with some "receptor" system.

The crystal packing arrangements are quite different in the three crystal structures reported here. The most extensive system of hydrogen bonding occurs in *trans*-**4** monohydrate (Figure 5), in which the molecules are linked as dimers by a pair of N10–H···N1 hydrogen bonds, and the dimers are interconnected to other dimers through water molecules, each of which is a hydrogen donor to an oxygen and tetrahedral nitrogen atom and a hydrogen acceptor from N4–H. In the structure of *trans*-**4**·$(CH_3)_2SO$ solvate, the only hydrogen bonds are from N10–H to the $(CH_3)_2SO$ oxygen and a weak interaction between N4–H and N7 of another molecule. The molecular arrangement in *cis*-**4** consists of chains of molecules linked by two N–H···O bonds at each end, similar to the situation in the cis cyclopropane analogue of ICRF-159,[1] with only van der Waals interactions between chains.

Acknowledgment. We thank D. T. Witiak and B. K. Trivedi for supplying the title compounds. Financial support from the Medical Research Council of Canada and from a USPHS grant (CA15879) is gratefully acknowledged.

Registry No. *trans*-**4**·H_2O, 84924-33-4; *trans*-**4**·Me_2SO, 84894-19-9; *cis*-**4**, 84894-20-2.

Supplementary Material Available: A listing of observed and calculated structure factors, hydrogen atom coordinates, and heavy-atom anisotropic thermal parameters for all three structures (39 pages). Ordering information is given on any current masthead page.

Stereochemistry of the Sakurai Reaction. Additions to Cyclohexenones and Cycloheptenones

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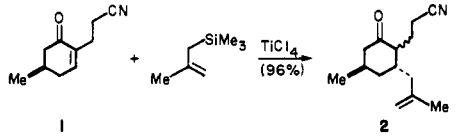
Abstract: The $TiCl_4$-mediated reactions of allyltrimethylsilane (Sakurai reaction) with cyclic enones **3–7** have been investigated. The stereochemistry of these reactions has been compared with the stereochemistry of the copper-catalyzed conjugate addition of *n*-propylmagnesium bromide with the same set of enones. It is shown that the major products formed in the Sakurai reactions are those favored on stereoelectronic grounds. In each case the copper-catalyzed Grignard addition affords less of the stereoelectronically preferred product, presumably as a result of steric hindrance to approach of the bulky cuprate cluster to the Lewis acid coordinated enone.

In our recent *Lycopodium* alkaloid synthesis we employed Sakurai's method for the conversion of cyanoenone **1** into compound **2**, in which the methallyl group has been introduced ex-



clusively trans to the methyl group at C-5.[1] This result represents a substantial improvement over the use of lithium dimethallylcuprate, which gives a mixture of products from which cyano ketone **2** can be isolated in only 66% yield. In addition, the allylsilane procedure is relatively simple compared with the lengthy and tedious procedures required for the preparation of allyllithium reagents.[2] Because of these desirable properties, we have carried out a systematic investigation of the stereochemistry of the Sakurai reaction with conformationally flexible α,β-unsaturated ketones. In this paper we report the results of additions to methylcyclohexenones **3**[3] and **4** and methylcycloheptenones **5–7**.[4]

Results

Allylsilane additions were carried out in the normal manner.[5,6] Reaction products were analyzed by ^{13}C NMR spectroscopy and,

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