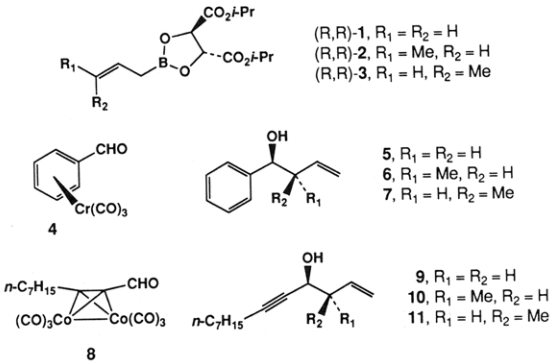
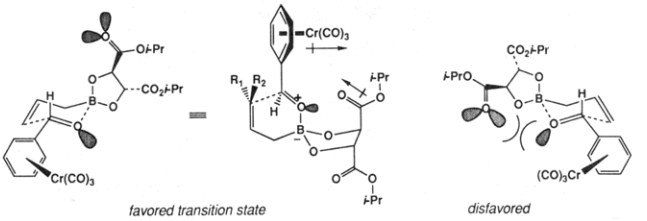
the enantioselectivity of the allyl- and crotylborations of α,β-unsaturated aldehydes is poor (62–74% ee for (*E*)-decenal and **1-3**),[5] and the masked acetylene unit of **8** can be viewed as a synthetic equivalent of both *E* and *Z* olefins in the reaction products. 2-Decynal, too, is a poor allylboration substrate: the reactions with **1–3** under standard conditions provide **9–11** with enantiomeric excesses of only 72%, 72%, and 58%, respectively. *It is thus significant that the reactions of* ***8*** *with (R,R)-**1**, (R,R)-**2**, and (R,R)-**3** (toluene, −78 °C, 4-Å sieves) followed by oxidative decomplexation (Fe(NO$_3$)$_3$, EtOH, 23 °C) provide* ***9***[10] *(92% ee),* ***10***[10] *(96% ee; 97:3 anti to syn), and* ***11***[10] *(86% ee; 97:3 syn to anti) in 85–95% yield.* Here again, the absolute stereochemical outcome is the same with both 2-decynal and the dicobalt hexacarbonyl complex **8**.[11]



These examples clearly demonstrate that the enantioselectivity of the asymmetric allylborations of aryl and propargylic aldehydes may be significantly improved by using appropriate metal carbonyl derivatives. The origin of this effect, however, cannot be explained by invoking previously established principles of metal carbonyl chemistry.[1-3] For example, while the Cr(CO)$_3$ unit of **4** is well known to have a significant inductive effect, comparable to a *p*-NO$_2$ substituent,[1c] this electronic effect is not responsible for the increased enantioselectivity: the allylboration of *p*-nitrobenzaldehyde with **1** proceeds with the same enantioselectivity as PhCHO.[12] The increased enantioselectivity also does not appear to be due to a steric effect, since the bulky metal carbonyl units can be positioned away from the allyl group in both the favored and disfavored transition states as indicated below for the reaction of **4**. Moreover, in the asymmetric allylborations of hindered substrates (e.g., pivalaldehyde) with **2** and **3**, enantioselectivity in fact decreases relative to less sterically demanding substrates.[5] Rather, we speculate that the stereochemically preferred transition state is stabilized by a favorable dipole–dipole interaction between the tartrate ester and the metal carbonyl unit as indicated in the three-dimensional structure presented below for **4**.[1c,13] Such interactions are possible only in the favored transition state.



In summary, we have shown that the enantioselectivity of the asymmetric allylborations of certain unsaturated aldehydes is significantly improved by using metal carbonyl derivatives as substrates. These results are also of considerable interest since the reaction products are chiral organometallic complexes that are potential substrates for a range of stereoselective transition metal mediated organic reactions, a line of investigation that we are actively pursuing.

Acknowledgment. This research was supported by a grant from the National Institute of General Medical Sciences (GM 38436).

(10) Satisfactory ^{1}H NMR, IR, mass spectra, and C, H analytical data were obtained for this compound.

(11) The relative and absolute stereostructures of **9–11** have been assigned by hydrogenation of each to the corresponding tridecanols that have been correlated with materials prepared by the Sharpless asymmetric epoxidation reactions (ref 8a,b).

(12) The asymmetric allylborations of para-substituted benzaldehydes (NO$_2$, Br, H, Me, OMe) proceed with 70–72% ee using **1** in THF: Roush, W. R.; Hoong, L. K., unpublished.

(13) (a) For evidence supporting the indicated transition-state conformation of the dioxaborolane unit: Roush, W. R.; Banfi, L. *J. Am. Chem. Soc.* **1988**, *110*, 3979. (b) Additional allylboration results have rationalized by invoking dipole–dipole interactions: Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Straub, J. A.; Palkowitz, A. D. *J. Org. Chem.*, submitted.

Enantiospecific Synthesis of an Aziridinobenzoazocinone, an Advanced Intermediate Containing the Core Nucleus of FR900482 and FK973

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Summary: A route to the enantiospecific synthesis of the aziridinobenzohexahydroazocine ketone **14**, containing the core nucleus of FR900482 and FK973, has been developed. It consists of coupling the two key intermediates, sulfonanilide **7** and methyl (2*S*,3*S*)-2,3-aziridino-4-hydroxybutyrate **12**, prepared from vinylglycine, followed by cyclization to the azocinone **14**.

In 1987 the isolation was reported of a potent antineoplastic agent from cultures of *Streptomyces sandaensis* No. 6897; it was designated FR900482, **1**.[1-3] This unique compound exists in two diastereomeric forms, A and B, due to the hydroxylamine hemiketal functionality. The A form is favored in neutral and acidic media possibly due

(1) Uchida, I.; Takase, S.; Kayakiri, H.; Kiyoto, S.; Hashimoto, M. *J. Am. Chem. Soc.* **1987**, *109*, 4108.

(2) Iwami, M.; Kiyoto, S.; Terano, H.; Kohsaka, M.; Aoki, H.; Imanaka, H. *J. Antibiot.* **1987**, *40*, 589.

(3) Kiyoto, S.; Shibata, T.; Yamashita, M.; Komori, T.; Okuhara, M.; Terano, H.; Kohsaka, M.; Aoki, H.; Imanaka, H. *J. Antibiot.* **1987**, *40*, 594.

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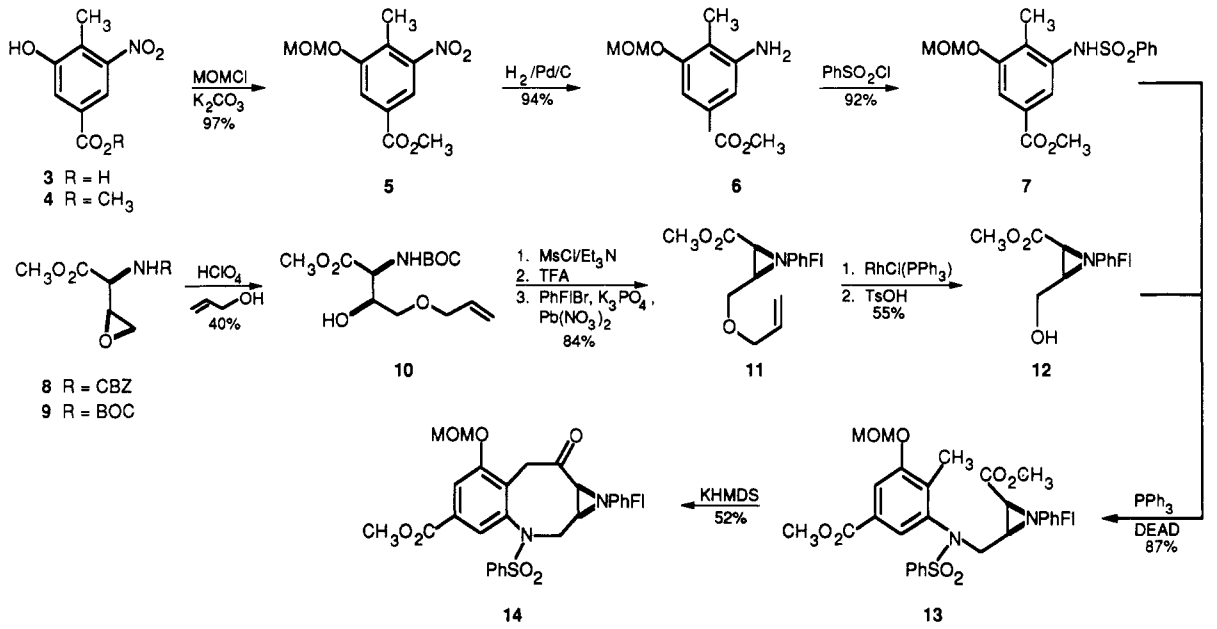
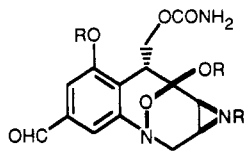
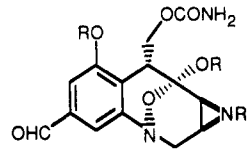
Scheme I



to hydrogen bonding between the aziridine NH and the bridging oxygen. The B form is predominant in the triacetate **2**, FK973, which was selected for biological screening.[4,5] The diastereomers presumably interconvert through the tautomeric tricyclic keto form C.[1]

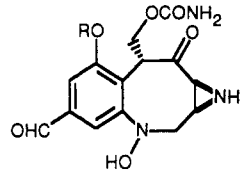


A



B

1 R = H
2 R = Ac



C

The triacetate FK973, **2**, has displayed a very promising biological profile. Showing activity against various transplanted human and murine tumors, FK973 is 3 times more potent than mitomycin C and significantly less toxic.[6-8] It has been proposed that FK973 is gradually activated in the cytoplasm of cells and the activated FK973 forms interstrand DNA–DNA and DNA–protein crosslinks.[7,8] It does not cause oxidative scission of single-stranded DNA.[7,8] Due to their potent antineoplastic activity and unique structures, FR900482 and FK973 are attractive candidates for synthesis.[9]

Our starting material for the synthesis of the aromatic portion of FR900482 is the nitrophenol **3**.[10] The methyl ester **4** was formed under Fischer esterification conditions with methanol and sulfuric acid in 93% yield.[11] Phenol **4** was then converted almost quantitatively into the methoxymethyl ether **5**, mp 60–61 °C, using potassium carbonate and chloromethyl methyl ether in acetone (see Scheme I). The nitro group of **5** was catalytically reduced to afford the aniline **6**, mp 99–100 °C, in 94% yield. Reacting this aniline derivative with benzenesulfonyl chloride, pyridine, and DMAP in acetonitrile gave a 92% yield of the protected aniline **7**,[12] mp 145.5–146.5 °C.

The precursor to the aliphatic portion of FR900482 was the optically pure CBZ epoxide **8**.[13] The CBZ group was exchanged for a BOC to afford epoxide **9**.[14] Opening BOC epoxide **9** with allyl alcohol and catalytic 60% aqueous $HClO_4$[15] gave a 40% yield of allyl ether **10** with the BOC moiety intact. Allyl ether **10** was then converted to the protected aziridine **11** in 84% overall yield by mesylation of the alcohol (MsCl, 200 mol %; triethylamine, 200 mol %); removal of the BOC group (TFA); aziridine formation and protection as its 9-phenylfluoren-9-yl (PhFl)[16] derivative (K_3PO_4, 300 mol %; $Pb(NO_3)_2$, 100 mol %; PhFlBr, 115 mol %). Removal of the allyl ether was accomplished in two steps. First the double bond was isomerized to the stable vinyl ether with Wilkison's catalyst ($RhCl(PPh_3)_3$, 10 mol %; DBU, 10 mol %; EtOH).[17] Subsequent hy-

(4) Shimomura, K.; Hirai, O.; Mizota, T.; Matsumoto, S.; Mori, J.; Shibayama, F.; Kikuchi, H. *J. Antibiot.* **1987**, *40*, 600.
(5) Hirai, O.; Shimomura, K.; Mizota, T.; Matsumoto, S.; Mori, J.; Kikuchi, H. *J. Antibiot.* **1987**, *40*, 607.
(6) Shimomura, K.; Manda, T.; Mukumoto, S.; Masuda, K.; Nakamura, T.; Mizota, T.; Matsumoto, S.; Nishigaki, F.; Oku, T.; Mori, J.; Shibayama, F. *Cancer Res.* **1988**, *48*, 1116.
(7) Masuda, K.; Nakamura, T.; Mizota, T.; Mori, J.; Shimomura, K. *Cancer Res.* **1988**, *48*, 5172.
(8) Masuda, K.; Nakamura, T.; Shimomura, K.; Shibata, T.; Terano, H.; Kohsaka, M. *J. Antibiot.* **1988**, *41*, 1497.
(9) Yasuda, N.; Williams, R. M. *Tetrahedron Lett.* **1989**, *30*, 3397.

(10) Nitrophenol **3** was prepared in two steps and 49% yield from commerically available 3,5-dinitrotoluic acid as described by Nielson, O. B. T.; Bruun, H.; Bretting, C.; Feit, P. W. *J. Med. Chem.* **1975**, *18*, 41.
(11) Satisfactory elemental analyses and spectral data were obtained for all new compounds.
(12) **7**: ^1H NMR ($CDCl_3$) δ 2.00 (s, 3 H, $ArCH_3$), 3.43 (s, 3 H, OCH_3), 3.86 (s, 3 H, CO_2CH_3), 5.19 (s, 2 H, OCH_2O), 7.14 (s, 1 H, ArH), 7.45 (d, 2 H, J = 7.8 Hz, ArH), 7.55 (d, 2 H, J = 1.5 Hz, ArH), 7.60 (d, 1 H, J = 1.16 Hz, ArH), 7.76 (m, 2 H, ArH); ^{13}C NMR ($CDCl_3$) δ 10.69, 52.25, 56.28, 94.60, 112.56, 119.41, 127.23, 127.44, 128.90, 129.09, 133.13, 135.29, 139.31, 155.51, 166.23.
(13) This epoxide was constructed from L-methionine in five steps and 41% overall yield following the procedure of Shaw, K. J.; Luly, J. R.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 4515.
(14) Yields varied from 70 to 90% by carrying out the hydrogenolysis in methanol with hydrogen at atmospheric pressure over 10% Pd/C in the presence of 250 mol % of $(BOC)_2O$; Truong, T.; Rapoport, H., manuscript in preparation.
(15) Fieser, L. F.; Goto, T. *J. Am. Chem. Soc.* **1960**, *82*, 1693.
(16) Christie, B. D.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 1239.

drolysis of the vinyl ether was more difficult than expected, requiring TsOH (15 mol %) and 18 h, and the alcohol **12**[18] was obtained in 55% yield, along with a significant amount of phenylfluorenyl alcohol from solvolysis of the product or intermediate.

Mitsunobu coupling[19] (PPh_3, 100 mol %; DMAD, 100 mol %; THF) of benzenesulfonamide **7** and aziridino alcohol **12** afforded the coupled (phenylsulfonyl)anilide **13**, mp 81-84 °C, as a mixture of conformational isomers in 87% yield. At this stage, we anticipated that the para ester group would sufficiently increase the acidity of the tolyl methyl protons of **13** to permit deprotonation and condensation with the aziridino methyl ester. Although such intramolecular condensations to form eight-membered rings are generally quite poor processes, the severe conformational constraints imposed by the fused benzene and aziridine rings were expected to overcome this barrier. In the event, treatment of the Mitsunobu product **13** with KHMDS (500 mol %, THF, -10 to 5 °C) afforded the ketone **14**,[20] mp 220-222 °C, in 52% yield. This completes the synthesis of the core (3*S*,4*S*)-3,4-aziridinobenzo[1,2-*b*]hexahydroazocine nucleus. To complete the synthesis of FR900482, introduction of the carbamoylmethyl group and the remaining functional group manipulations with ketone **14** are being pursued.

Acknowledgment. Michael Carrasco, President's Undergraduate Fellow, provided valuable assistance in the preparation of intermediates.

Supplementary Material Available: Complete experimental details and ^1H and ^{13}C NMR data for numbered compounds in the synthetic sequence (**4**, **5**, **6**, **7**, **10** and its mesylate, **11**, **12**, **13**, **14**) (7 pages). Ordering information is given on any current masthead page.

(17) Corey, E. J.; Suggs, J. W. *J. Org. Chem.* **1973**, *38*, 3224.

(18) **12**: ^1H NMR ($CDCl_3$) δ 1.74 (q, 1 H, J = 6.6 Hz, H_β), 2.52 (d, 1 H, J = 6.6 Hz, H_α), 3.56 (b d, 1 H, J = 4.5 Hz, H_γ), 3.72 (s, 3 H, CO_2CH_3), 7.14-7.49 (m, 11 H, ArH), 7.71 (m, 2 H, ArH); ^{13}C NMR δ 37.36 (1), 40.39 (1), 51.75 (3), 59.83 (2), 75.15, 119.81 (1), 125.26 (1), 125.95 (1), 126.57 (1), 126.92 (1), 127.24 (1), 127.75 (1), 128.0 (1), 128.56 (1), 128.74 (1), 139.60, 141.11, 142.23, 144.72, 147.79, 169.71.

(19) Mitsunobo, O. *Synthesis* **1981**, 1. A similar application to aliphatic amines has just appeared: Henry, J. R.; Marcin, L. R.; McIntosh, M. C.; Scola, P. M.; Harris, G. D., Jr.; Weinreb, S. M. *Tetrahedron* **1989**, *30*, 5709.

(20) **14**: ^1H NMR ($CDCl_3$) δ 1.96 (d, 1 H, J = 6.6 Hz, H_α), 2.47 (q, 1 H, J = 3.3 Hz, H_β), 3.50 (d, 1 H, J = 14.3 Hz, H_γ), 3.51 (d, 1 H, J = 18.1 Hz, H_{Bn}), 3.56 (s, 3 H, OCH_3), 3.79 (d, 1 H, J = 18.0 Hz, H_{Bn}), 3.93 (s, 3 H, CO_2CH_3), 4.29 (dd, 1 H, J = 3.4, 14.3 Hz, H_γ), 5.29 (d, 1 H, J = 6.6 Hz, CH_2), 5.46 (d, 1 H, J = 6.6 Hz, CH_2), 6.62-7.92 (m, 20 H, ArH); ^{13}C NMR ($CDCl_3$) δ 42.37 (1), 42.53 (2), 45.34 (1), 47.97 (2), 52.36 (3), 56.62 (3), 75.43, 95.10 (2), 115.25 (1), 120.10 (1), 120.31 (1), 121.44 (1), 124.91 (1), 126.35 (1), 126.44 (1), 127.01 (1), 127.18 (1), 127.77 (1), 127.95 (1), 127.99 (1), 128.74 (1), 129.04 (1), 129.26 (1), 129.42 (1), 133.32 (1), 136.35, 138.03, 139.13, 140.47, 142.07, 142.14, 142.55, 147.74, 154.31, 165.79, 204.13.

Reaction of Trithiolanes with Dihalocarbenes under Phase-Transfer Catalysis. A Convenient Synthesis of Trithiocarbonates and Thionocarbonates

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Summary: The reaction of trithiolanes with both dichloro- and dibromocarbene under phase-transfer catalysis has been studied in detail. The primary product is the trithiocarbonate, which undergoes further reaction to give the thionocarbonates. A mechanism for this reaction is discussed.

Recently we reported on the oxidation of norbornane trithiolanes with a variety of reagents.[1] This study indicated that simple norbornane trithiolanes have the potential to serve as good models for investigating trisulfide chemistry. Here we describe the reaction of trithiolanes with dihalocarbenes. Although we have been unable to find any example in the literature on the reactivity of trithiolanes (or trisulfides for that matter) with dihalocarbenes, there are quite a few reports on the reaction with disulfides.

In the earliest study of the reaction of disulfides with carbenes, Searles and Wann found that dichlorocarbene led to (dichloromethyl)alkyl disulfides and alkenes (eq 1).[2]

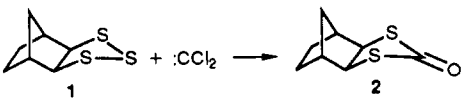
$$(CH_3)_3CSSC(CH_3)_3 + :CCl_2 \rightarrow (CH_3)_3CSSCHCl_2 + CH_2{=}C(CH_3)_2 \quad (1)$$

Aryl disulfides on the other hand do not react with dichlorocarbene.[3] Recently dichlorocarbene has been shown to act as both as an oxidizing and reducing agent for organosulfur compounds under phase-transfer catalysis.[4,5] With this information in hand the following study was undertaken.

Table I. Ratio of 2 and 3 with Time

time, h	2/3	1, %
0.17	2.9	52
1	2.9	24
7	2.3	16
17	2.3	16

Heating a mixture of *exo*-3,4,5-trithiatricyclo[5.2.1.$0^{2,6}$]decane (**1**),[6] excess NaOH and benzyltriethylammonium chloride (TEBAC) in $CHCl_3$ at reflux gave a 60% yield of *exo*-3,5-dithia-4-oxotricyclo[5.2.1.$0^{2,6}$]decane (**2**)[7] as the only product. If the reaction is carried out at



1 **2**

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(2) Searles, S., Jr.; Wann, R. E. *Tetrahedron Lett.* **1965**, 2899-2902.

(3) Field, L.; Banks, C. H. *J. Org. Chem.* **1975**, *40*, 2774-2779.

(4) Soysa, D. S. H.; Weber, W. P. *Tetrahedron Lett.* **1978**, 1969-1970.

(5) Evans, S. H., Jr.; Dyer, J. C. *J. Org. Chem.* **1980**, *45*, 5350-5355.

(6) Bartlett, P. D.; Ghosh, T. *J. Org. Chem.* **1987**, *52*, 4937-4943.

0022-3263/90/1955-1146$02.50/0