Table I. Final Cell, Refinement, and Atom Parameters for $Nb_{1.72}Ta_{3.28}S_2$[a]

		occupancy, %	z	B_{eq}, Å^2	U_{11}	U_{33}
M1	2a	88.3 Ta + 11.7 Nb	0	0.98 (9)	0.011 (1)	0.015 (2)
M2	4e	82.6 Ta + 17.4 Nb	0.4248 (1)	0.68 (5)	0.0098 (7)	0.006 (1)
M3	4c	37.3 Ta + 62.7 Nb	0.1560 (1)	0.74 (8)	0.009 (1)	0.010 (2)
S	4e		0.3024 (4)	0.7 (2)	0.011 (4)	0.005 (6)

[a] Tetragonal, space group $I4/mmm$, a = 3.3203 (9) Å, c = 21.619 (12) Å, Z = 2, 124 unique reflections ($I \geq 3\sigma I$), 15 variables, R = 0.035, R_W = 0.038. x, y = 0 for all atoms; $U_{22} = U_{11}$, $U_{ij} = 0$. $B_{eq} = 8\pi^2/3\ (U_{11} + U_{22} + U_{33})$.

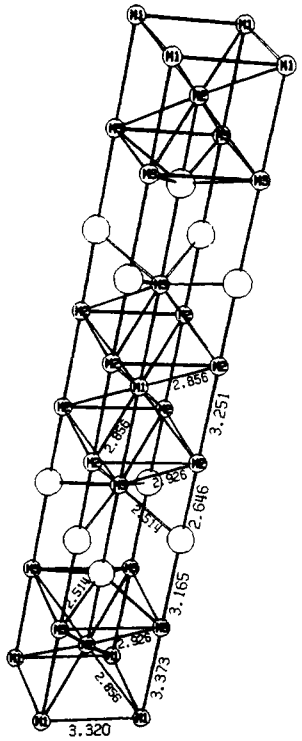

Figure 1. Picture of one unit cell for $Nb_{1.72}Ta_{3.28}S_2$. Larger circle represents S.

Zr-Zr-Cl and the homoatomic analogue structure is *ccp*-type.

The coordination of M1 is as follows: eight M2 (2.856 Å) at the corners of a distorted capped cube, four M1 (3.320 Å) and two M3 (3.373 Å) as capping atoms. Around M2 there are four M1 (2.856 Å) and four M3 (2.926 Å) at the corners of a distorted capped cube, five M2 (four at 3.320 Å and one at 3.251 Å), and one S (2.646 Å) as capping atoms. The corners of the distorted capped cube around M3 are four M2 (2.926 Å) and four S (2.514 Å) while the capping atoms are one M1 (3.373 Å) and four M3 (3.320 Å), respectively.

As the identifying number of the metal increases, the Nb/Ta ratio on that position also increases. The number of coordinating sulfurs for M1, M2, and M3 are 0, 1, and 4, respectively; i.e., the more Nb in the position, the more S bonded to this position. This is the fourth example supporting the suggestion[7] that Nb-S binding energy is greater than that of Ta-S in the metal-rich sulfides. The shortest distance between sulfur atoms (3.26 Å) in neighboring layers indicates interlayer van der Waals interactions, consistent with the graphitic character and the tendency of the compound to disorder.

The layered disulfides (TiS_2, MoS_2, NbS_2, etc.) have been studied extensively[10] because they intercalate both organic and inorganic substances into the interlayer van der Waals gap between adjacent sulfur layers. The compound reported here introduces the possibility of studying intercalates in a new setting, namely, in a compound with a robustly metallic region separating the van der Waals layers. This compound also raises again the intriguing chemical question posed previously by $Nb_{4.92}Ta_{6.08}S_4$[6] and $Nb_{6.74}Ta_{5.26}S_4$,[7] namely: what are the properties of mixed Nb-Ta that cause compounds of the mixed metals to differ substantially in M/S ratio and structure from the binary sulfides of Nb and Ta?

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Supplementary Material Available: Tables of crystal data and bonding distances for $Nb_{1.72}Ta_{3.28}S_2$ (3 pages); table of observed and calculated structure factors (1 page). Ordering information is given on any current masthead page.

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Total Synthesis of Deoxybouvardin and RA-VII: Macrocyclization via an Intramolecular Ullmann Reaction

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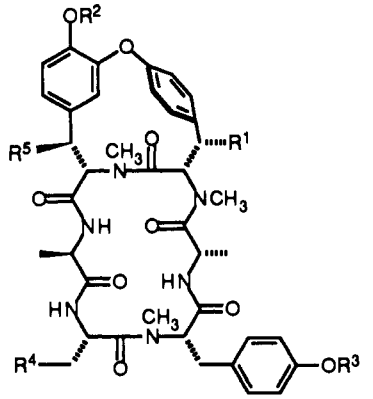
Bouvardin (**8**, NSC 259968) and deoxybouvardin (**2**), bicyclic hexapeptides isolated initially from *Bouvardia ternifolia* (Rubiacea) and identified by single-crystal X-ray structure analysis (bouvardin) and chemical correlation (deoxybouvardin),[1] represent the initial members of a growing class of potent antitumor antibiotics now including the bicyclic hexapeptides RA-I - RA-VII.[2-7] Synthetic efforts on **1-8** have been characterized by the



	R1	R2	R3	R4	R5	
1	H	CH_3	CH_3	H	H	O-methyl deoxybouvardin, (RA-VII)
2	H	H	CH_3	H	H	deoxybouvardin, (RA-V)
3	H	H	CH_3	OH	H	RA-I
4	H	CH_3	H	H	H	RA-II
5	H	CH_3	CH_3	OH	H	RA-III
6	H	CH_3	CH_3	H	OH	RA-IV
7	OH	CH_3	CH_3	H	H	O-methyl bouvardin, (RA-VI)
8	OH	H	CH_3	H	H	bouvardin

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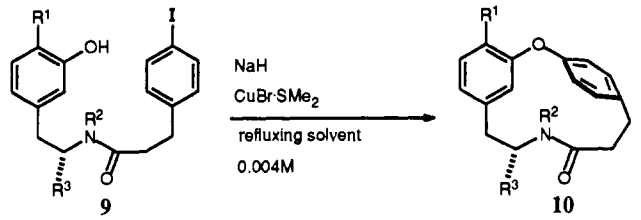
Table I



9	R^1	R^2	R^3	NaH, equiv	$CuBr{\cdot}SMe_2$, equiv	solvent[a]	time, h	10	yield, % (RSM,[b] %)	S:R[c]
9a	H	H	H	2.0	10	pyridine	18	**10a**	58 (20)	
9a	H	H	H	2.0	10	dioxane	18	**10a**	51 (24)	
9b	H	CH_3	H	1.2	10	pyridine	18	**10b**[d]	49 (36)	
9c	OCH_3	H	H	2.0	10	pyridine	18	**10c**	46 (29)	
9d	OCH_3	CH_3	H	1.2	10	pyridine	18	**10d**	45 (22)	
9e	OH	H	CO_2CH_3	2.0	10	pyridine	9	**10e**	51 (20)	nd
9f	OCH_3	H	CO_2CH_3	2.0	10	pyridine	9	**10f**	51 (8)	55:45
9f	OCH_3	H	CO_2CH_3	2.0	10	dioxane	9	**10f**	31 (17)	96:4
9f	OCH_3	H	CO_2CH_3	2.0	10	collidine	9	**10f**	50 (12)	93:7

[a] Reaction temperatures: pyridine, 130 °C (bath); collidine, 185 °C (bath); dioxane, 115 °C (bath). [b] RSM = recovered starting material. [c] Ratio of S:R enantiomers; nd = not determined. Starting **9f**, S:R = 99:1. [d] Structure established by X-ray, ref 17.

failure of conventional macrolactamization techniques and direct diaryl ether cyclization procedures to provide the elusive 14-membered ring.[8-10] Consequently an indirect thallium trinitrate promoted two-step method for achieving the intramolecular phenol coupling has been introduced by Yamamura and co-workers,[11-14] required the use of dichloro- and/or dibromophenol coupling partners, and has been applied by Inoue and co-workers in the synthesis of RA-VII (**1**) and deoxybouvardin (**2**) albeit in low yields (ca. 2%).[15-16] In contrast to earlier reports, herein we detail successful studies on the implementation of an intramolecular Ullmann condensation reaction for direct closure to the 14-membered diaryl ethers that have proven inaccessible or less accessible by alternative routes and the use of this key macrocyclization reaction in the total synthesis of RA-VII (**1**) and deoxybouvardin (**2**).

Preliminary studies of the viability of the intramolecular Ullmann reaction for direct formation of 14-membered diaryl ethers **10** were conducted, and the optimized results of the conversion of **9a–f** to **10a–f** are detailed in Table I.[17] Routine macrocyclization conversions in the range of 45–60% were realized under moderately dilute reaction conditions (0.004 M pyridine) with a full range of substrates including those bearing an alkoxy or hydroxy substituent ortho to the participating phenol. Importantly, the racemization of substrate **9f** observed in pyridine was suppressed with reactions conducted in collidine or dioxane. In addition to the improved conversions available through use of the Ullmann reaction, the procedure permits the use of readily available amino acids and directly provides the functionalized diaryl ethers without resorting to the use of the less accessible and less applicable dichloro- or dibromophenols.[11-16]

With the established viability of the key Ullmann macrocyclization reaction and the modifications that effectively address potential substrate racemization in hand, its application to the total synthesis of **1** and **2** were pursued. Single step O- and N-methylation[18] of *N*-carbobenzyloxy-3-acetyl-L-tyrosine methyl ester (**11**)[19] followed by Baeyer–Villiger oxidation and subsequent acid-catalyzed methanolysis of the resulting acetate provided the selectively protected *N*-methyl-L-DOPA derivative **14**, Scheme I. Catalytic hydrogenolysis of **14** served to remove the CBZ protecting group, and coupling of the resultant amine **15** with *N*-carbobenzyloxy-*N*-methyl-4-iodo-L-phenylalanine (**17**) provided the key dipeptide **18**. Subjection of **18** to the prescribed conditions for effecting the strategic intramolecular Ullmann condensation reaction provided **19** (30%) without evidence of racemization.[20] In contrast to the natural products but consistent with expectations based on conformational analysis, **19** exists in a rigid solution conformation ($CDCl_3$) possessing a trans C^{11}–N^{10} amide bond.[20] Amine deprotection (CBZ hydrogenolysis) and coupling of **20** with the tetrapeptide **21**[21] provided **22**. Sequential C-2 methyl ester hydrolysis, N-3 BOC deprotection, and diphenyl phosphorazidate promoted macrocyclization with C^2–N^3 amide bond formation strategically conducted employing a D-amino acid amine terminus[22] under the recently introduced and improved reaction conditions[23] provided RA-VII [**1**, $[\alpha]^{22}_D$ −222° (c = 0.1, $CHCl_3$], identical in all compared respects with a sample of natural material [TLC, ^{1}H NMR, ^{13}C NMR, IR, EIMS, $[\alpha]^{21}_D$ −229° (c = 0.1, $CHCl_3$)[3]]. Selective C-24 methyl ether removal provided deoxybouvardin [**2**, $[\alpha]^{22}_D$ −219° (c = 0.05, $CHCl_3$)], identical in all compared respects with a sample of natural material [TLC, ^{1}H NMR, ^{13}C

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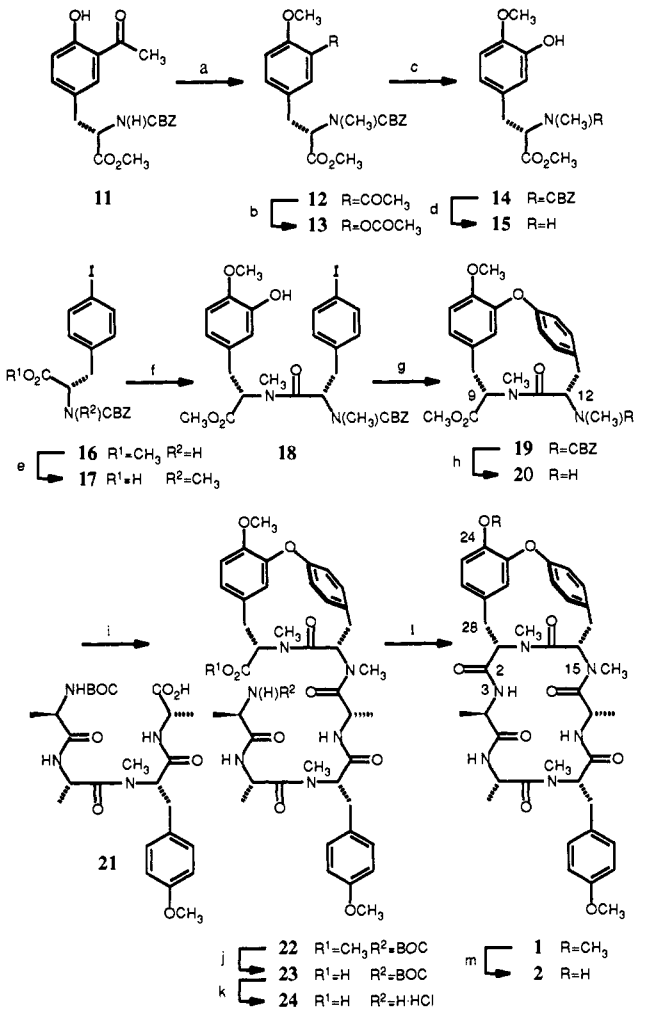
Scheme I



[a] (a) NaH (2.2 equiv), 3.5 equiv of MeI, THF/DMF (10:1), 85 °C, 6 h, 89%; (b) 2.0 equiv of *m*CPBA, CH_2Cl_2, 40 °C, 24 h; (c) 1.0 equiv of HCl, MeOH, 25 °C, 3 h, 91%; (d) 0.1 wt equiv of 10% Pd/C, 1 atm of H_2, CH_3OH, 25 °C, 6 h, 97%; (e) 1.1 equiv of NaH, 1.2 equiv of MeI, DMF, 0–25 °C, 3 h; 1.0 equiv of $LiOH·H_2O$, THF/MeOH/H_2O (3:1:1), 25 °C, 3 h, 80%; (f) 1.4 equiv of **15**, 1.0 equiv of EDCI, 1.0 equiv of $HOBt·H_2O$, DMF, 25 °C, 16 h, 69%; (g) 2.0 equiv of NaH, 10.0 equiv of CuBr–SMe_2, collidine, 130 °C, 8 h, 28%; 24–30%; (h) 0.1 wt equiv of 10% Pd/C, 1 atm of H_2, CH_3OH, 25 °C, 6 h, 98%; (i) 2.0 equiv of **21**, 2.0 equiv of EDCI, 2.0 equiv of $HOBt·H_2O$, DMF, 25 °C, 16 h, 53%; (j) 3.0 equiv of $LiOH·H_2O$, THF/MeOH/H_2O (3:1:1), 25 °C, 2 h; (k) 3.0 M HCl/EtOAc, 25 ° C, 1 h, 92% from **22**; (l) 1.5 equiv of DPPA, 5 equiv of $NaHCO_3$, DMF, 0 °C, 72 h, 58%; (m) 2.0 equiv of BBr_3, CH_2Cl_2, −78 to 0 °C, 3 h, 57%.

NMR, IR, EIMS, $[\alpha]^{21}_D$ −225° (c = 0.3, $CHCl_3$)[3].

The successful implementation of the Ullmann macrocyclization reaction for direct formation of the elusive 14-membered diaryl ether representative of that found in **1–8** has been achieved.[24] Efforts to improve the macrocyclization procedure and its application in the preparation of conformational analogues of the natural products are in progress.

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Supplementary Material Available: A general procedure for conduct of the Ullmann macrocyclization and full spectroscopic and physical characterization of **10a–f**, **12**, **14**, **17–19**, **22**, **1**, and **2** (11 pages). Ordering information is given on any current masthead page.

(24) Efforts to close the 14-membered ring with C^{11}–N^{10} amide bond formation employing conventional macrolactamization techniques, efforts to close the 14-membered ring with diaryl ether formation through use of the reversed intramolecular Ullmann reaction (O^2–C^3 versus O^2–C^1 bond formation), or oxidative phenolic coupling on *O-seco*-deoxybouvardin[8] have not yet proven successful.

Novel Dimetal Complex Containing M(VI) and M(II) Centers United by a Short Metal–Metal Bond: $O_3ReReCl_2(Me_2PCH_2PMe_2)_2$

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The ability of multiply bonded dimetal complexes[1] to undergo *intramolecular disproportionation* reactions to yield products in which a multiple bond is retained offers some fascinating prospects for further developments in the chemistry of this class of compounds. However, very few such systems have been encountered to date, noteworthy examples being $(RO)_2X_2ReReX_2(PPh_3)_2$ (X = Cl, Br; R = Me, Et, *n*-Pr, *i*-Pr),[2] $Cl_4ReReCl(dth)_2$ (dth = $Me_2SCH_2CH_2SMe_2$),[3] $(Me_3SiCH_2)_2Mo[\mu\text{-}(CH_2)_2SiMe_2]Mo(PMe_3)_3$,[4] and $(i\text{-}PrO)_4MoMo(dmpe)_2$ (dmpe = $Me_2PCH_2CH_2PMe_2$).[5] In these cases the M–M bond orders can be considered to be 4, 3.5, 3, and 3, respectively, and the *formal* oxidation states are Re(IV)Re(II), Re(IV)Re(I), Mo(III)Mo(I), and Mo(IV)Mo(0).[6] We now report the isolation and structural characterization of the dirhenium(VI,II) complex $O_3ReReCl_2(dmpm)_2$ (**4**) (dmpm = $Me_2PCH_2PMe_2$) that has not only a disparity in metal oxidation states equal to that in $(i\text{-}PrO)_4MoMo(dmpe)_2$[5] but also a difference in coordination numbers (4 and 7) that is unprecedented in the chemistry of metal–metal-bonded dimetal species.

This complex was obtained as one of three products from the reaction of *cis*-$Re_2(O_2CCH_3)_2Cl_4(H_2O)_2$ (**1**) with a solution of dmpm in toluene (1.3 M). A quantity of **1** (0.20 g, 0.299 mmol) in 15 mL of ethanol was admixed with 0.46 mL of dmpm/toluene (0.598 mmol) and the mixture stirred at room temperature for 15 min. A quantity of brown insoluble $Re_2(\mu\text{-}O_2CCH_3)Cl_4(\mu\text{-}dmpm)_2$ (**2**) was filtered off [0.09 g (36%) after recrystallization],[7,8] the filtrate evaporated to dryness, and the residue treated

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(7) This product was recrystallized from CH_2Cl_2/hexane. Anal. Calcd for $C_{12}H_{31}Cl_4O_2P_4Re_2$: C, 17.04; H, 3.67. Found: C, 16.76; H, 3.65. The identity of this paramagnetic complex is supported by the similarity of its ESR spectrum and electrochemical properties to those of its structurally characterized dppm analogue $Re_2(\mu\text{-}O_2CCH_3)Cl_4(\mu\text{-}dppm)_2$ (dppm = $Ph_2PCH_2PPh_2$).[8]

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