M solution of borane–dimethyl sulfide complex. The mixture was stirred at 0 °C for an additional 1 h and was then allowed to warm to room temperature over a span of 30 min. The mixture was then poured into 50 mL of ice–water, 40 mL of saturated bicarbonate was added, and the whole was extracted with three 50-mL portions of ether. The combined organic layers were washed with a 50-mL portion of brine, dried over $MgSO_4$, and filtered, and the solvent was removed with a rotary evaporator to give 750 mg (79%) of methyl (1α,2β,3β)-2-(methoxycarbonyl)-3-(2-hydroxyethyl)-α,α-dimethylcyclopentaneacetate as a viscous liquid: ^{1}H NMR δ 3.64 (s, 3 H), 3.60 (s, 3 H), 2.82–2.62 (m, 2 H), 2.20–2.04 (m, 1 H), 1.88–1.14 (m, 9 H), 1.11 (s, 6 H); ^{13}C NMR δ 177.6, 176.4, 61.4, 51.5, 51.2, 50.7, 48.8, 44.5, 40.9, 33.8, 31.7, 27.5, 23.3, 22.1; IR (neat). Anal. Calcd for $C_{14}H_{24}O_5$: C, 61.74; H, 8.88. Found: C, 61.38; H, 8.76. A solution of 1.90 g (6.99 mmol) of this alcohol in 2.20 g (21.8 mmol) of NEt_3 and 25 mL of toluene was added to a solution of 2.00 g (10.5 mmol) of 4-nitrobenzoyl chloride in 75 mL toluene at 0 °C. After being stirred for 75 min at 0 °C and overnight at 23 °C, the mixture was extracted with two 50-mL portions of 0.5 N HCl, the organic layer was washed with two 30-mL portions of saturated sodium bicarbonate, and the organic layer was dried over $MgSO_4$. Filtration and solvent removal with a rotary evaporator was followed by flash chromatography of the residue on a 9-in. × 26-mm silica gel column using 20% EtOAc/petroleum ether as eluent to afford 2.10 g (71%) of 41 as light yellow solid. Recrystallization of the solid by slow evaporation from a solution of absolute ethanol afforded crystals suitable for X-ray analysis: mp 51–53 °C; ^{1}H NMR δ 8.30–8.15 (m, 4 H), 4.36 (t, J = 6.8 Hz), 3.66 (s, 3 H), 3.60 (s, 3 H), 2.85 (dd, J = 9.0 Hz, 6.0 Hz, 1 H), 2.75–2.60 (m, 1 H), 2.20–2.10 (m, 1 H), 1.99–1.30 (m, 6 H), 1.12 (s, 6 H); ^{13}C NMR δ 177.5, 176.1, 164.6, 150.5, 135.6, 130.7, 123.5, 64.9, 51.6, 51.5, 50.9, 48.8, 44.6, 41.2, 31.8, 29.9, 27.6, 23.6, 22.3. Anal. Calcd for $C_{21}H_{27}NO_8$: C, 59.85; H, 6.46; N, 3.32. Found: C, 60.10; H, 6.28; N, 3.26.

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Supplementary Material Available: X-ray crystallographic data for 41 (16 pages). Ordering information is given on any current masthead page.

Conjugate Addition Reactions of Organosamarium Species via in Situ Transmetalation to Cu(I) Salts

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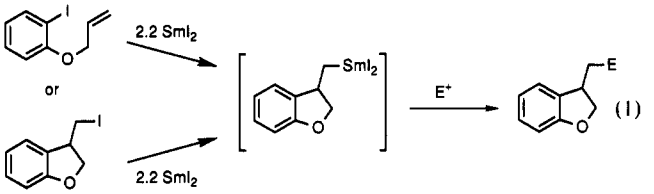
Preformed organosamarium species, available by reduction of aryl or alkyl halides with SmI_2, were treated with copper(I) salts to effect in situ transmetalation and conjugate addition to enones. In a series of copper(I) salts, CuI·P(OEt)$_3$ gave best results in combination with 2 equiv of organosamarium reagent. This new method allows the multiple formation of carbon–carbon bonds through a combination of radical and cuprate chemistry.

Applications of samarium(II) iodide (SmI_2) in synthetic organic chemistry have grown rapidly in recent years.[1] Representative examples include Barbier-type reactions,[2] pinacol couplings,[3] and the preparation of α-ketols[4] and vicinal carbonyl compounds.[5] Recently, samarium(II) iodide mediated radical or ketyl cyclizations have been applied in conjunction with carbonyl addition reactions (eq 1, E^+ = aldehyde, ketone).[6] Experimental observations



(1)

support the intermediacy of solution-stable organosamarium species in this[6a] and probably many other samarium-mediated processes.[2f] These mechanistic observations[6a] led to the development of conditions for the direct reduction of alkyl iodides to alkylsamarium species. These alkylsamarium species then react with a wide variety of electrophiles, including many that are not stable to the SmI_2 reagent used to generate the samarium alkyls (E^+ = PhSSPh, Bu_3SnCl, etc.).[6c]

As expected, alkylsamarium reagents add in a 1,2-fashion to unsaturated ketones.[6a,c] In order to extend the usefulness of these new reagents, we decided to develop conditions to effect 1,4-additions to unsaturated ketones. We now report the first conjugate additions of preformed

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(6) (a) Curran, D. P.; Fevig, T. L.; Totleben, M. J. *Synlett* **1990**, 773. (b) Curran, D. P.; Wolin, R. L. *Synlett* **1991**, 317. (c) Curran, D. P.; Totleben, M. Manuscript submitted for publication. (d) Molander, G. A.; Kenny, C. *J. Org. Chem.* **1991**, *56*, 1439.

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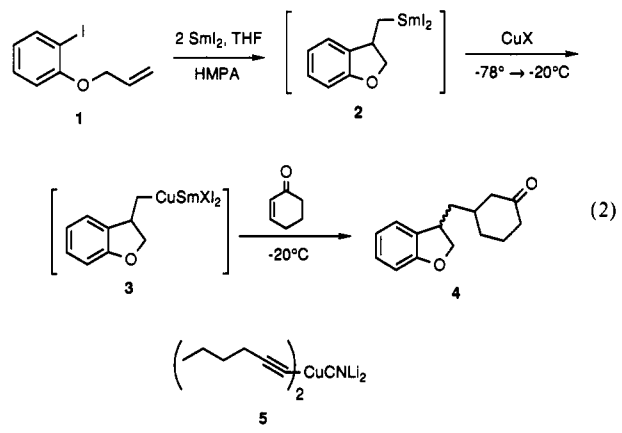
organosamarium derivatives via in situ transmetalation to copper(I) salts.[7] This new protocol combines the unique features of samarium chemistry with the broad scope of organocopper reagents. Because no highly reactive, strongly basic precursors of cuprates (such as organolithium or organomagnesium species) are involved, the transmetalation of organosamarium reagents to copper(I) salts also offers a potential access to larger and more highly functionalized cuprate reagents.[8]

Results and Discussion

Organosamarium reagent **2** is the presumed product of the samarium iodide mediated radical cyclization of aryl ether **1** in THF/HMPA at room temperature.[6a,9] In order to test the feasibility of a transmetalation of such a species, the reaction mixture was added to copper(I) complexes at −78 °C, followed by addition of 2-cyclohexenone at −20 °C (eq 2).



(2)

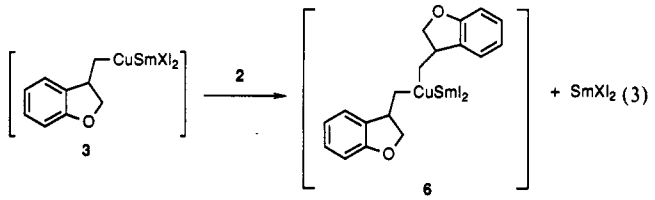
Initial attempts to effect the desired transmetalation with higher order cyanocuprates such as bishexynylcopper cyanide **5**[8b] failed to produce any of the desired 1,4 adduct **4**. Likewise, addition of a catalytic amount of copper triflate to alkylsamarium **2**, followed by addition of methyl vinyl ketone, gave only a small amount of the 1,2 adduct. Because it was unclear whether cyano or hexynyl ligands were interfering in the reaction sequence, we shifted our attention toward less reactive copper(I) salts. With these reagents, 1,4-addition product **4** was found in variable yields as a 1/1 mixture of diastereomers. Table I summarizes the results of a series of model studies performed with various copper(I) salts and additives.

Yields of 1,4-addition product **4** were generally low with CuBr·DMS,[10] CuSPh,[11] CuCN, CuCN·2LiCl,[12] or CuI in the absence of phosphite ligands. The transmetalation with CuI in the presence of 1 equiv of $P(OEt)_3$ (entry 4),[13,14] followed by reaction with 2-cyclohexenone for 2 h at −20 °C, led to a 36% yield of conjugate addition product **4**. An increase in the amount of phosphite ligand, however, dramatically reduced the isolated yield to 9% (entry 7). Addition of TMSCl to the reaction mixture was of no consequence (entry 6).[15] Finally, a 57% overall yield of ketone **4** was obtained with a 2:1 ratio of aryl iodide **1** to cyclohexenone (entry 8). Even in the low yielding reactions, no 1,2-addition products were isolated. We therefore reason that the formation of some type of monoalkyl copper samarium species **3** from organosamarium **2** and copper salt proceeds readily;[16] however, the reactivity of this species toward electrophiles is only marginal. In the presence of a second equivalent of organosamarium reagent, copper complex **6** may be formed, and this may account for an increase in the yield of transfer of alkyl ligands to enone acceptor systems (eq 3).

Table I. Transmetalation of Organosamarium 2 with Cu(I) Complexes To Provide Ketone 4

entry	CuX	additive	ratio 1/CuX	% isolated yield[a]
1	CuI	none	1	17
2	CuI	none	2	31
3	CuI	PBu_3 (2.2 equiv)	1	<20[b]
4	CuI	$P(OEt)_3$	1	36
5	CuI	$P(OEt)_3$	1	16[c]
6	CuI	$P(OEt)_3$, TMSCl	1	35
7	CuI	$P(OEt)_3$ (3 equiv)	1	9
8	CuI	$P(OEt)_3$	2	57
9	CuBr	DMS	1	30[d]
10	CuBr	DMS	1	11[e]
11	CuBr	DMS	2	19[e]
12	CuSPh	none	1	11
13	CuCN (1.1 equiv)	none	1	19
14	CuCN (2 equiv)	none	1	19
15	CuCN	LiCl (2 equiv)	1	3[f]

[a] Based on 2-cyclohexenone. [b] Traces of phosphine were still present in the NMR of the product. [c] Enone was added at −78 °C, followed by warming up to −20 °C. [d] Solid complex was added to organosamarium **2**. [e] Organosamarium **2** was added to a suspension of the copper complex in THF. [f] Some minor impurities remained as determined by NMR.



As outlined in Table II, this procedure is quite general for the synthesis of a variety of 3-alkylated ketones from organosamarium reagents. The use of 2 equiv of halide, 4 equiv of SmI_2, 1 equiv of CuI·$P(OEt)_3$ complex, and 1 equiv of 1,4-enone reliably provides the expected conjugate addition products in moderate to good yield.[17] With

(7) For the preparation of spirolactones in a mixture of cycloalkanone, methyl acrylate, and SmI_2, see: Otsubo, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 5763.

(8) For recent applications of in situ transmetalation protocols for the formation of cuprates, see: (a) Wipf, P.; Smitrovich, J. H. *J. Org. Chem.* **1991**, *56*, 6494. (b) Ireland, R. E.; Wipf, P. *J. Org. Chem.* **1990**, *55*, 1425. (c) Lipshutz, B. H.; Ellsworth, E. L. *J. Am. Chem. Soc.* **1990**, *112*, 7440. (d) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390.

(9) Reduction of organic halides and formation of organosamarium proceeds very sluggishly at temperatures below −20 °C. The cosolvent HMPA is probably not required for the actual transmetalation, but it is necessary for a rapid, high-yielding preparation of the organosamarium precursor.

(10) For the preparation of cuprates from CuBr·DMS, see: LaLima, N. J., Jr.; Levy, J. *J. Org. Chem.* **1978**, *43*, 1279.

(11) For the preparation of cuprates from CuSPh, see: (a) Posner, G. H.; Brunelle, D. J.; Sinoway, L. *Synthesis* **1974**, 662. (b) Kende, A. S.; Jungheim, L. N. *Tetrahedron Lett.* **1980**, *21*, 3849.

(12) For the preparation of cuprates from CuCN·2LiCl, see: ref 8d and Yeh, M. C. P.; Knochel, P. *Tetrahedron Lett.* **1988**, *29*, 2395.

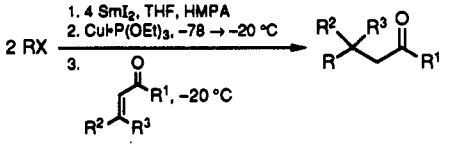
(13) For the preparation of cuprates from CuI·$P(OEt)_3$, see: Ziegler, F. E.; Mikami, K. *Tetrahedron Lett.* **1984**, *25*, 131.

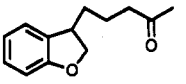
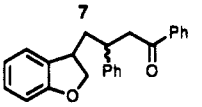
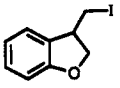
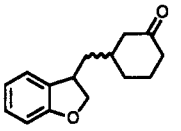
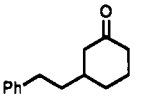
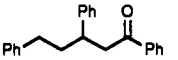
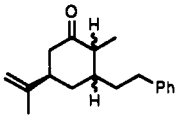
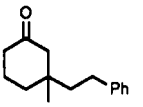
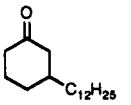
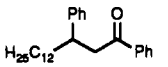
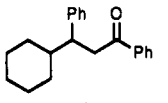
(14) A solid, preformed complex and a complex generated in situ showed no difference in reactivity. Equimolar amounts of CuI and $P(OEt)_3$ in THF form a turbid solution after 10–15 min stirring at room temperature.

(15) For examples of rate accelerations of TMSCl in cuprate additions, see: (a) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6019. (b) Matsuzawa, S.; Horiguchi, Y.; Nakamura, E.; Kuwajima, I. *Tetrahedron* **1989**, *45*, 349.

(16) In the absence of copper(I) salts, addition of enones to organosamarium **2** leads to the formation of 1,2-addition products, see refs 5a and 6a,c.

Table II. Copper(I)-Mediated Conjugate Additions of Organosamarium Species to Enones



entry	RX	enone	product	% isolated yield[a]
1	1	methyl vinyl ketone	 7	30
2	1	chalcone	 8	40[b]
3	 9	2-cyclohexen-1-one	 4	55[b]
4	 10	2-cyclohexen-1-one	 11	67
5	10	chalcone	 12	64
6	10	(*R*)-(−)-carvone	 13	62[c]
7	10	3-methyl-2-cyclohexen-1-one	 14	45[d]
8	dodecyl iodide (15)	2-cyclohexen-1-one	 16	82
9	15	chalcone	 17	72
10	cyclohexyl bromide (18a)	chalcone	 19	33
11	cyclohexyl iodide (18b)	chalcone		44[e]

[a] Based on enone. [b] Mixture of diastereomers. [c] Unassigned mixture of three isomers (73/17/10 (GC)). [d] 48% of the enone was recovered. [e] Ratio of 18b/SmI_2/chalcone = 4/4/1.

halides such as allyl aryl ether 1, the radical ring closure preceeds the transmetalation process.

In all experiments, the organosamarium species were formed before addition to copper(I) salts and enones. As expected,[1] alkyl and aryl iodides are significantly more reactive in this process than the corresponding bromides. Whereas the preparation of the organosamarium reagent from cyclohexyl bromide (18a, entry 10) required nearly 30 min at room temperature, the organometallic reagent is usually formed within 1–5 min from iodides. Hydrogen atom abstraction from the solvent or disproportionation of the secondary radical could account for the lower yield observed with bromide 18a and iodide 18b (entries 10 and 11).[6c] Interestingly, addition of additional cyclohexyl iodide (18b) to SmI_2 was necessary to effect a complete

(17) The analogous copper(I)-mediated coupling of organosamarium species to acrylonitrile did not lead to any addition products under our conditions. Also, attempts to trap the copper or samarium enolate formed by conjugate addition to enones with allyl bromide have so far been unsuccessful. However, conjugate addition product of the enolate with unreacted enone was identified by NMR and MS as a minor side product in most examples.

conversion of the samarium(II) iodide, resulting in a total ratio of 18b/SmI_2/chalcone of 4/4/1.[18]

Conclusions

Transmetalation of organosamarium species to copper(I) salts has been successfully applied for the formal conjugate addition of aryl and alkyl halides to enones and the multiple formation of carbon–carbon bonds through a cascade of radical and ionic reactions. This protocol provides a further extension of the synthetic utility of SmI_2 and presents additional compelling evidence for the presence of organometallic intermediates in SmI_2 induced processes. At present, the major limitation of this combination of samarium and copper chemistry is the requirement for an excess of halide. Further applications of this transmetalation method and investigations of the structure of the intermediate organocopper–samarium species are planned.

Experimental Section

General. *O*-Allyl-2-iodophenol (1) and 3-(iodomethyl)-2,3-dihydrobenzofuran (9) were prepared and purified as described elsewhere.[6a,c] Other starting materials were commercially available and were distilled before use. Samarium powder (40 mesh, Aldrich) was used without further purification. THF was distilled from sodium/benzophenone under Ar, HMPA was distilled from CaH_2 under high vacuum and stored over 4-Å molecular sieves under N_2. Triethyl phosphite and tri-*n*-butyl phosphine were distilled under N_2. CuI was purified by recrystallization as described in the literature.[19] CuBr·DMS and copper(I) thiophenoxide were commercially available and used without further purification. CuCN and LiCl were dried in vacuo with periodic heating prior to use. Chlorotrimethylsilane was distilled from CaH_2 under N_2. NMR spectra were recorded at 300 MHz for protons and at 75 MHz for ^{13}C.

Preparation of 0.1 M SmI_2 in THF.[20] A suspension of samarium powder (1.82 g, 12 mmol) and I_2 (2.54 g, 10 mmol) in dry THF (100 mL) was stirred vigorously at 25 °C for at least 2 h, during which time the color changed from purple to rust-brown to green and finally to Prussian blue.[21] This procedure gave a 0.1 M solution of SmI_2, and the titer was checked by titration with a 0.1 M solution of I_2 in THF (the endpoint is reached when the solution turns yellow and SmI_3 precipitates out).[20]

General Procedures for Transmetalation and Conjugate Additions. To a 0.1 M THF solution of SmI_2 (20 mL, 2 mmol) and HMPA (1.20 mL, 7 mmol) was added dropwise over 5 min at 25 °C a solution of an alkyl or aryl halide (1.1 mmol) in dry THF (3 mL). The solution was stirred for 5 min at 25 °C (until the color of the solution changed to dark or yellow-brown), cooled to −78 °C, and added via cannula to a cooled (−78 °C) solution of CuI (0.095 g, 0.5 mmol) and $P(OEt)_3$ (86 μL, 0.5 mmol) in dry THF (10 mL). The reaction mixture was stirred at −78 °C for 10 min and then at −20 °C for 20–30 min. The neat enone (0.5 mmol) was added (resulting in immediate color change to yellow), and the reaction was stirred at −20 °C for 2 h and 20 °C for 30 min. After dropwise addition of a 0.5 M aqueous solution of HCl, the reaction mixture was poured into 0.5 M HCl solution and extracted 3× with a mixture of petroleum ether/ether (1:1). The organic extracts were combined and washed twice with H_2O, once with 3% $Na_2S_2O_3$, and once with brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated. Unless specified otherwise, the residues were purified by flash chromatography in hexanes/EtOAc.

3-[[3-(2*H*,3*H*-benzofurfuryl)]methyl]cyclohexan-1-one (4). Prepared from iodide 1 or iodide 9. Chromatography with hexanes/EtOAc (4/1) gave 65 mg (0.28 mmol, 57%; yield from iodide 9: 55%) of a viscous yellow oil (1/1 mixture of diastereomers): IR (neat) 3048, 2930, 1711, 1608, 1597, 1481, 1460, 1228, 1016, 968, 837, 752 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.1 (m, 2 H), 6.90–6.70 (m, 2 H), 4.60 (t, J = 9 Hz, 1 H), 4.15 (m, 1 H), 3.48 (m, 1 H), 2.48 (m, 1 H), 2.37 (broad s, 1 H), 2.30 (m, 1 H), 2.10 (m, 2 H), 2.0–1.58 (m, 5 H), 1.45 (m, 1 H); ^{13}C NMR ($CDCl_3$, expect 30 peaks, see 19) δ 210.9, 159.7, 130.5, 128.3, 124.2, 124.1, 120.4, 109.6, 77.0, 76.8, 48.3, 47.7, 42.1, 41.4, 39.2, 37.0, 31.7, 31.1, 25.1; MS (EI) m/e 230 (32), 212 (9), 145 (10), 132 (60), 119 (100), 97 (83), 91 (100), (45), 55 (55); HRMS (EI) m/e calcd for $C_{15}H_{18}O_2$ 230.1307, found 230.1307.

5-[3-(2*H*,3*H*-Benzofurfuryl)]pentan-2-one (7). Chromatography with hexanes/EtOAc (4/1) gave 30 mg (0.15 mmol, 30%) of a pale yellow oil: IR (neat) 2932, 2890, 1714, 1595, 1481, 1458, 1360, 1228, 1161, 1016, 964, 752 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.12 (m, 2 H), 6.83 (m, 2 H), 4.61 (t, J = 9 Hz, 1 H), 4.21 (dd, J = 6, 9 Hz, 1 H), 3.40 (m, 1 H), 2.45 (t, J = 7 Hz, 2 H), 2.12 (s, 3 H), 1.80–1.55 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 208.4, 159.8, 130.6, 128.2, 124.3, 120.3, 109.5, 76.6, 43.5, 41.8, 34.4, 29.9, 21.2; MS (EI) m/e 204 (35), 186 (11), 144 (13), 119 (100), 91 (70), 59 (84), 49 (97); HRMS (EI) m/e calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1150.

4-[3-(2*H*,3*H*-Benzofurfuryl)]-1,3-diphenylbutan-1-one (8). The crude product was purified by HPLC in hexanes/EtOAc (24/1) to give 69 mg (0.20 mmol, 40%) of a viscous pale yellow oil as a mixture of diastereoisomers, in a ratio of 62:38 by ^1H NMR: IR (neat) 3060, 3025, 2920, 2900, 1684, 1595, 1479, 1456, 1230, 960, 750, 700, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.85 (d, J = 8 Hz, 2 H), 7.58–7.20 (m, 8 H), 7.18–7.0 (m, 2 H), 6.9–6.7 (m, 2 H), 4.58, 4.36, 4.19, 3.81 (4t, J = 9, 8 Hz, 4 H), 3.58, 3.30, 3.16 (3m, 4 H), 2.21 (m, 1 H), 1.95 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 198.3, 159.5, 143.5, 136.8, 132.9, 130.6, 128.6, 128.4, 128.0, 127.8, 127.5, 126.6, 124.3, 123.6, 120.2, 109.3, 77.1, 76.2, 45.8, 42.0, 41.3, 40.6, 39.8, 39.4, 39.1; MS (EI) m/e 342 (20), 222 (34), 210 (15), 131 (25), 118 (50), 105 (100), 91 (69), 77 (61); HRMS (EI) m/e calcd for $C_{24}H_{22}O_2$ 342.1620, found 342.1620.

3-(2-Phenethyl)cyclohexan-1-one (11). Chromatography with hexanes/EtOAc (6/1) gave 68 mg (0.33 mmol, 67%) of a light yellow oil: IR (neat) 2930, 2858, 1711, 1495, 1454, 1226, 748, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.27 (m, 2 H), 7.15 (m, 3 H), 2.61 (t, J = 8 Hz, 2 H), 2.44 (m, 1 H), 2.32 (m, 1 H), 2.26 (m, 1 H), 2.04 (m, 2 H), 1.93 (broad, 1 H), 1.80 (m, 1 H), 1.66 (m, 3 H), 1.38 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 211.6, 141.9, 128.4, 128.3, 125.8, 48.0, 41.5, 38.5, 38.4, 32.9, 31.2, 25.1; MS (EI) m/e 202 (11), 184, 97 (100), 91 (50), 55 (12); HRMS (EI) m/e calcd for $C_{14}H_{18}O$ 202.1358, found 202.1358.

1,3,5-Triphenylpentan-1-one (12). The crude product was purified by MPLC in hexanes/EtOAc (24/1) to give 101 mg (0.32 mmol, 64%) of a pale yellow solid: mp 63–66 °C ($CHCl_3$); IR (neat) 3125, 3050, 2953, 2870, 1682, 1493, 1450, 750, 700, 686 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.85 (d, J = 7 Hz, 2 H), 7.55–7.06 (m, 13 H), 3.37 (m, 1 H), 3.27 (m, 2 H), 2.47 (broad t, J = 8 Hz, 2 H), 2.17–2.0 (broad m, 1 H), 2.0–1.90 (broad m, 1 H); ^{13}C NMR ($CDCl_3$) δ 198.9, 144.4, 142.1, 137.1, 132.9, 128.6, 128.0, 127.7, 126.5, 125.7, 46.0, 41.0, 37.9, 33.7; MS (EI) m/e 314 (10), 209 (75), 194 (55), 105 (100), 91 (40), 77 (45); HRMS (EI) m/e calcd for $C_{23}H_{22}O$ 314.1671, found 314.1671.

2-Methyl-3-(2-phenethyl)-5-(2-propenyl)cyclohexan-1-one (13). Chromatography with hexanes/EtOAc (19/1) and Kugelrohr distillation (~80 °C (~0.5 mmHg)) to remove the remaining carvone gave 79 mg (0.31 mmol, 62%) of a pale yellow oil, which was a mixture of diastereomers in a ratio of 10:73:17 by GC (no internal standard): IR (neat) 3086, 3028, 2936, 2864, 1711, 1645, 1603, 1496, 1454, 1377, 893, 748, 700, 669 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.27 (m, 2 H), 7.16 (broad m, 3 H), 4.76 (m, 2 H), 2.79–2.35 (m, 3 H), 2.32 (m, 2 H), 2.22–2.11 (m, 1 H), 2.08–1.97 (m, 1 H), 1.74 (s, 3 H), 1.68–1.56 (m, 2 H), 1.45 (m, 2 H), 1.10, 1.04, 0.98 (3d, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 215.0, 213.7, 212.6, 212.3, 147.6, 147.5, 147.4, 146.8, 142.1, 141.9, 141.7, 128.4, 128.2, 125.8, 111.3, 110.0, 109.7, 49.4, 49.2, 48.6, 47.5, 46.6, 45.1, 44.8, 44.1, 43.6, 42.2, 40.8, 40.5, 40.4, 39.7, 39.4, 36.3, 35.9, 35.5, 34.5, 33.4, 33.1, 32.4, 31.2, 31.0, 28.5, 21.4, 20.6, 20.4, 14.3, 11.7, 11.5, 10.8; MS (EI) m/e

(18) After the initial addition of 0.5 equiv of cyclohexyl iodide to SmI_2, the color of the reaction mixture remained blue, indicating an incomplete consumption of SmI_2. The solution changed from dark-blue to yellow-brown only during the addition of another 0.5 equiv of iodide.

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(21) A slight excess of samarium powder was used to increase the shelf-life of the SmI_2 stock solution. This remained as a solid at the bottom of the flask.

256 (19), 213 (12), 185 (10), 151 (28), 95 (20), 91 (100), 81 (18), 67 (22), 55 (26); HRMS (EI) m/e calcd for $C_{18}H_{24}O$ 256.1827, found 256.1827.

3-Methyl-3-(2-phenethyl)cyclohexan-1-one (14). Chromatography with hexanes/EtOAc (7/1) gave 48% recovered enone and 49 mg (0.23 mmol, 45%) of a yellow oil: IR (neat) 3026, 2938, 2890, 1709, 1655, 1647, 1496, 1454, 1228, 750, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.25 (m, 2 H), 7.15 (m, 3 H), 2.54 (m, 2 H), 2.28 (m, 2 H), 2.22 (m, 2 H), 1.88 (m, 2 H), 1.65 (m, 2 H), 1.55 (m, 2 H), 1.00 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 211.9, 142.4, 128.4, 128.3, 125.8, 53.6, 43.9, 41.0, 38.7, 35.9, 30.0, 24.9, 22.1; MS (EI) m/e 216 (3), 131 (4), 111 (100), 97 (10), 91 (35), 55 (20); HRMS (EI) m/e calcd for $C_{15}H_{20}O$ 216.1574, found 216.1574.

3-Dodecylcyclohexan-1-one (16). Chromatography with hexanes/EtOAc (9/1) gave 33 mg (0.12 mmol, 82%) of a light yellow oil: IR (neat) 2922, 2851, 1716, 1464, 1458, 1313, 1225, 721 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40-2.20 (m, 3 H), 2.00 (m, 2 H), 1.85 (m, 1 H), 1.70-1.55 (m, 3 H), 1.40-1.18 (broad s, 22 H), 0.85 (t, J = 6.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 212.2, 53.4, 48.2, 41.5, 39.1, 36.6, 31.9, 31.3, 29.6, 29.4, 26.6, 25.3, 22.7, 14.1; MS (EI) m/e 266 (1.5), 223 (1.6), 97 (100), 69 (10), 57 (10), 55 (12); HRMS (EI) m/e calcd for $C_{18}H_{34}O$ 266.2610, found 266.2610.

1,3-Diphenylpentadecan-1-one (17). Chromatography with hexanes/EtOAc (24/1) gave 137 mg (0.36 mmol, 72%) of a pale yellow solid: mp 68-71 °C ($CHCl_3$); IR (neat film) 2914, 2847, 1674, 1440, 1425, 750, 700, 682 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.88 (m, 2 H), 7.51 (m, 1 H), 7.43 (m, 2 H), 7.10-7.30 (m, 5 H), 3.29 (m, 3 H), 1.66 (m, 2 H), 1.40-1.00 (broad, 20 H), 0.86 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 199.1, 145.1, 137.3, 132.8, 128.5, 128.4, 128.0, 127.5, 126.2, 46.0, 41.3, 36.4, 31.9, 29.6, 29.5, 29.4, 27.5, 22.7, 14.2; MS (EI) m/e 378 (1.5), 258 (78), 209 (87), 131 (10), 117 (30), 105 (100), 91 (47), 77 (39), 57 (21); HRMS (EI) m/e calcd for $C_{27}H_{38}O$ 378.2923, found 378.2923.

3-Cyclohexyl-1,3-diphenylpropan-1-one (19). Chromatography with hexanes/EtOAc (19/1) gave 40 mg (0.17 mmol, 33% from bromide **18a**; yield from iodide **18b**: 44% (ratio **18b**/SmI_2/chalcone = 4/4/1)) of a pale yellow solid: mp 120-122 °C; IR (neat film) 2930, 2900, 2850, 1690, 1630, 1540, 1490, 1425, 750, 700, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.84 (m, 2 H), 7.49 (m, 1 H), 7.41 (m, 2 H), 7.10-7.30 (m, 5 H), 3.37 (m, 2 H), 3.17 (m, 1 H), 1.85 (m, 1 H), 1.70-1.45 (broad, 4 H), 1.40-1.00 (broad m, 4 H), 0.99 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 199.5, 143.8, 137.4, 132.8, 128.5, 128.4, 128.1, 126.1, 47.1, 43.2, 42.4, 31.4, 30.8, 26.6, 26.4; MS (EI) m/e 209 ($M^+ - cC_6H_{11}$, 19), 172 (75), 105 (100), 91 (22), 81 (12), 77 (40), 55 (20); HRMS (EI) m/e calcd for $C_{15}H_{13}O$ ($M^+ - cC_6H_{11}$) 209.0966, found 209.0966.

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Registry No. 1, 24892-63-5; (*R**,*S**)-4, 138695-36-0; (*R**,*R**)-4, 138695-37-1; 7, 138695-38-2; (*R**,*R**)-8, 138695-39-3; (*R**,*S**)-8, 138695-40-6; 9, 78739-83-0; 10, 17376-04-4; 11, 108011-20-7; 12, 123200-56-6; 13, 138695-45-1; 14, 138695-41-7; 15, 4292-19-7; 16, 138695-42-8; 17, 138695-43-9; 18a, 108-85-0; 18b, 626-62-0; 19, 138695-44-0; CuI, 7681-65-4; CuBr, 7787-70-4; CuSPh, 1192-40-1; CuCN, 544-92-3; PBu_3, 998-40-3; $P(OEt)_3$, 122-52-1; TMSCl, 75-77-4; DMS, 75-18-3; SmI_2, 32248-43-4; Sm, 7440-19-9; methyl vinyl ketone, 78-94-4; chalcone, 94-41-7; 2-cyclohexen-1-one, 930-68-7; (*R*)-(*N*)-carvone, 6485-40-1; 3-methyl-2-cyclohexen-1-one, 1193-18-6.

Supplementary Material Available: ^1H NMR and ^{13}C NMR spectra for compounds 4, 7, 8, 11, 12, 13, 14, 16, 17, and 19 (23 pages). Ordering information is given on any current masthead page.

Model Studies on the Synthesis of Carboxylate-Binding Pocket Analogues of Vancomycin Using Arene-Ruthenium Chemistry

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Preparation of several protected (D)-chlorophenylalanine derivatives in high optical purity and their complex formation with the $[RuCp]^+$ moiety are described. The complexation reaction, as well as subsequent photochemical decomplexations, proceeds with retention of optical purity. Reactions of these chloroarene complexes with 3-hydroxyphenylglycine derivatives proceed under mild conditions to give aryl ether-ruthenium complexes, which can be converted to diaryl ethers in which both aromatic rings have protected amino acid or peptide side chains. Efforts to effect cycloamidation to give vancomycin carboxylate-binding pocket analogues, using a number of known coupling reagents, were unsuccessful.

While it is well-established that nucleophilic displacement of halogen on halobenzene-$FeCp$[1] and -$Mn(CO)_3$[2] cationic complexes proceeds under very mild conditions, and that the corresponding tricarbonylchromium complexes require much more reactive nucleophiles,[3] the application of such methodology to the synthesis of highly functionalized aromatic compounds is still in its infancy.[4] The most serious limitations posed by the use of the iron or manganese complexes is the inability of sensitive functional groups to withstand the rather drastic conditions required for the attachment of the metal to the aromatic ring and/or the failure even to achieve such complexation in certain cases. For example, in our laboratory[5] conversion of protected 4-chlorophenylalanine

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