J|A|C|S
ARTICLES
Published on Web 01/12/2007

Rhenium(VII) Oxide Catalyzed Heteroacylative Ring-Opening Dimerization of Tetrahydrofuran

H. Christine Lo,[†] Hongna Han,[†] Lawrence J. D'Souza,[†] Subhash C. Sinha,*[,†] and Ehud Keinan*[,†,‡]

Contribution from the Department of Molecular Biology and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037, and Department of Chemistry and Institute of Catalysis Science and Technology, Technion − Israel Institute of Technology, Haifa 32000, Israel

Received September 28, 2006; E-mail: keinan@tx.technion.ac.il; subhash@scripps.edu

Abstract: Re_2O_7, which is known primarily as a strong oxidant, was found to be a highly selective Lewis acid catalyst that affects the heteroacylative dimerization of THF at room temperature. This multicomponent reaction, which involves THF, trifluoroacetic anhydride (TFAA), and a carboxylic acid, produces a nonsymmetrical diester, $RCO_2(CH_2)_4O(CH_2)_4OCOCF_3$, in high yields. The reaction is quite general with respect to the carboxylic acid but is highly selective for unsubstituted THF in preference to other cyclic ethers. It is also highly selective for TFAA in preference to other anhydrides. Isotope labeling experiments indicate that two of the five oxygen atoms in the product originate from THF; one comes from rhenium oxide, and the two carbonyl oxygens originate from the carboxylic acid and from TFAA. The catalytic cycle, which is proposed on the basis of these experiments, involves a multistep sequence of nucleophilic attacks, starting with an attack of a rhenium oxo ligand on a coordinated THF, then attack of the resultant alkoxide ligand on a second coordinated THF, nucleophilic addition of the resultant alkoxide ligand to the coordinated carboxylic acid (an intramolecular metal−oxygen bond metathesis), and, finally, electrophilic cleavage of the other coordinated alkoxide by TFAA to produce the nonsymmetrical diester. This synthetically useful reaction highlights the unique, frequently avoided Lewis acidity of transition-metal oxides.

Introduction

High-oxidation-state transition metal oxides are attractive synthetic reagents and catalysts because they are strong oxidants and Lewis acids and can accommodate a high coordination number of ligands. The latter property allows for highly controlled synthetic transformations to occur intramolecularly within the metal coordination sphere. These advantages have been manifested by the many synthetic applications of rhenium(VII) oxides in various oxidation reactions,[1] including the use of CH_3ReO_3 in olefin epoxidation reactions[2,3] and of Re_2O_7 in oxidative cyclization of bis-homoallylic alcohols.[4] The latter reaction has found useful applications in highly selective total syntheses of natural products containing THF and poly-THF fragments, such as the Annonaceous acetogenins.[5] Surprisingly, the Lewis acid property of Re(VII) oxides has remained unexplored, and this property has often been mentioned in the literature as a disadvantage. For example, pyridine has been employed in the CH_3ReO_3-catalyzed olefin-epoxidation reaction in order to diminish the Lewis acidity of the catalyst and prevent further ring opening of the epoxide product.[3] This report reveals a new reaction, heteroacylative ring-opening dimerization of tetrahydrofurans, based on the unique Lewis acidity of Re(VII) oxides.

The reaction was discovered serendipitously while attempting to expand the substrate scope of the oxidative cyclization reaction to include not only bis-homoallylic alcohols but also other analogous compounds, including the γ,δ-unsaturated carboxylic acid, **1a**. Unexpectedly, treatment of **1a** with Re_2O_7 and trifluoroacetic anhydride (TFAA) in THF and CH_2Cl_2 did not produce the expected oxidative cyclization product, **2**[6] (Scheme 1). Instead, the nonsymmetrical diester, **3a**, was obtained in high yield and high purity.

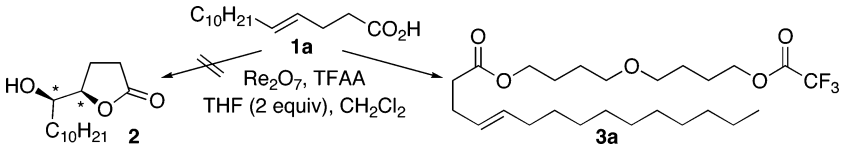
Ring-opening reactions of cyclic ethers are important synthetic transformations because they provide an effective approach to difunctional intermediates and monomers.[7] Tetrahydrofuran, in particular, has been the most studied cyclic ether in this regard because the resultant 4-carbon building block has many applications in organic synthesis and in polymer chemistry.[7a,8] Several Lewis acids[9] and transition metals[8,10,11] have been

[†] The Scripps Research Institute.
[‡] Technion − Israel Institute of Science.

(1) (a) Romão, C. C.; Kühn, F. E.; Herrmann, W. A. *Chem. Rev.* **1997**, *97*, 3197. (b) Kühn, F. E.; Herrmann, W. A. *Struct. Bonding* **2000**, *97*, 213.
(2) Herrmann, W. A.; Fischer, R. W.; Marz, D. W. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1638.
(3) Rudolph, J.; Reddy, K. L.; Chiang, J. P.; Sharpless, K. B. *J. Am. Chem. Soc.* **1997**, *119*, 6189.
(4) Keinan, E.; Sinha, S. C. *Pure Appl. Chem.* **2002**, *74*, 93 and references cited therein.
(5) For selected examples, see: (a) Sinha, S. C.; Sinha-Bagchi, A.; Keinan, E. *J. Am. Chem. Soc.* **1995**, *117*, 1447. (b) Han, H.; Sinha, M. K.; D'Souza, L. J.; Keinan, E.; Sinha, S. C. *Chem.—Eur. J.* **2004**, *10*, 2149. (c) Das, S.; Li, L.-S.; Abraham, S.; Chen, Z.-Y. Sinha, S. C. *J. Org. Chem.* **2005**, *70*, 5922 and references therein.
(6) Keinan, E.; Sinha, S. C.; Sinha-Bagchi, A.; Wang, Z.-M.; Zhang, X.-L.; Sharpless, K. B. *Tetrahedron Lett.* **1992**, *33*, 6411.

10.1021/ja0668668 CCC: $37.00

Scheme 1



reported to catalyze the ring opening of THF. Nonetheless, most of the known examples have resulted in either monomeric products[9,10b−e] or complex mixtures of oligomers.[8,11] The few reports on the dimerization of THF describe harsh reaction conditions (120−180 °C)[10a,12] and stoichiometric amounts of the acidic reagent.[13] Furthermore, no method has been described for nonsymmetric ring-opening dimerization reaction of THF to produce a product with two different end groups.

Here we report on the scope and characteristics of this newly discovered reaction and show that rhenium(VII) oxide can be used as a highly selective Lewis acid catalyst. We show that, in the presence of TFAA and a carboxylic acid at room temperature, Re_2O_7 catalyzes the ring-opening dimerization of THF to produce a nonsymmetrical diester at room temperature. Furthermore, we show that this reaction is highly selective for unsubstituted THF and propose a catalytic cycle on the basis of isotope labeling experiments.

Results and Discussion

Our first goal was to define the reaction conditions and the appropriate proportions of the various reactants in this multicomponent ring opening reaction. In our initial experiments with acid **1a**, the choice of the rhenium(VII) reagent was based on our protocol for the oxidative cyclization reactions,[4,5] where Re_2O_7 was premixed with TFAA and 2 equiv of THF in order to form either $(THF)_2ReO_3(\eta^1\text{-}O,O\text{-}CF_3CO_2)$ or $(THF)ReO_3\text{-}(\eta^2\text{-}O,O\text{-}CF_3CO_2)$ in situ.[14] Obviously, the key question from both practical and mechanistic standpoints was whether rhenium(VII) oxide could be used in catalytic amounts. Assuming that other acids could be used instead of **1a**, we employed benzoic acid, **1b**, in our exploratory reactions. Thus, using Re_2O_7 (1 equiv), THF (2 equiv), **1b** (1 equiv), and TFAA (1.3 equiv) in CH_2Cl_2 at room temperature for 24 h afforded compound **3b** in over 90% yield (based on **1b**). By varying the amount of Re_2O_7 we found that with 10 mol % Re_2O_7 product **3b** was obtained in excellent yield (95%). Lower catalyst loadings at a mmol scale could also be used, but the reaction progressed at slower rates. Interestingly, using THF as solvent rather than CH_2Cl_2 resulted in very low yields of **3b**.

Obviously, the carboxylic acid, **1**, plays a crucial role in this reaction because no reaction occurred in its absence. To verify the generality of the reaction with respect to this component, we carried out the reaction in the presence of various aliphatic and aromatic carboxylic acids, **1a**−**j**, and found that in all cases the corresponding acylated THF dimers, **3a**−**j**, were obtained in high yields (78−95%, Table 1). All aryl carboxylic acids examined, bearing either an electron-donating or an electron-withdrawing group, exhibited high reactivity. Likewise, various alkyl carboxylic acids were used successfully in this reaction. The only isolated side products were the corresponding monomeric and trimeric analogues of the main product. For example, in the reaction of **1b** the dimeric product, **3b** (95%), was accompanied by the monomeric, **4b** (∼4%), and trimeric, **5b** (<1%), analogues. Interestingly, trifluoroacetic acid (entry 11) was found to be essentially inactive in this reaction with no reaction being observed even after 5 days at room temperature (<1%). These findings explain why we did not observe this reaction in our previous studies on the oxidative cyclization reactions.

Next, we examined the scope of the reaction with respect to the cyclic ether (Table 2). Interestingly, the reaction was found to be quite selective for unsubstituted THF. For example, unlike the reaction with THF (entry 1), the reactivity of either oxetane or THP (entries 2 and 3) under the same conditions was quite poor, and the expected products **6** and **7** were obtained in no more than 10% yields. In fact, in a competition experiment using acid **1b** and a 1:1 mixture of THF and THP in the presence of TFAA and a catalytic amount (10%) of Re_2O_7, only the acylative dimerization of THF, **3b**, was noticed by NMR. In the case of 2-methyl-THF (entry 4) only the two monomeric ring-opening products, **8a** and **8b**, were isolated (5:1, 62%). Similarly, the reaction with 2,5-dimethyl-THF resulted only in the monomeric product **9** in 59% yield (entry 5).

We have also examined the ring-opening reaction with respect to the anhydride partner and found that the reaction is quite selective for TFAA (entry 1, Table 3). When TFAA was replaced by either acetic anhydride (entries 2, 3) or pivalic anhydride (entries 4, 5), essentially no ring-opening products could be isolated in a reaction of THF with various acids even after 5 days. Even with benzoic anhydride, which is more electron deficient, yields did not exceed 5% after 48 h at 36 °C (entry 6).

Role of Re_2O_7. Several experiments were carried out in order to gain insight into the reaction mechanism and the origin of product selectivity. Re_2O_7 is known to react with TFAA in THF to produce the carboxylate complex **10** in high yields (Scheme 2),[14,15] which can be readily converted to **11** via a carboxylate exchange reaction.[15b] We prepared both complexes **10** and **11** and used each one of them in control experiments. When **10**

(7) (a) Dreyfuss, P.; Dreyfuss, M. P; Pruckmayr, G. *Encyclopedia of Polymer Science and Engineering*, 2nd ed.; John Wiley & Sons: New York, 1989; Vol. 16, p 649. (b) Penczek, S.; Kubisa, P.; Matyjaszewski, K. *Adv. Polym. Sci.* **1980**, *37*, 1. (c) Rosowski, A. In *Heterocyclic Compounds with Three and Four Membered Rings, Part 1*; Weissberger, A., Ed.; Interscience: New York, 1964.

(8) (a) Drysdale, N. E. U.S. Patent 5,990,264, 1999. (b) Drysdale, N. E.; Bockrath, R. E.; Herron, N.; Citron, J. D. U.S. Patent 5,770,678, 1998. (c) Kobayashi, S.; Sugiura, M.; Kitagawa, H.; Lam, W. W.-L. *Chem. Rev.* **2002**, *102*, 2227.

(9) For selective examples, see: (a) Wang, B.; Gu, Y.; Gong, W.; Kang, Y.; Yang, L.; Suo, J. *Tetrahedron* **2004**, *45*, 6599. (b) Yasuhiro, T.; Hamada, M.; Kai, N.; Nagai, T. *J. Heterocycl. Chem.* **2000**, *37*, 1351.

(10) (a) Miles, W. H.; Ruddy, D. A.; Tinorgah, S.; Geisler, R. L. *Synth. Commun.* **2004**, *34*, 1871. (b) Kwon, D. W.; Kim, Y. H.; Lee, K. *J. Org. Chem.* **2002**, *67*, 9488. (c) Pri-Bar, I.; Stille, J. K. *J. Org. Chem.* **1982**, *47*, 1215. (d) Miyoshi, N.; Hatayama, Y.; Ryu, I.; Kamble, N.; Murai, T.; Muria, S.; Sonoda, N. *Synthesis* **1988**, 175. (e) Guo, Q.; Miyaji, T.; Hara, R.; Shen, B.; Takahashi, T. *Tetrahedron* **2002**, *58*, 7327.

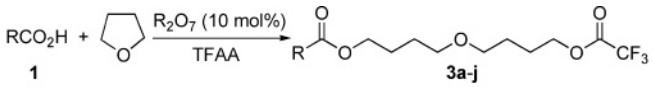
(11) Kucera, M.; Zahradnicková, A.; Majerová, K. *Polymer* **1976**, *17*, 528.

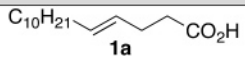
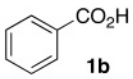
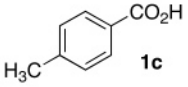
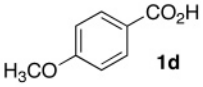
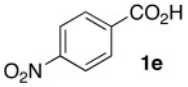
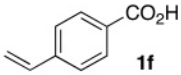
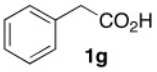
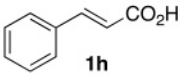
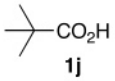
(12) (a) Wuonola, M. A.; Sheppard, W. A. *J. Org. Chem.* **1971**, *36*, 3640. (b) Alexander, K.; Schniepp, L. E. *J. Am. Chem. Soc.* **1948**, *70*, 1839.

(13) (a) Delaney, P. A.; Johnstone, R. A. W. *J. Chem. Soc., Perkin Trans. I* **1986**, 1855. (b) Edwards, J. D.; Gerrard, W.; Lappert, M. F. *J. Chem. Soc.* **1957**, 348.

(14) There are two steps in a typical Re_2O_7-mediated oxidative cyclization reaction. In the first step, $(THF)ReO_3(\eta^2\text{-}O,O\text{-}CF_3CO_2)$, **10**, was generated quantitatively. See: Scheme 2 for details.

Table 1. Re_2O_7-Catalyzed Heteroacylative Ring-Opening Dimerization of THF[a]



Entry	RCO_2H, 1	Time (h)	Product (yield)
1	 **1a**	24	**3a** (R = $C_{10}H_{21}CHCHCH_2CH_2$, 80%)
2	 **1b**	24	**3b** (R = C_6H_5, 95%)
3	 **1c**	24	**3c** (R = *p*-$CH_3C_6H_4$, 92%)
4	 **1d**	24	**3d** (R = *p*-$CH_3OC_6H_4$, 91%)
5	 **1e**	36	**3e** (R = *p*-$NO_2C_6H_4$, 86%)
6	 **1f**	24	**3f** (R = *p*-$(CH_2{=}CH)C_6H_4$, 92%)
7	 **1g**	24	**3g** (R = $C_6H_5CH_2$, 92%)
8	 **1h**	24	**3h** (R = $C_6H_5CH{=}CH$, 78%)
9	CH_3CO_2H **1i**	42	**3i** (R = CH_3, 87%)
10	 **1j**	42	**3j** (R = t-Bu, 82%)
11	CF_3CO_2H **1k**	120	**3k** (R = CF_3, < 1%)

[a] Yields of isolated products are based on substrate **1**. All reactions were carried out in CH_2Cl_2 at room temperature with molar ratio of Re_2O_7/**1**/THF/TFAA = 1:10:25:15. Small amounts of monomeric products, **4** (<4%), and trimeric products, **5** (<1%), were also isolated in all cases.

was treated with **1b**, TFAA, and THF, compound **3b** was obtained in high yields. The same result was achieved when **11** was used for the same reaction in the absence of **1b**.[15c] We conclude that Re_2O_7 is a catalyst precursor and that complexes **10** and **11** are probably the actual species that participate in the catalytic cycle.

Origin of the Oxygen Atoms in the Product. To reveal the origin of the three oxygen atoms in the saturated portion of **3b**, several isotope-labeling experiments were conducted. First, a stoichiometric amount of $Re_2{}^{18}O_7$ (>90 At%-^{18}O)[16] was used in the reaction with **1b**. In the high-resolution mass spectrum (HRMS, ESI-TOF) of the isolated product **3b**, a distinct peak at m/z = 387.1288, consistent with incorporation of one ^{18}O in [**3b** · Na^+] ion, was observed along with a peak at m/z = 385.1239, consistent with its ^{16}O-isotopomer.[17] No indication for the incorporation of more than one ^{18}O could be detected. These observations indicate that one Re═O bond is involved in the THF ring-opening step.

Next, we prepared a doubly labeled benzoic acid ($PhC^{18}O_2H$, > 92 At%-^{18}O)[18] and used it in a stoichiometric reaction with Re_2O_7. Unexpectedly, the HRMS of the isolated product revealed that only one out of the two ^{18}O atoms in **1b** was incorporated into **3b** (ESI-TOF, m/z = 387.1282). The same result was obtained when **11**-(η^2-*O*,*O*-$^{18}O_2$CPh),[19] which was prepared from **10** using $PhC^{18}O_2H$, was employed instead of Re_2O_7 under the same conditions. The identity of ^{18}O in the

(15) (a) Edwards, P.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1984**, 2695. (b) Complex **11** can be prepared by addition of **1b** to a (THF)ReO_3(η^2-*O*,*O*-RCO_2) complex, where R = CF_3, CH_3, or $C(CH_3)_3$. However, the carboxylate exchange with the trifluoroacetoxyl ligand would be the most kinetically favorable. These Re-carboxylate complexes are all moisture-sensitive and thermally unstable.

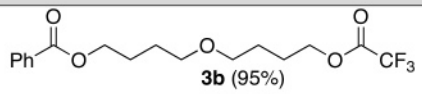
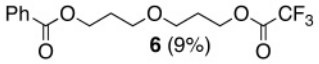
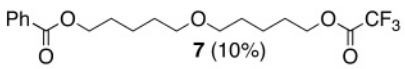
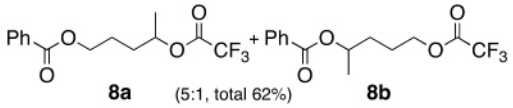
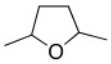
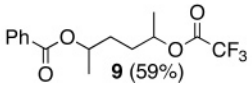
(16) (a) Schmidt, M.; Schmidbaur, H. *Inorg. Syn.* **1967**, *4*, 149. (b) Herrmann, W. A.; Kühn, F. E.; Roesky, P. W. *J. Organomet. Chem.* **1995**, *485*, 243. (c) We thank Dr. F. E. Kühn for his helpful suggestions on the preparation of isotope-labled Re_2O_7.

(17) Theoretical mass: 387.1276 for $^{18}O_1$-[**3b**·Na^+]; 385.1233 for ^{16}O-[**3b**·Na^+].

(18) The ^{18}O-labeled **1b** has been previously prepared; see: Wnuk, S. F.; Chowdhury, S. M.; Garcia, P. I., Jr.; Robins, M. J. *J. Org. Chem.* **2002**, *67*, 1816 and references therein.

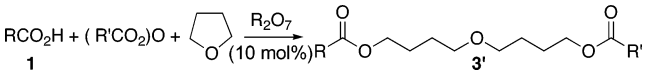
(19) The integrity of $PhC^{18}O_2$-ligand was verified by ESI-TOF. In the CH_2Cl_2 extract of a hydrolyzed solution of **11**-(η^2-*O*,*O*-$^{18}O_2$CPh), a distinct peak at m/z = 125.0376 attributed to $PhC^{18}O_2$-anion was observed.

Table 2. Re_2O_7-Catalyzed Heteroacylative Ring Opening of Various Cyclic Ethers with **1b** and TFAA[a]

Entry	Ether	Time (h)	Product (yield)
1		24	 **3b** (95%)
2		50	 **6** (9%)
3		50	 **7** (10%)
4		50	 **8a** (5:1, total 62%) **8b**
5		50	 **9** (59%)

[a] All reactions were carried out under the conditions mentioned in Table 1. Yields are based on benzoic acid, **1b**.

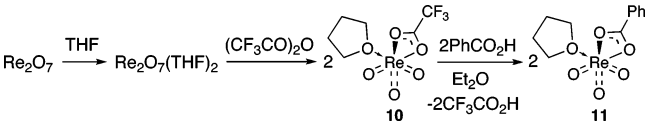
Table 3. Re_2O_7-Catalyzed Acylative Ring-Opening Dimerization of THF[a]



entry	R	R′	time (h)	product (yield)
1	Ph	CF_3	24	**3b** (95%)
2	CH_3	CH_3	120	**3l** (1%)
3	Ph	CH_3	72	
4	$(CH_3)_3C$	$(CH_3)_3C$	120	
5	Ph	$(CH_3)_3C$	72	
6	Ph	Ph	48 (at 36 °C)	**3m** (5%)

[a] Yields of isolated products are based on substrate **1**. All reactions were carried out under the general conditions described in Table 1 with the appropriate changes of the carboxylic acid and anhydride.

Scheme 2



product was further determined by $^{13}C\{^1H\}$ NMR experiments, taking advantage of the fact that ^{18}O-isotopes are known to induce an upfield-shift in $^{13}C\{^1H\}$ NMR.[20] Thus, when a 1:1 mixture of **1b** and **1b**-$^{18}O_2$ was used stoichiometrically, the resultant $^{13}C\{^1H\}$ NMR spectrum confirmed that only the carbonyl oxygen in **3b** remained ^{18}O-labeled ($\Delta\delta = \delta(C^{16}O) - \delta(C^{18}O) = 0.031$ ppm).[21] Overall, two of the five oxygen atoms in **3b** originate from THF, one comes from rhenium oxide, and the two carbonyl oxygens originate from **1b** and from TFAA. These findings represent the first example of oxygen incorporation from a transition-metal oxide into the ring-opening products of THF.

Proposed Mechanism. Our proposed catalytic cycle (Scheme 3) starts with **10**, which undergoes facile carboxylate exchange to give **11** (Scheme 2).[15] In solution the carboxylate ligand in both **10** and **11** is likely to undergo fast equilibrium between its η^1 and η^2 modes.[15a,22] Complexation of the second carboxylate oxygen in **11** activates the *trans* oxo ligand to undergo nuclophilic attack on the adjacent THF ligand,[23,24] resulting in a dioxometallacycle, **A**. This nucleophilic attack is reminiscent of the known reaction between CH_3ReO_3 and an epoxide.[25] Coordination of a second THF to give **B** followed by a nucleophilic attack of the alkoxide ligand on that THF leads to a second ring-opening step to produce **C**. Although complex **C** is analogous to **A**, the central oxygen in the diolate ligand in **C** can coordinate to Re and thereby shift the carboxylate η^2/η^1 equilibrium toward η^1 (C′/C″) rather than η^2 (C). The η^1-carboxylate in C′/C″, a 14e Re dioxide, would then undergo facile metal−oxygen bond metathesis with concomitant coordination of a THF molecule to give a 16e Re trioxide species, **D**. An analogous conversion of a 14e Re dioxide to a 16e Re trioxide has been recently reported.[26] Finally, electrophilic cleavage of the metal oxygen bond in **D** with TFAA leads to product **3b** which regenerates the catalyst, **10**.

This proposed catalytic cycle could also explain the observation that the main product, **3b**, is accompanied by small amounts of the monomeric analogue, **4b** (<4%), and trimeric one, **5b** (<1%).[27a] Formation of **4b** could result from an η^1/η^2 equilibrium between **A** and **A′**, followed by metal−oxygen bond metathesis with concomitant coordination of a THF molecule to produce **E**, which then reacts with TFAA to produce **4b**, the

(20) Risley, J. M.; van Etten, R. L. In *NMR Basic Principles Progress*; Diehl, P., Fluck, E., Günther, E., Kosfeld, R., Seeling, J., Eds.; Springer: Berlin, 1990; Vol. 22.

(21) (a) A difference of 0.031 ppm in ^{13}C NMR is consistent with the average value for one ^{18}O-incorporated isotopomers. The observed two ^{13}C signals were not in equal intensity (~2:1), indicating a kinetic isotope effect may be involved. (b) The ^{13}C resonance difference between $PhCO_2H$ and $PhC^{18}O_2H$ is 0.046 ppm.

(22) In solid state, the carboxylate ligand exits in its η^2 mode. See: ref 15a.

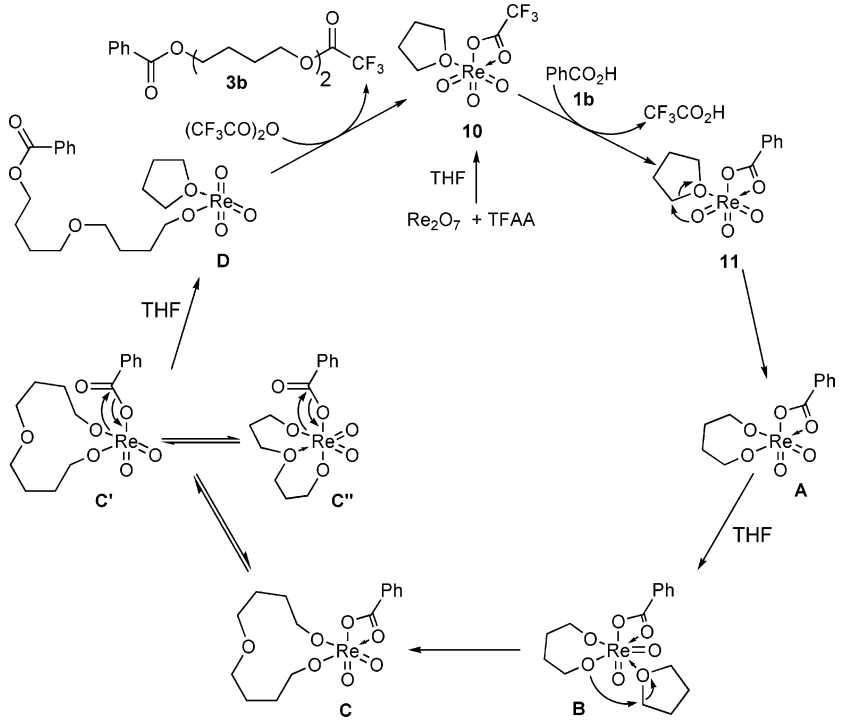
(23) (a) Three resonance structures of a Re═O bond, $Re^+—O^-$, Re═O, and $Re^-≡O^+$ have been analyzed; see: Herrmann, W. A., et al. *J. Am. Chem. Soc.* **1991**, *113*, 6527. (b) Upon complexation of a ligand, the increased electron density on the trans ligand could be attributable to a situation similar to a *trans influence* on the trans ligand; see: Cotton F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 5th ed.; John Wiley & Sons: New York, 1988; p 1300.

(24) (a) The THF ligand is believed to undergo fast exchange. As **3** was not generated in reactions conducted in THF, this result could be attributable to the fact that the THF is constantly undergoing exchange rather than sticking to Re, resulting in no ring opening of THF. (b) The presence of TFAA and CF_3CO_2H, generated in situ, can slow down the THF exchange rate and thereby promote ring opening of a bound THF.

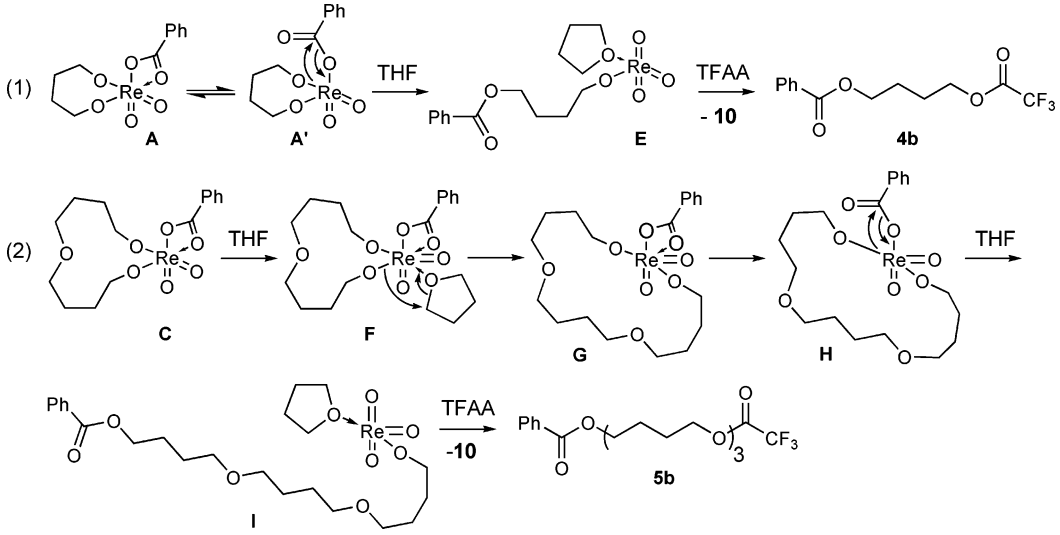
(25) (a) Al-Ajlouni, A. M.; Espenson, J. H. *J. Am. Chem. Soc.* **1995**, *117*, 9243. (b) Zhu, Z.; Al-Ajlouni, A. M.; Espenson, J. H. *Inorg. Chem.* **1996**, *35*, 1408.

(26) Herrmann, W. A.; Wojtczak, W. A.; Artus, G. R. J.; Kühn, F. E.; Mattner, M. R. *Inorg. Chem.* **1997**, *36*, 465. See: Scheme 2 on p 468.

Scheme 3. Proposed Catalytic Cycle



Scheme 4. Proposed Mechanism for the Formation of **4b** and **5b**



smaller analogue of **3b** (Scheme 4). Formation of **5b** reflects a minor route of THF coordination to **C**, leading to **F**, which could continue via **G**, **H**, then a metal alkoxide, **I**, and finally to **5b**. One possible mechanistic route to **3b** could involve a concerted ring-opening reaction in $ReO_3(THF)_2(\eta^1\text{-}O\text{-}OCOPh)$, where two THF ligands are concurrently bound to the metal.[27b] This model, however, cannot explain the formation of the trimeric products, **5b**, because a third THF ligand will bring the total electron count from 18 to 20. Therefore, it is more likely that the acylative dimerization reaction proceeds via a stepwise fashion with one coordinated THF at a time.

As some ring-opening reactions of THF have been reported to be governed by equilibrium control,[8b,10a,28] we conducted a series of control experiments to examine this possibility. A CH_2Cl_2 solution of **5b** was treated with a catalytic amount (10 mol %) of Re_2O_7, **10**, **11**, or CF_3CO_2H, separately, but no **3b** could be observed by TLC over a period of 24 h. Therefore, we exclude the equilibrium-control mechanism.

Apparently, TFAA plays an essential role in this reaction. On one hand, the coordinated trifluoroacetate in **10** is too electron-deficient to activate an oxo ligand for a nucleophilic attack on the coordinated THF (Table 1, entry 11). All other carboxylic acids examined, **1a**−**j**, seem to be sufficiently electron-rich to activate the oxo ligand (Table 1, entries 1−10). On the other hand, the low electrophilicity of other anhydrides examined (Table 3, entries 2−6) does not allow them to complete the last step of the catalytic cycle. Thus, the role of

(27) (a) Compounds **4** and **5** are further characterized by partial hydrolysis. See: Supporting Information for details. (b) Such a model would be entropy disfavored.

(28) Delfs, P. B. 717, O.T.S., U.S. Department of Commerce.

TFAA is twofold, first, to form a labile carboxylate complex, **10**, and, second, to cleave the metal−oxygen bond in complex **D**, producing **3** and regenerating the actual catalyst, **10**.

Conclusions

An effective Re-catalyzed THF ring opening/dimerization was discovered with Re_2O_7 serving as a convenient catalyst precursor. This catalyst exhibits high selectivity for unsubstituted THF, providing the most effective method currently available for ring opening of THF. The methodology is of synthetic value, particularly for polymer chemistry. Since isotope-labeled $Re_2{}^{17}O_7$ and $Re_2{}^{18}O_7$ can be easily prepared, the transfer of one oxygen atom from Re to the product can be utilized as a useful tool for the synthesis of oxygen-labeled organic molecules. Overall, this study has not only expanded the scope of rhenium catalysis but also highlighted the unique, frequently avoided Lewis acidity of transition-metal oxides.

Experimental Section

General Methods. Unless otherwise stated, all NMR spectral data were acquired in $CDCl_3$ at room temperature, in which ^1H and ^{13}C NMR spectra were obtained on a Varian-Mercury 300 MHz (75.5 MHz for ^{13}C) spectrometer, and $^{19}F\{^1H\}$ NMR data were obtained on a Bruker-AMX 400 MHz spectrometer. The ^1H and ^{13}C NMR chemical shifts are reported in ppm downfield from tetramethylsilane and referenced to residual solvent resonances (^1H NMR: δ 7.24 for $CDCl_3$; ^{13}C NMR: δ 77.00 for $CDCl_3$), where the ^1H NMR chemical shifts are given followed by multiplicity, coupling constants J in hertz, and integration in parentheses. For complex coupling patterns, e.g., δ (dt, J = 7.7, 4.8, 1H), the doublet (d) represents the larger coupling (7.7 Hz), and the triplet (t) indicates the smaller coupling (4.8 Hz). The $^{19}F\{^1H\}$ NMR chemical shifts are referenced to an external perfluorobenzene solution. Assignments are provided for key moieties only. High-resolution mass spectra were obtained on an Agilent ESI-TOF mass spectrometer. For ^{18}O-labeled starting materials, a technique of desorption/ionization on silicon (DIOS) was used with an Applied Biosystems Voyager-DE STR mass spectrometer, and the ^{18}O-labeled percentage was calculated according to published methods. Chromatography was carried out on silica gel (230-400 mesh) from Merck, or with a Harrison Research Chromatotron, where silica gel plates were used under an argon atmosphere. Thin-layer chromatography (TLC) was performed on aluminum- or glass-backed silica gel 60-F_{254} sheets from Merck and was visualized under a UV lamp and by a cerium(IV) sulfate or cerium(IV) molybdate staining agent. All reactions were conducted under argon unless otherwise stated.

Materials. Et_2O and THF were distilled over sodium benzophenone ketyl and potassium metal, respectively, and CH_2Cl_2 was distilled over CaH_2 under argon prior to use. Trifluoroacetic anhydride (TFAA) and liquid carboxylic acids were purified according to published procedures. Oxetane, tetrahydropyran, and substituted THF were distilled over potassium metal. Solid carboxylic acids were dried by azeotropic evaporation with CH_2Cl_2 repeatedly under a vacuum. Re_2O_7 was purchased from Strem. Labeled $H_2{}^{18}O$ (98.07 At%) was purchased from Rotem Industries, Israel. Labeled $Re_2{}^{18}O_7$ was prepared according to modified literature methods, and the ^{18}O-labeled percentage of Re_2O_7 was determined by the DIOS mass spectra obtained from ^{18}O-labeled $AgReO_4$. Complexes **10** and **11** were prepared either in situ or in their isolated form prior to use.

PhC$^{18}O_2$H. Benzoic acid (514 mg, 4.2 mmol) was dissolved in a mixture of $H_2{}^{18}O$ (98 At%, 1 mL) and a solution of HCl in Et_2O (2 mL, 1M) in a 25 mL reaction bomb. The reaction vessel was heated at 65 °C with vigorous stirring under a closed condition for 24 h. Volatile species was then removed, and the process was repeated once. The obtained residue was redissolved in Et_2O (20 mL), and the resulting solution was concentrated to a volume of ca. 1.5 mL. The solution part was removed, and the obtained solid was further dried in vacuo over KOH to afford the title compound as a white crystalline solid (450 mg, 85%). The ^{18}O-incorporation of the title compound is estimated to be >92%, as calculated from the obtained mass spectra according to literature methods. ESI-DIOS: m/z 125 (100, $PhC^{18}O_2^-$), 123 (9, $PhC^{18}O^{16}O^-$), 121 (2, $PhCO_2^-$).

$Re_2{}^{18}O_7$. The isotope-enriched Re_2O_7 has been previously prepared (eqs 1−3).

$$Re_2O_7 + H_2O \rightarrow [2\ HReO_4] \xrightarrow[-2\ HNO_3]{2\ AgNO_3} 2\ AgReO_4 \qquad (1)$$

$$AgReO_4 + (CH_3)_3SiCl \xrightarrow{-AgCl} (CH_3)_3SiOReO_3 \qquad (2)$$

$$2(CH_3)_3SiOReO_3 + 2\ THF \xrightarrow{-[(CH_3)_3Si]_2O} Re_2O_7(THF)_2 \qquad (3)$$

AgRe$^{18}O_4$. To ensure high ^{18}O-isotope incorporation into the rhenium oxide bonds, the procedure for the preparation of $AgRe^{18}O_4$ was modified. Re_2O_7 (485 mg, 1.0 mmol) was dissolved in 1 mL of $H_2{}^{18}O$ (98 At%), and the resulting solution was stirred at room temperature for 4 h. Volatile species was then removed under a vacuum, and the process was repeated twice. In a separate flask, $AgNO_3$ (341 mg, 2.0 mmol) was dissolved in 1 mL of $H_2{}^{18}O$ (98 At%) in a 25 mL reaction bomb, and the resulting solution was heated at 65 °C with vigorous stirring under a closed condition for 24 h. Volatile species was removed under a vacuum, and the process was repeated once. The $H_2{}^{18}O$-treated $AgNO_3$ salt was then added to the previous reaction flask containing ^{18}O-labeled $HRe^{18}O_4$, and 1 mL of $H_2{}^{18}O$ (98 At%) was added with stirring. A white precipitate was observable immediately. The resulting mixture was allowed to stir at room temperature for 1 h under subdued room light. The white precipitate was collected with a glass-fritted funnel and washed with Et_2O (2 × 10 mL), and was further dried in vacuo over KOH to afford the title complex as a white powder (656 mg). The ^{18}O-incorporation of the title compound is estimated to be >90%, as calculated from the obtained ESI-DIOS mass spectra and the computer-simulated isotope pattern.

Ring Opening/Dimerization Reactions of THF. Catalytic Reactions. (*Method a*) Using **1b** as an example. In a typical reaction, Re_2O_7 (130 mg, 0.268 mmol) was placed in a Schlenk flask under argon and the flask was capped with a septum. CH_2Cl_2 (8 mL) was added via syringe, followed by the addition of TFAA (570 μL, 4.035 mmol) and THF (550 μL, 6.780 mmol). Under positive argon pressure, **1b** (332 mg, 2.718 mmol) was added, and the reaction mixture was allowed to stir at room temperature for 24 h. The reaction mixture was worked up with saturated $NaHCO_3$ aqueous solution (8 mL) and H_2O_2 (35 wt %, 2 mL) and was extracted with ether (3 × 25 mL). The ether extract was dried with $MgSO_4$ and concentrated under a vacuum and was purified by column chromatography (hexanes/EtOAc = 5:1) to afford **3b** (935 mg, 95%), **4b** (24 mg, 3%), and **5b** (11 mg, < 1%) as a colorless oil, respectively. The yield is based on **1b**.

(*Method b*) In a typical reaction, Re_2O_7 (130 mg, 0.268 mmol) was placed in a Schlenk flask under argon and the flask was capped with a septum. THF (550 μL, 6.780 mmol) was added via syringe, and the solution was allowed to stir until Re_2O_7 was completely dissolved. CH_2Cl_2 (8 mL) was added and a clear solution resulted. TFAA(570 μL, 4.035 mmol) and **1b** (332 mg, 2.718 mmol) were then added, respectively, and the reaction mixture was allowed to stir under argon for 24 h. The result obtained was almost the same as that described in *method a*.

Stoichiometric Reactions. Similar to the procedure described in the catalytic reactions. In a typical reaction, the reaction was conducted in CH_2Cl_2 (8 mL) with the molar ratio of Re_2O_7/TFAA/**1b** : THF being equal to 1.15:3.45:2.0:6.90, in which 332 mg of **1b** were used. The reaction mixture was allowed to stir at room temperature for 24 h, and the workup was carried out as stated in the catalytic reactions.

Isotope Labeling Experiments. The procedure described in the stoichiometric reactions was followed, and $PhC^{18}O_2H$ and $Re_2{}^{18}O_7$ were used in separate reactions, respectively. According to the ESI-TOF mass spectra of the isolated products, isopotomers with one ^{18}O-incorporation were observed along with peaks associated with their ^{16}O-analogues. Isotopomers with two or more ^{18}O-incorporation were not observed. The same result was obtained from **3b**, **4b**, and **5b**. HRMS *m*/*z* 385.1237 (**3b**·Na^+ = 385.1233), 387.1280 (**3b**·$Na^+ - {}^{18}O_1$ = 387.1276); 313.0677 (**4b**·Na^+ = 313.0658), 315.0713 (**4b**·$Na^+ - {}^{18}O_1$ = 315.0701); 457.1816 (**5b**·Na^+ = 457.1808), 459.1858 (**5b**·$Na^+ - {}^{18}O_1$ = 459.1851).

Compound 1a: Homoallylic carboxylic acid **1a** was obtained by hydrolysis of its corresponding ethyl ester, which was prepared from undecanal (Aldrich) according to conventional methods described for the syntheses of homoallylic alcohols.[5b] ^{1}H NMR δ 11.25 (br s, 1H), 5.50−5.30 (m, 2H), 2.42−2.36 (m, 2H), 2.32−2.27 (m, 2H), 1.96−1.93 (m, 2H), 1.40−1.20 (m, 16H), 0.88−0.83 (m, 3H).

Compound 3a: ^{1}H NMR (600 MHz) δ 5.45−5.35 (m, 2H), 4.37 (t, J = 6.6, 2H, CH_2OC(O)CF_3), 4.07 (t, J = 6.5, 2H, CH_2OC(O)CH_2-CH_2—), 3.43 (t, J = 6.0, 2H), 3.41 (t, J = 6.0, 2H), 2.35−2.32 (m, 2H, HC═CH—CH_2CH_2CO_2—), 2.30−2.27 (m, 2H, HC═CH—CH_2CH_2-CO_2—), 1.95−1.93 (m, 2H, HC═CH—C$H_2C_9H_{19}$), 1.84−1.82 (m, 2H, CH_2CH_2OC(O)CF_3), 1.69−1.59 (m, 6H), 1.32−1.23 (m, 16H), 0.86 (vt, J = 5.9, 3H); ^{13}C NMR (150.9 MHz) δ 173.32, 157.51 (q, J = 41.3, *C*O*C*F_3), 131.85 (HC═*C*H$C_{10}H_{21}$), 127.84 (H*C*═CH$C_{10}H_{21}$), 114.45 (q, J = 285.8, *C*F_3), 70.35, 69.88, 68.06 (*C*H_2OC(O)CF_3), 64.06 (*C*H_2OC(O)CH_2CH_2—), 34.39, 32.49, 31.89, 29.62 (for 2 C), 29.49, 29.43, 29.33, 29.13, 27.93, 26.19, 25.81, 25.50, 25.22, 22.66, 14.09 (*C*H_3). The assignment is based on COSY, HMBC, and APT spectra.

Compound 3b: ^{1}H NMR δ 8.02 (app d, J = 7.8, 2H), 7.53 (app t, J = 7.2, 1H), 7.41 (app t, J = 7.6, 2H), 4.35 (t, J = 6.3, 2H, CH_2-OCO*C*F_3), 4.32 (t, J = 6.6, 2H, CH_2OCOPh), 3.45 (t, J = 6.0, 2H), 3.43 (t, J = 6.0, 2H), 1.85−1.60 (m, 8H); ^{13}C NMR δ 166.56, 157.46 (q, J = 42.1, *C*O*C*F_3), 132.82, 130.34, 129.49, 128.28, 114.49 (q, J = 285.8, *C*F_3), 70.34, 69.87, 68.06, 64.70 (*C*H_2OCOPh), 26.28, 25.79, 25.59, 25.20; ^{19}F NMR δ −74.83. HRMS *m*/*z* 385.1219 385.1236 (MNa^+ = 385.1233).

Compound 3c: ^{1}H NMR δ 7.90 (d, J = 8.0, 2H), 7.21 (d, J = 8.0, 2H), 4.36 (t, J = 6.6, 2H), 4.30 (t, J = 6.6, 2H), 3.45 (t, J = 5.4, 2H), 3.43 (t, J = 6.0, 2H), 2.38, (s, 3H), 1.85−1.60 (m, 8H); ^{13}C NMR δ 166.69, 157.49 (q, J = 41.2, *C*O*C*F_3), 143.49, 129.52, 129.00, 127.58, 114.49 (q, J = 258.8, *C*F_3), 70.37, 69.88, 68.07, 64.53, 26.28, 25.79, 25.59, 25.20, 21.60 (*C*H_3).

Compound 3d: ^{1}H NMR δ 7.96 (d, J = 8.7, 2H), 6.88 (d, J = 8.7, 2H), 4.35 (t, J = 6.5, 2H), 4.28 (t, J = 6.3, 2H), 3.44 (t, J = 6.0, 2H), 3.42 (t, J = 6.0, 2H), 1.85−1.60 (m, 8H); ^{13}C NMR δ 166.33, 163.24, 157.45 (q, J = 42.1, *C*O*C*F_3), 131.49, 122.74, 114.47 (q, J = 285.8, *C*F_3), 113.50, 70.35, 69.85, 68.06, 64.38, 55.34 (O*C*H_3), 26.28, 25.77, 25.61, 25.19.

Compound 3e: ^{1}H NMR δ 8.26 (AB pattern d, J = 8.7, 2H), 8.19 (AB pattern d, J = 8.7, 2H), 4.38 (t, J = 6.3, 2H), 4.37 (t, J = 6.6, 2H), 3.46 (t, J = 6.3, 2H), 3.44 (t, J = 6.0, 2H), 1.90−1.60 (m, 8H); ^{13}C NMR δ 164.71, 157.52 (q, J = 42.1, *C*O*C*F_3), 150.48, 135.72, 130.66, 123.52, 114.50 (q, J = 285.8, *C*F_3), 70.27, 70.02, 68.06, 65.77, 26.24, 25.79, 25.58, 25.25.

Compound 3f: ^{1}H NMR δ 7.97 (d, J = 8.4, 2H), 7.43 (d, J = 8.4, 2H), 6.72 (dd, J = 17.7, 10.8, 1H, C*H*═CH_2), 5.84 (d, J = 17.7, 1H), 5.35 (d, J = 10.8, 1H), 4.36 (t, J = 6.6, 2H), 4.32 (t, J = 6.3, 2H), 3.45 (t, J = 6.0, 2H), 3.43 (t, J = 5.7, 2H), 1.87−1.59 (m, 8H); ^{13}C NMR δ 166.37, 157.47 (q, J = 42.1, *C*O*C*F_3), 141.84, 135.95 (*C*H═CH_2), 129.81, 129.42, 126.03, 116.41 (CH═*C*H_2), 114.49 (q, J = 285.6, *C*F_3), 70.35, 69.89, 68.06, 64.70, 26.26, 25.77, 25.58, 25.19.

Compound 3g: ^{1}H NMR δ 7.40−7.20 (m, 5H), 4.35 (t, J = 6.6, 2H), 4.09 (t, J = 6.3, 2H), 3.60 (s, 2H), 3.39 (t, J = 6.3, 2H), 3.37 (t, J = 6.3, 2H), 1.86−1.76 (m, 2H), 1.73−1.52 (m, 6H); ^{13}C NMR δ 171.54, 157.42 (q, J = 42.1, *C*O*C*F_3), 134.06, 129.16, 128.45, 126.95, 114.47 (q, J = 285.8, *C*F_3), 70.19, 69.76, 68.03, 64.58, 41.33 (*C*H_2-Ph), 26.02, 25.73, 25.38, 25.16.

Compound 3h: ^{1}H NMR δ 7.66 (d, J = 15.9, 1H), 7.52−7.49 (m, 2H), 7.37−7.35 (m, 3H), 6.42 (d, J = 15.9, 1H), 4.37 (t, J = 6.6, 2H), 4. 21 (t, J = 6.3, 2H), 3.44 (t, J = 6.2, 4H), 1.86−1.60 (m, 8H); ^{13}C NMR δ 167.03, 157.51 (q, J = 42.1, *C*O*C*F_3), 144.67, 134.37, 130.24, 128.86, 128.03, 118.10, 114.50 (q, J = 285.8, *C*F_3), 70.36, 69.89, 68.08, 64.31, 26.23, 25.82, 25.59, 25.22.

Compound 3i: ^{1}H NMR δ 4.36 (t, J = 6.5, 2H), 4.06 (t, J = 6.5, 2H), 3.42 (t, J = 6.0, 2H), 3.40 (t, J = 5.4, 2H), 2.03 (s, 3H), 1.85−1.76 (m, 2H), 1.73−1.50 (m, 6H); ^{13}C NMR δ 170.99, 157.32 (q, J = 41.2, *C*O*C*F_3), 114.41 (q, J = 285.8, *C*F_3), 70.17, 69.74, 67.96, 64.10, 26.03, 25.67, 25.34, 25.10, 20.72 (*C*H_3); HRMS *m*/*z* 323.1074 (MNa^+ = 323.1082).

Compound 3j: ^{1}H NMR δ 4.37 (t, J = 6.5, 2H), 4.05 (t, J = 6.2, 2H), 3.42 (t, J = 6.3, 2H), 3.41 (t, J = 5.4, 2H), 1.86−1.75 (m, 2H), 1.70−1.55 (M, 6H), 1.17 (s, 9H); ^{13}C NMR δ 178.58, 157.48 (q, J = 42.1, *C*O*C*F_3), 114.49 (q, J = 285.8, *C*F_3), 70.37, 69.85, 68.06, 64.09, 38.69 (*C*Me_3), 27.14 (*C*H_3), 26.18, 25.79, 25.48, 25.22.

Compound 3k: ^{1}H NMR δ 4.36 (t, J = 6.6, 4H), 3.43 (t, J = 6.0, 4H), 1.86−1.78 (m, 4H), 1.69−1.60 (m, 4H); ^{19}F NMR δ −74.85. HRMS *m*/*z* 377.0803 (MNa^+ = 377.0794).

Compound 3l: ^{1}H NMR δ 4.06 (t, J = 6.3, 4H), 3.41 (t, J = 6.2, 4H), 2.03 (s, 6H), 1.72−1.58 (m, 8H). HRMS *m*/*z* 269.1357 (MNa^+ = 269.1359).

Compound 3m: ^{1}H NMR δ 8.02 (app d, J = 7.8, 4H), 7.53 (app t, J = 7.2, 2H), 7.41 (app t, J = 7.6, 4H), 4.33 (t, J = 6.6, 4H, CH_2-OC(O)Ph), 3.47 (t, J = 6.0, 4H), 1.90−1.68 (m, 8H); ^{13}C NMR δ 166.62, 132.84, 130.37, 129.53, 128.31, 70.33, 64.79, 26.35, 25.63. HRMS *m*/*z* 393.1677 (MNa^+ = 393.1672).

Compound 4b: ^{1}H NMR δ 8.02 (app d, J = 7.8, 2H), 7.56 (app t, J = 7.2, 1H), 7.43 (app t, J = 7.7, 2H), 4.42 (t, J = 6.0, 2H), 4.36 (t, J = 6.0, 2H), 1.92−1.87 (m, 4H); ^{19}F NMR δ −74.77.

Compound 5b: ^{1}H NMR δ 8.02 (app d, J = 8.1, 2H), 7.54 (app t, J = 7.2, 1H), 7.42 (app t, J = 7.7, 2H), 4.36 (t, J = 6.6, 2H), 4.33 (t, J = 6.6, 2H), 3.48−3.38 (m, 8H), 1.90−1.58 (m, 12H); ^{13}C NMR, partial spectrum (carbon signals for *C*O*C*F_3 are not provided) δ 166.63, 132.84, 130.38, 129.52, 128.31, 70.75, 70.68, 70.22, 69.80, 68.11, 64.80, 26.47 (with high intensity, two ^{13}C signals overlapping), 26.35, 25.83, 25.62, 25.42; ^{19}F NMR δ −74.85. HRMS *m*/*z* 457.1806 (MNa^+ = 457.1808).

Partial Hydrolysis of 3b. Compound **3b** was further characterized by partial hydrolysis to remove the trifluoroacetyl group. Compound **3b** (20 mg) was dissolved in CH_2Cl_2 (5 mL), and a small amount of silica gel was added. The resulting mixture was allowed to stir overnight at room temperature. The solvent of the reaction mixture was evaporated, and the residue was purified by column chromatography (hexanes/EtOAc = 2.5 :1) to afford the partially hydrolyzed product, $PhCO_2(CH_2)_4O(CH_2)_4OH$, in quantitative yield. ^{1}H NMR δ 8.00 (app d, J = 8.0, 2H), 7.51 (app t, J = 7.5, 1H), 7.39 (app t, J = 7.6, 2H), 4.31 (t, J = 6.5, 2H), 3.60 (t, J = 6.2, 2H), 3.46 (t, J = 6.3, 2H), 3.43 (t, J = 5.7, 2H), 2.70 (br s, 1H, O*H*), 1.88−1.58 (m, 8H); ^{13}C NMR δ 166.59, 132.80, 130.23, 129.45, 128.25, 70.85, 70.32, 64.67, 62.58 (*C*H_2OH), 30.10, 26.69, 26.16, 25.51.

Partial Hydrolysis of 5b. Compound **5b** (5 mg) was partially hydrolyzed, as described in the case of **3b**, to afford $PhCO_2(CH_2)_4O$-$(CH_2)_4O(CH_2)_4OH$ in quantitative yield. ^{1}H NMR δ 8.02 (app d, J = 8.0, 2H), 7.54 (app t, J = 7.5, 1H), 7.42 (app t, J = 7.8, 2H), 4.32 (t, J = 6.3, 2H), 3.64−3.60 (m, 2H), 3.47−3.39 (m, 8H), 2.50 (br s, 1H, O*H*), 1.90−1.58 (m, 12H); ^{13}C NMR δ 166.65, 132.84, 130.39, 129.53, 128.31, 70.88, 70.83, 70.63, 70.22, 64.83, 62.78 (*C*H_2OH), 30.44, 26.99, 26.43, 26.40, 26.36, 25.63.

Reactivity of Other Cyclic Ethers and Substituted THF. The procedure described in the catalytic reactions of THF was followed. See Tables 2 and 3 for yields.

Compound 6: ^{1}H NMR δ 8.06 (app d, J = 7.6, 2H), 7.58 (app t, J = 7.2, 1H), 7.43 (app t, J = 7.6, 2H), 4.37 (t, J = 6.2, 4H), 3.42 (t, J = 6.0, 4H), 1.96−1.88 (m 4H); ^{13}C NMR δ 162.18, 157.27 (q, J = 42.1, *C*OCF$_3$), 134.43, 130.43, 128.76, 120.07, 114.40 (q, J = 285.8, *C*F$_3$), 66.57 (with high intensity, two ^{13}C signals overlapping), 65.23 (with high intensity, two ^{13}C signals overlapping), 28.50 (with high intensity, two ^{13}C signals overlapping).

Compound 7: ^{1}H NMR δ 8.02 (app d, J = 8.1, 2H), 7.53 (app t, J = 7.2, 1H), 7.41 (app t, J = 7.5, 2H), 4.33 (t, J = 6.6, 2H), 4.31 (t, J = 6.4, 2H), 3.42 (t, J = 6.5, 2H), 3.40 (t, J = 6.1, 2H), 1.84−1.70 (m, 4H), 1.67−1.40 (m, 8H); ^{13}C NMR δ 166.36, 157.50 (q, J = 42.1, *C*OCF$_3$), 132.65, 130.24, 129.34, 128.14, 114.39 (q, J = 285.8, *C*F$_3$), 70.70, 70.40, 68.15, 64.95, 29.49, 29.29, 28.70, 28.09, 22.93, 22.50.

Compound 8a: ^{1}H NMR δ 8.02 (app d, J = 8.2, 2H), 7.55 (app t, J = 7.2, 1H), 7.43 (app t, J = 7.8, 2H), 5.20−5.13 (m, 1H), 4.37−4.30 (m, 2H), 1.92−1.72 (m, 4H), 1.38 (d, J = 6.3, 3H); ^{13}C NMR δ 166.39, 157.03 (q, J = 42.1, *C*OCF$_3$), 132.94, 130.03, 129.45, 128.32, 114.49 (q, J = 285.8, *C*F$_3$), 75.89 (*C*HCH$_3$), 64.08 (*C*H$_2$OCOPh), 31.97, 24.41, 19.36 (*C*H$_3$). The characterization is based on APT and the ^{13}C NMR data of the product isolated from the reaction with ^{13}C-labeled **1b**.

Compound 8b: ^{1}H NMR δ 8.03 (app d, J = 7.5, 2H), 7.53 (app t, J = 7.2, 1H), 7.41 (app t, J = 7.8, 2H), 5.28−5.10 (m, 1H), 4.37−4.30 (m, 2H), 1.92−1.72 (m, 4H), 1.37 (d, J = 6.3, 3H); ^{13}C NMR, partial spectrum, δ 166.04, 132.82, 132.76, 128.26, 71.03 (*C*HCH$_3$), 64.57 (*C*H$_2$OCOCF$_3$), 32.51, 24.80, 19.98 (*C*H$_3$).

Compound 9 (syn and anti): ^{1}H NMR, combined spectra, δ 8.02 (app d, J = 7.2, 2H), 7.55 (app t, J = 7.2, 1H), 7.43 (app t, J = 7.7, 2H), 5.23−5.05 (m, 2H), 1.90−1.60 (m, 4H), 1.35 (d, J = 6.3, 6H); ^{13}C NMR, combined spectra, δ 166.05, 157.09 (q, J = 42.1, *C*OCF$_3$), 132.91, 130.43, 129.49, 128.34, 114.52 (q, J = 286.2, *C*F$_3$), 76.21, 75.98, 70.96, 70.62, 31.58, 31.48, 31.42, 31.23, 20.04, 20.02, 19.46 (2 × C).

Acknowledgment. We thank the Israel-US Binational Science Foundation, the German-Israeli Project Cooperation (DIP), and the Skaggs Institute for Chemical Biology. S.C.S thanks the NIH for Grant GM63914-2. E.K. is the incumbent of Benno Gitter and Ilana Ben-Ami chair of Biotechnology, Technion.

JA0668668