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Metal-Free Reductive Cleavage of C−O σ-bonds in Acyloin Derivatives by an Organic Neutral Super-Electron-Donor†

Sylvain P. Y. Cutulic,‡ Neil J. Findlay,‡ Sheng-Ze Zhou,‡ Ewan J. T. Chrystal,§ and John A. Murphy*,‡

‡WestCHEM, Department of Pure and Applied Chemistry, University of Strathclyde, Thomas Graham Building, 295 Cathedral Street, Glasgow, G1 1XL, United Kingdom, and §Syngenta, Research International Centre, Bracknell RG42 6EY, United Kingdom

john.murphy@strath.ac.uk

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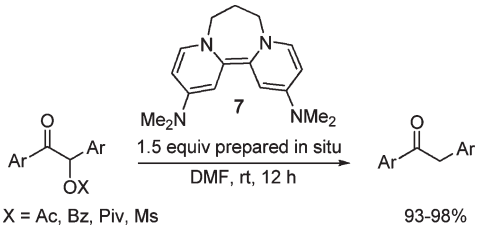

Neutral organic electron-donor **7**, formally a pyridinylidene carbene dimer, effects reductive cleavage of C−O σ-bonds in acyloin derivatives Ar(CO)CRR′OX (X = OAc, OPiv, OBz, OMs) and this represents the first cleavage of C−O σ-bonds by a neutral organic electron-donor. The methodology is applicable to a large array of substrates and the reduced counterparts were isolated in good to excellent yields. For certain substrates, donor **7** behaves as a base, effecting condensation reactions with some acetate ester derivatives of acyloins, leading to butenolides. The variation in reactivity among the different substrates was rationalized.

Introduction

Benzoins are classically prepared by the cyanide-mediated benzoin condensation of aromatic aldehydes,[1] and, more generally, acyloins (α-hydroxyketones and aldehydes) have long been efficiently synthesized from esters by the acyloin condensation by using dissolving metals, with or without trimethylchlorosilane.[2] Spectacular recent advances have greatly increased access to acyloins and related compounds, using aldehydes and ketones in reactions that are mediated by *N*-heterocyclic carbenes present either as enzyme cofactors[3] or as reagents in organic solution.[4,5]

The assembly of the two carbonyl components to form an acyloin is a useful C−C bond formation, but the products have wider use when they can be converted into simple ketones by reductive cleavage of the α-hydroxy group. Methodologies have been developed recently to perform this reductive C−O bond cleavage. Yamaguchi reduced benzoin derivatives using a complex system containing 1,3-propanedithiol, *N*-methylmorpholine, and tetrabutylammonium fluoride hydrate. (We assume that this works through oxidation of the thiolate.[6]) Metal-based methodologies have also been developed: acyloin derivatives have been successfully

† This paper is dedicated to the memory of the late Dr. Ewan J. T. Chrystal.

(1) Woehler, F.; von Liebig, J. *Ann. Pharm.* **1832**, *3*, 249–282. Lapworth, A. J. *J. Chem. Soc., Trans.* **1904**, *85*, 1206–1214.

(2) Finley, K. T. *Chem. Rev.* **1964**, *64*, 573–589. Rühlmann, K. *Synthesis* **1971**, 236–253. Makosza, M.; Grela, K. *Synlett* **1997**, 267–268. Kashimura, S.; Murai, Y.; Ishifune, M.; Masuda, H.; Murase, H.; Shono, T. *Tetrahedron Lett.* **1995**, *36*, 4805–4808. Bloomfield, J. J.; Owsley, D. C.; Ainsworth, C.; Robertson, R. E. *J. Org. Chem.* **1975**, *40*, 393–402.

(3) For reviews, see: Sukumaran, J.; Hanefeld, U. *Chem. Soc. Rev.* **2005**, *34*, 530–542. Muller, M.; Gocke, D.; Pohl, M. *FEBS J.* **2009**, *276*, 2894–2904.

(4) Ugai, T.; Tanaka, S.; Dokawa, S. *J. Pharm. Soc. Jpn.* **1943**, *63*, 269. Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719–3726. Stetter, H.; Rämsch, R. Y.; Kuhlmann, H. *Synthesis* **1976**, 733–735. Teles, J. H.; Stetter, H.; Rämsch, R. Y. *Synthesis* **1981**, 477–478. Melder, J.-P.; Ebel, K.; Schneider, R.; Gehrer, E.; Harder, W.; Brode, S.; Enders, D.; Breuer, K.; Raabe, G. *Helv. Chim. Acta* **1996**, *79*, 61. Murry, J. A.; Frantz, D. E.; Soheili, A.; Tillyer, R.; Grabowski, E. J. J.; Reider, P. J. *J. Am. Chem. Soc.* **2001**, *123*, 9696–9397. Enders, D.; Kallfass, U. *Angew. Chem., Int. Ed.* **2002**, *41*, 1743–1745. Dudding, T.; Houk, K. N. *Proc. Nat. Acad. Sci. U.S.A.* **2004**, *101*, 5770–5775. Mattason, A. E.; Scheidt, K. A. *Org. Lett.* **2004**, *6*, 4363–4366. Mennen, S. M.; Gipson, J. D.; Kim, Y. R.; Miller, S. J. *J. Am. Chem. Soc.* **2005**, *127*, 1654–1655. Linghu, X.; Bausch, C. C.; Johnson, J. S. *J. Am. Chem. Soc.* **2005**, *127*, 1833–1840. Demir, A. S.; Esiringü, I.; Göllü, M.; Reis, Ö. *J. Org. Chem.* **2009**, *74*, 2197–2199.

(5) For reviews, see: Enders, D; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606–5655. Rovis, T. *Chem. Lett.* **2008**, *37*, 2–7. Enders, D.; Niemeier, O. *Synlett* **2004**, 2111–2114. Marion, N.; Diez-Gonzalez, S.; Nolan, I. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2988–3000.

(6) Ueki, M.; Okamura, A.; Yamaguchi, J. *Tetrahedron Lett.* **1995**, *41*, 7467–7470.

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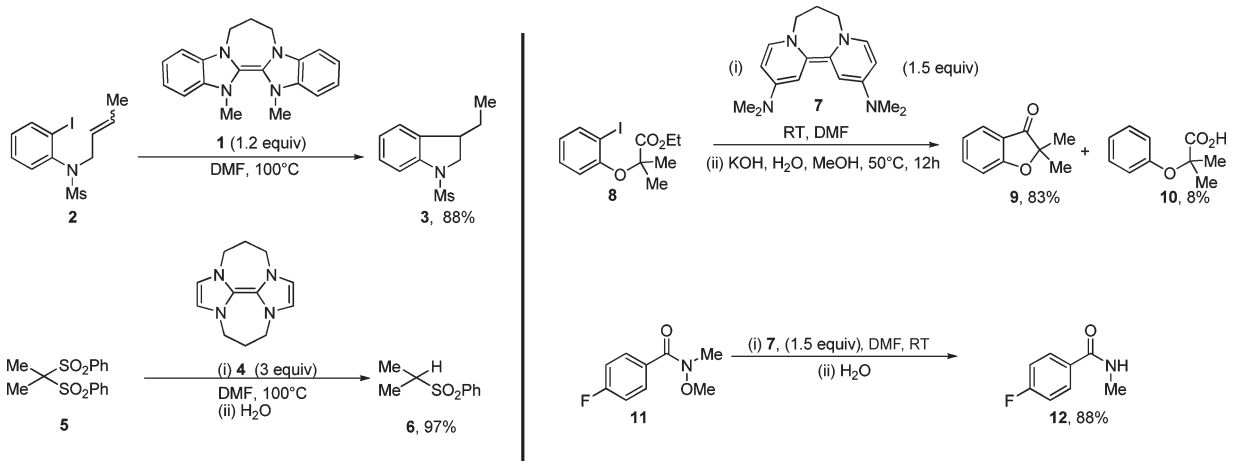
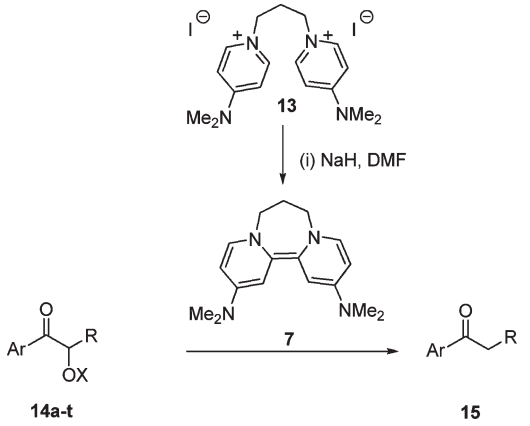
SCHEME 1. Reduction of Substrates by Super-Electron-Donors 1, 4, and 7



reduced into their ketone counterparts with use of zinc and ammonium chloride in ethanol under reflux,[7] titanium on activated graphite,[8] Raney nickel,[9] or metallic salts, such as titanium chloride in combination with zinc[10] or samarium(II) diiodide.[11] Alternative approaches have used phenyldimethylsilyllithium[12] and a vanadium complex $[V_2Cl_3(THF)_6]_2[Zn_2Cl_6]$, prepared in situ from vanadium trichloride and zinc dust.[13] Hence this is a very active area of wide interest to synthetic chemists.

Our aim was to develop a tailored organic reagent for this reduction. Along these lines, neutral ground state "super-electron-donor" reagents [defined as organic ground state electron-donors that are powerful enough to dehalogenate haloarenes] have recently been developed in our laboratories.[14−20] Reagent **1**, formally a dimer of a benzimidazolylidene carbene, reduced aryl and alkyl iodides to aryl and alkyl radicals, respectively; in appropriate substrates,[14] these radicals underwent cyclization reactions as shown for iodoarene **2** in Scheme 1. Recently, two more powerful neutral ground state electron-donors, **4** and **7**, have been developed within our laboratories.[15−20] These reagents readily transfer two electrons, converting aryl iodides into aryl anions, performing reductive cleavages of sulfones and reductively cleaving N−O bonds in Weinreb amides (Scheme 1).[19] This paper now explores the first cleavages of C−O σ-bonds with the strong, neutral organic electron-donor **7**.

SCHEME 2. Reduction of Substrates 14 with Donor 7, Prepared in Situ from Salt 13



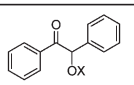
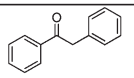
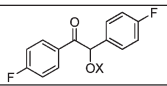
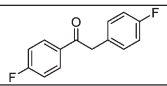
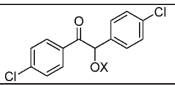
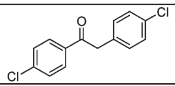
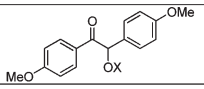
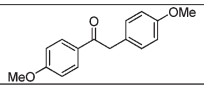
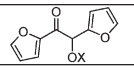
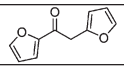
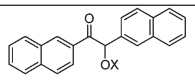
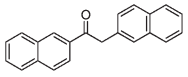
Results and Discussion

Acyloins were purchased commercially or prepared by reaction of *N*-heterocyclic carbenes with the appropriate aldehydes. The acyloin OH groups were then converted into ether and ester derivatives.

Different substrates were reacted as shown in Scheme 2 with electron-donor **7**, prepared in situ from precursor **13**.[17] Results of these reactions are summarized in Table 1. Methylated benzoin derivative **14a** was first selected. At 20 °C, no reaction was seen. Even when the temperature of the reaction mixture was brought to 100 °C, very little reductive C−O bond cleavage was observed (tentative identification was estimated at 5% maximum from the ^{1}H NMR spectrum of the unpurified reaction mixture). However, when the methoxy group was replaced by a more electron-withdrawing group (substrates **14b−e**) efficient reduction was achieved at room temperature to afford desoxybenzoin **15** in excellent

(7) Yao, Z.; Ye, D.; Liu, H.; Chen, K.; Jiang, H. *Synth. Commun.* **2007**, *37*, 149–156.
(8) Fuerstner, A.; Jumbam, D. N. *Tetrahedron* **1992**, *48*, 5991–6010.
(9) Satoh, T.; Hayashi, Y.; Mizu, Y.; Yamakawa, K. *Tetrahedron Lett.* **1992**, *33*, 7181–7184.
(10) Fuerstner, A.; Hupperts, A.; Ptock, A.; Janssen, E. *J. Org. Chem.* **1994**, *59*, 5215–5229.
(11) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693–2698.
(12) Fleming, I.; Roberts, R. S.; Smith, S. C. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1215–1228.
(13) Inokuchi, T.; Kawafuchi, H.; Torii, S. *Chem. Lett.* **1992**, 1895–1896.
(14) Murphy, J. A.; Khan, T. A.; Zhou, S.; Thomson, D. W.; Mahesh, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1356–1360. This work emanated from previous electron transfer studies with tetrathiafulvalene: Fletcher, R. J.; Lampard, C.; Murphy, J. A.; Lewis, N. *J. Chem. Soc., Perkin Trans. 1* **1995**, 623–633. Lampard, C.; Murphy, J. A.; Lewis, N. *J. Chem. Soc., Chem. Commun.* **1993**, 295–297.
(15) Murphy, J. A.; Zhou, S.; Thomson, D. W.; Schoenebeck, F.; Mahesh, M.; Park, S. R.; Tuttle, T.; Berlouis, L. E. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 5178–5183.
(16) Schoenebeck, F.; Murphy, J. A.; Zhou, S.; Uenoyama, Y.; Miclo, Y.; Tuttle, T. *J. Am. Chem. Soc.* **2007**, *129*, 13368–13369.
(17) Murphy, J. A.; Garnier, J.; Park, S. R.; Schoenebeck, F.; Zhou, Z.-S.; Turner, A. T. *Org. Lett.* **2008**, *10*, 1227–1230.
(18) Garnier, J.; Murphy, J. A.; Zhou, S.-Z.; Turner, A. T. *Synlett* **2008**, 2127–2131.
(19) Cutulic, S. P. Y.; Murphy, J. A.; Farwaha, H.; Zhou, S.-Z.; Chrystal, E. *Synlett* **2008**, 2132–2136.
(20) Murphy, J. A.; Schoenebeck, F.; Findlay, N. J.; Thomson, D. W.; Zhou, S.-Z.; Garnier, J. *J. Am. Chem. Soc.* **2009**, *131*, 6475–6479.

TABLE 1. Reduction of Substrates 14 with Donor 7

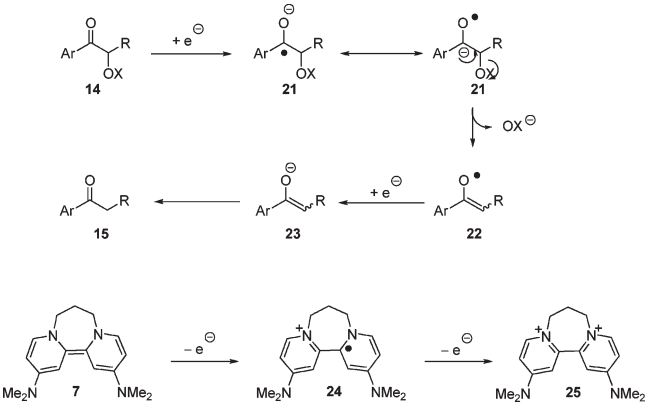
Entry	*Substrate*	*Product*	*Yield*
			
1	**14a**, X = Me	**15**	<5%[a]
2	**14b**, X = Ms		93%
3	**14c**, X = Ac		95%
4	**14d**, X = Piv		98%
5	**14e**, X = Bz		97%
			
6	**14f**, X = Ms	**16**	94%
7	**14g**, X = Ac		92%
8	**14h**, X = Piv		93%
			
9	**14i**, X = Ms	**17**	95%
10	**14j**, X = Ac		97%
11	**14k**, X = Piv		98%
			
12	**14l**, X = Ac	**18**	93%
13	**14m**, X = Piv		96%
			
14	**14n**, X = Ac	**19**	88%
15	**14o**, X = Piv		90%
			
16	**14p**, X = Ac	**20**	92%
17	**14q**, X = Piv		94%

[a]From ^{1}H NMR spec of crude reaction product.

yields (93−98%). The reaction was then successfully extended to benzoin-related compounds with either electron-withdrawing substituents (entries **14f**−**k**) or electron-donating substituents (**14l**,**m**) on the arene rings. In both cases, C−O bond reductive cleavage was performed with 1.5 equiv of donor **7** at room temperature and their reduced counterparts **16**, **17**, and **18** were isolated in excellent yields (92−98%). The same reaction also proved successful on benzoin-related compounds derived from either furans (**14n**,**o**) or naphthalenes (**14p**,**q**) to afford their reduced counterparts **19** and **20** in very good yields (88−94%).

The results can be rationalized (Scheme 3). Initial single electron transfer (S.E.T.) from the neutral electron-donor **7** to the LUMO of the substrate **14** [computations with Spartan (Hartree−Fock 6-31G**) indicate that the LUMO is delocalized over the aroyl unit] generates the ketyl radical

SCHEME 3. Reduction of Acyloin Derivatives 14 and Oxidation of Donor 7



anion **21**, leading to cleavage of the C−O bond and affording the enolyl radical **22**. The latter can then receive another electron from **7** (or from the radical-cation **24**) to generate enolate **23**, protonation of which yields ketone **15**. The electronic character of the O−X group can therefore be important both for decreasing the energy of the LUMO of the acyloin system and for facilitating the departure of the leaving group as an anion.

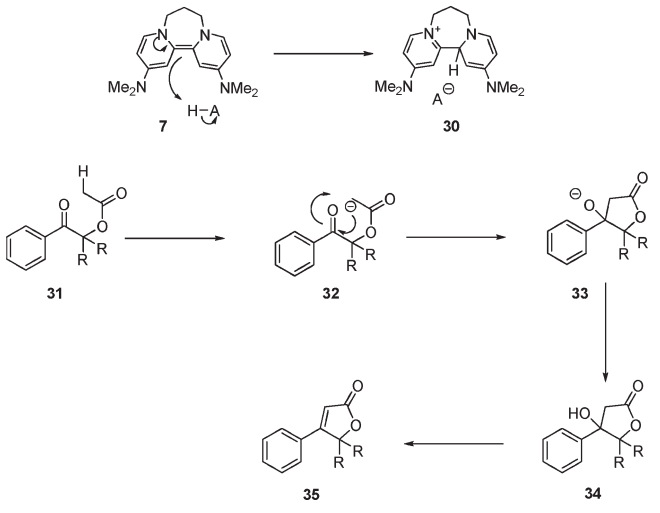
The use of an organic reducing agent, **7**, leads to intermediates such as the ketyl **21** and the enolate **23** that differ from normal ketyls and enolates in that the counterion (**24**/**25**) is organic. Although the cations **24** and **25** derived from **7** are potentially electrophilic, the high yields of desired products obtained indicate that reaction with the intermediate ketyls **21** and enolates **23** is unfavorable; this is undoubtedly influenced by the twist undergone by the cations **24** and **25**,[17] giving steric protection to the unsubstituted 6-positions of both pyridinium rings.

With the above benzoin derivatives and analogues, high yields of reduced products were observed. Substrates **14r**−**w** (Table 2) then explored the replacement of the aryl group β to the carbonyl group by aliphatic groups. In the *gem*-dimethyl substrates, the mesylate **14r** and pivalate **14s** examples afforded the expected product **26** cleanly. However, the acetate derivative **14t** afforded none of the desoxyacyloin product **26**, and instead afforded the butenolide **27** in high yield (86%).

The related substrates **14u**−**w** were then tested. Once again, the mesylate **14u** and pivalate **14v** examples cleanly afforded the desired desoxy product **28** (63% and 62%, respectively), while the acetate derivative **14w** again afforded a butenolide, **29**, in high yield (85%).

The formation of butenolides from substrates **14t**,**w** merits comment. By comparison with the pivalates **14s**,**v** these substrates are similarly activated for electron transfer to occur from donor **7**. However, this reaction is not observed, and instead the donor acts as a base, transforming the substrate to an ester enolate **32**, which then attacks the benzoyl carbonyl affording the β-hydroxylactone product **34**, which undergoes easy dehydration to give the butenolide product **35** (Scheme 4). The basic character of the donor **7** can be easily rationalized, since protonation will lead to the pyridinium salt **30**, and the gain in aromaticity will be a good driving force for this reaction.

SCHEME 4. Donor 7 Behaves also as a Base: Formation of Butenolides 35



The interesting question that arises is why acetates **14t**,**w** undergo butenolide formation while the earlier examples **14c**,**g**,**j**,**l**,**n**,**p** do not. Both the electron transfer to the substrates **14** to form the corresponding radical-anions and the deprotonation of the acetate substrates are likely to be endothermic reactions for donor **7**, associated with unfavorable equilibria. [The first reduction potential of **14c** is seen at $E_p = -1.76$ V vs. Ag/AgCl/KCl (sat), while that of **14t** occurs at $E_p = -1.81$ V; the redox potential of **7** is $E_{1/2}$(DMF) $= -1.13$ V[17]]. Factors that favor one pathway within these substrates could lead to the observed preferences. For the radical-anions of the 1,2-diaryl substrates **14c**, **g**,**j**,**l**,**n**,**p**, departure of the acetate leaving group affords a very conjugated π-system spanning both the aryl rings; the transition state leading to the loss of the acetate anion may therefore be relatively encouraged. With the *gem*-dialkyl substrates **14t**,**w** (entries 3 and 6, Table 2) on the other hand, loss of the acetate ion does not lead to such extended conjugation. By contrast, cyclization of the ester enolates of substrates **14t**,**w** could be accelerated due to the *gem*-dialkyl effect and the reactive rotamer effect.[21] This effect would not be present to encourage cyclizations of the ester enolates of substrates **14c**,**g**,**j**,**l**,**n**,**p**.

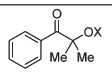
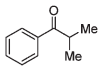
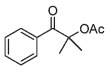
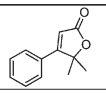
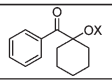
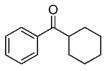
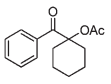
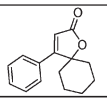
In conclusion, we disclosed a novel reactivity for neutral electron-donors. Electron-donor **7** reductively cleaves the C−O σ-bonds of acyloin derivatives in very good yields with the reaction proving successful for a diverse range of substrates.

Experimental Section

Example of the Preparation of Acyloins. 1,2-Bis(4-fluorophenyl)-2-hydroxyethanone: Sodium hydride (0.8 g, 20 mmol, 0.2 equiv) was added to a suspension of 4-fluorobenzaldehyde (12.4 g, 100 mmol, 1 equiv) and 1,3-dimethyl-1*H*-imidazol-3-ium iodide (2.23 g, 10 mmol, 0.1 equiv) in anhydrous tetrahydrofuran (150 mL) at room temperature under argon. The resulting mixture was then heated to reflux under argon overnight. The reaction mixture was then concentrated under reduced pressure and the residue was taken in dichloromethane (100 mL) and water (100 mL). The aqueous phase was then washed with dichloromethane (2 × 100 mL) and the combined organic fractions were further washed with water (3 × 100 mL) and brine (100 mL). The resulting organic phase was eventually dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was then adsorbed onto silica and purified by flash chromatography on silica gel (PE/EtOAc 75/25) to afford 1,2-bis(4-fluorophenyl)-2-hydroxyethanone, isolated as a fine yellow powder (9.68 g, 78%): mp. 86−88 °C (lit.[22] mp 81−82 °C); ν_{max} (film)/cm^{-1} 3432, 3113, 3076, 2918, 1682, 1599, 1508, 1412, 1387, 1300, 1276, 1234, 1156, 1104, 1075; found $[M + Na]^+$ (ES^+) 271.0545, $C_{14}H_{10}F_2O_2$ requires $[M + Na]^+$, 271.0541; δ_H ($CDCl_3$, 500 MHz) 4.50 (2H, d, $J = 5.9$ Hz), 5.90 (2H, d, $J = 5.9$ Hz), 7.01−7.05 (2H, m), 7.07−7.11 (2H, m), 7.29−7.32 (2H, m), 7.92−7.95 (2H, m); δ_C ($CDCl_3$, 125 MHz) 75.4, 116.1 (d, $J_{C-}{}^{19}F = 21.3$ Hz), 116.2 (d, $J_{C-}{}^{19}F = 20.4$ Hz), 129.5 (d, $J_{C-}{}^{19}F = 8.5$ Hz), 129.7, 131.9 (d,

(21) Jung, M. E. *Synlett* **1990**, 186–190.
(22) Hicks, L. D.; Hyatt, J. L.; Moak, T.; Edwards, C. C.; Tsurkan, L.; Wierdl, M.; Ferreira, A. M.; Wadkins, R. M.; Potter, P. M. *Bioorg. Med. Chem.* **2007**, *15*, 3801–3817.

TABLE 2. Reductive Cleavage from Substrates 14r,s,u,v and Butenolides Arising from Acetoxy-Substituted Substrates 14t,w

Entry	*Substrate*	*Product*	*Yield*
			
1 2	**14r**, X = Ms **14s**, X = Piv	**26**	51% 71%
			
3	**14t**	**27**	86%
			
4 5	**14u**, X = Ms **14v**, X =Piv	**28**	63% 62%
			
6	**14w**	**29**	85%

$J_{C-}{}^{19}F$ = 9.3 Hz), 134.8 (d, $J_{C-}{}^{19}F$ = 2.9 Hz), 163.4 (d, $J_{C-}{}^{19}F$ = 409.2 Hz), 165.4 (d, $J_{C-}{}^{19}F$ = 417.6 Hz), 197.2; *m*/*z* (ES^+) 519 ($[2M + Na]^+$, 22%), 271 ($[M + Na]^+$, 100), 231 (14).

Preparation of Substrates 14. 2-Methoxy-1,2-diphenylethanone, 14a:. Methyl iodide (2.8 mL, 45 mmol, 6 equiv) was added to a suspension of benzoin (1.59 g, 7.5 mmol, 1 equiv) and silver(I) oxide (3.48 g, 15 mmol, 2 equiv) in chloroform (40 mL). The resulting mixture was then heated to reflux for 24 h. The reaction mixture was then cooled and 1 mL of methyl iodide was added to the mixture. The resulting suspension was heated for another 2 h and allowed to cool to room temperature. The reaction mixture was then treated with decolorizing activated charcoal (1 g) and filtered on Celite. The filtrate was then dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was then adsorbed onto silica and purified by flash chromatography on silica gel (gradient petroleum ether/EtOAc from 95/5 to 90/10) to afford 2-methoxy-1,2-diphenylethanone **14a**[23] as a yellowish oil slowly crystallizing into white rosettes (1.31 g, 77%): mp 50−52 °C (lit.[21] mp 49−51 °C); ν_{max} (film)/cm^{-1} 3063, 3030, 3004, 2934, 2827, 1692, 1597, 1581, 1493, 1449, 1316, 1275, 1260, 1224, 1194, 1178, 1106, 1020, 1001; found $[M + H]^+$ (ESI^+) 227.1063, $C_{15}H_{14}O_2$ requires $[M + H]^+$ 227.1067; δ_H ($CDCl_3$, 400 MHz) 3.46 (3H, s), 5.52 (1H, s), 7.28−7.41 (5H, m), 7.45−7.43 (3H, m), 7.98−8.01 (2H, m); δ_C ($CDCl_3$, 100 MHz) 57.5, 86.5, 127.6, 128.5, 128.6, 128.8, 129.1, 133.3, 136.0, 139.1, 197.1; *m*/*z* (ESI^+) 227 ($[M + H]^+$, 100%).

Example of the Preparation of Mesylates. 2-Oxo-1,2-diphenylethylmethanesulfonate, 14b: Triethylamine (4.21 mL, 30 mmol, 1.5 equiv) was added dropwise to a solution of benzoin (4.24 g, 20 mmol, 1 equiv) and methanesulfonyl chloride (2.33 mL, 30 mmol, 1.5 equiv) in dichloromethane under argon at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and allowed to warm to room temperature. The reaction progress was monitored by TLC until no starting material was observed. After being stirred for 2 h at room temperature, the reaction mixture was successively washed with a saturated aqueous solution of sodium bicarbonate (3 × 100 mL) and brine (3 × 100 mL). The organic extract was eventually dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was then adsorbed onto silica and purified by flash chromatography on silica gel (gradient PE/EtOAc 95/5 to 80/20) to afford 2-oxo-1,2-diphenylethylmethanesulfonate **14b** as a fine white powder (4.20 g, 72%) and 2-chloro-1,2-diphenylethanone as white rosettes (0.722 g, 16%).

Data for 2-oxo-1,2-diphenylethylmethanesulfonate, 14b: mp 120−122 °C (lit.[24] mp 120−121 °C); ν_{max} (film)/cm^{-1} 3383, 3064, 3033, 2938, 2851, 1700, 1597, 1580, 1495, 1449, 1412, 1354, 1259, 1223, 1174, 1100, 1033, 1022, 1001; found $[M + NH_4]^+$ (ES^+) 308.0955, $C_{15}H_{14}O_4S$ requires $[M + NH_4]^+$, 308.0951; δ_H ($CDCl_3$, 400 MHz) 3.08 (3H, s), 7.41−7.45 (5H, m), 7.46−7.48 (2H, m), 7.49−7.51 (1H, m), 7.91−7.95 (2H, m); δ_C ($CDCl_3$, 125 MHz) 39.6, 82.6, 128.8, 128.9, 129.0, 129.4, 130.1, 132.5, 133.9, 134.0, 192.3; *m*/*z* (CI^+) 308 ($[M + NH_4]^+$, 82%), 214 (100), 197 (50), 105 (49).

Data for 2-chloro-1,2-diphenylethanone: mp 66−68 °C (lit.[25] mp 68 °C); found $[M^+]$ (EI^+) 230.0492, $C_{14}H_{11}{}^{35}ClO$ requires $[M^+]$, 230.0493; ν_{max} (film)/cm^{-1} 3374, 3063, 3031, 3006, 2926, 2853, 1904, 1810, 1783, 1697, 1596, 1580, 1496, 1448, 1319, 1277, 1208, 1175, 1075, 1000; δ_H ($CDCl_3$, 400 MHz) 6.32 (1H, s), 7.31−7.42 (3H, m), 7.43−7.46 (2H, m), 7.47−7.51 (2H, m), 7.53−7.58 (1H, m), 7.95−7.99 (2H, m); δ_C ($CDCl_3$, 100 MHz) 69.6, 127.6, 127.9, 128.6, 128.8, 129.2, 133.1, 136.2, 136.7, 188.8; *m*/*z* (EI^+) 230 ($[M^+]$ (^{35}Cl), 100%).

Example of Preparation of Acetates. 2-Oxo-1,2-diphenylethyl acetate, 14c: Acetic anhydride (1.42 mL, 15 mmol, 1 equiv) was

(23) Reddy, G. D.; Usha, G.; Ramanathan, K. V.; Ramamurthy, V. *J. Org. Chem.* **1986**, *51*, 3085–3093.

(24) Borowitz, I. J.; Rusek, P. E.; Virkhaus, R. J. *Org. Chem.* **1969**, *34*, 1595–1600.

(25) Buck, J. S.; Ide, W. S. *J. Am. Chem. Soc.* **1932**, *54*, 4359–4365.

added to a solution of benzoin (2.12 g, 10 mmol, 1 equiv) in pyridine (25 mL) at room temperature under argon. The reaction mixture was then stirred at room temperature under argon overnight. The reaction mixture was then concentrated under reduced pressure. The residue was then dissolved in diethyl ether (100 mL) and successively washed with aqueous hydrochloric acid (1 N, 3 × 100 mL), a saturated aqueous solution of sodium bicarbonate (3 × 100 mL), and brine (3 × 100 mL). The resulting organic extract was then dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was then adsorbed onto silica and purified by flash chromatography on silica gel (PE/EtOAc 95/5) to afford 2-oxo-1,2-diphenylethyl acetate **14c** as a colorless oil, slowly crystallizing as white rosettes (2.49 g, 98%): mp 80−81 °C (lit.[26] mp 81 °C); ν_{max} (film)/cm^{-1} 3381, 3064, 3033, 1740, 1697, 1597, 1579, 1495, 1448, 1373, 1230, 1180, 1160, 1079, 1055, 1029, 1004; found $[M + NH_4]^+$ (ES^+) 272.1281, $C_{16}H_{14}O_3$ requires $[M + NH_4]^+$ 272.1281; δ_H ($CDCl_3$, 500 MHz) 2.21 (3H, s), 6.87 (1H, s), 7.32−7.42 (5H, m), 7.45−7.49 (2H, m), 7.51−7.55 (1H, m), 7.92−7.96 (2H, m); δ_C ($CDCl_3$, 100 MHz) 20.7, 78.6, 127.6, 128.4, 128.6, 129.2, 129.6, 133.0, 136.5, 136.7, 169.1, 194.2; *m*/*z* (CI^+) 272 ($[M + NH_4]^+$, 100%), 255 ($[M + H]^+$, 22), 212 (41), 197 (18), 105 (36).

Example of Preparation of Pivalates. 2-Oxo-1,2-diphenylethyl pivalate, 14d: Pivaloyl chloride (3.70 mL, 30 mmol, 1.5 equiv) was added dropwise to a solution of benzoin (4.24 g, 20 mmol, 1 equiv) in pyridine (25 mL). The resulting solution was stirred at room temperature under argon overnight. The reaction mixture was then concentrated under reduced pressure. The residue was then dissolved in dichloromethane (100 mL) and successively washed with aqueous hydrochloric acid (1 N, 3 × 100 mL), a saturated aqueous solution of sodium bicarbonate (3 × 100 mL), and brine (3 × 100 mL). The resulting organic extract was then dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was then adsorbed onto silica and purified by flash chromatography on silica gel (PE/EtOAc 90/10) to afford 2-oxo-1,2-diphenylethyl pivalate[27] **14d** as a pale yellow oil (5.39 g, 91%): ν_{max} (film)/cm^{-1} 3065, 3033, 2972, 2934, 2872, 1731, 1687, 1597, 1496, 1478, 1449, 1396, 1364, 1287, 1225, 1151, 1045; found $[M + H]^+$ (ES^+) 297.1486, $C_{19}H_{20}O_3$ requires $[M + H]^+$, 297.1485; δ_H ($CDCl_3$, 500 MHz) 1.29 (9H, s), 6.80 (1H, s), 7.31−7.43 (5H, m), 7.46−7.54 (3H, m), 7.93−7.96 (2H, m); δ_C ($CDCl_3$, 125 MHz) 27.1, 38.7, 77.3, 128.3, 128.6, 128.8, 129.0, 129.1, 133.4, 133.9, 134.9, 178.0, 194.3; *m*/*z* (ES^+) 615 ($[2M + Na]^+$, 10%), 297 ($[M + H]^+$, 100), 195 (56).

Example of Preparation of Benzoates. 14e: Benzoyl chloride (3.48 mL, 30 mmol, 1.5 equiv) was added dropwise to a solution of benzoin (4.24 g, 20 mmol, 1 equiv) in pyridine (25 mL). The resulting solution was stirred at room temperature under argon overnight. The reaction mixture was then concentrated under reduced pressure. The residue was then dissolved in dichloromethane (100 mL) and successively washed with aqueous hydrochloric acid (1 N, 3 × 100 mL), a saturated aqueous solution of sodium bicarbonate (3 × 100 mL), and brine (3 × 100 mL). The resulting organic extract was then dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The resulting residue was then adsorbed onto silica and purified by flash chromatography on silica gel (PE/EtOAc 90/10) to afford 2-oxo-1,2-diphenylethyl benzoate **14e** as a pale yellow oil, which slowly crystallized into white rosettes (5.57 g, 88%): mp 124−126 °C (lit.[28] mp 123.5−125 °C); ν_{max} (film)/cm^{-1} 3063, 3033, 1719, 1696, 1598, 1495, 1316, 1280, 1250, 1226, 1176, 1109, 1070, 1025; found $[M + H]^+$ (ES^+) 317.1173, $C_{21}H_{16}O_3$ requires $[M + H]^+$, 317.1172]; δ_H ($CDCl_3$, 500 MHz) 7.12 (1H, s), 7.38−7.47 (7H, m), 7.53−7.60 (4H, m), 8.01−8.03 (2H, m), 8.14−8.15 (2H, m); δ_C ($CDCl_3$, 125 MHz) 78.0, 128.4, 128.7, 128.9, 129.2, 129.3, 129.4, 130.0, 133.4, 133.5, 133.8, 134.8, 166.1, 193.7; *m*/*z* (ES^+) 650 ($[2M + NH_4]^+$, 30%), 317 ($[M + H]^+$, 100), 195 (48).

General Procedure for Reducing Substrates, 14. In a centrifuge tube under argon at room temperature, DMAP-derived salt **13** (0.810 g, 1.5 mmol, 1.5 equiv) and sodium hydride (0.6 g, 15 mmol, 15 equiv) were washed three times with anhydrous hexane. An excess of hexane was removed by a flow of argon. Anhydrous *N*,*N*-dimethylformamide (15 mL) was then added to the resulting fine white powder and the resulting mixture was stirred at room temperature under argon for 3 h. The resulting dark purple suspension was then centrifuged and the upper liquid phase was transferred to substrate **14** (1 mmol, 1.0 equiv) via a cannula. The resulting mixture was then stirred at room temperature under argon overnight. The reaction mixture was then washed with EtOAc (100 mL) and water (100 mL). The aqueous phase was further extracted with EtOAc (2 × 50 mL). Combined organic phases were then further washed with water (2 × 50 mL) and brine (50 mL). The resulting organic extract was eventually dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was then adsorbed onto silica and purified by flash chromatography on silica gel (PE/EtOAc 95/5) to afford product.

15 from **14b**: 1,2-diphenylethanone **15** was isolated as a fine white powder (0.182 g, 93%); mp 60−62 °C (lit.[29] mp 59 °C); found $[M^+]$ (EI^+) 196.0882, $C_{14}H_{12}O$ requires $[M^+]$, 196.0883]; ν_{max} (film)/cm^{-1} 3086, 3059, 3028, 2924, 2852, 1686, 1596, 1579, 1448, 1411, 1337, 1213, 1176, 1101, 1075; δ_H ($CDCl_3$, 400 MHz) 4.30 (2H, s), 7.24−7.29 (3H, m), 7.32−7.36 (2H, m), 7.45−7.49 (2H, m), 7.55−7.59 (1H, m), 8.02−8.05 (2H, m); *m*/*z* (EI^+) 196 ($[M^+]$, 100%), 165 (89), 157 (52).

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Supporting Information Available: Spectroscopic data for the preparation of all compounds except those described in the above Experimental Section, together with ^{1}H and ^{13}C NMR spectra of compounds **14a**−**w**, **15**−**20**, and **26**, **28**, and **29**. This material is available free of charge via the Internet at http://pubs.acs.org.

(26) Hattori, K.; Sajiki, H.; Hirota, K. *Tetrahedron* **2001**, *57*, 4817–4824.
(27) Evans, D. A.; Nagorny, P.; Xu, R. *Org. Lett.* **2006**, *8*, 5669–5671.
(28) Stevens, C. L.; Weiner, M. L.; Freeman, R. C. *J. Am. Chem. Soc.* **1953**, *75*, 3977–3980.
(29) Mathey, F.; Lampin, J.-P. *Tetrahedron Lett.* **1972**, *13*, 1949–1952.