Preparation and Reactivity of Highly Functionalized Organometallics at the α Position of Oxygen or Nitrogen

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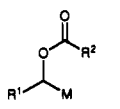
α-Halogenoalkyl carboxylates (FG-R^1CH(X)($OCOR^2$); FG = COOR, CN, SR; X = I, Br) were readily prepared by the addition of an acid chloride or bromide (R^2COX; X = Br or Cl) to an aldehyde (FG-RCHO) in the presence of a catalytic amount of $ZnCl_2$. They insert efficiently zinc dust in THF–DMSO (X = Br, 8–10 °C, 6–10 h) affording the corresponding zinc organometallics at the α position to oxygen FG-RCH(ZnBr)(OAc). After the addition of the THF-soluble copper salt CuCN·2LiCl, the corresponding copper reagents FG-RCH(Cu(CN)ZnBr)(OAc) are formed and reacted with various classes of electrophiles such as acid chlorides, aldehydes, enones, allylic and alkynyl halides, activated alkynes, nitro olefins and alkylidenemalonates providing polyfunctional molecules in excellent yields. Similarly, zinc organometallics at the α position to the nitrogen of cyclic imides were prepared by the zinc insertion to cyclic α-chloromethyl (or α-chloroethyl) imides. After their transmetalation to the corresponding copper organometallic (($(R^1CO)_2$NCH(R)(Cu(CN)ZnCl); R = Me or H), they were reacted with allylic and alkynyl halides and ethyl propiolate affording polyfunctional imides. The reaction of cyclic *N*-(chloromethyl)imides with aldehydes in the presence of chromium(II) chloride in THF furnishes protected amino alcohols in 36–95% yield.

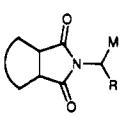
Introduction

Functionalized organometallics are important intermediates in organic synthesis. The preparation and the reaction of lithium carbanions at the α-position to oxygen or nitrogen has been an active area of research leading to numerous synthetic applications.[2,3] However, the high reactivity of the carbon–lithium bond has prevented the presence of most organic functionalities in these molecules and has limited the synthetic scope of these reagents.

Recently, we have found that in strong contrast to lithium, magnesium, and aluminum organometallics organozinc halides tolerate the presence of most organic functional groups.[4] Here, we wish to report our work concerning a general preparation and study of the reactivity of functionalized zinc and copper organometallics **1** at the α position to the oxygen of a carboxylate as well as some new zinc, copper, and chromium organometallics **2** α to the nitrogen of imides.



1: M = ZnX or Cu(CN)ZnX



2: M = ZnX, Cu(CN)ZnX or CrX_2

R = H, Me

Results and Discussion

Organozinc halides are best prepared by the insertion of zinc to organic halides.[5] The required α-halogenoalkyl carboxylates and imides were readily available by using methods described in the literature. Iodomethyl pivalate (**3**) is prepared from commercially available chloromethyl pivalate[6] and iodomethyl crotonate (**4**) is obtained in two

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(2) (a) Peterson, D. *J. Organomet. Chem. Rev. A* **1972**, *7*, 295. (b) Baldwin, J. E.; Hofle, G. A.; Lever, O. W., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 7125. (c) Still, W. C.; Macdonald, T. L. *J. Am. Chem. Soc.* **1974**, *96*, 5561. (d) Beak, P., McKinnie, B. G. *J. Am. Chem. Soc.* **1977**, *99*, 5213. (e) Beak, P.; Baillangeon, M.; Carter, L. G. *J. Org. Chem.* **1978**, *43*, 4255. (f) Schlecker, R.; Seebach, D.; Lubosch, W. *Helv. Chim. Acta* **1978**, *61*, 512. (g) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481. (h) Meyer, N.; Seebach, D. *Chem. Ber.* **1980**, *113*, 1290. (i) Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* **1980**, *102*, 1201. (j) Cohen, T.; Matz, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 6900. (k) Magnus, P.; Roy, G. *J. Chem. Soc., Chem. Commun.* **1979**, 822. (l) Burke, S. D.; Shearouse, S. A.; Burch, D. J.; Sutton, R. W. *Tetrahedron Lett.* **1980**, *21*, 1285. (m) Beak, P.; Carter, L. G. *J. Org. Chem.* **1981**, *46*, 2363. (n) Hoppe, D.; Bronneke, A. *Synthesis* **1982**, 1045. (o) Corey, E. J.; Eckrich, T. M. *Tetrahedron Lett.* **1983**, *24*, 3163. (p) Corey, E. J.; Eckrich, T. M. *Tetrahedron Lett.* **1983**, *24*, 3165. (q) Cohen, T.; Lin, M.-T. *J. Am. Chem. Soc.* **1984**, *106*, 1130. (r) Lehmann, R.; Schlosser, M. *Tetrahedron Lett.* **1984**, *25*, 745. (s) McGarvey, G. J.; Kimura, M. *J. Org. Chem.* **1985**, *50*, 4655. (t) Fetizon, M.; Hanna, I.; Rens, J. *Tetrahedron Lett.* **1985**, *26*, 3453. (u) McDougal, P. G.; Rico, J. G.; VanDerveer, D. *J. Org. Chem.* **1986**, *51*, 4492. (v) Linderman, R. J.; Godfrey, A.; Horne, K. *Tetrahedron Lett.* **1987**, *28*, 3911. (w) Sawyer, J. S.; Kucerovy, A.; MacDonald, T. L.; McGarvey, G. J. *J. Am. Chem. Soc.* **1988**, *110*, 842. (x) Shiner, C. S.; Tsunoda, T.; Goodman, B. A.; Ingham, S.; Lee, S.; Vorndam, P. E. *J. Am. Chem. Soc.* **1989**, *111*, 1381. (y) Rychnovsky, S. D.; Mickus, D. E. *Tetrahedron Lett.* **1989**, *30*, 3011. (z) Rychnovsky, S. D. *J. Org. Chem.* **1989**, *54*, 4982.

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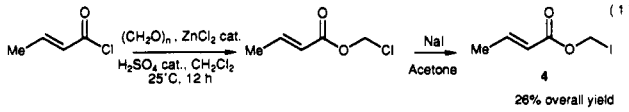
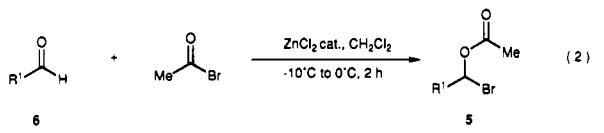
steps[7] from crotonyl chloride ((i)$(CH_2O)_n$, $ZnCl_2$ cat., H_2SO_4 cat., 25 °C, 12 h; 33% yield; (ii) NaI, acetone, 25 °C, 3 h; 79% yield; eq 1). The substituted α-iodoalkyl



(1)

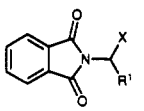
carboxylates are not stable; however, the corresponding α-bromoalkyl acetates **5** can be readily obtained according to Neuenschwander's method.[8-11]

The treatment of an aldehyde **6** with freshly distilled acetyl bromide (1.2 equiv) in CH_2Cl_2 in the presence of a catalytic amount of $ZnCl_2$ (1.5 mol %) at −10 to 0 °C for 2 h provides the desired α-bromoalkyl acetates **5** in excellent yields (ca. 90% yield; eq 2). The reaction

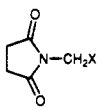


6 5 (2)

tolerates the presence of an ester, cyanide, and thioester in the starting aldehyde. The *N*-(halomethyl)imides **7–11** were obtained by using literature methods.[12] The halides **3–5** and **7–11** could be converted to zinc, copper, or



7 : R' = H ; X = Cl
8 : R' = H ; X = Br
9 : R' = CH3 ; X = Cl



10 : X = Cl
11 : X = I

chromium organometallics and reacted with a variety of electrophiles. Thus, the iodomethyl pivalate and crotonate, **3** and **4**, react rapidly with cut zinc foil[13] in THF (12–13 °C, 0.1–1 h) and produce the desired organozinc reagent **12** and **13** in over 85% yield. These zinc compounds are converted to the more reactive copper reagents **14** and **15** (Table I) by the addition of the THF-soluble copper salt[4,14] CuCN·2LiCl (1 equiv, −30 °C, 5 min). Similarly, an insertion of zinc dust[15] to the α-bromoalkyl acetates **5** in a mixture of THF and DMSO (7:2) affords the desired organozinc reagents **16** in over 85% yield (Zn dust (2 equiv), 8–10 °C, 6–10 h). After a transmetalation with CuCN·2LiCl (1 equiv, 0 °C, 5 min), the corresponding copper compounds of type **17** were obtained. The reaction shows an excellent functional group tolerance and reagents of type **17** bearing an ester, cyanide, or thioether function can be readily prepared (eq 3 and Table I). The reaction of the copper reagents **14**, **15**, and **17a–k** with electrophiles such as acid chlorides, aldehydes, enones, allylic and alkynyl halides, activated alkynes, nitro olefins, and alkylidenemalonates furnishes the polyfunctional molecules **18a–m**, **19a–b**, and **20a–y** in good to excellent yields. The reactivity of α-oxygenated zinc and copper organometallics is lower than the one of alkylcopper–zinc reagents but is satisfactory with many classes of electrophiles. Thus, the addition of an acid chloride to **14**, **15**, or **17a** produces α-carboxy ketones in good yields (RCOCl (0.6 equiv), −78 to −20 °C, −20 to 0 °C, 1–3 h; entries 1–4, 14, 27). Aromatic acid chlorides react especially well, and in the case of 4-chlorobutyryl chloride it was found advantageous to use the cadmium-derived copper reagent **21**: $PivOCH_2Cu(CN)CdI$ prepared from Cd dust[16] and **3** which afforded the desired ketone **18d** in 68% yield instead of 42% if the zinc–copper reagent **14** is used (entry 4). Aldehydes react in 73–89% yield with **14** (entries 5 and 6) in the presence of BF_2·OEt_2 (2 equiv, −30 to −20 °C, 12 h); however, the reagents **17** did not undergo this reaction cleanly. Various Michael acceptors add **14** and **17**, giving only the 1,4-adducts. For example, cyclohexenone reacts with **14** in the presence of Me_3SiCl (1.1 equiv; −78 to +25 °C, 12 h)[17] and gives an intermediate silyl enol ether which was converted to the ketone **18g** (entry 7) by treatment with Bu_4NF (1.1 equiv, 25 °C, 5 min, 59% yield). The use of more than 1.1 equiv of Me_3SiCl leads to a considerable amount of Me_3SiCH_2OPiv. The reaction with β-disubstituted enones like 3-methyl-2-cyclohexen-1-one is best performed in the presence of BF_3·OEt_2 (4 equiv; −30 °C, 36 h; entry 8)[18] and gives the γ-pivaloyloxy ketone **18h** in 71% yield. Especially reactive toward organocopper reagents are β-halo ketones, and 3-iodo-2-cyclohexen-1-one ((0.55 equiv), −78 to 0 °C; 0 °C, 2 h; 25 °C, 1 h) reacts in very high yields with **14**, **17a**, and **17g** furnishing the 3-substituted cyclohexenones **18i** (97% yield, entry 9), **20c** (97% yield, entry 18), and **20t** (75% yield, entry 35). The reaction with 2-(phenylsulfonyl)nitroethylene[19,20] (**22**) allows an approach to new allylic acetates bearing a nitro group in position 2 (**20f**, **20x**, **20y**; see entries 21, 39, 40).[21] The crude reaction mixture of the reaction of **17a** with **22** contains 10% of (*E*)-3-acetoxy-4-methyl-1-(phenylsulfonyl)-1-pentene which results from an addition elimination at the carbon bearing the nitro group. The addition to activated alkynes[22] such as ethyl propiolate or dimethyl acetylenedicarboxylate does not proceed cleanly with **14**; however, the substituted reagent **17a** reacts in high yields with these alkynes providing with high stereoselectivity the unsaturated esters (**20d**: 93% (>97% *Z*); **20e**: 93% (>96% *E*); **20r**: 77% (>98% *Z*); entries 19, 20, 33). Interestingly, whereas the Michael addition of **17a** to benzylidenemalononitrile gives the expected product **20h**

(6) Aldrich Chemical Co. or Lancaster Synthesis Ltd.
(7) Bodor, N.; Sloan, K. B.; Kaminski, J. J.; Shih, C.; Pogany, S. *J. Org. Chem.* **1983**, *48*, 5280.
(8) Kyburz, R.; Schaltegger, H.; Neuenschwander, M. *Helv. Chim. Acta* **1971**, *54*, 1037.
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(11) Neuenschwander, M.; Bigler, P.; Christen, K.; Iseli, R.; Kyburz, R.; Muhle, H. *Helv. Chim. Acta* **1978**, *61*, 2047.
(12) *N*-(Chloromethyl)- and *N*-(bromomethyl)phthalimide were purchased from Lancaster Synthesis Ltd. whereas *N*-(1-chloroethyl)phthalimide was prepared according to: (a) Worley, J. W. *J. Org. Chem.* **1979**, *44*, 1178. (b) Zaugg, H. E. *Synthesis* **1970**, 49.
(13) The zinc foil was purchased from Alfa (0.62-mm thick, purity 3 N).
(14) (a) Knochel, P.; Chou, T. S.; Chen, H. G.; Yeh, M. C. P.; Rozema, M. J. *J. Org. Chem.* **1989**, *54*, 5202. (b) Chou, T. S.; Knochel, P. *J. Org. Chem.* **1990**, *55*, 4791.
(15) Zinc dust (−325 mesh) was purchased from Aldrich Chemical Co.
(16) Cadmium dust (Aldrich), washed successively with diluted aqueous HCl, ethanol, and ether and dried under vacuum (5 h, 0.1 mmHg), was used.
(17) (a) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6015 and 6019. (b) Alexakis, A.; Berlan, J.; Besace, Y. *Tetrahedron Lett.* **1986**, *27*, 1047. (c) Horiguchi, Y.; Matsuzawa, S.; Nakamura, E.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4025. (d) Nakamura, E.; Matsuzawa, S.; Horiguchi, Y.; Kuwajima, I. *Tetrahedron Lett.* **1986**, *27*, 4029.
(18) (a) Yeh, M. C. P.; Knochel, P.; Santa, L. E. *Tetrahedron Lett.* **1988**, *29*, 3887. (b) See also: Yamamoto, Y. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 947; *Angew. Chem.* **1986**, *98*, 945. (c) Lipshutz, B. H. *Synthesis* **1987**, 325. (d) Lipshutz, B. H.; Ellworth, E. L.; Siahaan, T. J. *J. Am. Chem. Soc.* **1989**, *111*, 1351.
(19) (a) Ono, N.; Kamimura, A.; Kaji, A. *Tetrahedron Lett.* **1986**, *27*, 1595. (b) Ono, N.; Kamimura, A.; Kaji, A. *J. Org. Chem.* **1986**, *51*, 2139.
(20) Jubert, C.; Knochel, P. *Tetrahedron Lett.* **1991**, *32*, 441.
(21) The addition of nucleophiles to the allylic nitroacetates of type **20f** is currently being investigated in our laboratories, manuscript in preparation.
(22) AchyuthaRao, S.; Knochel, P. *J. Am. Chem. Soc.* **1991**, *113*, 5735.

Table I. Products 18a–m, 19a–b, and 20a–y Obtained by the Reaction of the α-Oxygenated Zinc–Copper Reagents 14, 15, and 17a–k with Electrophiles

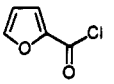
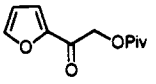
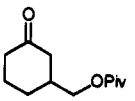
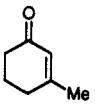
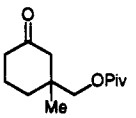
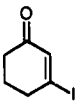
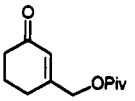
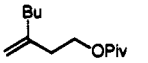
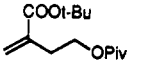
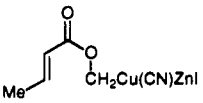
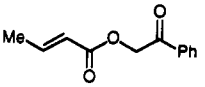
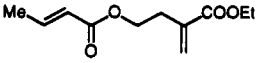
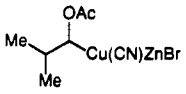
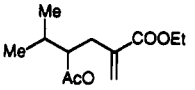
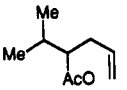
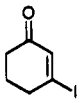
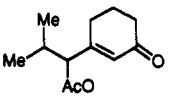
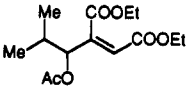
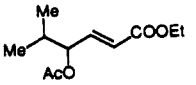
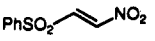
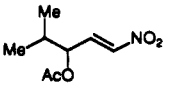
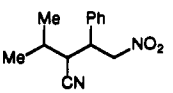
entry	copper–zinc reagent	electrophile	products		yield[a] (%)
1	$PivOCH_2Cu(CN)ZnI$ (14)	PhCOCl	$PhCOCH_2OPiv$	18a	81
2	14			18b	90
3	14	c-HexCOCl	$c\text{-HexCOCH}_2OPiv$	18c	66
4	14	$Cl(CH_2)_3COCl$	$Cl(CH_2)_3COCH_2OPiv$	18d	42 (68)[b]
5	14	PhCHO	$PhCH(OH)CH_2OPiv$	18e	89
6	14	HexCHO	$HexCH(OH)CH_2OPiv$	18f	73
7	14			18g	59[c]
8	14			18h	71
9	14			18i	97
10	14			18j	95
11	14			18k	94
12	14	Bu_3SnCl	$PivOCH_2SnBu_3$	18l	93
13	14	$BrC{\equiv}C\text{-Hex}$	$HexC{\equiv}CCH_2OPiv$	18m	72
14	 15	PhCOCl		19a	93
15	15			19b	96
16	 17a			20a	95
17	17a			20b	85
18	17a			20c	97
19	17a	$MeOOCC{\equiv}CCOOMe$	 (>97% *Z*)	20d	93
20	17a	$HC{\equiv}CCOOEt$	 (>96% *E*)	20e	91
21	17a		 (100% *E*)	20f	74
22	17a			20g	72[d]

Table I. (Continued)

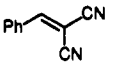
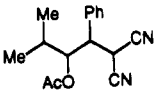
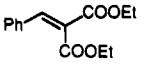
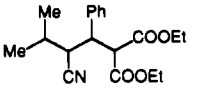
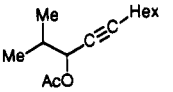
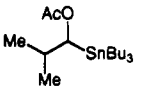
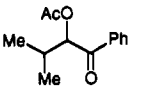
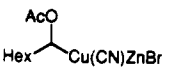
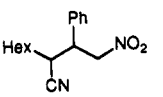
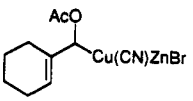
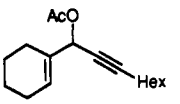
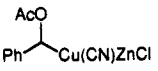
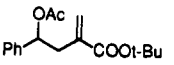
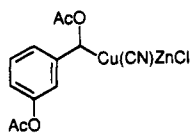
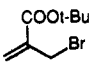
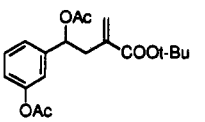
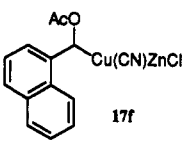
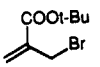
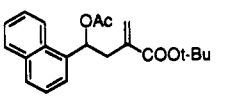
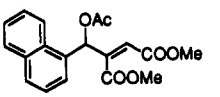
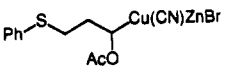
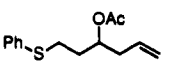
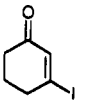
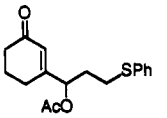
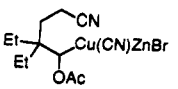
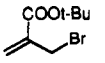
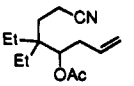
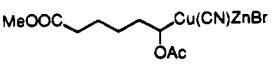
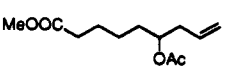
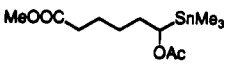
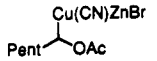
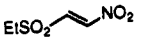
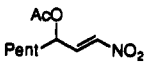
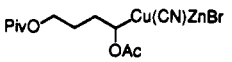
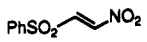
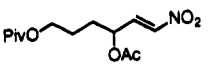
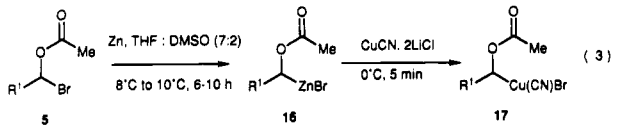
entry	copper–zinc reagent	electrophile	products		yield[a] (%)
23	**17a**			**20h**	89[e]
24	**17a**			**20i**	86[d]
25	**17a**	HexC≡CBr		**20j**	76
26	**17a**	Bu_3SnCl		**20k**	90
27	**17a**	PhCOCl		**20l**	82
28	 **17b**			**20m**	68[e]
29	 **17c**	BrC≡C–Hex		**20n**	86
30	 **17d**			**20o**	91
31	 **17e**			**20p**	89
32	 **17f**			**20q**	71
33	**17f**	MeOOCC≡CCOOMe	 (>98% *Z*)	**20r**	77
34	 **17g**			**20s**	86
35	**17g**			**20t**	75
36	 **17h**			**20u**	92
37	 **17i**			**20v**	95

Table I. (Continued)

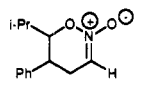
entry	copper–zinc reagent	electrophile	products		yield[a] (%)
38	**17i**	Me_3SnCl		**20w**	78
39	 **17j**			**20x**	80
40	 **17k**			**20y**	74

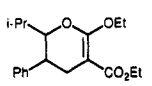
[a] All yields refer to isolated yields of compounds being over 98% pure by GC analysis. [b] This reaction has been performed with the organocadmium reagent $PivOCH_2Cu(CN)CdI$. [c] The intermediate TMD–enol ether was converted to the ketone by treatment with Bu_4NF. [d] Ca. 1:1 mixture of diastereoisomers. [e] Ca. 60:40 mixture of diastereoisomers.



(3)

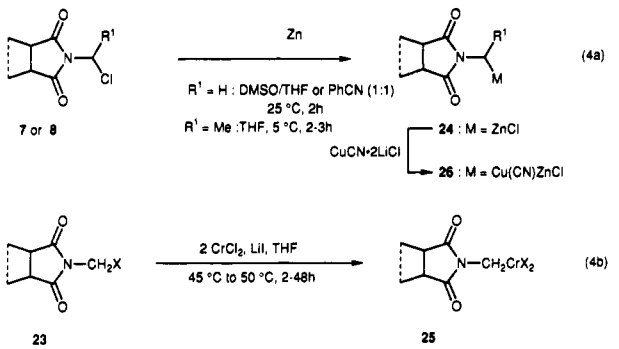
(25 °C, 8 h; 90% yield; entry 23), the reaction of **17a** with nitrostyrene[4d] (0 °C, 12 h; 72% yield; entry 22) provides the γ-nitro nitrile **20g**. The same behavior is observed with diethyl benzylidenemalonate which leads to the γ-cyano malonate **20i** (−25 °C, 8 h; 86% yield; entry 24). This is explained by postulating that the nitronate and malonate anions initially produced in these reactions displace intramolecularly the acetoxy group giving, respectively, the intermediates **23a** and **23b** which undergo


23a


23b

in a second step a ring opening with cyanide leading, respectively, to **20g** and **20i**. The formation of such intermediates is not possible in the preparation of **20h** explaining why no substitution of the acetoxy group has taken place in this case. Alternatively, the cyano group coordinated to the intermediate copper nitronate or enolate which is in close proximity to the carbon atom bearing the acetate can undergo a direct substitution of the acetoxy group. The coupling of **14** or **17** with allylic halides is a high-yield reaction (0 °C, 1 h) and produces homoallylic pivalates such as **18j** (95%) and **18k** (94%; entries 10 and 11) and functionalized homoallylic acetates (entries 16, 17, 30–32, 34, 36, 37). Alkynyl bromides react under even milder conditions (−50 °C, 8 h) affording propargylic carboxylates (**18m** (72%); **20j** (76%); **20n** (86%); see entries 13, 25, 29). The reaction of **14** or **17** with chlorotrialkylstannanes furnishes α-acetoxy or -(pivaloyloxy) organotin derivatives **18l** (93%), **20k** (90%), and **20w** (78%) (entries 12, 26, and 38).

In the course of our studies, we found also that the reaction of *N*-(chloromethyl)succinimides and -phthalimides **7** or **8** with zinc metal or chromium(II) chloride[23] provides, respectively, intermediate zinc(II) or chromium(III) organometallics at the α position to nitrogen of type **24** and **25** in good yields (eq 4 and Tables II and III).



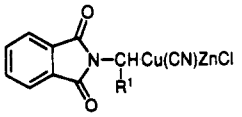
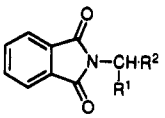
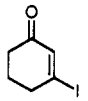
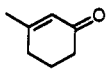
It was necessary due to their lack of reactivity to transmetalate the zinc reagent **24** to the corresponding copper derivatives **26** by the addition of CuCN·2LiCl (1 equiv). Thus, the reaction of *N*-(chloromethyl)phthalimide (**7**) with zinc dust (2–3 equiv) in a mixture of THF–DMSO (1:1) at 25 °C affords the zinc organometallic **24** in 70–80% yield accompanied by variable amounts of 1,2-bis(phthalimido)ethane (ca. 15%). In strong contrast to the corresponding lithium reagent, **24** and its copper derivative **26** are stable at 25 °C for several hours and no attack of the imide carbonyl groups has been observed.[24] The use of benzonitrile and DMSO as solvent mixture is advantageous in some cases. Thus, the allylation of **26a** with ethyl α-(bromomethyl)acrylate[25] (0.5 equiv) gives the expected product **27a** in THF–DMSO (1:1) (45% yield), whereas a yield of 72% is obtained in PhCN–DMSO (1:1 (entry 1 of Table II). The reaction is completed within 0.5 h (−60 to 0 °C) and proceeds well with the α-substituted copper reagent **26b** (entry 8). The carbocupration of ethyl propiolate (0.5 equiv; −60 to +25 °C, 12 h) with **26a** furnishes the (*E*)-γ-amino acrylate **27c** (*E*/*Z* = 97/3) in 69% yield (entry 3). Coupling reaction with 1-bromoalkynes (0.6 equiv) produces the propargylic phthalimides **27d** and **27e** (−60 to 0 °C, 8 h; entries 4 and 5) in, respectively, 79% and 76% yield. The addition–elimination of **26a** to 3-iodo-2-cyclohexen-1-one[26] (0.5 equiv) gives the desired 3-substituted cyclohexenone **27f** (−60 to 0 °C, 12 h, then 0–40 °C, 8 h, 72% yield), whereas the stannylation of **4a** with Me_3SnCl (0.5 equiv, 0–25 °C, 2 h) gives the tin derivative **27g** in 64% yield.

Compared to the primary alkylcopper reagents (RCu(CN)ZnX), the nitrogen-substituted zinc and copper

(23) The insertion of chromium(II) halides into allylic, alkenyl, alkynyl, propargyl, and aryl halides has been reported: (a) Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179. (b) Hiyama, T.; Okude, Y.; Kimura, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 561. (c) Takai, K.; Kimura, K.; Kuroda, T. Hiyama, T.; Nozaki, H. *Tetrahedron Lett.* **1983**, *24*, 5281. (d) Takai, K.; Kuroda, T.; Nakatsukasa, S.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, 5585. (e) Wender, P. A.; Wisniewski Grisson, J.; Hoffmann U.; Mah, R. *Tetrahedron Lett.* **1990**, *31*, 6605. (f) For an insertion of $CrCl_2$ to α-iodosulfides see: Nakatsukasa, S.; Takai, K.; Utimoto, K. *J. Org. Chem.* **1986**, *51*, 5045.

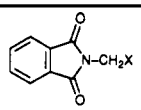
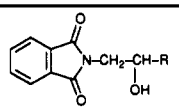
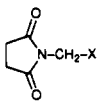
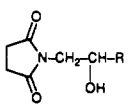
(24) Schlecker, R.; Seebach, D. *Helv. Chim. Acta* **1977**, *60*, 1459.
(25) Villieras, J.; Rambaud, M. *Synthesis* **1982**, 924.
(26) Piers, E.; Nagakura, I. *Synth. Commun.* **1975**, *5*, 193.

Table II. N-Substituted Imides 27a–h Obtained by the Reaction of the Copper Derivatives 26a–b with Electrophiles

entry	copper reagent	electrophile	product of type 27	yield (%)
				
1	**26a**: R^1 = H	ethyl α-(bromomethyl)acrylate	**27a**: R^1 = H; R^2 = $CH_2C(CO_2Et)=CH_2$	72 (45)[b]
2	**26a**	2-(bromomethyl)-1-hexene	**27b**: R^1 = H; R^2 = $CH_2C(Bu)=CH_2$	72
3	**26a**	ethyl propiolate	**27c**: R^1 = H; R^2 = $CH=CHCO_2Et$	69
4	**26a**	HexC≡CBr	**27d**: R^1 = H; R^2 = C≡C-Hex	79[b]
5	**26a**	$THPOCH_2C{\equiv}CBr$	**27e**: R^1 = H; R^2 = $C{\equiv}CCH_2OTHP$	76[b]
6	**26a**			72[b]
7	**26a**	Me_3SnCl	**27g**: R^1 = H; R^2 = $SnMe_3$	64
8	**26b**	ethyl α-(bromomethyl)acrylate	**27h**: R^1 = CH_3; R^2 = $CH_2C(CO_2Et)=CH_2$	76

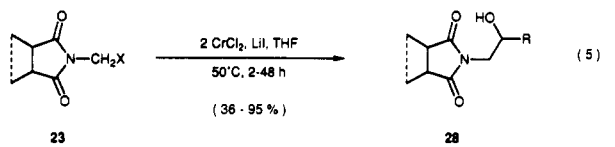
[a] The zinc reagent was prepared from a 1:1 mixture of PhCN and DMSO.

Table III. Protected 1,2-Amino Alcohols 28a–i Obtained by the Reaction of Cyclic *N*-Halomethyl Imides with Aldehydes in the Presence of Chromium(II) Chloride and Lithium Iodide

entry	*N*-(halomethyl)imide 7a, 9, 10, or 11	aldehyde	protected amino alcohol 28	yield[a] (%)
				
1	**7a**: X = Cl	PhCHO	**28a**: R = Ph	81
2	**7a**: X = Cl	c-HexCHO	**28b**: R = c-Hex	95
3	**7a**: X = Cl	PentCHO	**28c**: R = Pent	88
4	**8**: X = Br	PentCHO	**28c**: R = Pent	93
5	**7a**: X = Cl	*p*-NCPhCHO	**28d**: R = *p*-NCPh	71
6	**7a**: X = Cl	*m*-AcOPhCHO	**28e**: R = *m*-AcOPh	76
7	**7a**: X = Cl	cinnamaldehyde	**28f**: R = (*E*)-PhCH=CH	36
				
8	**10**: X = Cl	PhCHO	**28g**: R = Ph	84
9	**10**: X = Cl	PentCHO	**28h**: R = Pent	81
10	**11**: X = I	$MeO_2C(CH_2)_4CHO$	**28i**: R = $(CH_2)_4COOMe$	68

[a] All yields refer to isolated yields of compounds being over 98% pure by GC analysis.

compounds **26** display a lower reactivity and electrophiles such as enones, nitro olefins, and aldehydes did not undergo a reaction. This led us to search for alternative organometallic reagents having a higher reactivity. We found that various cyclic *N*-(halomethyl)imides readily insert $CrCl_2$ in THF and in the presence of lithium iodide (1 equiv),[22f] furnishing intermediate[22] chromium(III) organometallics **25** which react with aldehydes (50 °C, 4–48 h) affording protected amino alcohols of type **28** in good to excellent yields (eq 5 and Table III). A complete con-



23 **28** (5)

version is usually reached after 5–10 h at 50 °C; however, the reaction of **7a** with cyclohexanecarboxaldehyde requires 48 h at 55 °C (entry 2 of Table III, 95% yield). Both aromatic (entries 1, 5, 6, 8) and aliphatic (entries 2–4, 9, 10) aldehydes can be used, but an α,β-unsaturated aldehyde such as cinnamaldehyde (entry 7) furnishes the desired alcohol **28f** only in 36% isolated yield. The reaction shows an excellent chemoselectivity and tolerates the presence of functional groups such as a cyano (entry 5) or an ester group (entries 6 and 10) providing an efficient entry to polyfunctional amino alcohols **28d–e** and **28i**.

In conclusion, we have developed a general approach to polyfunctional zinc and copper organometallics at the α position to oxygen and studied their reactivity toward various classes of electrophiles. Using the same approach, it was also possible to prepare zinc, copper, and chromium organometallics at the α position to the nitrogen of imides. However, in this case, the relatively low reactivity of these reagents limits the choices of electrophiles to allylic and alkynyl halides, ethyl propiolate (M = Cu(CN)ZnCl), and aldehydes (M = $CrCl_2$).

Experimental Section

General Considerations. Unless otherwise indicated, all reactions were carried out under argon. Solvents (THF and diethyl ether) were dried and freshly distilled from sodium/benzophenone. Reactions were monitored by gas–liquid-phase chromatography (GC) or thin-layer chromatography (TLC) analysis of aliquots taken from the reaction mixture and quenched with saturated aqueous NH_4Cl. Unless otherwise indicated, the reactions were worked up as follows: the reaction mixture was added to a stirred ether/saturated aqueous NH_4Cl mixture. After filtration of the insoluble salts, the two layers were separated and the aqueous layer was extracted twice with ether. The combined ethereal extracts were then washed with distilled water and saturated sodium chloride, dried ($MgSO_4$), and filtered, and the solvent was removed by rotary evaporation.

Starting Materials. 2-(Bromomethyl)-1-hexene was prepared from 2-butyl-2-propen-1-ol and PBr_3.[27] 1-Bromooctyne,[28] *N*-(1-chloroethyl)phthalimide (**9**),[9] *N*-(chloromethyl)succinimide (**10**),[29] *N*-(iodomethyl)succinimide (**11**),[29] and methyl 6-oxohexanoate[30] were prepared according to the literature. *N*-(Chloromethyl)- and *N*-(bromomethyl)succinimide (**7** and **8**) were purchased from Aldrich Chemical Co.

Iodomethyl Pivalate (3). A solution of freshly distilled chloromethyl pivalate (8 g, 53 mmol) and sodium iodide (18 g, 120 mmol) in 50 mL of acetone was stirred 2.5 h at 25 °C under nitrogen. GC analysis showed the completion of the reaction, and hexane (200 mL) was added. The precipitate was filtered, and the solvents were evaporated. The crude residue was purified by distillation (bp ca. 35 °C/0.1 mmHg) affording 10.39 g (81% yield) of pure iodomethyl pivalate. IR (neat): 2976 (s), 2873 (s), 1735 (s), 1480 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.95 (s, 2 H), 1.2 (s, 9 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 176.1, 38.8, 31.2, 26.5. Mass spectra (CI with ammonia): 260 (MNH_4^+, 53), 136 (100), 119 (27). HRMS: calcd for $C_6H_{11}O_2INH_4$ 260.0147, found 260.0160.

Iodomethyl Crotonate (4). (a) Chloromethyl Crotonate. A three-necked flask containing crotonyl chloride (20.9 g, 0.2 mol) and $ZnCl_2$ (400 mg) in CH_2Cl_2 (200 mL) was connected to a flask containing paraformaldehyde (16.0 g, 533 mmol) and 7 drops of concd H_2SO_4. The solid paraformaldehyde was heated so that the formaldehyde condensed into the stirred solution of the crotonyl chloride. The reaction was stirred 12 h at 25 °C and worked up as usual. The crude product was purified by distillation (bp 93 °C/50 mmHg) affording 8.0 g (34% yield) of the pure chloromethyl crotonate. IR (neat): 2980 (s), 1742 (s), 1657 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.10 (h, 1 H, J = 7.5 Hz), 5.83 (d, 1 H, J = 18 Hz), 5.78 (s, 2 H), 1.92 (d, 3 H, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 164.0, 147.8, 121.2, 68.7, 18.2; MS (EI, 70 eV): 134 (2), 104 (15), 69 (100). HRMS: calcd for $C_5H_7ClO_2$ 134.0134, found 134.0130.

(b) Iodomethyl Crotonate (4). A solution of chloromethyl crotonate (4.58 g, 30 mmol) and sodium iodide (7.5 g, 50 mmol in acetone (50 mL) was stirred for 3 h at 25 °C and worked up as described above for iodomethyl pivalate (**3**) affording after distillation (42 °C, 0.1 mmHg) 5.35 g (79% yield) of iodomethyl crotonate (**4**). IR (neat): 3061 (s), 2973 (s), 1738 (s), 1656 (s), 1442 (s), 1424 (s). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.1 (d, 1 H, J = 7.5 Hz), 5.95 (s, 2 H), 5.8 (d, 1 H, J = 15.6 Hz), 1.86 (d, 3 H, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 164.0, 147.4, 121.4, 30.7, 18.0. MS (CI with ammonia): 244 (MNH_4^+, 100), 136 (54). HRMS: calcd for $C_5H_7IO_2NH_4$ 243.9836, found 243.9838.

Typical Preparation of an α-Bromoalkyl Acetate 5. Preparation of 1-Bromo-2-methylpropyl Acetate (5a; R = *i*-Pr). According to ref 8, isobutyraldehyde (3.6 g, 50 mmol) was added dropwise within 30 min at −10 °C to a solution of freshly distilled acetyl bromide (7.4 g, 60 mmol) and zinc chloride (100 mg, 0.75 mmol) in 10 mL of CH_2Cl_2. After 2 h of stirring between −5 and 0 °C, the reaction mixture was filtered through alumina (5 g of aluminum oxide, activated, neutral, Brockmann I) affording a clear yellowish solution. After evaporation of the solvent[9g] (90%), an oil was obtained which was found to be over 95% pure by ^{1}H NMR and was used without purification for the preparation of the corresponding zinc organometallic.

Preparation of (Pivaloyloxy)methylzinc Iodide (12). A solution of iodomethyl pivalate (6.44 g, 25 mmol) in THF (16 mL) was slowly added at 10–12 °C to zinc dust (3.25 g, 50 mmol; Aldrich −325 mesh) which has been activated with dibromoethane (200 mg) and Me_3SiCl (0.1 mL).[4] After the addition, a GC analysis of a hydrolyzed aliquot showed a yield of 80–90% (*n*-decane was used as an internal standard). The corresponding cadmium reagent ((pivaloyloxy)methylcadmium iodide) was prepared in a similar way (the reaction temperature was kept below 15 °C). The reaction was almost complete after the addition. (Crotonyloxy)methylzinc iodide (**13**) was prepared similarly (10–12 °C, reaction complete after the slow addition of the reagent **4**).

Typical Preparation of an Organozinc Reagent Derived from an α-Bromoalkyl Acetate 16. Preparation of 1-Acetoxy-2-methylpropylzinc Bromide (16a). A three-necked, 25-mL flask equipped with an argon inlet, a stirring bar, and a low-temperature and an addition funnel was charged under argon with zinc dust (Aldrich −325 mesh; 1 g, 15 mmol), DMSO (2 mL), and THF (2 mL). The mixture was cooled to 0 °C, and 1-bromo-2-methylpropyl acetae (**5a**: R = *i*-Pr, 1.95 g, 10 mmol) in THF (5 mL) prepared as described above was added dropwise within 10 min. The reaction mixture was warmed to 8–10 °C and stirred at this temperature overnight (10 h) leading to an almost quantitative formation of the corresponding zinc organometallic as indicated by GC analysis of a hydrolyzed reaction aliquot.

General Procedure of the Reaction of (Pivaloyloxy)methylcopper (PivOCH$_2$Cu(CN)ZnI) 14 with Electrophiles. A THF solution of the zinc reagent **12** (10 mmol) prepared as described above was added at −20 °C to a THF (10 mL) solution of CuCN (0.9 g, 10 mmol) and LiCl (0.84 g, 20 mmol). The reaction mixture was allowed to reach 0 °C and was stirred for 5 min at this temperature. The copper derivative **14** formed in this way was cooled to −78 °C, and 0.7–0.8 equiv of the electrophile was added. (i) In the case of acid chlorides, the reaction mixture was warmed to −20 °C and stirred 1 h at this temperature and then 0.5 h at 0 °C; (ii) for aldehydes, the electrophile was added at −78 °C, followed by the addition of BF_3·OEt_2 (1.35 equiv). The reaction mixture was stirred overnight at −30 °C, 2 h at −20 °C, and worked up; (iii) for cyclohexenone, Me_3SiCl (1.1 equiv) was added at −78 °C, followed by the enone. The reaction was allowed to warm to 25 °C overnight worked up as usual and the crude reaction mixture dissolved in THF and treated with a THF solution of Bu_4NF (1.1 equiv, 5 °C, 5 min); (iv) for 3-methylcyclohexenone, 4 equiv of BF_3·OEt_2 was added at 78 °C, and the reaction mixture was stirred at −30 °C for 3 days and worked up; (v) 3-iodocyclohexenone was added at −78 °C, and the reaction mixture was stirred at −30 °C overnight allowed to warm to −5 °C, and worked up after 2 h at this temperature; (vi) the allylic bromide and tributyltin chloride were in each case added at −40 °C, and the reaction mixture was warmed to 25 °C and stirred for 0.5 h; (vii) 1-bromooctyne was added at −78 °C, and the reaction mixture was stirred overnight at −50 °C and worked up.

General Procedure for the Preparation of a Zinc–Copper Reagent 17 and Its Allylation. Preparation of Ethyl 2-(2-Acetoxy-3-methylbutyl)-2-propenoate (20a). The THF solution of 1-acetoxy-2-methylpropylzinc bromide (10 mmol) prepared as described above was added via syringe at −78 °C to a suspension of LiCl (0.7 g, 16 mmol) and CuCN (0.72 g, 8 mmol) in THF (3 mL). A solution of ethyl α-(bromomethyl)acrylate (0.97 g, 5 mmol) in THF (3 mL) was added, and the reaction mixture was warmed to 0 °C. The reaction was completed after 0.5 h as shown by GC analysis. The reaction mixture was then diluted with ether (50 mL) and poured in saturated aqueous NH_4Cl (25 mL). The organic and aqueous layers were separated, and the aqueous layer was extracted twice with ether (25 mL). The combined organic phase was successively washed with H_2O (2 × 20 mL) and brine (10 mL). After the solution was dried over $MgSO_4$ and filtered, the solvent was evaporated and the crude oil was purified by flash chromatography (hexane/ether (20–10:1)) yielding 1.08 g (95%) of the analytically pure product **20a** (>98% by capillary GC analysis).

Alternative Preparation of the Reagents 17 Using Zinc Dust Activated with 1,2-Dibromoethane. The Addition of the Copper–Zinc Reagent 17j to 2-(Ethylsulfonyl)nitroethylene (22).[19,20] Preparation of (*E*)-3-Acetoxy-1-nitro-1-octene (20x). (a) Preparation of the Zinc–Copper Reagent 17j. To a suspension of zinc dust (0.98 g, 15 mmol) previously activated with 1,2-dibromoethane (0.1 mL) and Me_3SiCl (0.05 mL) in a mixture of THF (3.5 mL) and DMSO (1 mL) was slowly added at 25 °C 1-bromohexyl acetate (1.12 g, 5 mmol). The addition was exothermic, and the temperature reached 40 °C. GC analysis of a hydrolyzed reaction aliquot shows the complete formation of the zinc reagent. The zinc reagent solution was allowed to settle and was added slowly to a solution of copper cyanide (0.4 g, 4.5 mmol) and lithium chloride (0.38 g, 9 mmol)

(27) 2-(Bromomethyl)-1-hexene has been prepared by the bromination of 2-butyl-2-propen-1-ol (Sarkar, D. C.; Das, A. R.; Rawu, B. C. *J. Org. Chem.* **1990**, *55*, 5799 with PBr_3 in ether (0 °C, 2 h).

(28) Brandsma, L. Preparative Acetylenic Chemistry, 2nd ed.; Elsevier: Amsterdam, 1988.

(29) (a) Wendeliu, W.; Gubitz, G.; Pracher, U. *J. Heterocycl. Chem.* **1987**, 1381. (b) Martell, M. J.; Ross, A. S.; Boothe, J. H. *J. Med. Chem.* **1967**, *10*, 359.

(30) (a) Schreiber, S. L.; Claus, R. E.; Reagan, J. *Tetrahedron Lett.* **1982**, *23*, 3867. (b) Claus, R. E.; Schreiber, S. L. *Org. Synth.* **1986**, *64*, 150.

in THF (2 mL) at −40 °C. The reaction mixture was then warmed to 0 °C and was ready to use.

(b) Reaction of 17j with 2-(Ethylsulfonyl)nitroethylene (22).[19,20] The previously prepared solution of **17j** was cooled to −78 °C, and 2-(ethylsulfonyl)nitroethylene (0.58 g, 3.5 mmol) in 5 mL of THF was slowly added. The reaction mixture was stirred at −60 °C for 30 min and worked up as usual. The residue was then purified by flash chromatography (hexane/Et_2O (97:3)) to afford 0.52 g (80% yield) of the analytically pure nitro olefin **20x**.

Products Described in Table I. (a) Products 18a–m. (Pivaloyloxy)methyl Phenyl Ketone (18a). Yield: 1.60 g (81%) using **14** (12 mmol) and benzoyl chloride (1.27 g, 9 mmol). Reaction conditions: −10 °C, 1 h, 0 °C, 1 h; purified by flash chromatography (hexane–ether (96:4)). IR (neat): 2987 (s), 1736 (s), 1697 (s), 1448 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.92 (d, 2 H), 7.6 (m, 1 H), 7.48 (t, 2 H), 5.42 (s, 2 H), 1.41 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 192.4, 177.8, 134.4, 133.6, 127.9, 65.8, 38.8, 27.2. Mass (EI, 70 eV): 220 (M^+, 1), 105 (100). HRMS: calcd for $C_{13}H_{16}O_3$ 220.1099, found 220.1100.

2-Furyl (Pivaloyloxy)methyl Ketone (18b). Yield: 1.04 g as a solid, mp 72 °C (90%) using **14** (10 mmol) and 2-furoyl chloride (910 mg, 5.5 mmol). Reaction conditions: −10 °C, 10 h. Purified by flash chromatography (hexane–ether (10:1)). IR (CH_2Cl_2): 2942 (m), 1737 (s), 1696 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.61 (s, 1 H), 7.26 (s, 1 H), 6.57 (m, 1 H), 5.16 (s, 2 H), 1.3 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 181.7, 177.6, 150.5, 146.5, 117.3, 112.2, 65.0, 38.6, 27.0. Mass (EI, 70 eV): 210 (M^+, 10), 57 (100). HRMS: calcd for $C_{11}H_{14}O_4$ 210.0892, found 210.0877.

Cyclohexyl (Pivaloyloxy)methyl Ketone (18c). Yield: 830 mg (66%) using **14** (10 mmol) and cyclohexanecarbonyl chloride (820 mg, 5.6 mmol). Reaction conditions: −10 °C, 8 h. Purified by flash chromatography (hexane–ether (10:1)). IR (neat): 2975.7 (s), 1740.5 (s), 1728.9 (s), 1481.0 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 4.62 (s, 2 H), 2.43 (m, 1 H), 1.72 (m, 4 H), 1.6 (m, 1 H), 1.2–1.4 (m, s, 14 H). ^{13}C-NMR ($CDCl_3$, 7.5 MHz): δ 206.2, 177.5, 66.4, 47.0, 38.5, 27.9, 27.0, 25.5, 25.3. Mass (EI, 70 eV): 226 (M^+, 2), 111 (37), 83 (100). HRMS: calcd for $C_{13}H_{22}O_3$ 226.1569, found 226.1568.

3-Chloropropyl (Pivaloyloxy)methyl Ketone (18d). Yield: 740 mg (42%) using **14** (10 mmol) and 4-chlorobutyroyl chloride (1.15 g, 8 mmol). Reaction conditions: −10 °C, 3 h. A yield of 62% (1.37 g) was obtained by using the corresponding copper–cadmium reagent ($PivOCH_2Cu(CN)CdI$; 14 mmol) and 4-chlorobutyroyl chloride (1.41 g, 10 mmol). Purified by flash chromatography (hexane–ether (95:5)). IR (neat): 2974 (s), 1730 (s), 1482 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 4.65 (s, 2 H), 3.57 (t, 2 H, J = 6.2 Hz), 2.63 (t, 2 H, J = 6.9 Hz), 2.09 (m, 2 H), 1.28 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 203.0, 177.7, 67.8, 44.0, 38.6, 35.3, 27.0, 25.7. Mass (CI): 223 (MH^+, 12), 185 (18), 119 (38), 85 (100). HRMS: calcd for $C_{18}H_{17}ClO_3H$ (MH^+) 221.0944, found 221.0946.

2-Hydroxy-2-phenylethyl Pivalate (18e). Yield: 1.09 g (89%) using **14** (8 mmol) and benzaldehyde (583 mg, 5.5 mmol) in the presence of $BF_3{\cdot}OEt_2$ (1.35 mL, 11 mmol). Reaction conditions: −30 °C, 16 h, −20 °C, 2 h. Purified by flash chromatography (hexane–ether (15:1)). IR (neat): 3450 (br), 2973 (s), 1730 (s), 1712 (s), 1480 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.2–7.4 (m, 5 H), 4.9 (dd, 1 H, J = 7.7, 3.8 Hz), 4.18 (dd, 1 H, J = 11.4, 7.7 Hz), 4.25 (dd, 1 H, J = 11.4, 3.8 Hz), 2.62 (brs, 1 H), 1.19 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 178.9, 140.4, 128.2, 121.7, 126.4, 72.8, 69.4, 27.5. Mass (CI): 223 (5), 205 (100), 151 (42). HRMS: calcd for $C_{13}H_{26}O_3H$ (MH^+) 231.1960, found 231.1966.

2-Hydroxyoctyl Pivalate (18f). Yield: 0.910 g (73%) using **14** (10 mmol) and heptanal (0.62 g, 5.4 mmol) in the presence of $BF_3{\cdot}OEt_2$ (1.42 g, 10 mmol). Reaction conditions: −30 °C, 2 h, −15 °C, 10 h. Purified by flash chromatography (hexane–ether (15:1)). IR (neat): 3540 (br), 2932 (s), 1732 (s), 1713 (s), 1164 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 4.18 (m, 1 H), 4.02 (m, 1 H), 3.86 (m, 1 H), 1.48 (m, 3 H), 1.32 (m, 6 H), 1.21 (s, 9 H), 0.8 (m, 3 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 178.4, 70.0, 68.4, 38.8, 33.3, 31.6, 29.1, 27.1, 25.2, 22.5, 13.9. Mass (CI): 231 (MH^+, 22), 213 (34), 111 (30), 103 (100), 85 (96). HRMS: (CI) calcd for $C_{13}H_{26}O_3H$ (MH^+) 231.1960, found 231.1966.

(3-Oxocyclohexyl)methyl Pivalate (18g). Yield: 1.16 g (59%) using **14** (8 mmol) and cyclohexenone (528 mg, 5.5 mmol) in the presence of chlorotrimethylsilane (0.76 mL, 6 mmol). Reaction conditions: −78 to −20 °C, 8 h, 0 °C, 6 h. After workup, the crude reaction mixture was treated with a THF solution of Bu_4NF (1 M solution, 4 mL, 4 mmol). Purified by flash chromatography (hexane–ether (80:20)). IR (neat): 2960 (s), 1728 (s), 1524 (s), 1284 (s), 1157 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 3.92 (m, 2 H), 2.4–2.0 (m, 6 H), 1.85 (m, 1 H), 1.56 (m, 2 H), 1.45 (m, 1 H), 1.16 (s, 9 H). ^{13}C-NMR ($CDCl_3$), 75.5 MHz): δ 209.3, 177.8, 67.5, 44.3, 40.9, 38.7, 38.1, 27.8, 27.1, 24.5. Mass (CI): 213 (MH^+, 85), 139 (25), 129 (22), 111 (100), 85 (49). HRMS: calcd for $C_{12}H_{20}O_3H$ 213.1490, found 213.1479.

(1-Methyl-3-oxocyclohexyl)methyl Pivalate (18h). Yield: 1.06 g (71%) using **14** (20 mmol) and 3-methylcyclohexenone (0.73 g, 6.6 mmol) in the presence of $BF_3{\cdot}OEt_2$ (5 mL, 40 mmol). Reaction conditions: −38 °C, 40 h, 25 °C, 5 h. Purified by flash chromatography (hexane–ether (90:10)). IR (neat): 2940 (m), 1730 (s), 1716 (s), 1392 (m), 1284 (s) cm^{-1}. ^1H-NMR ($CDCl_3$), 300 MHz): δ 3.81 (s, 2 H), 2.4 (m, 3 H), 2.1 (m, 1 H), 1.9 (m, 2 H), 1.7 (m, 1 H), 1.6 (m, 1 H), 1.2 (s, 9 H), 0.9 (s, 3 H). ^{13}C-NMR ($CDCl_3$, 90.5 MHz): δ 210.5, 177.9, 71.5, 49.9, 40.7, 39.2, 38.8, 32.9, 27.1, 26.9, 22.4, 21.5. Mass (CI): 227 (MH^+, 6), 153 (11), 143 (10), 125 (100). HRMS: calcd for $C_{13}H_{22}O_3H$ (MH^+) 227.1647, found 227.1637.

(3-Oxo-1-cyclohexenyl)methyl Pivalate (18i). Yield: 1.12 g (97%) using **14** (8 mmol) and 3-iodo-2-cyclohexen-1-one[26] (1.27 g, 5.5 mmol). Reaction conditions: −30 °C, 8 h, −5 °C, 6 h. Purified by flash chromatography (hexane–ether (80:20)). IR (neat): 2936 (s), 1734 (s), 1677 (s), 1498 (m) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 6.02 (m, 1 H), 4.68 (m, 2 H), 2.42 (t, 2 H, J = 7.3 Hz), 2.30 (brt, 2 H, J = 7.3 Hz), 2.08 (m, 1 H), 1.23 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 210.1, 188.9, 169.9, 135.5, 76.1, 50.1, 48.9, 38.4, 37.5, 33.6. Mass (EI): 210 (M^+, 4), 126 (27), 108 (7), 98 (15), 85 (19), 81 (9), 57 (100). HRMS: calcd for $C_{12}H_8O_3H$ (MH^+) 210.1256, found 210.1257.

3-Butyl-3-butenyl Pivalate (18j). Yield: 1.21 g (95%) using **14** (10 mmol) and 2-(bromomethyl)-1-hexene[27] (1.06 g, 6 mmol). Reaction conditions: 0 °C, 1 h. Purified by flash chromatography (hexane–ether (95:5)). IR (neat): 2950 (s), 2850 (s), 1710 (s), 1480 (s), 1390 (s), cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 4.76 (s, 1 H), 4.73 (s, 1 H), 4.13 (t, 2 H, J = 7.5 Hz), 2.32 (t, 2 H, J = 6.4 Hz), 1.62 (t, 2 H, J = 7.8 Hz), 1.15–1.14 (m, 4 H), 1.27 (s, 9 H), 0.87 (t, 3 H, J = 3.8 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 178.4, 145.8, 110.9, 62.8, 38.7, 35.8, 35.0, 29.9, 27.2, 22.4, 13.9. Mass (EI, 70 eV): 212 (M^+, 1), 110 (20), 95 (27), 68 (100). HRMS: calcd for $C_{13}H_{24}O_2$ (MH^+) 213.1854, found 213.1842.

***tert*-Butyl [2-(Pivaloyloxy)ethyl]acrylate (18k).** Yield: 1.33 g (94%) using **14** (8 mmol) and *tert*-butyl α-(bromomethyl)-acrylate[25] (1.21 g, 5.5 mmol). Reaction conditions: −78 to 0 °C, 0.5 h. Purified by flash chromatography (hexane–ether (10:1)). IR (neat): 2935 (s), 1730 (s), 1714 (s), 1481 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 6.18 (s, 1 H), 5.52 (s, 1 H), 4.17 (t, 2 H, J = 7.5 Hz), 2.61 (t, 2 H, J = 7 Hz), 1.49 (s, 9 H), 1.24 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 178.2, 165.7, 138.2, 125.8, 80.7, 62.5, 31.5, 28.0, 27.08. Mass (CI): 257 (MH^+, 7), 201 (45), 183 (19), 99 (100), 85 (36). HRMS: calcd for $C_{14}H_{24}O_4H$ (MH^+) 257.1753, found 257.1758.

(Tributylstannyl)methyl Pivalate (18l). Yield: 1.56 g (93%) using **14** (6 mmol) and chlorotributylstannane (1.37 g, 4.2 mmol). Reaction conditions: −78 to 25 °C, 8 h. Purified by flash chromatography (hexane–ether (98:2)). IR (neat): 2956 (s), 1712 (s), 1480 (s), 1463 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz) δ 4.18 (s, 2 H), 1.52 (m, 6 H), 1.32 (m, 6 H), 1.18 (s, 9 H), 0.92 (m, 15 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 179.3, 53.7, 38.9, 29.0, 27.3, 13.7, 9.5. Mass (CI): 405 (MH^+, 7), 349 (100), 235 (27), 177 (20). HRMS: (CI) calcd for $C_{18}H_{38}SnO_2H$ (MH^+) 405.1815, found 405.1817.

2-Nonynyl Pivalate (18m). Yield: 0.86 g (72%) using **14** (8 mmol) and 1-bromo-1-octyne[28] (1.04 g, 5.5 mmol). Reaction conditions: −50 °C, 8 h. Purified by flash chromatography (hexane–ether (98:2)). IR (neat): 2958 (s), 1739 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 4.62 (t, 2 H), 2.21 (m, 2 H), 1.52 (m, 2 H), 1.29–1.50 (m, 7 H), 1.21 (s, 9 H), 0.89 (t, 3 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 177.6, 87.1, 74.3, 52.7, 38.6, 31.3, 28.4, 27.0, 22.5, 18.7, 13.9. Mass (CI): 225 (MH^+, 61), 141 (22), 131 (21), 123 (61), 107 (11), 103 (25), 95 (14), 85 (45), 81 (100). HRMS: (CI) calcd for $C_{14}H_{24}O_2H$ (MH^+) 225.1854, found 225.1860.

(*E*)-2-Oxo-2-phenylethyl Crotonate (19a). Yield: 0.89 g (93%) using **15** (10 mmol) and benzoyl chloride (0.69 g, 4.7 mmol). Reaction conditions: −78 to −14 °C, 8 h. Purified by flash chromatography (hexane–ether (10:1)). IR (KBr): 1723 (s), 1705 (s), 1657 (m) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.92–7.89 (m, 2 H), 7.61–7.55 (m, 1 H), 7.48–7.43 (m, 2 H), 7.10 (dq, 1 H, *J* = 15, 6.3 Hz), 5.98 (bd, 1 H, *J* = 15 Hz), 5.37 (s, 2 H), 1.90 (dd, 3 H, *J* = 6, 1.5 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 192.4, 165.7, 146.3, 134.5, 133.8, 128.8, 127.8, 121.8, 65.8, 18.0. MS (EI): 204 (M^+, 0.2), 118 (15), 105 (100). Exact mass for $C_{12}H_{12}O_3$: calcd 204.0788, obsd 204.0786.

3-Carbethoxy-3-butenyl Crotonate (19b). Yield: 1.0 g (96%) using **15** (10 mmol) and ethyl α-(bromomethyl)acrylate[25] (98% purity, 1.01 g, 5 mmol). Reaction conditions: −78 to −25 °C, 2 h. Purified by flash chromatography (hexane–ether (10:1)). IR (neat): 2981 (s), 1720 (s), 1660 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 6.96 (dq, 1 H, *J* = 18, 6 Hz), 6.23 (s, 1 H), 5.80 (d, 1 H, *J* = 18 Hz), 5.61 (s, 1 H), 4.27 (t, 2 H, *J* = 6 Hz), 4.21 (t, 2 H, *J* = 6 Hz), 2.67 (t, 2 H, *J* = 6 Hz), 1.88 (d, 3 H, *J* = 6 Hz), 1.30 (t, 3 H, *J* = 6 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 166.3, 166.0, 144.4, 136.7, 126.6, 122.4, 62.2, 60.6, 31.3, 17.7, 14.0. MS (EI): 212 (M^+, 0.13), 69 (100). Exact mass for $C_{11}H_{16}O_4$: calcd 212.1049, obsd 212.1039.

Ethyl 2-(2-Acetoxy-3-methylbutyl)-2-propenoate (20a). Yield: 1.08 g (95%) using **17a** (8 mmol) and ethyl α-(bromomethyl)acrylate[25] (0.97 g, 5 mmol). Reaction conditions: −78 to 0 °C, 0.5 h. Purified by flash chromatography (hexane–ether (20:1)). IR (neat): 2965 (s), 1739 (s), 1720 (s), 1372 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 6.13 (d, 1 H, *J* = 1.2 Hz), 5.52 (s, 1 H), 4.90 (ddd, 1 H, *J* = 9.7, 5.7, 2.3 Hz), 4.19 (qd, 2 H, *J* = 8.1, 1.0 Hz), 2.66 (dd, 1 H, *J* = 14.1, 3.3 Hz), 2.32 (dd, 1 H, *J* = 14.1, 9.9 Hz), 1.96 (s, 3 H), 1.82 (octet, 1 H, *J* = 6.3 Hz), 1.28 (t, 3 H, *J* = 7.2 Hz), 0.91 (d, 3 H, *J* = 6.8 Hz), 0.90 (d, 3 H, *J* = 6.8 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 170.1, 166.2, 137.2, 126.2, 76.2, 60.4, 34.1, 31.5, 20.5, 18.1, 17.3, 13.8. Mass (EI): 115 (10), 114 (31), 97 (10), 43 (100). Exact mass for $C_{12}H_{20}O_4H^+$: calcd 229.1440, obsd 229.1425.

1-Isopropyl-3-butenyl Acetate (20b). Yield: 670 mg (85%) using **17a** (10 mmol) and allyl bromide (0.6 g, 5 mmol). Reaction conditions: −78 to −5 °C, 0.5 h. Purified by distillation: bp 88 °C/20 mmHg. IR (neat): 2966 (s), 1738 (s), 1643 (m) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 5.70–5.56 (m, 1 H), 4.98 (m, 1 H), 4.93 (m, 1 H), 2.25–2.12 (m, 2 H), 1.92 (s, 3 H), 1.76–1.69 (m, 1 H), 0.78 (s, 3 H), 0.60 (s, 3 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 170.7, 134.1, 117.1, 77.4, 35.9, 30.9, 20.8, 18.5, 17.4. MS (EI): 115 (22), 43 (100). Exact mass for $C_9H_{16}O_2H^+$: calcd 157.1228, obsd 157.1243.

1-(3-Oxo-1-cyclohexenyl)-2-methylpropyl Acetate (20c). Yield: 1.32 g (97%) using **17a** (10 mmol) and 3-iodo-2-cyclohexen-1-one[26] (1.4 g, 6.5 mmol). Reaction conditions: 0 °C, 2 h, then 25 °C, 1 h. Purified by flash chromatography (hexane–EtOAc (95:5)). IR (neat): 2965 (s), 1742 (s), 1672 (s), 1631 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 5.91 (d, 1 H, *J* = 1.3 Hz), 4.99 (d, 1 H, *J* = 5.6 Hz), 2.37 (t, 2 H, *J* = 6.7 Hz), 2.27 (q, 2 H, *J* = 6.2 Hz), 2.08 (s, 3 H), 1.98 (octet, 1 H, *J* = 6.4 Hz), 0.92 (d, 3 H, *J* = 6.8 Hz), 0.88 (d, 3 H, *J* = 6.8 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 198.9, 169.9, 161.8, 125.3, 79.6, 37.4, 30.2, 26.5, 22.3, 20.4, 18.9, 16.8. MS (EI): 210 (M^+, 2), 168 (27), 126 (35), 125 (54). Exact mass for $C_{12}H_{18}O_3$: calcd 210.1256, obsd 210.1246.

(*Z*)-Methyl 4-Acetoxy-3-carbethoxy-5-methyl-2-hexenoate (20d). >97% *Z* by GC analysis. Yield: 1.11 g (93%) using **17a** (10 mmol) and dimethyl acetylenedicarboxylate (0.71 g, 4.6 mmol). Reaction conditions: −30 °C, 1 h. Purified by flash chromatography (hexane–EtOAc (96:4)). IR (neat): 2937 (s), 1730 (s), 1655 (s), 1462 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 5.93 (d, 1 H, *J* = 1.2 Hz), 5.21 (dd, 1 H, *J* = 6.5, 1.2 Hz), 3.80 (s, 3 H), 3.71 (s, 3 H), 2.02 (octet, 1 H, *J* = 6.7 Hz), 0.93 (d, 3 H, *J* = 6.8 Hz), 0.91 (d, 3 H, *J* = 6.7 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.5, 166.4, 164.7, 146.7, 121.5, 77.6, 52.2, 51.8, 30.4, 20.4, 18.7, 17.0. MS (EI): 199 (13), 174 (21), 43 (100). Exact mass for $C_{12}H_{18}O_6H^+$: calcd 259.1182, obsd 259.1176.

(*E*)-Ethyl 4-Acetoxy-5-methyl-2-hexenoate (20e). >96% *E* by GC analysis. Yield: 0.98 g (91%) using **17a** (10 mmol) and ethyl propiolate (0.49 g, 5 mmol). Reaction conditions: 25 °C, 4 h. Purified by flash chromatography (hexane–EtOAc (98:2)). IR (neat): 2928 (s), 1739 (s), 1721 (s), 1662 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 6.82 (dd, 1 H, *J* = 15.6, 5.5 Hz), 5.90 (dd, 1 H, *J* = 15.6, 1.6 Hz), 5.21 (td, 1 H, *J* = 5.5, 1.6 Hz), 4.17 (q, 2 H, *J* = 7.2 Hz), 2.09 (s, 3 H), 1.93 (octet, 1 H, *J* = 5.7 Hz), 1.27 (t, 3 H, *J* = 7.2 Hz), 0.94 (d, 3 H, *J* = 7.8 Hz), 0.93 (d, 3 H, *J* = 7.8 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.8, 165.8, 143.9, 122.4, 76.7, 60.3, 31.8, 20.6, 17.9, 17.6, 14.0. MS (EI): 130 (37), 127 (24), 43 (100). Exact mass for $C_{11}H_{18}O_4H^+$: calcd 215.1283, obsd 215.1286.

1-Isopropyl-3-nitro-2-propenyl Acetate (20f). Yield: 0.83 g (74%; 100% *E*) prepared form **17a** (8 mmol) and 2-(phenylsulfonyl)nitroethylene **22**[20] (1.28 g, 6 mmol). Reaction conditions: −78 to −60 °C, 2 h. Purified by flash chromatography (hexane–EtOAc (97:3)). IR (neat): 2970 (s), 2937 (s), 1748 (s), 1657 (m), 1531 (s), 1355 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.12 (dd, 1 H, *J* = 5, 13.3 Hz), 7.00 (d, 1 H, *J* = 13.4 Hz), 5.31 (m, 1 H), 2.09 (s, 3 H), 2.01 (m, 1 H), 0.94 (m, 6 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.6, 140.7, 137.9, 73.9, 32.0, 20.4, 17.7, 17.5. MS (EI): 188 (M^+, 29), 145 (29), 128 (97). Exact mass for $C_8H_{13}NO_4H^+$: calcd 188.0923, obsd 188.0915.

2-Isopropyl-4-nitro-3-phenylbutanenitrile (20g). Mixture of diastereoisomers (ca. 50:50). Yield: 735 mg (72%) using **17a** (6 mmol) and nitrostyrene (0.66 g, 4.4 mmol). Reaction conditions: −78 to 0 °C, 12 h. Purified by flash chromatography (hexane–EtOAc (96:4)). IR (neat): 2968 (m), 1603 (w), 1556 (s), 1373 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.41–7.29 (m, 4 H), 7.19–7.16 (m, 1 H), 4.97–4.69 (m, 2 H), 3.82–3.67 (m, 1 H), 2.83 (dd, *J* = 10.8, 4.0 Hz), 2.71 (dd, *J* = 8.5, 5.7 Hz, 1 H), 1.69–1.53 (m, 1 H), 1.12–0.89 (m, 6 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 135.2, 134.7, 129.1, 128.9, 128.6, 128.4, 127.9, 127.3, 118.6, 118.3, 78.8, 77.9, 43.6, 42.3, 42.1, 42.0, 27.7, 26.9, 21.3, 20.4, 19.9, 16.7. MS (EI): 232 (M^+, 4), 185 (21), 143 (46), 104 (100). Exact mass for $C_{13}H_{16}N_2O_2$: calcd 232.1212, obsd 232.1216.

2-Acetoxy-3-methyl-2-phenylbutylmalonitrile (20h). Mixture of two diastereoisomers; 60:40 ratio. Yield: 865 mg as a solid. Mp: 74 °C (89%) using **17a** (5 mmol) and benzylidenemalononitrile (0.55 g, 3.6 mmol). Reaction conditions: 25 °C, 8 h. Purified by flash chromatography (hexane–EtOAc (98:2)). IR (neat): 2969 (s), 2935 (s), 2916 (s), 2256 (m), 1743 (s), 1604 (w) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): two diastereoisomers with a ratio of 60:40; 7.46–7.35 (m, 5 H), 5.5 (dd, *J* = 10.8, 2.4 Hz), 5.20 (dd, *J* = 9.3, 2.4 Hz, 1 H), 4.79 (d, *J* = 6.4 Hz), 4.29 (d, *J* = 5.4 Hz, 1 H), 3.49 (dd, *J* = 6.6, 3.7 Hz), 3.44 (dd, *J* = 10.8, 5.4 Hz, 1 H), 2.21 (s), 2.18 (s, 3 H), 1.72–1.62 (m, 1 H), 0.87 (dd, *J* = 12.3, 6.6 Hz), 0.83 (dd, *J* = 9.0, 6.9 Hz, 6 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 170.8, 170.7, 134.4, 133.1, 129.6, 129.4, 129.2, 129.1, 128.4, 112.0, 111.9, 111.7, 111.5, 77.9, 76.5, 48.5, 47.9, 30.4, 29.6, 27.8, 27.3, 20.8, 19.6, 18.6, 18.4, 14.7. MS (EI): 270 (M^+, 0.2), 43 (100). Exact mass for $C_{16}H_{18}N_2O_2$: calcd 270.1368. Obsd: 270.1368.

Diethyl 2-Cyano-3-methyl-1-phenylbutylmalonate (20i). Ca. 50:50 mixture of diastereoisomers). Yield: 1.28 g (86%) using **17a** (10 mmol) and diethyl benzylidenemalonate (1.12 g, 4.5 mmol). Reaction conditions: 25 °C, 10 h. Purified by flash chromatography (hexane–EtOAc (96.4)). IR (neat): 2978 (s), 2236 (w), 1750 (s), 1734 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.39–7.36 (m, 1 H), 7.29–7.20 (m, 4 H), 4.29 (q, *J* = 7.0 Hz, 2 H (major diast.)), 4.14 (q, *J* = 7.2 Hz, 2 H (minor diast.)), 4.08 (d, *J* = 11.6 Hz, 1 H (major diast.)), 3.92 (m, 2 H, (major diast.)), 3.91 (d, *J* = 7.6 Hz, minor diast.), 3.80 (m, 2 H (minor diast.)), 3.71–3.64 (m, 1 H), 3.15 (dd, *J* = 10.9, 3.4 Hz, 1 H (minor diast.)), 2.86 (dd, *J* = 9.6, 4.4 Hz, 1 H, (major diast.)), 1.57–1.40 (m, 1 H), 1.27 (t, *J* = 7.2 Hz, 3 H (major diast.)), 1.18 (t, *J* = 7.0 Hz, 3 H (minor diast.)), 1.01 (t, *J* = 7.2 Hz, 3 H (minor diast.)), 0.98 (s, 3 H), 0.96 (s, 3 H), 0.84 (t, *J* = 7.2 Hz, 3 H (major diast.)). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 167.8, 167.7, 167.1, 167.0, 137.5, 135.9, 129.2, 128.8, 128.6, 128.5, 128.1, 127.9, 119.8, 118.9, 61.9, 61.8, 61.4, 61.3, 56.8, 56.2, 44.7, 43.6, 43.3, 42.3, 28.3, 27.4, 21.7, 21.3, 20.3, 16.7, 13.9, 13.7, 13.6, 13.5. MS (EI): 331 (M^+, 8), 160 (70), 135 (100), 131 (74), 130 (32), 103 (30). Exact mass for $C_{19}H_{25}NO_4$: calcd 331.1783, obsd 331.1771.

1-Isopropyl-2-nonynyl Acetate (20j). Yield: 0.92 g (76%) using **17a** (10 mmol) and 1-bromo-1-octyne[28] (0.95 g, 5 mmol). Reaction conditions: −30 °C, 3 h. Purified by flash chromatography (hexane–EtOAc (96:4)). IR (neat): 2962 (s), 2234 (s), 1743 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 5.19 (dt, 1 H, *J* = 5.5, 2.0 Hz), 2.19 (td, 2 H, *J* = 6.9, 2.0 Hz), 2.06 (s, 3 H), 1.57 (octet, 1 H, *J* = 7.5 Hz), 1.5–1.3 (m, 8 H), 0.98 (d, 3 H, *J* = 6.8 Hz), 0.95 (d, 3 H, *J* = 6.8 Hz), 0.86 (t, 3 H, *J* = 6.7 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.9, 86.6, 76.2, 69.4, 32.5, 31.2, 28.5, 28.4,

22.4, 20.9, 18.6, 18.1, 17.4, 13.8. MS (EI): 224 (M^+, 0.03), 43 (100). Exact mass for $C_{14}H_{24}O_2NH_4^+$: calcd 242.2120, obsd 242.2110.

2-Methyl-1-(tributylstannyl)propyl Acetate (20k). Yield: 1.98 g (90%) using **17a** (10 mmol) and chlorotributylstannane (1.7 g, 5.2 mmol). Reaction conditions: −20 °C, 10 h. Purified by flash chromatography (hexane). IR (neat): 2957 (s), 1722 (s), 1464 (m), 1243 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 4.63 (d, 1 H, J = 9.6 Hz), 2.16–2.01 (m, 1 H), 2.00 (s, 3 H), 1.49–1.40 (m, 6 H), 1.28 (sextet, 6 H, J = 6.9 Hz), 0.92–0.83 (m, 21 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 171.1, 78.5, 32.0, 29.0, 27.4 (t, J = 75 Hz), 20.3 (t, J = 60 Hz), 13.6, 10.0 (t, J = 330 Hz). MS (EI): 349 (13), 293 (29), 291 (27), 179 (95), 177 (100). Exact mass for $C_{18}H_{28}O_2{}^{120}SnNH_4^+$: calcd 424.2238, obsd 424.2236.

1-Acetoxy-2-methylpropyl Phenyl Ketone (20l). Yield: 0.91 g (82%) using **17a** (10 mmol) and benzoyl chloride (0.71 g, 5 mmol). Reaction conditions: −20 °C, 8 h. Purified by flash chromatography (hexane–ether (25:1)). IR (neat): 2969 (s), 1741 (s), 1697 (s), 1131 (s), 1038 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.92 (d, 2 H, J = 8.4 Hz), 7.53 (t, 1 H, J = 7.4 Hz), 7.45 (t, 2 H, J = 6.9 Hz), 5.72 (d, 1 H, J = 4.8 Hz), 2.26 (m, 1 H), 2.15 (s, 3 H), 1.02 (d, 3 H, J = 6.9 Hz), 0.91 (d, 3 H, J = 6.8 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 196.2, 170.6, 135.9, 133.2, 128.7, 128.3, 79.3, 30.1, 20.4, 19.3, 16.9. MS (EI): 220 (M^+, 0.1), 105 (100). Exact mass for $C_{13}H_{16}O_3H^+$: calcd 221.1178, obsd 221.1163.

2-(2-Nitro-1-phenylethyl)octanenitrile (20m). Ca. 60:40 mixture of two diastereoisomers. Yield: 0.56 g (68%) using **17b** (8 mmol) and nitrostyrene (0.45 g, 3 mmol). Reaction conditions: 0 °C, 10 h. Purified by flash chromatography (hexane–EtOAc (96:4)). IR (neat): 2956 (s), 2250 (w), 1734 (m), 1556 (s), 1378 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.40–7.28 (m, 4 H), 7.20–7.15 (m, 1 H), 4.95–4.72 (m, 2 H), 3.69–3.60 (m, 1 H), 3.01–2.92 (m, 1 H), 2.89–2.82 (m, 1 H), 1.65–1.12 (m, 8 H), 0.91–0.79 (m, 5 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 135.8, 134.6, 129.4, 129.3, 129.0, 128.8, 128.3, 127.6, 119.8, 119.4, 78.1, 77.7, 45.6, 44.6, 35.5, 34.8, 31.4, 31.3, 30.4, 30.3, 28.5, 28.4, 27.1, 26.8, 22.4, 13.8. MS (EI): 274 (M^+, 2), 143 (68), 104 (100), 84 (63). Exact mass for $C_{16}H_{22}N_2O_2H^+$: calcd 275.1760, obsd 275.1751.

1-Cyclohexenyl-2-nonynyl Acetate (20n). 1:1 mixture of diastereoisomers. Yield: 1.13 g (86%) using **17c** (10 mmol) and 1-bromo-1-octyne[28] (0.95 g, 5 mmol). Reaction conditions: −78 to 0 °C, 6 h. Purified by flash chromatography (hexane–EtOAc (98:2)). IR (neat): 2955 (s), 1743 (s), 1653 (w) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 5.66 (bs, 2 H), 5.28 (m, 1 H), 2.18 (td, 2 H, J = 7.0, 2.0 Hz), 2.11–2.03 (bs, 6 H), 2.02–1.72 (m, 3 H), 1.53–1.21 (m, 9 H), 0.86 (t, 3 H, J = 7.0 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.7, 126.7, 126.6, 125.5, 125.4, 86.8, 86.6, 76.3, 76.2, 68.1, 68.0, 38.3, 38.1, 31.1, 28.4, 28.3, 27.2, 26.8, 24.8, 24.7, 24.5, 24.1, 22.5, 22.4, 20.7, 18.6, 13.8, 13.8. MS (EI): 262 (M^+, 0.1), 220 (30), 179 (14), 43 (100). Exact mass for $C_{17}H_{26}O_2H^+$: calcd 263.2011, obsd 263.2015.

***tert*-Butyl 2-(2-Acetoxy-2-phenylethyl)-2-propenoate (20o).** Yield: 1.54 g (91%) using **17d** (10 mmol) and *tert*-butyl α-(bromomethyl)acrylate[25] (1.2 g, 5.5 mmol). Reaction conditions: −78 to 20 °C, 0.5 h. Purified by flash chromatography (hexane–EtOAc (96:4)). IR (neat): 1743 (s), 1712 (s), 1368 (s), 1235 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.33–7.28 (m, 5 H), 6.10 (d, 1 H, J = 1.5 Hz), 5.96 (dd, 1 H, J = 3.0, 1.5 Hz), 5.44 (d, 1 H, J = 1.5 Hz), 2.77–2.74 (m, 2 H), 2.03 (s, 3 H), 1.46 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.6, 165.4, 140.1, 137.6, 128.2, 127.7, 126.8, 126.2, 80.6, 74.1, 39.3, 27.9, 20.9. MS (EI): 234 (22), 191 (26), 175 (41), 149 (50), 107 (100). Exact mass for $C_{17}H_{22}O_4NH_4^+$: calcd 308.1862, obsd 308.1862.

***tert*-Butyl 2-[2-Acetoxy-2-(3-acetoxyphenyl)ethyl]propenoate (20p).** Yield: 980 mg (89%) using **17e** (5 mmol) and *tert*-butyl α-(bromomethyl)acrylate[25] (0.66 g, 3 mmol). Reaction conditions: −15 °C, 2 h. Purified by flash chromatography (hexane–EtOAc (96:4)). IR (neat): 1768 (s), 1744 (s), 1710 (s), 1369 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.32 (t, 1 H, J = 7.8 Hz), 7.11 (m, 1 H), 7.05 (m, 1 H), 6.98 (m, 1 H), 6.10 (d, 1 H, J = 1.5 Hz), 5.98 (dd, 1 H, J = 8.4, 5.1 Hz), 5.44 (m, 1 H), 2.81–2.66 (m, 2 H), 2.28 (s, 3 H), 2.02 (s, 3 H), 1.48 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.3, 168.6, 165.2, 150.5, 141.7, 137.3, 129.0, 126.8, 123.5, 120.8, 119.2, 80.5, 73.3, 39.2, 27.7, 20.7, 20.6. MS (EI): 165 (28), 57 (33), 43 (100). Exact mass for $C_{19}H_{24}O_6NH_4^+$: calcd 366.1917, obsd 366.1918.

Ethyl 2-[2-Acetoxy-2-(1-naphthyl)ethyl]-2-propenoate (20q). Yield: 724 mg (71%) using **17f** (5.3 mmol) and ethyl α-(bromomethyl)acrylate[25] (0.66 g, 3 mmol). Reaction conditions: −10 °C, 2 h. Purified by flash chromatography (hexane–EtOAc (96:4)). IR (neat): 1744 (s), 1706 (s), 1632 (m), 1368 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 8.28 (d, 1 H, J = 8.7 Hz), 7.83 (d, 1 H, J = 9.6 Hz), 7.77 (d, 1 H, J = 8.1 Hz), 7.57–7.41 (m, 4 H), 6.76 (dd, 1 H, J = 9.3, 5.4 Hz), 6.13 (d, 1 H, J = 1.8 Hz), 5.50 (s, 1 H), 3.04 (ddd, 1 H, J = 14.1, 4.2, 1.0 Hz), 2.80 (dd, 1 H, J = 13.8, 9.3 Hz), 2.08 (s, 3 H), 1.49 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.6, 137.8, 136.3, 133.6, 130.2, 128.6, 128.2, 127.0, 126.1, 125.5, 125.1, 123.3, 80.7, 71.2, 39.2, 27.9, 20.9. MS (EI): 340 (M^+, 4), 199 (25), 158 (12), 157 (100), 43 (92). Exact mass for $C_{21}H_{24}H_4$: calcd 340.1675, obsd 340.1675.

***(Z)*-Methyl 1-(Naphthylacetoxymethyl)-2-carbomethoxy-2-propenoate (20r).** >98.5% *Z*. Yield: 0.79 g (77%) using **17f** and dimethyl acetylenedicarboxylate (0.42 g, 3 mmol). Reaction conditions: −15 °C, 10 h. Purified by flash chromatography (hexane–EtOAc (96:4)). IR (neat): 2952 (s), 1746 (s), 1727 (s), 1655 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 8.04 (d, 1 H, J = 6.3 Hz), 7.88–7.82 (m, 2 H), 7.59–7.42 (m, 4 H), 7.33 (s, 1 H), 5.87 (s, 1 H), 3.70 (s, 3 H), 3.68 (s, 3 H), 2.12 (s, 3 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.1, 166.3, 165.1, 146.5, 134.0, 131.5, 130.8, 130.0, 128.9, 126.9, 126.6, 126.1, 125.2, 123.6, 123.0, 71.6, 52.4, 52.0, 20.7. MS (EI): 342 (M^+, 7), 236 (20), 223 (21), 43 (100). Exact mass for $C_{19}H_{18}O_6$: calcd 342.1103, obsd 342.1092.

1-[2-(Phenylthio)ethyl]-3-butenyl Acetate (20s). Yield: 1.08 g (86%) using **17g** (9.5 mmol) and allyl bromide (0.61 g, 5 mmol). Reaction conditions: −20 °C, 2 h. Purified by flash chromatography (hexane–EtOAc (96:4)). IR (neat): 2928 (s), 1737 (s), 1642 (m) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.35–7.25 (m, 4 H), 7.20–7.15 (m, 1 H), 5.80–5.62 (m, 1 H), 5.21–4.96 (m, 3 H), 2.95–2.79 (m, 2 H), 2.28 (t, 2 H, J = 15 Hz), 2.04 (s, 3 H), 1.90–1.30 (m, 2 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 170.4, 136.2, 133.1, 129.5, 128.8, 126.1, 117.9, 72.2, 38.5, 33.4, 29.9, 21.0. MS (EI): 250 (M^+, 3), 123 (59), 43 (100). Exact mass for $C_{14}H_{18}O_2S$: calcd 250.1028, obsd 250.1007.

3-[3-(Phenylthio)-1-acetoxypropyl]-2-cyclohexen-1-one (20t). Yield: 1.14 g (75%) using **17g** and 3-iodo-2-cyclohexen-1-one[26] (1.11 g, 5 mmol). Reaction conditions: −10 °C, 5 h, then 5 °C, 2 h. Purified by flash chromatography (hexane–EtOAc). IR (neat): 1744 (s), 1717 (w), 1688 (s), 1675 (s), 1230 (s) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 7.30–7.15 (m, 5 H), 5.91 (s, 1 H), 5.29 (t, 1 H, J = 6.3 Hz), 2.92–2.83 (m, 2 H), 2.32 (t, 2 H, J = 6.6 Hz), 2.21–2.14 (m, 2 H), 2.04 (s, 3 H), 1.97–1.90 (m, 4 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 198.8, 169.7, 161.5, 129.9, 129.0, 126.6, 124.9, 117.3, 74.0, 37.5, 32.6, 29.3, 26.2, 22.4, 20.7. MS (EI): 304 (M^+, 30), 262 (65), 139 (38), 135 (32), 124 (56), 123 (100). Exact mass for $C_{17}H_{20}O_3S$: calcd 304.1133, obsd 304.1146.

5-Acetoxy-4,4-diethyl-7-octenenitrile (20u). Yield: 1.63 g (92%) using **17h** (8 mmol) and *tert*-butyl α-(bromomethyl)-acrylate[25] (1.07 g, 5 mmol). Reaction conditions: −10 °C, 3 h. Purified by flash chromatography (hexane–EtOAc (96:4)). IR (neat): 2974 (s), 2246 (w), 1742 (s), 1710 (s), 1633 (m) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 6.05 (d, 1 H, J = 1.6 Hz), 5.46 (s, 1 H), 5.07 (dd, 1 H, J = 11.0, 1.9 Hz), 2.69 (d, 1 H, J = 13.5 Hz), 2.52–2.29 (m, 2 H), 2.19 (dd, 1 H, J = 13.5, 11.1 Hz), 1.96 (s, 3 H), 1.82–1.63 (m, 2 H), 1.48 (s, 9 H), 1.41–1.22 (m, 4 H), 0.88 (t, 3 H, J = 7.5 Hz), 0.83 (t, 3 H, J = 7.5 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.6, 165.3, 138.5, 126.1, 120.0, 80.6, 75.6, 41.4, 32.9, 29.7, 27.9, 26.3, 24.9, 20.6, 12.1, 7.7, 7.5. MS (EI): 154 (11), 97 (31), 43 (100). Exact mass for $C_{19}H_{31}NO_4NH_4^+$: calcd 355.2597, obsd 355.2613.

Methyl 6-Acetoxy-8-nonenoate (20v). Yield: 0.43 g (95%) using **17i** (3.4 mmol) and allyl bromide (0.25 g, 2 mmol). Reaction conditions: −78 to 25 °C, 2 h. Purified by flash chromatography (hexane–EtOAc (25:1)). IR (neat): 2951 (m), 1738 (s), 1437 (m), 1241 (s), 1167 (m), 1023 (m) cm^{-1}. ^1H-NMR ($CDCl_3$, 300 MHz): δ 5.78–5.64 (m, 1 H), 5.08–5.04 (d, 1 H, J = 6.9 Hz), 5.02 (t, 1 H, J = 1.2 Hz), 4.88 (quintet, 1 H, J = 6.2 Hz), 3.64 (s, 3 H), 2.31–2.25 (m, 4 H), 2.01 (s, 3 H), 1.66–1.50 (m, 4 H), 1.37–1.23 (m, 2 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 173.5, 170.4, 133.4, 117.4, 72.8, 51.2, 38.4, 33.7, 33.0, 24.6, 24.5, 20.9. MS (EI): 155 (15), 145 (65), 113 (64), 43 (100). Exact mass for $C_{12}H_{20}O_4H^+$: calcd 229.1440, obsd 229.1434.

Methyl 6-Acetoxy-6-(trimethylstannyl)hexanoate (20w). Yield: 0.55 g (78%) using **17i** (3.4 mmol) and chlorotrimethyl-

stannane (0.4 g, 2 mmol). Reaction conditions: −78 to 25 °C, 2 h. Purified by flash chromatography (hexane–EtOAc (20:1)). IR (neat): 2948 (s), 2938 (s), 1739 (s), 1719 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 4.50 (dd, 1 H, J = 9.0, 5.7 Hz), 3.65 (s, 3 H), 2.30 (t, 2 H, J = 7.4 Hz), 2.01 (s, 3 H), 1.92–1.55 (m, 4 H), 1.46–1.24 (m, 2 H), 0.74 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 173.7, 171.3, 71.7, 51.3, 33.8, 32.9, 26.9, 24.5, 20.6, −9.6. MS (EI): 352 (M^+, 0.2), 337 (46), 335 (30), 209 (30), 165 (70), 163 (47), 43 (100). Exact mass for $C_{12}H_{24}O_4{}^{120}SnH^+$: calcd 353.0775, obsd 353.0786.

1-Pentyl-3-nitro-2-propenyl Acetate (20x). Yield: 0.52 g (80%) using **17j** (5 mmol) and 2-(ethylsulfonyl)nitroethylene[20] (0.58 g, 3.5 mmol). Reaction condtions: −78 °C, 30 min. Purified by flash chromatography (hexane–Et_2O (97:3)). IR (neat): 2958 (s), 1658 (m), 1531 (s), 1354 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.15 (dd, 1 H, J = 5.0, 13.3 Hz), 7.04 (d, 1 H, J = 13.4 Hz), 5.50 (m, 1 H), 2.11 (s, 3 H), 1.72 (m, 2 H), 1.30 (m, 6 H), 0.88 (t, 3 H, J = 6.7 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.6, 139.8, 139.3, 69.4, 33.4, 31.1, 24.2, 22.1, 20.5, 13.6. MS (CI, NH_4): 233 (100), 136 (50). Exact mass for $C_{10}H_{17}NO_4NH_4^+$: calcd 233.1501, obsd 233.1497.

4-Acetoxy-6-nitro-5-hexenyl Pivalate (20y). Yield: 0.53 g (74%) using **17k** (3.5 mmol) and 2-(phenylsulfonyl)nitroethylene **22**[20] (0.53 g, 2.5 mmol). Reaction conditions: −78 to −60 °C, 2 h. Purified by flash chromatography (hexane–Et_2O (4:1)). IR (neat): 2972 (s), 1659 (m), 1582 (m), 1532 (s), 1354 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 360 MHz): δ 7.15 (dd, 1 H, J = 5, 13.3 Hz), 7.06 (d, 1 H, J = 13.4 Hz), 5.55 (m, 1 H), 4.07 (t, 2 H, J = 6.2 Hz), 2.13 (s, 3 H), 1.73 (m, 4 H), 1.19 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 90 MHz): δ 178.2, 169.5, 140.1, 138.7, 68.9, 63.1, 38.6, 30.0, 27.0, 24.0, 20.6. MS (CI, NH_4^+): 305 (MNH_4^+, 25), 213 (23), 198 (58), 136 (100). Exact mass for $C_{13}H_{21}NO_6NH_4^+$: calcd 305.1713, obsd 305.1719.

Typical Procedure for the Preparation of the Copper–Zinc Reagent 26 and Its Reaction with an Electrophile. Preparation of *N*-(2-Nonyl)phthalimide (27d). A solution of *N*-(chloromethyl)phthalimide (7) (2.0 g, 10 mmol) in DMSO (2 mL) and PhCN (2 mL) was slowly added to a suspension of Zn (2 g, 30 mmol) in 3 mL of DMSO at 25 °C under argon. GC analysis of hydrolyzed reaction aliquots shows the completion of the zinc reagent formation after 2 h. The excess zinc was allowed to decant, and the clear solution of the organozinc compound **24l** was added via syringe at −60 °C to a solution of CuCN (720 mg, 8 mmol) and LiCl (670 mg, 16 mmol) in THF (8 mL). The reaction was allowed to warm to 0 °C for 5 min and cooled back to −60 °C, and 1-bromooctyne (940 mg, 5 mmol) was added. The reaction temperature was allowed to raise to 0 °C, and the reaction was stirred at this temperature for 3 h. GC analysis shows the consumption of 1-bromooctyne. The reaction mixture was worked up as usual and the residue obtained after evaporation of the solvents was purified by flash chromatography (hexane–ether (5:1)) yielding 1.05 g (79% yield) of analytically pure **27d**.

Products 27a–h Described in Table II. *N*-(3-Carbethoxy-3-butenyl)phthalimide (27a). Yield: 0.98 g as a solid. Mp: 30 °C (72%) using the copper reagent **26a** (9 mmol) and ethyl α-(bromomethyl)acrylate[25] (1.0, 5 mmol). Reaction conditions: −78 to 0 °C, 1 h. Purified by flash chromatography (hexane–EtOAc (95:5)). IR (neat): 2982 (m), 1773 (m), 1712 (s), 1615 (m), cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.77–7.73 (m, 2 H), 7.70–7.62 (m, 2 H), 6.08 (d, 1 H, J = 1.3 Hz), 5.46 (q, 1 H, J = 1.1 Hz), 4.17 (q, 2 H, J = 7.2 Hz), 3.83 (t, 2 H, J = 6.9 Hz), 2.64 (td, 2 H, J = 6.9, 0.9 Hz), 1.25 (t, 3 H, J = 7.2 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 168.1, 166.3, 137.5, 133.8, 132.1, 126.9, 123.1, 60.7, 36.9, 31.2, 14.0. MS (EI): 273 (M^+, 2), 160 (100.0). Exact mass for $C_{15}H_{15}NO_4$: calcd 273.1001, obsd 273.0977.

***N*-(3-Butyl-3-butenyl)phthalimide (27b).** Yield: 277 mg (72%) using **26a** (4.4 mmol) and 2-(bromomethyl)-2-hexene[27] (0.26 g, 1.5 mmol). Reaction conditions: 25 °C, 8 h. Purified by flash chromatography (hexane–EtOAc (96:4)). A yield of 95% was obtained by using THF–DMSO as solvent. IR (neat): 2985 (s), 1773 (s), 1721 (s), 1645 (m), 1086 (s), 1006 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.80–7.76 (m, 2 H), 7.69–7.63 (m, 2 H), 4.70 (d, 1 H, J = 1.3 Hz), 4.68 (s, 1 H), 3.76 (t, 2 H, J = 7.2 Hz), 2.35 (t, 2 H, J = 7.2 Hz), 2.06 (t, 2 H, J = 7.3 Hz), 1.43–1.22 (m, 4 H), 0.86 (t, 3 H, J = 7.3 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 168.1, 146.2, 133.7, 132.2, 123.0, 111.2, 36.6, 35.3, 34.5, 22.3, 13.8. MS (EI): 257 (M^+, 4), 200 (14), 160 (100), 110 (56). Exact mass for $C_{16}H_{19}NO_2$: calcd 257.1416, obsd 257.1411.

***N*-(3-Carbethoxy-2-propenyl)phthalimide (27c).** Yield: 893 mg as a solid. Mp: 82 °C (69%) using **26a** (8 mmol) and ethyl propiolate (0.49 g, 5 mmol). Reaction conditions: −78 to 25 °C, 12 h. Purified by flash chromatography (hexane–EtOAc (95:5)). IR (KBr): 1775 (s), 1753 (s), 1728 (s), 1713 (s), 1605 (m) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.87–7.82 (m, 2 H), 7.76–7.71 (m, 2 H), 6.90 (dt, 1 H, J = 15.6, 5.7 Hz), 5.86 (dt, 1 H, J = 15.6, 1.8 Hz), 4.42 (dd, 2 H, J = 5.1, 1.8 Hz), 4.15 (q, 2 H, J = 6.9 Hz), 1.23 (t, 3 H, J = 7.2 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 167.5, 165.6, 140.6, 134.2, 132.0, 123.5, 123.3, 60.5, 38.1, 14.1. MS (EI): 259 (M^+, 6), 214 (36), 213 (100), 186 (84), 185 (53). Exact mass for $C_{14}H_{13}NO_4$: calcd 259.0844, obsd 259.0848.

***N*-(2-Nonynyl)phthalimide (27d).** Yield: 1.07 g (79%) using **26a** (8 mmol) and 1-bromo-1-octyne (0.84 g, 5 mmol). Reaction conditions: −78 to 0 °C; 0 °C, 3 h. Purified by flash chromatography (hexane–ether (5:1)). IR (KBr): 1773 (w), 1712 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.87–7.81 (m, 2 H), 7.73–7.68 (m, 2 H), 4.40 (t, 2 H, J = 2.0 Hz), 2.10 (tt, 2 H, J = 7.0, 2.0 Hz), 1.47–1.38 (m, 2 H), 1.35–1.13 (m, 6 H), 0.83 (t, 3 H, J = 7.0 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 167.1, 134.0, 132.3, 123.4, 83.8, 73.5, 31.2, 28.4, 27.5, 22.4, 18.6, 13.9. MS (EI): 269 (M^+, 0.4), 199 (100), 160 (80), 122 (56). Exact mass for $C_{17}H_{19}NO_2H^+$: calcd 270.1494, obsd 270.1486.

***N*-[4-(Tetrahydropyranyloxy)-2-butynyl]phthalimide (27e).** Yield: 800 mg as a solid. Mp: 77 °C (76%) using **26a** (4.4 mmol) and 1-bromo-4-(tetrahydropyranyloxy)-1-propyne (0.7 g, 3.5 mmol). Reaction conditions: −78 to 0 °C; 0 °C, 10 h. Purified by flash chromatography (hexane–ether (5:1)). IR (neat): 1725 (s), 1422 (m), 1390 (m) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.87–7.82 (m, 2 H), 7.74–7.70 (m, 2 H), 4.75 (t, 1 H, J = 3.3 Hz), 4.47 (t, 2 H, J = 2.0 Hz), 4.25 (dt, 1 H, J = 16.0, 2.0 Hz), 4.17 (dt, 1 H, J = 15.9, 2.0 Hz), 3.81–3.74 (m, 1 H), 3.51–3.44 (m, 1 H), 1.76–1.48 (m, 6 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 166.8, 134.0, 132.1, 123.4, 96.8, 79.3, 79.2, 61.9, 54.1, 30.2, 27.3, 25.3, 19.0. MS (EI): 200 (15), 199 (80), 198 (100), 147 (33), 104 (36), 85 (65). Exact mass for $C_{17}H_{17}NO_4H^+$: calcd 300.1236, obsd 300.1230.

***N*-(3-Oxo-1-cyclohexenyl)phthalimide (27f).** Yield: 0.92 g as a solid. Mp: 152 °C (72%) using **26a** (8 mmol) and 3-iodo-2-cyclohexen-1-one[26] (1.1 g, 5 mmol). Reaction conditions: 42 °C, 8 h. Purified by flash chromatography (hexane–EtOAc (6:1)). IR (CCl_4): 1721 (s), 1663 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.88–7.83 (m, 2 H), 7.80–7.72 (m, 2 H), 5.75 (t, 1 H, J = 1.5 Hz), 4.38 (s, 2 H), 2.36 (q, 4 H, J = 6.6 Hz), 2.04 (m, 2 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 199.7, 167.6, 158.0, 134.4, 131.9, 125.0, 123.7, 42.1, 37.3, 27.5, 22.3. MS (EI): 255 (M^+, 1), 103 (18), 56 (100). Exact mass for $C_{15}H_{13}NO_3H^+$: calcd 256.0974, obsd 256.0961.

***N*-[(Trimethylstannyl)methyl]phthalimide (27g).** Yield: 0.79 g (64%) using **26a** and chlorotrimethylstannane (0.8 g, 4 mmol). Reaction conditions: −78 to 25 °C, 8 h. Purified by flash chromatography (hexane–EtOAC (98:2)). IR (KBr): 1779 (m), 1760 (w), 1704 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.79–7.76 (m, 2 H), 7.66–7.64 (m, 2 H), 3.19 (s, 2 H), 0.17 (s, 9 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 168.8, 133.5, 132.3, 122.8, 22.8, −8.6. MS (EI): 310 (33), 165 (35), 160 (100). Exact mass for $C_{11}H_{12}NO_2{}^{120}Sn$: calcd 309.9890, obsd 309.9884.

***N*-(3-Carbethoxy-1-methyl-3-butenyl)phthalimide (27h).** Yield: 219 mg (76%) using **26a** (2 mmol) and ethyl α-(bromomethyl)acrylate[25] (0.2 g, 1 mmol). Reaction conditions: −78 to 0 °C, 2 h. Purified by flash chromatography (hexane–EtOAc (98:2)). IR (neat): 1771 (m), 1707 (s), 1631 (m) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.77–7.72 (m, 2 H), 7.68–7.62 (m, 2 H), 6.04 (d, 1 H, J = 1.2 Hz), 5.45 (s, 1 H), 4.66–4.56 (m, 1 H), 4.16 (q, 2 H, J = 7.2 Hz), 3.00 (dd, 1 H, J = 13.8, 10.2 Hz), 2.76 (dd, 1 H, J = 13.8, 5.1 Hz), 1.48 (d, 3 H, J = 7.2 Hz), 1.17 (t, 3 H, J = 7.5 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 168.3, 166.5, 137.7, 133.8, 132.0, 127.3, 123.0, 60.8, 46.2, 36.6, 18.4, 14.1. MS (EI): 287 (M^+, 0.3), 174 (100). Exact mass for $C_{16}H_{17}NO_4N^+$: calcd 288.1236, obsd 288.1238.

Typical Procedure for the Preparation of Amino Alcohol Derivatives 28 by the Reaction of 7, 8, 10, or 11 with Aldehydes in the Presence of $CrCl_2$. Preparation of *N*-(2-Hydroxy-2-phenylethyl)succinimide (28g). A solution containing $CrCl_2$ (500 mg, 4 mmol), LiI (280 mg, 2 mmol), benzaldehyde (130 mg, 1.2 mmol), and *N*-(chloromethyl)succinimide (10) (300 mg, 2 mmol) in THF (5 mL) was warmed

under argon to 50 °C (internal temperature). After 6 h at this temperature, GC analysis of a reaction aliquot shows that no more benzaldehyde was present. The reaction mixture was worked up in the usual way. The residue obtained after the evaporation of the solvents was purified by flash chromatography (hexane–ethyl acetate (100:0–1:10)) affording 218 mg (84% yield) of the analytically pure amino alcohol **28g**.

Products 28a–28i Described in Table III. *N*-(2-Hydroxy-2-phenylethyl)phthalimide (28a). Yield: 540 mg as a solid, mp 148 °C (81%) using *N*-(chloromethyl)phthalimide (**7a**) (0.96 g, 5 mmol), $CrCl_2$ (1.23 g, 10 mmol), benzaldehyde (0.26 g, 2.5 mmol), and LiI (0.67 g, 5 mmol) in THF (20 mL). Reaction conditions: 50 °C, 5 h. Purified by flash chromatography (CH_2Cl_2–EtOAc (95:5)). IR (KBr): 3467 (s), 1772 (s), 1699 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.87–7.80 (m, 2 H), 7.75–7.68 (m, 2 H), 7.47–7.42 (m, 2 H), 7.40–7.24 (m, 3 H), 5.06 (dd, 1 H, *J* = 6.0, 3.0 Hz), 4.01 (dd, 1 H, *J* = 12.0, 6.0 Hz), 3.91 (dd, 1 H, *J* = 12.0, 3.0 Hz), 3.02 (bs, 1 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 168.7, 141.2, 134.1, 132.0, 128.6, 128.1, 125.9, 123.4, 72.6, 45.8. MS (EI): 267 (M^+, 5), 161 (100). Exact mass for $C_{16}H_{13}NO_3$: calcd 267.0895, obsd 267.0905.

***N*-(2-Cyclohexyl-2-hydroxyethyl)phthalimide (28b).** Yield: 648 mg (95%) using *N*-(chloromethyl)phthalimide (**7a**) (1.0 g, 5 mmol), LiI (0.67 g, 5 mmol), $CrCl_2$ (1.23 g, 10 mmol), and cyclohexanecarboxaldehyde (0.28 g, 2.5 mmol) in 20 mL of THF. Reaction conditions: 55 °C, 48 h. Purified by flash chromatography (CH_2Cl_2–EtOAc (95:5)). IR (KBr): 3516 (m), 3461 (m), 1694 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.92–7.80 (m, 2 H), 7.73–7.67 (m, 2 H), 3.87–3.55 (m, 3 H), 2.01–1.63 (m, 6 H), 1.47–1.03 (m, 6 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.0, 134.0, 132.1, 123.4, 74.6, 42.6, 42.3, 29.1, 27.7, 26.4, 27.1, 26.0. MS (EI): 273 (M^+, 0.3), 254 (100), 161 (77). Exact mass for $C_{16}H_{19}NO_3$: calcd 273.1365, obsd 273.1372.

***N*-(2-Hydroxyheptyl)phthalimide (28c).** Yield: 576 mg (88%) using the same quantities as described above and hexanal (0.25 g, 2.5 mmol). Reaction conditions: 45 °C, 5 h. Purified by flash chromatography (CH_2Cl_2–EtOAc (98:2)). A yield of 93% was obtained using *N*-(bromomethyl)phthalimide **7b** instead of **7a**. The product **28c** was purified by flash chromatography (CH_2Cl_2–EtOAc (98:2)). IR (KBr): 3516 (m), 1691 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.83–7.79 (m, 2 H), 7.71–7.67 (m, 2 H), 3.86 (bs, 1 H), 3.78–3.68 (m, 2 H), 3.37 (d, 1 H, *J* = 6.0 Hz), 1.47–1.22 (m, 8 H), 0.85 (t, 3 H, *J* = 6.3 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.0, 134.1, 132.1, 123.4, 70.6, 44.5, 35.1, 31.7, 25.1, 22.0, 13.9. MS (EI): 216 (M^+, 0.3), 162 (11), 161 (100). Exact mass for $C_{15}H_{19}NO_3H^+$: calcd 262.1443, obsd 262.1434.

***N*-[2-(4-Cyanophenyl)-2-hydroxyethyl]phthalimide (28d).** Yield: 414 mg (71%) using *N*-(chloromethyl)phthalimide (**7a**) (0.8 g, 4 mmol), LiI (0.56 g, 4 mmol), $CrCl_2$ (1.0 g, 8 mmol), and 4-cyanobenzaldehyde (0.26 g, 2 mmol) in THF (10 mL). Purified by flash chromatography (CH_2Cl_2–EtOAc (95:5)). IR (KBr): 3442 (s), 2226 (m), 2231 (m), 1707 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.84–7.79 (m, 2 H), 7.75–7.69 (m, 2 H), 7.63–7.60 (m, 2 H), 7.55–7.53 (m, 2 H), 5.14–5.08 (m, 1 H), 4.01 (dd, 1 H, *J* = 14.4, 7.2 Hz), 3.93 (dd, 1 H, *J* = 14.4, 3.9 Hz), 3.40 (d, 1 H, *J* = 5.1 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 168.7, 146.3, 134.4, 132.4, 131.7, 126.7, 123.7, 118.6, 112.0, 72.2, 45.6. MS (EI): 292 (M^+, 0.5), 161 (100), 160 (69). Exact mass for $C_{17}H_{12}N_2O_3$: calcd 292.0847, obsd 292.0833.

***N*-[2-(3-Acetoxyphenyl)-2-hydroxyethyl]phthalimide (28e).** Yield: 620 mg (76%) prepared by using *N*-(chloromethyl)-phthalimide (**7a**) (1.0 g, 5 mmol), LiI (0.67 g, 5 mmol), $CrCl_2$ (1.23 g, 10 mmol), and 3-acetoxybenzaldehyde (0.41 g, 2.5 mmol) in THF (10 mL). Reaction conditions: 55 °C, 4 h. Purified by flash chromatography (CH_2Cl_2–EtOAc (90:10)). IR (KBr): 3442 (s), 1768 (s), 1734 (s), 1707 (s), 1695 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.84–7.80 (m, 2 H), 7.73–7.68 (m, 2 H), 7.37–7.27 (m, 2 H), 7.19–7.18 (m, 1 H), 7.02–6.98 (m, 1 H), 5.07–5.01 (m, 1 H), 3.97 (dd, 1 H, *J* = 14.1, 3.6 Hz), 3.03 (d, 1 H, *J* = 4.8 Hz), 2.26 (s, 3 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 169.3, 168.7, 151.1, 143.1, 134.1, 132.0, 129.6, 123.5, 123.3, 121.3, 119.2, 72.1, 45.7, 21.0. MS (EI): 325 (M^+, 2), 161 (100). Exact mass for $C_{18}H_{15}NO_5$: calcd 325.0950, obsd 325.0966.

***N*-(2-Hydroxy-4-phenyl-3-butenyl)phthalimide (28f).** Yield: 264 mg as a solid. Mp: 170 °C (36%) using the same quantities as described above and cinnamaldehyde (0.33 g, 2.5 mmol). Reaction conditions: 45 °C, 8 h. Purified by flash chromatography (CH_2Cl_2–EtOAc (95:5)). IR (KBr): 3451 (m), 1699 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.85–7.81 (m, 2 H), 7.72–7.68 (m, 2 H), 7.36–7.21 (m, 5 H), 6.69 (dd, 1 H, *J* = 15.9, 1.2 Hz), 6.22 (dd, 1 H, *J* = 15.9, 6.0 Hz), 4.66–4.62 (m, 1 H), 3.97–3.87 (m, 2 H), 2.60 (d, 1 H, *J* = 5.4 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 168.7, 136.3, 134.0, 132.0, 131.9, 128.6, 128.5, 127.8, 126.6, 123.4, 71.1, 44.0. MS (EI): 293 (M^+, 4), 161 (35), 160 (23), 146 (25), 133 (100). Exact mass for $C_{18}H_{15}NO_3$: calcd 293.1052, obsd 293.1042.

***N*-(2-Hydroxy-2-phenylethyl)-2,5-pyrrolidinedione (28g).** Yield: 224 mg as a solid. Mp: 162 °C (84%) using *N*-(chloromethyl)succinimide (**8a**) (0.3 g, 2 mmol), LiI (0.28 g, 2 mmol), $CrCl_2$ (0.5 g, 4 mmol), and benzaldehyde (0.13 g, 1.2 mmol). Reaction conditions: 50 °C, 6 h. Purified by flash chromatography (ethyl acetate). IR (KBr): 3498 (m), 3467 (m), 1699 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.41–7.26 (m, 5 H), 4.98–4.95 (m, 1 H), 3.87 (dd, 1 H, *J* = 14.1, 8.7 Hz), 3.76 (dd, 1 H, *J* = 13.8, 3.3 Hz), 2.89 (d, 1 H, *J* = 5.4 Hz), 2.70 (s, 4 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 177.6, 140.9, 128.5, 128.0, 125.7, 72.0, 46.4, 28.1. MS (EI): 219 (M^+, 2), 120 (36), 113 (100), 107 (72). Exact mass for $C_{12}H_{13}NO_3$: calcd 219.0895, obsd 219.0903.

***N*-(2-Hydroxyheptyl)-2,5-pyrrolidinedione (28h).** Yield: 170 mg (81%) using *N*-(chloromethyl)succinimide (0.3 g, 2 mmol), LiI (0.28 g, 2 mmol), $CrCl_2$ (0.5 g, 4 mmol), and hexanal (100 mg, 1 mmol) in THF (5 mL). Reaction conditions: 45 °C, 2 h. Purified by flash chromatography (hexane–EtOAc (3:1)). IR (KBr): 3478 (m), 2952 (s), 1774 (m), 1690 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 3.72–3.70 (m, 1 H), 3.49 (s, 1 H), 3.47 (d, 1 H, *J* = 1.2 Hz), 2.67 (s, 4 H), 2.62 (d, 1 H, *J* = 5.7 Hz), 1.38–1.16 (m, 8 H), 0.81 (t, 3 H, *J* = 6.9 Hz). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 179.0, 169.7, 45.1, 35.1, 31.6, 28.0, 24.9, 22.4, 13.8. MS (EI): 213 (M^+, 0.2), 142 (19), 113 (100). Exact mass for $C_{11}H_{19}NO_3H^+$: calcd 241.1443, obsd 214.1446.

***N*-(6-Carbomethoxy-2-hydroxyhexyl)-2,5-pyrrolidinedione (28i).** Yield: 175 mg (68%) using $CrCl_2$ (0.5 g, 4 mmol), methyl 6-oxohexanoate (0.15 g, 1 mmol), *N*-(iodomethyl)-succinimide (0.42 g, 2 mmol). Reaction conditions: 55 °C, 8 h. Purified by flash chromatography (EtOAc). IR (KBr): 3405 (m), 2953 (m), 1765 (m), 1736 (s), 1691 (s), 1674 (s) cm^{-1}. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 3.84–3.73 (bs, 1 H), 3.64 (s, 3 H), 2.58 (m, 2 H), 2.74 (s, 4 H), 2.41–2.34 (m, 1 H), 2.30 (t, 2 H, *J* = 7.2 Hz), 1.70–1.57 (m, 2 H), 1.56–1.34 (m, 4 H). ^{13}C-NMR ($CDCl_3$, 75.5 MHz): δ 177.9, 173.9, 69.8, 51.3, 45.2, 34.8, 33.8, 28.1, 24.8, 24.7. MS (EI): 145 (57), 142 (23), 113 (100). Exact mass for $C_{12}H_{19}NO_5H^+$: calcd 258.1341, obsd 258.1328.

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Supplementary Material Available: ^{1}H NMR spectra of all new compounds (64 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.