Diethylzinc: A Chain-Transfer Agent in Intermolecular Radical Additions. A Parallel with Triethylborane

Michèle P. Bertrand,* Laurence Feray, Robert Nouguier, and P. Perfetti

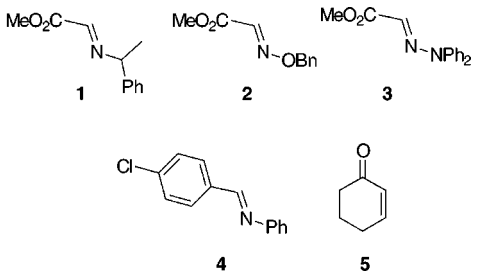
Laboratoire de Chimie Moléculaire Organique, UMR 6517, Boite 562, Faculté des Sciences St-Jérôme, Université d'Aix-Marseille III, Avenue Normandie-Niemen, 13397 Marseille, Cedex 20, France

Received August 5, 1999

In the presence of oxygen, diethylzinc can be used to promote radical additions to C═N bond containing radical acceptors and to enones. In these reactions, it plays at the same time the role of the initiator and the role of the chain-transfer reagent. A parallel with triethylborane-mediated reactions is established. The methodology is restricted to secondary and tertiaryalkyl radicals generated from the corresponding alkyl iodides. It could not be extended either to C═C bond containing radical acceptors such as methyl methacrylate and nitrocyclohexene or to diethylazodicarboxylate.

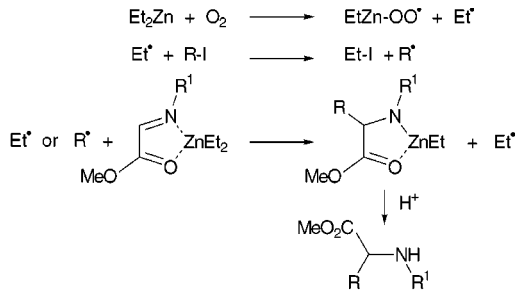
We have recently shown that diethylzinc could be used to promote radical additions to glyoxylate imines.[1,2] In these reactions, diethylzinc plays exactly the same role as triethylborane that was used in previous experiments.[3,4] Like Et_3B, Et_2Zn is able to initiate the formation of ethyl radical through reaction with oxygen. As a Lewis acid, it activates the reactivity of the substrate; it also acts as the chain-transfer agent by regenerating the chain carrier in the last propagation step (Scheme 1).

The aim of this paper is to demonstrate that this reactivity could be extended to other C═N double bonds containing radical acceptors (glyoxylic oxime ether **2**, hydrazone **3**, and Schiff base **4**) and to acceptors containing C═C bonds such as cyclohexenone (**5**).

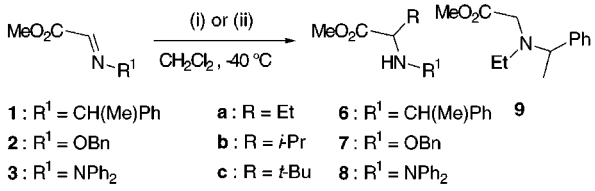


All the above substrates, in 0.2 M solution in dichloromethane, were treated with Et_2Zn (alone or in the presence of 6 equiv of a secondary (*i*-PrI) or a tertiary alkyl iodide (*t*-BuI)) at low temperature (−40 °C) while air (20 mL) was injected into the solution (we observed that it was necessary to use at least 1.5 equiv of Et_2Zn to reach completion).

Scheme 1



Scheme 2



1 : R^1 = CH(Me)Ph **a** : R = Et **6** : R^1 = CH(Me)Ph
2 : R^1 = OBn **b** : R = *i*-Pr **7** : R^1 = OBn
3 : R^1 = NPh_2 **c** : R = *t*-Bu **8** : R^1 = NPh_2

(i) Et_3B (3 equiv), RI (none or 6 equiv), air;
(ii) Et_2Zn (2 equiv), RI (none or 6 equiv), air.

We have first compared the reactivity of oxime ether **2** and hydrazone **3** to that of imine **1**. The results obtained under various experimental conditions (including some Et_3B-mediated reactions, run under similar conditions in regard to temperature and concentration, to establish a parallel) are given in Scheme 2 and Table 1.

The first difference between **2** and **3** compared to imine **1** is the fact that no product resulting from the formation of a C−N bond (according to a nucleophilic mechanism[1,5,6]) was isolated, either when Et_2Zn was used alone

* To whom correspondence should be addressed. Fax: (33) 4 91 67 09 44. E-mail: michele.bertrand@LCMO.u-3mrs.fr.

(1) Bertrand, M. P.; Feray, L.; Nouguier, R.; Perfetti, P. *Synlett* **1999**, 1148−1150.

(2) (a) For the initiation of tinhydride-mediated reductions of alkyl halides by Et_2Zn, see: Ryu, I.; Araki, F.; Minakata, S.; Komatsu, M. *Tetrahedron Lett.* **1998**, *39*, 6335−6336. (b) For radical allylation reactions initiated with $ZnCl_2$, see: Yamamoto, Y.; Onuki, S.; Yumoto, M.; Asao, N. *J. Am. Chem. Soc.* **1994**, *116*, 421−422.

(3) Bertrand, M. P.; Feray, L.; Nouguier, R.; Stella, L. *Synlett* **1998**, 780−782.

(4) For closely related additions onto oxime ethers and hydrazones using using Et_3B in the presence of RI with or without Bu_3SnH see: (a) Miyabe, H.; Ushiro, C.; Naito, T. *J. Chem. Soc., Chem. Commun.* **1997**, 1789−1790. (b) Miyabe, H.; Shibata, R.; Ushiro, C.; Naito, T. *Tetrahedron Lett.* **1998**, *39*, 631−634. (c) Miyabe, H.; Shibata, R.; Sangawa, M.; Ushiro, C.; Naito, T. *Tetrahedron* **1998**, *54*, 11431−11444. (d) Miyabe, H.; Yoshioka, N.; Ueda, M.; Naito, T. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3659−3660. (e) Miyabe, H.; Fujishima, Y.; Naito, T. *J. Org. Chem.* **1999**, *64*, 2174−2175. (f) Miyabe, H.; Ueda, M.; Yoshioka, N.; Naito, T. *Synlett* **1999**, 465−467.

(5) (a) Van Vliet, M. R. P.; Van Koten, G.; Buysingh, P.; Jastrzebski, J. T. B. H.; Spek, A. L. *Organometallics* **1987**, *6*, 537−546. (b) Van Vliet, M. R. P.; Jastrzebski, J. T. B. H.; Klaver, W. J.; Goubitz, K.; Van Koten, G. *Recl. Trav. Chim. Pays-Bas* **1987**, *106*, 132−134. (c) Wissing, E.; Havenith, R. W. A.; Boersma, J.; Van Koten, G. *Tetrahedron Lett.* **1992**, *33*, 7933−7936.

10.1021/jo9912404 CCC: $18.00
Published on Web 11/20/1999

Table 1. Et_2Zn-Mediated Additions to 1−3, a Parallel with Et_3B-Promoted Reactions

entry	substrate	conditions[a]	RI	products; yield (%)	
a	**1**	i	none[3]	**6a**; 56	
b	**1**	i	*t*-BuI[3]	**6a**; 0	**6c**; 48
c	**1**	ii	none[1]	**6a**; 49	**9**; 9
d	**1**	ii	*t*-BuI[1]	**6a**; 0	**6c**; 66
e	**2**	i	none	**7a**; 87	
f	**2**	i	*i*-PrI	**7a**; 31	**7b**; 57
g	**2**	i	*t*-BuI	**7a**; 7	**7c**; 85
h	**2**	ii	none	**7a**; 88	
i	**2**	ii	*i*-PrI	**7a**; 51	**7b**; 34
j	**2**	ii	t-BuI	**7a**; 16	**7c**; 74
k	**3**	i	none	**8a**; 89	
l	**3**	i	*i*-PrI	**8a**; 17	**8b**; 68
m	**3**	i	*t*-BuI	**8a**; 8	**8c**; 82
n	**3**	ii	none	**8a**; 88	
o	**3**	ii	*i*-PrI	**8a**; 38	**8b**; 48
p	**3**	ii	*t*-BuI	**8a**; 17	**8c**; 72

[a] Key: (i) Et_3B (3 equiv), RI (none or 6 equiv), −40 °C, air; (ii) Et_2Zn (2 equiv), RI (none or 6 equiv), −40 °C, air.

or in the presence of an alkyl iodide. Due to the electron-donating substituent, the nitrogen atom is far less electrophilic.

The second observation that is worth noting is that the overall yields are far better in the cases of the oxime ether and the hydrazone than in the case of the imine. This is in agreement with previously reported data according to which oxime ethers and hydrazones are better acceptors than imines in intramolecular processes (5-exo ring closure onto C=N bond is approximately 40 times faster with hydrazones than with imines).[7] The greater reactivity has, however, some drawbacks since, in the presence of a secondary or a tertiary alkyl iodide, the addition of ethyl radical competes with the iodine atom transfer, so that two different products are formed. The faster the iodine atom transfer the lower the yield in **7a** and **8a**. In this respect, Et_3B-mediated reactions are more chemoselective, which is probably due to the fact that it is less strongly coordinated to the substrate. It can be emphasized that TEMPO (4 equiv) inhibits completely the reaction (the inhibition experiment was conducted on the reaction of **2** with Et_2Zn). This is not surprising since alkylzinc reagents are known to react very rapidly with nitroxides.[8]

The few data concerning intermolecular radical addition onto imino groups available in the literature point out the low reactivity of the C=N bond. Unless there is no steric hindrance to approach the carbon atom,[9] activation is needed for the reaction to be efficient. This can be achieved either through substitution with an electron-withdrawing group,[10] through association with a Lewis acid, or both.[1,3,4,11] Both triethylborane and diethylzinc mediation made possible radical additions to imine **4**, which was unreactive when the radicals were generated by the tributyltin hydride methodology in the absence of a Lewis acid (Scheme 3). In regard to diethylzinc-mediated reactions, only the expected product (**10a** or **10b**) was isolated in the absence of any alkyl iodide or in the presence of isopropyl iodide; however, **11** was the unique product in the presence of *tert*-butyl iodide. Monitoring the reaction by GPC showed that in fact **10c** is the primary product of the reaction (of course as a zinc amide) and that it is progressively transformed into **11** in the presence of excess *t*-BuI. It is likely that **11** results from a Friedel−Crafts alkylation after radical addition. With this substrate no improvement of the yield could be observed when the reaction was carried out at −40 °C.

Reference can be made to classical organometallic reactivity of organozinc reagents with respect to imines. With the exception of allylzinc,[12] reactions between diethylzinc and imines need activation by TMSCl[13] or by an appropriate substituent on nitrogen atom.[14] Our procedure offers an alternative to introduce secondary or tertiary alkyl groups.

The radical addition of alkylboranes to enones is well known,[15] and the reaction proceeds also with *B*-alkylcatecholboranes.[16] The use of triethylborane as chain-transfer agent in the reaction of alkyl iodides with α-sulfinyl enones has recently been reported.[17] Since, like Et_3B, Et_2Zn was able to mediate radical additions to imines, in all likelihood, it should also mediate the addition of secondary and tertiary alkyl radicals to enones. The results obtained with cyclohexenone (**5**) are reported in Scheme 4. It can be noted that whereas additions onto the imino group are completed within less than 1 h, additions onto **5** need approximately 5 h to reach completion (in this case, 2 equiv of Et_2Zn was needed).

1,4-Conjugated additions of organozinc derivatives have been extensively studied.[18,19] These reactions are

(6) It is to be noted that Naito and co-workers[4c] have reported the incorporation of two ethyl groups via, respectively, C−C and C−N bond formation, in the triethylborane-promoted addition of ethyl radical to **3**. However, in this case the N-alkylated product resulted from nucleophilic substitution of ethyl iodide (used as coreagent) by **8a**.

(7) Kim, S. *Tetrahedron* **1997**, *53*, 73−80.

(8) Nagashima, T.; Curran, D. P. *Synlett* **1996**, 330−332.

(9) (a) Hart, D. J.; Seely, F. L. *J. Am. Chem. Soc.* **1988**, *110*, 1631−1633. (b) Hart, D. J.; Krishnamurthy, R.; Pook, L. M.; Seely, F. L. *Tetrahedron Lett.* **1993**, *34*, 7819−7822. (c) Bhat, B.; Swayze, E. E.; Wheeler, P.; Dimock, S.; Perbost, M.; Sanghvi, Y. S. *J. Org. Chem.* **1996**, *61*, 8186−8199.

(10) (a) Kim, S.; Lee, I. Y.; Yoon, J.-Y.; Oh, D. H. *J. Am. Chem. Soc.* **1996**, *118*, 5138−5139. (b) Kim, S.; Yoon, J.-Y.; Lee, I. Y. *Synlett* **1997**, 475−476.

(11) Russell, G. A.; Wang, L.; Rajaratnam, R. *J. Org. Chem.* **1996**, *61*, 8988−8991.

(12) (a) Hanessian, S.; Yang, R.-H. *Tetrahedron Lett.* **1996**, *37*, 8997−9000. (b) Nakamura, M.; Hirai, A.; Nakamura, E. *J. Am. Chem. Soc.* **1996**, *118*, 8489−8490. (c) Jones, P.; Knochel, P. *J. Org. Chem.* **1999**, *64*, 186−195 and refs cited therein.

(13) Hou, X. L.; Zhen, X. L.; Dai, L. X. *Tetrahedron Lett.* **1998**, *38*, 6949−6952.

(14) (a) Katritzky, A. R.; Harris, P. A. *Tetrahedron*: *Asymmetry* **1992**, *3*, 437−442. (b) Soai, K.; Hatanaka, T.; Miyazawa, T. *J. Chem. Soc., Chem. Commun.* **1992**, 1097−1098. (c) Suzuki, T.; Narisada, N.; Shibata, T.; Soai, K. *Tetrahedron*: *Asymmetry* **1996**, *7*, 2519−2522. (d) Andersson, P. G.; Guijarro, D.; Tanner, D. *J. Org. Chem.* **1997**, *62*, 7364−7375. (e) Guijarro, D.; Pinho, P.; Andersson, P. G. *J. Org. Chem.* **1998**, *63*, 2530−2535. (f) Jimeno, C.; Vidal-Ferran, A.; Moyano, A.; Pericas, M. A.; Riera, A. *Tetrahedron Lett.* **1999**, *40*, 777−780.

(15) (a) Brown, H. C.; Kabalka, G. W. *J. Am. Chem. Soc.* **1970**, *92*, 714−716. (b) Brown, H. C.; Negishi, E. *J. Am. Chem. Soc.* **1971**, *93*, 3777−3779.

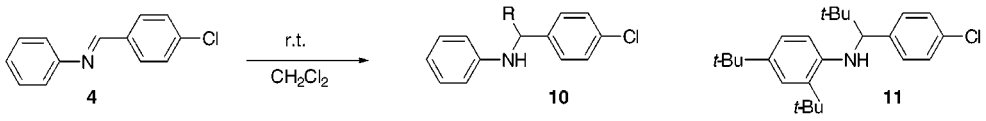
(16) *B*-Alkylcatecholboranes, readily available from the reaction of various olefins and catecholborane, have been used to perform radical additions to α,β-unsaturated ketones and aldehydes. See: Ollivier, C.; Renaud, P. *Chem. Eur. J.* **1999**, *5*, 1468−1473.

(17) Mase, N.; Watanabe, Y.; Ueno, Y.; Toru, T. *J. Org. Chem.* **1997**, *62*, 7794−7800.

(18) For general reviews on organozinc mediated reactions see: (a) Knochel, P.; Almene Perea, J. J.; Jones, P. *Tetrahedron* **1998**, *54*, 8275−8319. (b) Knochel, P. In *Transition Metals for Organic Synthesis: Building Blocks and Fine Chemicals*; Beller, M., Bolm, C., Eds; Wiley−VCH: Weinheim, 1998; Vol. 1, pp 467−503.

(19) For examples of reactions of organozinc reagents with enones, see: (a) Hanson, M. V.; Rieke, R. D. *J. Am. Chem. Soc.* **1995**, *117*, 10775−10776. (b) Charette, A. B.; Beauchemin, A.; Marcoux, J.-F. *J. Am. Chem. Soc.* **1998**, *120*, 5114−5115. (c) Alexakis, A.; Vastra, J.; Burton, J.; Benhaim, C.; Mangeney, P. *Tetrahedron Lett.* **1998**, *39*, 7869−7872. (d) Yan, M.; Yang, L.-W.; Wong, K.-Y.; Chan, A. S. C. *J. Chem. Soc., Chem. Commun.* **1999**, 11−12.

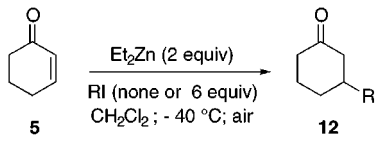
Scheme 3



Conditions	(i)	(i)	(i)	(ii)	(ii)	(ii)
RI	none	*i*-PrI	*t*-BuI	none	*i*-PrI	*t*-BuI
Product; Yield (%)	**10a** ; 64	**10b** ; 68	**10c** ; 76	**10a** ; 55	**10b** ; 53	**11** ; 40

(i) Et_3B (3 equiv), RI (none or 6 equiv), air;
(ii) Et_2Zn (2 equiv), RI (none or 6 equiv), air.
a : R = Et; b : R = *i*-Pr; c : R = *t*-Bu

Scheme 4

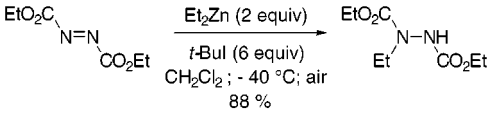


RI	Product ; Yield (%)
none	**12a** ; 61
i-PrI	**12b** ; 63
t-BuI	**12c** ; 64

a : R = Et; b : R = *i*-Pr; c : R = *t*-Bu

usually performed in the presence of an activating Lewis acid. Since, as previously, the contrathermodynamics exchange between zinc and an iodine is unlikely, a radical mechanism is highly probable for the oxygen-promoted reactions.[20] No competitive addition of ethyl radical is detected under the above experimental conditions in the presence of *i*-PrI or *t*-BuI. The question arises about whether the addition proceeds via the enone complexed to the metal or not.

No similar additions could be performed onto ethyl methacrylate or onto nitrocyclohexene,[18,20] although they are good radical acceptors. This seems to indicate that the radical formed through the addition step must have a spin density greater on the heteroatom than on carbon for the reaction to proceed. The alternative explanation would be that the functional group in conjugation with the double bond should be basic enough to shift the equilibrium toward the complexed starting material, which would be the reactive species.



Finally, we had a look at the reactivity of strong electrophiles such as DEAD. The reaction of dialkylazodicarboxylates with organozinc halides was shown to be an efficient pathway for electrophilic amination.[21] Under our standard experimental conditions in the presence of an excess of *tert*-butyl iodide (up to 20 equiv), no incorporation of the tertiary group was detected. The only product, isolated in 88% yield, resulted from the nucleophilic attack of diethylzinc onto the N=N bond (eq).[21,22]

In conclusion, diethylzinc-mediated radical additions have been generalized to various C=N bond containing radical acceptors. Since the alkyl radical is produced through iodine transfer from an alkyl iodide toward ethyl radical, they are efficient, provided the alkyl iodide is secondary or tertiary. These oxygen-promoted reactions can be extended to enones, they are easy to carry out, and they offer an alternative to previously developed methodologies. Further studies are in progress, and their results will be reported in due course.

Experimental Section

All chemicals and reagents were purchased from Aldrich Chemical Co. NMR spectra (^1H, ^{13}C, and DEPT) were registered in $CDCl_3$; chemical shifts are relative to TMS as internal reference. Coupling constants are reported in Hz.

Starting materials **1**,[23] **2**,[24] **3**,[4c] and **4**[25] were prepared according to known procedures, and spectral data were in accordance with literature.

General Procedures for Radical Addition. Method A (Conditions i). The alkyl iodide (6 equiv) was added (when necessary), under argon at −40 °C, to a 0.2 M solution of substrate, in dichloromethane. Triethylborane (3 equiv, 1 M solution in hexane) was then introduced, and the reaction was stirred at −40 °C while air (20 mL) was injected through a needle into the solution over 1 h. The reaction was monitored by TLC and GPC. After completion, the solvent was evaporated under reduce pressure and the crude product was purified by FC.

Method B (Conditions ii). The alkyl iodide (6 equiv) was added (when necessary), under argon at −40 °C, to a 0.2 M solution of substrate, in dichloromethane. Diethylzinc (2 equiv, 1 M solution in hexane) was then added, and the reaction was stirred at −40 °C while air (20 mL) was injected through a needle into the solution over 1 h. The reaction was monitored by TLC and GPC. The reaction mixture was treated with saturated NH_4Cl (10 mL) and extracted with CH_2Cl_2 (×3). The organic layer was dried (Na_2SO_4), filtered, and concentrated. The crude product was purified by FC.

Methyl 2-(1-Phenylethylamino)butanoate (6a). Treating **1** (222 mg, 1.16 mmol) according to method A, in the absence of any alkyl iodide, led to **6a** (143 mg, 0.65 mmol, 56%),

(20) It has been shown that under oxygen atmosphere Et_2Zn could promote asymmetric epoxidation of enones and nitro alkenes; see: (a) Enders, D.; Zhu, J.; Kramps, L. *Liebigs Ann.* **1997**, 1101−1113. (b) Enders, D.; Kramps, L.; Zhu, J. *Tetrahedron: Asymmetry* **1998**, *9*, 3959−3962.

(21) (a) Velarde-Ortiz, R.; Guijarro, A.; Rieke, R. D. *Tetrahedron Lett.* **1998**, *39*, 9157−9160. (b) Guijarro, A.; Rieke, R. D. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1679−1681.

(22) Under similar conditions Et_3B behaves as a reducing reagent.

(23) Barreau, M.; Commerçon, A.; Mignani, S.; Mouysset, D.; Perfetti, P.; Stella, L. *Tetrahedron* **1998**, *54*, 11501−11516.

(24) Kolasa, T.; Sharma, S. K.; Miller, M. J. *Tetrahedron* **1988**, *44*, 5431−5440.

(25) Nonkunsarn, P.; Ramsden, C. A. *Tetrahedron* **1997**, *53*, 3805−3830.

isolated as a colorless oil after purification by FC (5% EtOAc/pentane). The diastereomeric ratio (58:42) was determined from ^{1}H NMR. ^{1}H NMR (200 MHz): (major isomer) δ 0.80 (t, 3H, J = 7.3), 1.25 (d, 3H, J = 6.6), 1.38−1.64 (m, 2H), 1.78 (br s,1H), 2.86 (t, 1H, J = 6.3), 3.63 (s, 3H), 3.60 (q, 1H, J = 6.6), 7.12−7.28 (m, 5H); (minor isomer) δ 0.82 (t, 3H, J = 7.3), 1.27 (d, 3H, J = 6.6), 1.38−1.64 (m, 2H), 1.78 (br s,1H), 3.17 (t, 1H, J = 6.3), 3.51 (s, 3H), 3.64 (q, 1H, J = 6.6), 7.12−7.28 (m, 5H). ^{13}C NMR (50 MHz): (major isomer) δ 10.2 (CH_3), 25.4 (CH_3), 27.1 (CH_2), 51.4 (CH_3), 56.6 (CH), 60.2 (CH), 126.9 (CH), 127.0 (CH), 128.3 (CH), 145.1 (C), 176.5 (C); (minor isomer) δ 9.9 (CH_3), 22.9 (CH_3), 26.3 (CH_2), 51.4 (CH_3), 56.2 (CH), 60.2(CH), 126.7 (CH), 126.8 (CH), 128.3 (CH), 145.3 (C), 175.6 (C=O). Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.56; H, 8.65. Found: C, 70.53; H, 8.61.

When treated according to method B, **1** (200 mg, 1.05 mmol) led to **6a** (50:50 mixture of diastereomers) and **9**[5] (132 mg, 0.59 mmol, 57%) as an inseparable mixture. The ratio **6a**:**9** (85:15) was determined by GPC and ^{1}H NMR on the crude mixture. ^{1}H NMR characteristic signals of **9** were deduced from the mixture: δ 0.99 (t, 3H, J = 7.1), 2.63 (q, 2H, J = 7.1), 3.34 (AB spectra, 2H, J = 17.3), 3.64 (s, 3H).

Methyl 3,3-Dimethyl-2-(1-phenylethylamino)butanoate (6c). When treated according to method A, in the presence of *tert*-butyl iodide, **1** (160 mg, 0.84 mmol) led to **6c** (93 mg, 0.38 mmol, 48%), isolated as a colorless oil after purification by FC (3% EtOAc/pentane). The diastereomeric ratio (70:30) was determined from ^{1}H NMR. ^{1}H NMR (400 MHz): (major isomer) δ 0.87 (s, 9H), 1.30 (d, 3H, J = 6.5), 1.82 (br s, 1H), 2.66 (s, 1H), 3.50 (q, 1H, J = 6.5), 3.68 (s, 3H), 7.18−7.31 (m, 5H); (minor isomer) δ 0.92 (s, 9H), 1.30 (d, 3H, J = 6.5), 1.82 (br s, 1H), 2.95 (s, 1H), 3.49 (s, 3H), 3,58 (q, 1H, J = 6.6), 7.18−7.31 (m, 5H). ^{13}C NMR (50 MHz): (major isomer) δ 25.7 (CH_3), 26.7 (3xCH_3), 33.7 (C), 50.9 (CH_3), 57.1 (CH), 67.7 (CH), 126.7 (CH), 127.1 (CH), 128.2 (CH), 145.1 (C), 176.1 (C=O); (minor isomer) δ 22.5 (CH_3), 26.6 (3x CH_3), 34.1 (C), 50.9 (CH_3), 57.6 (CH), 68.1 (CH), 126.8 (CH), 126.9 (CH), 128.2 (CH). Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30. Found: C, 72.57; H, 9.69.

When treated according to method B, in the presence of *tert*-butyl iodide, **1** (100 mg, 0.52 mmol) gave **6c** (85 mg, 0.34 mmol, 66%) as a 40:60 mixture of isomers.

Methyl 2-(Benzyloxyamino)butanoate (7a).[26] When treated according to method A, in the absence of any alkyl iodide, **2** (100 mg, 0.52 mmol) gave **7a** (100 mg, 0.45 mmol, 87%), isolated as a colorless oil after purification by FC (3% EtOAc/pentane). When treated according to method B, in the absence of any alkyl iodide, **2** (100 mg, 0.52 mmol) gave **7a** (102 mg, 0.46 mmol, 88%). Spectral data were in accordance with the literature.

Methyl 2-(Benzyloxyamino)-3-methylbutanoate (7b). When treated according to method A, in the presence of isopropyl iodide, **2** (100 mg, 0.52 mmol) led to **7a** (35 mg, 0.15 mmol, 31%) and **7b** (70 mg, 0.29 mmol, 57%), isolated as colorless oils after purification by FC (3% EtOAc/pentane). ^{1}H NMR (200 MHz): δ 0.87 (d, 3H, J = 6.8), 0.90 (d, 3H, J = 6.8), 1.79 (oct, 1H, J = 6.8), 3.34 (d, 1H, J = 6.8), 3.73 (s, 3H), 4.66 (s, 2H), 5.97 (br s, 1H), 7.24−7.35 (m, 5H). ^{13}C NMR (50 MHz): δ 19.2 (2xCH_3), 29.1 (CH), 51.6 (CH_3), 69.5 (CH), 75.9 (CH_2), 127.6 (CH), 128.1 (CH), 128.5 (CH), 137.8 (C), 174.4 (C=O). Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07. Found: C, 65.77; H, 7.80.

When treated according to method B, in the presence of isopropyl iodide, **2** (100 mg, 0.52 mmol) led to **7a** (60 mg, 0.27 mmol, 51%) and **7b** (40 mg, 0.17 mmol, 34%).

Methyl 2-(Benzyloxyamino)-3,3-dimethylbutanoate (7c). When treated according to method A, in the presence of *tert*-butyl iodide, **2** (100 mg, 0.52 mmol) led to **7a** (10 mg, 0.04 mmol, 7%) and **7c** (110 mg, 0.44 mmol, 85%), isolated as colorless oils after purification by FC (3% EtOAc/pentane). ^{1}H NMR (200 MHz): δ 0.91 (s, 9H), 3.32 (s, 1H), 3.74 (s, 3H), 4.65 (s, 2H), 6.09 (br s, 1H), 7.31−7.34 (m, 5H). ^{13}C NMR (50 MHz): δ 26.9 (3xCH_3), 32.9 (C), 51.4 (CH_3), 71.9 (CH), 75.7 (CH_2), 127.6 (CH), 128.1 (CH), 128.6 (CH), 137.8 (C), 174.4 (C=O). Anal. Calcd for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42. Found: C, 66.80; H, 8.08.

When treated according to method B, in the presence of *tert*-butyl iodide, **2** (100 mg, 0.52 mmol) led to **7a** (20 mg, 0.09 mmol, 16%) and **7c** (96 mg, 0.38 mmol, 74%).

Methyl 2-(*N*,*N*-Diphenylhydrazino)butanoate (8a).[4c] When treated according to method A, in the absence of any alkyl iodide, **3** (100 mg, 0.40 mmol) led to **8a** (101 mg, 0.36 mmol, 89%), isolated as a colorless oil after purification by FC (5% EtOAc/pentane). When treated according to method B, in the absence of any alkyl iodide, **3** (100 mg, 0.40 mmol) gave **8a** (100 mg, 0.35 mmol, 88%). Spectral data were in accordance with literature.

Methyl 2-(*N*,*N*-Diphenylhydrazino)-3-methylbutanoate (8b). When treated according to method A, in the presence of isopropyl iodide, **3** (100 mg, 0.40 mmol) led to **8a** (20 mg, 0.07 mmol, 17%) and **8b** (80 mg, 0.27 mmol, 68%), isolated as a colorless oils after purification by FC (2% EtOAc/pentane). ^{1}H NMR (200 MHz): δ 0.97 (d, 3H, J = 6.8), 1.07 (d, 3H, J = 6.8), 2.00 (oct, 1H, J = 6.6), 3.46 (s + superimposed m, 4H), 4.39 (br s, 1H), 6.96−7.32 (m, 10H). ^{13}C NMR (50 MHz): δ 18.9 (CH_3), 19.3 (CH_3), 30.6 (CH), 51.3 (CH_3), 67.8 (CH), 120.9 (CH), 122.7 (CH), 129.0 (CH), 148.1 (C), 173.9 (C=O). Anal. Calcd for $C_{18}H_{22}N_2O_2$: C, 72.46; H, 7.43. Found: C, 72.78; H, 7.29.

When treated according to method B, in the presence of isopropyl iodide, **3** (100 mg, 0.40 mmol) gave **8a** (43 mg, 0.15 mmol, 38%) and **8b** (57 mg, 0.19 mmol, 48%).

Methyl 2-(*N*,*N*-Diphenylhydrazino)-3,3-dimethylbutanate (8c). When treated according to method A, in the presence of *tert*-butyl iodide, **3** (100 mg, 0.40 mmol) led to **8a** (9 mg, 0.03 mmol, 8%) and **8c** (102 mg, 0.32 mmol, 82%), isolated as colorless oils after purification by FC (2% EtOAc/pentane). ^{1}H NMR (200 MHz): δ 1.03 (s, 9H), 3.33 (d, 1H, J = 7.3), 3.36 (s, 3H), 4.34 (d, 1H, J = 7.3), 6.98−7.32 (m, 10H). ^{13}C NMR (50 MHz): δ 26.9 (3 × CH_3), 34.2 (C), 50.9 (CH_3), 71.4 (CH), 121.3 (CH), 122.9 (CH), 129.1 (CH), 148.4 (C), 173.9 (C=O). Anal. Calcd for $C_{19}H_{24}N_2O_2$: C, 73.05; H, 7.74. Found: C, 73.03; H, 7.77.

When treated according to method B, in the presence of *tert*-butyl iodide, **3** (100 mg, 0.40 mmol) gave **8a** (20 mg, 0.07 mmol, 17%) and **8c** (90 mg, 0.29 mmol, 72%).

***N*-[1-(4-Chlorophenyl)propyl]phenylamine (10a).** When treated according to method A, in the absence of any alkyl iodide, **4** (120 mg, 0.55 mmol) led to **10a** (87 mg, 0.35 mmol, 64%), isolated as a colorless oil after purification by FC (10% EtOAc/pentane). ^{1}H NMR (200 MHz): δ 0.85 (t, 3H, J = 7.3), 1.62−1.72 (m, 2H), 3.90 (br s, 1H), 4.10 (t, 1H, J = 6.8), 6.39 (d, 2H, J = 7.6), 6.55 (pseudo t, 1H, J = 7.3), 6.99 (pseudo t, 2H, J = 7.3), 7.19 (s, 4H). ^{13}C NMR (50 MHz): δ 10.7 (CH_3), 31.6 (CH_2), 59.1 (CH), 113.2 (CH), 117.4 (CH), 127.8 (CH), 128.6 (CH), 129.1 (CH), 132. 3 (C), 142.5 (C), 147.1 (C). Anal. Calcd for $C_{15}H_{16}NCl$: C, 73.31; H, 6.56. Found: C, 72.18; H, 6.68.

When treated according to method B, in the absence of any alkyl iodide, **4** (150 mg, 0.69 mmol) gave **10a** (93 mg, 0.37 mmol, 55%).

***N*-[1-(4-Chlorophenyl)-2-methylpropyl]phenylamine (10b).** When treated according to method A, in the presence of isopropyl iodide, **4** (150 mg, 0.69 mmol) led to **10b** (122 mg, 0.46 mmol, 68%), isolated as a colorless oil after purification by FC (7% EtOAc/pentane). ^{1}H NMR (200 MHz): δ 0.88 (d, 3H, J = 6.6), 0.94 (d, 3H, J = 6.6), 1.95 (oct, 1H, J = 6.6), 4.07 (d, 1H, J = 6.6), 6.45 (pseudo d, 2H, J = 7.6), 6.61 (pseudo t, 1H, J = 7.3), 7.05 (pseudo t, 2H, J = 7.3), 7.17 (s, 4H). ^{13}C NMR (50 MHz): δ 18.4 (CH_3), 19.5 (CH_3), 34.7 (CH), 63.1 (CH),-113.1 (CH), 117.2 (CH), 128.3 (CH), 128.5 (CH), 129.0 (CH), 132.2 (C), 141.0 (C), 147.3 (C). Anal. Calcd for $C_{16}H_{18}NCl$: C, 73.98; H, 6.98. Found: C, 73.30; H, 6.40.

When treated according to method B, in the presence of isopropyl iodide, **4** (150 mg, 0.69 mmol) gave **10b** (95 mg, 0.36 mmol, 53%).

***N*-[1-(4-Chlorophenyl)-2,2-dimethylpropyl]phenylamine (10c).**[11] When treated according to method A, in the

(26) Shimizu, K.; Nakayama, K.; Akiyama, M. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2456−2462.

presence of *tert*-butyl iodide, **4** (150 mg, 0.69 mmol) led to **10c** (144 mg, 0.52 mmol, 76%), isolated as a yellow solid after purification by FC (5% EtOAc/pentane). ^{1}H NMR (200 MHz): δ 1.01 (s, 9H), 4.05 (s, 1H), 4.25 (br s, 1H), 6.49 (pseudo d, 2H, J = 8.5), 6.65 (pseudo t, 1H, J = 6.7), 7.10 (pseudo t, 2H, J = 7.6), 7.29 (br s, 4H). ^{13}C NMR (50 MHz): δ 26.9 (CH_3), 34.8 (C), 66.6 (CH), 113.1 (CH), 117.2 (CH), 127.9 (CH), 129.0 (CH), 129.7 (CH), 132.4 (C), 139.7 (C), 147.3 (C). Anal. Calcd for $C_{17}H_{20}NCl$: C, 74.57; H, 7.36. Found: C, 73.13; H, 7.15.

***N*-[1-(4-Chlorophenyl)-2,2-dimethylpropyl]-2,4-di-*tert*-butylphenylamine (11).** When treated according to method B, in the presence of *tert*-butyl iodide, **4** (150 mg, 0.69 mmol) led to **11** (106 mg, 0.27 mmol, 40%), isolated as a white solid after purification by FC (5% EtOAc/pentane). ^{1}H NMR (200 MHz): δ 1.04 (s, 9H), 1.25 (s, 9H), 1.57 (s, 9H), 4.12 (d, 1H, J = 5.1), 4.45 (br d, 1H, J = 4.6), 6.24 (d, 1H, J = 8.5), 6.92 (dd, 1H, J = 2.4, 8.5), 7.25−7.30 (m, 4H); ^{13}C NMR (50 MHz): δ 27.4 (CH_3), 30.3 (CH_3), 31.6 (CH_3), 33.9 (C), 34.5 (C), 35.0 (C), 66.8 (CH), 111.7 (CH), 123.0 (CH), 123.4 (CH), 127.9 (CH), 129.9 (CH), 132.3 (C), 132.4 (C), 138.6 (C), 140.2 (C), 142.2 (C). Anal. Calcd for $C_{25}H_{36}NCl$: C, 77.79; H, 9.4. Found: C, 78.47; H, 8.93.

3-Ethylcyclohexanone (12a).[27] When **5** (200 μL, 2.08 mmol) was allowed to react with Et_2Zn, according to method B, in the absence of any alkyl iodide, **12a** (160 mg, 1.27 mmol, 64%) was isolated as a colorless oil after purification by FC (5% EtOAc/pentane). ^{1}H NMR (200 MHz): δ 0.91 (t, 3H, J = 7.3), 1.22−2.48 (m, 11H). ^{13}C NMR (50 MHz): δ 10.9 (CH_3), 25.1 (CH_2), 29.1 (CH_2), 30.7 (CH_2), 40.6 (CH), 41.3 (CH_2), 47.7 (CH_2), 211.8 (C=O).

3-Isopropylcyclohexanone (12b).[27] When **5** (200 μL, 2.08 mmol) was allowed to react with Et_2Zn, according to method B, in the presence of isopropyl iodide, **12b** (188 mg, 1.30 mmol, 63%) was isolated as a colorless oil after purification by FC (5% EtOAc/pentane). ^{1}H NMR (200 MHz): δ 0.85 (d, 3H, J = 6.3), 0.86 (d, 3H, J = 6.3), 1.28−2.35 (m, 10H). ^{13}C NMR (50 MHz): δ 19.2 (CH_3), 19.4 (CH_3), 25.4 (CH_2), 28.2 (CH_2), 32.4 (CH), 41.4 (CH_2), 45.2 (CH_2), 45.3 (CH), 212.5 (C=O).

3-*tert*-Butylcyclohexanone (12c).[27] When **5** (200 μL, 2.08 mmol) was allowed to react with Et_2Zn, according to method B, in the presence of *tert*-butyl iodide, **12c** (189 mg, 1.23 mmol, 61%) was isolated as a colorless oil after purification by FC (5% EtOAc/pentane). ^{1}H NMR (200 MHz): δ 0.85 (s, 9H), 1.16−1.65 (m, 3H), 1.85−2.46 (m, 6H). ^{13}C NMR (50 MHz): δ 25.6 (CH_2), 26.0 (CH_2), 27.0 (3xCH_3), 32.6 (C), 41.2 (CH_2), 43.5 (CH_2), 49.2 (CH), 212.8 (C=O).

Supporting Information Available: ^{1}H and ^{13}C NMR for compounds **10a**,**b** and **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9912404

(27) Wheeler, O. H. *J. Org. Chem.* **1964**, *29*, 3634−3636.