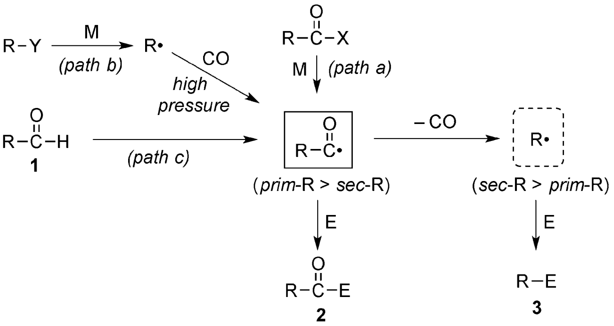
DOI: 10.1002/ange.201406513

Metal-Free C–H Bond Activation of Branched Aldehydes with a Hypervalent Iodine(III) Catalyst under Visible-Light Photolysis: Successful Trapping with Electron-Deficient Olefins

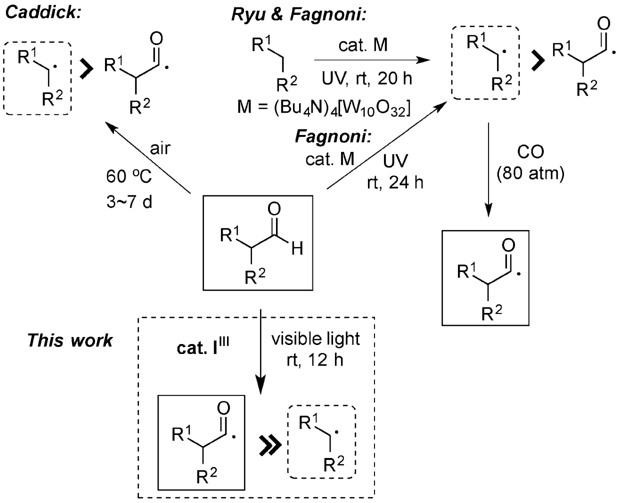
*Shin A. Moteki, Asuka Usui, Sermadurai Selvakumar, Tiexin Zhang, and Keiji Maruoka**

Abstract: *Direct acyl radical formation of linear aldehydes (RCH_2-CHO) and subsequent hydroacylation with electron-deficient olefins can be effected with various types of metal and nonmetal catalysts/reagents. In marked contrast, however, no successful reports on the use of branched aldehydes have been made thus far because of their strong tendency of generating alkyl radicals through the facile decarbonylation of acyl radicals. Here, use of a hypervalent iodine(III) catalyst under visible light photolysis allows a mild way of generating acyl radicals from various branched aldehydes, thereby giving the corresponding hydroacylated products almost exclusively. Another characteristic feature of this approach is the catalytic use of hypervalent iodine(III) reagent, which is a rare example on the generation of radicals in hypervalent iodine chemistry.*

Construction of C–C bonds through the use of carbon-centered radicals is one of the growing fields in synthetic organic chemistry.[1] Various efficient and practical approaches have been developed, and the generation of C–C bonds through addition of acyl radicals to olefins is very challenging.[2,3] A most widely used strategy in the generation of acyl radicals is to employ modified acyl derivatives such as acyl selenides, tellurides, and thioesters (Scheme 1, path a).[4] Alternatively, acyl radicals can be generated in situ by carbonylation of aryl, alkyl, and vinyl radicals with carbon monoxide under high pressure (Scheme 1, path b).[5] However, the most attractive approach, being free of harmful precursors and/or extra synthetic steps, is the direct generation of acyl radicals from the corresponding aldehydes **1** (Scheme 1, c). To this end, several approaches have been developed, and include acetyl peroxide/UV light, photogeneration of alkoxy radicals, use of various photoinitiators, and aerobic auto-oxidation.[6–8] Unfortunately, the efficiency of these approaches are rather limited to the use of linear aldehydes. Because of their higher stability, acyl radicals generated from linear aldehydes can be efficiently trapped by electrophiles (E) to form the ketone derivatives **2**. In marked contrast, acyl radicals generated from branched aldehydes tend to undergo facile decarbonylation to produce alkyl radicals, which subsequently form the alkylated products **3**.[4j] Therefore, as shown in Scheme 2, only limited reports on hydroacylation by branched aldehydes have been reported so far. Fagnoni and co-workers conducted the hydroacylation of electrophilic olefins through photocatalyzed activation of various aldehydes.[7] The catalytic use of tetrabutylammonium decatungstate (TBADT), which has a maximum light absorbance around $\lambda = 323$ nm, effectively generates acyl radicals under UV irradiation. However, for branched aldehydes, use of such high-energy light causes a significant decarbonylation of acyl radicals at ambient temperature. Decarbonylation of acyl radicals can be minimized by lowering the reaction temperature (−20–−50 °C), and hydroacylation products were obtained in up to approximately 45 % yield after 24 hours. To overcome this drawback, Ryu, Fagnoni, and co-workers efficiently generated acyl radicals through carbon-



Scheme 1. Generation of acyl radicals.



Scheme 2. Acyl radical formation from branched aldehydes.

---

[*] Dr. S. A. Moteki, A. Usui, Dr. S. Selvakumar, Dr. T. Zhang, Prof. Dr. K. Maruoka
Laboratory of Synthetic Organic Chemistry and Special Laboratory of Organocatalytic Chemistry, Department of Chemistry, Graduate School of Science, Kyoto University
Sakyo, Kyoto 606-8502 (Japan)
E-mail: maruoka@kuchem.kyoto-u.ac.jp

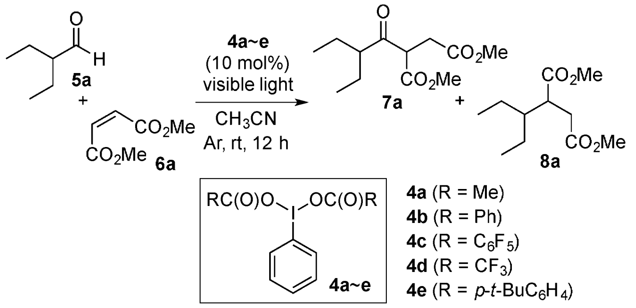
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201406513.

ylation of alkyl radicals with CO under high pressure (up to 80 atm).[5e] Although this approach is effective toward generation of branched acyl radicals, the applicability is limited to unsubstituted cyclic alkanes because of an issue with site specificity in generating carbon radicals from substituted cyclic or acyclic alkanes. More recently, Caddick and coworkers have taken the aldehyde auto-oxidation approach to generate acyl radicals.[8] However, this approach was effective only for linear aldehydes, and issues such as low reactivity, major decarbonylation of acyl radicals, as well as prolonged reaction times, with respect to branched aldehydes, need to be addressed.

We believe the key to minimizing the decarbonylation of branched acyl radicals lies in an appropriate choice of radical catalyst, which can effectively activate the C(O)−H bond under mild reaction conditions. Accordingly, we are interested in the possibility of using hypervalent iodine(III) catalysts,[9] which easily undergo photodecomposition by weak UV light or visible light to furnish iodanyl and carboxyl radicals, for the smooth generation of acyl radicals.[10]

To probe the potency on the effective use of hypervalent iodine(III) reagents with visible light, the hydroacylation reaction between 2-ethylbutyraldehyde (**5a**) and dimethyl maleate (**6a**) was investigated (Table 1). The in situ generation of acyl radicals from branched aldehydes and its subsequent trapping with electrophiles have not been previously developed to a synthetically useful level.[11] To our delight, catalytic use of DIB (**4a**) under the irradiation by visible light gave the hydroacylation product **7a** in 32 % yield with high selectivity for ketone formation (**7a**/**8a** = 8.0:1; entry 1). Only trace amounts of reaction products were detected in the absence of **4a** (entry 2) or visible light (entry 3) under the given conditions. These results strongly indicate that the reaction undergoes a radical pathway, thus generating acyl radicals in the reaction mixture. In addition, the reaction can be conveniently conducted using pyrex glassware, so use of an expensive quartz reactor is not necessary. We also investigated other iodine(III) catalysts (**4b**–**e**; entries 4–7), and found that **4b** and **4e** gave satisfactory results (entries 4 and 7), whereas **4c** and **4d** exhibited lower reactivity and selectivity (entries 5 and 6). In general, we prefer the use of **4e** because of the high solubility in CH_3CN. Use of a light source containing a short-wavelength UV light (100 W high-pressure mercury lamp or $\lambda = 365$ nm black light) accelerated the overall reaction rate, however, it increased the amount of the alkylated product **8a** (entries 8 and 9). Among the various solvents screened, CH_3CN provided the best result. The concentration of the reaction mixture is also important for obtaining the high yield as well as selectivity, and indeed use of a more concentrated CH_3CN (1.6 M) solution significantly enhanced both the selectivity (> 24:1) and the yield (89 %) in favor of **7a** (entry 10). Lowering the catalyst loading decelerates the reaction progress, however, high yield was obtained with a prolonged reaction time (entry 11).

Table 1: Hydroacylation of 2-ethylbutylaldehyde with dimethyl maleate by hypervalent iodine(III) catalysts (**4a**–**e**).[a]

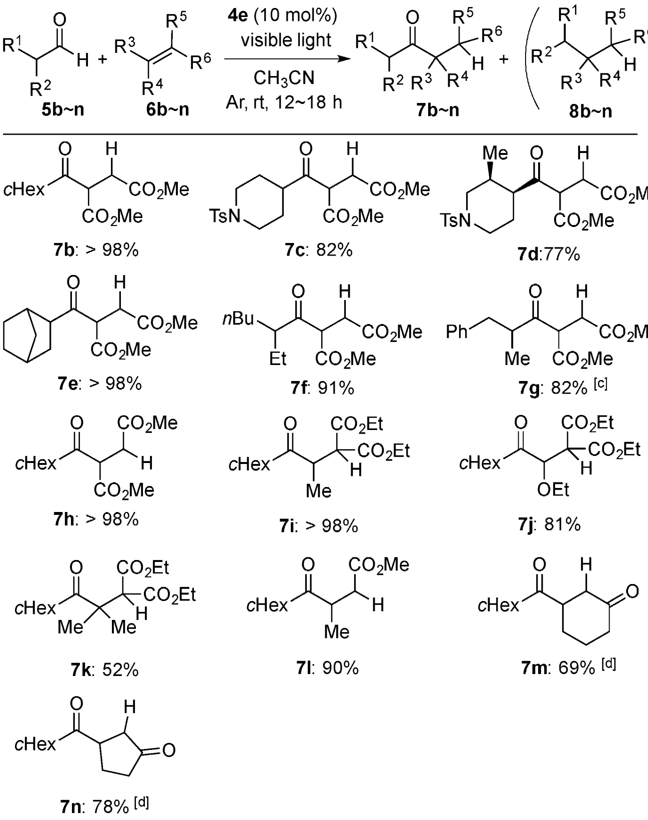


Entry	Catalyst	Yield [%][b]	**7a**/**8a**[c]
1	**4a**	32	8.0:1
2	none	trace	n.d.
3[d]	**4a**	trace	n.d.
4	**4b**	39	8.1:1
5	**4c**	24	7.9:1
6	**4d**	11	7.6:1
7	**4e**	41	8.1:1
8	**4e**[e]	> 98	3.2:1
9	**4e**[f]	97	5.3:1
10	**4e**	89 (82)[h]	> 24:1
11	**4e**[i]	83	> 24:1

[a] Unless otherwise specified, reaction of **5a** (0.75 mmol) and **6a** (0.5 mmol) was conducted in the presence of the catalyst **4** (10 mol %) in CH_3CN (0.5 M) with irradiation by visible light under the given conditions. [b] Yield was obtained for crude reaction mixture of **7a** and **8a** by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as internal standard. [c] The ratio of the hydroacylation versus alkylation product was obtained by ^1H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. [d] Reaction in the dark. [e] Use of 100 W mercury lamp in quartz reactor. [f] Use of $\lambda = 365$ nm black light. [g] Reaction in 1.6 M CH_3CN. [h] Yield of isolated product. [i] Reaction with 5 mol % **4e** for 20 h.

With the optimum reaction conditions in hand, we examined the applicability of other branched aldehydes as well as electrophilic olefins (Table 2). First, various branched aldehydes were screened against dimethyl maleate. None of the alkylated product **8b** was obtained in the reaction with cyclohexanecarbaldehyde (**5b**), thus giving the hydroacylation product **7b** almost exclusively in 98 % yield. In contrast, the same reaction using an aerobic protocol gave a mixture of **7b** and **8b** in 56 and 21 % yield, respectively, after ten days.[8c] Introduction of a heteroatom into the cyclohexane ring can be tolerated (**7c**), and does not affect stereocenters on heterocyclic rings (**7d**). The alteration of ring geometry has no effect on the yield (**7e**). It is noteworthy that the stereocenter in *endo*-**5e** was maintained during the reaction, thus giving *endo*-**7e** in nearly quantitative yield. 2-Ethylhexanal was previously reported to give a significant amount of the alkylated product **8f**.[8c] However, the extremely high preference for the hydroacylation product **7f** was observed when using our mild approach. No benzylic oxidation of the substrate **5g** was observed under the given reaction conditions (**7g**). Having confirmed the tolerance to various branched aldehydes, we screened substituted alkenes having distinct geometries as well as different electrophilicities. The high selectivity toward hydroacylation appears to be independent of the alkene geometry, as dimethyl fumarate (**6h**; $R^3 = R^6 = H$; $R^4 = R^5 = CO_2Me$) resulted in high selectivity for hydroacylation (**7h**). No alkylation was observed with the trisubstituted alkene **6i** ($R^3 = H$; $R^4 = Me$; $R^5 = R^6 = CO_2Et$),

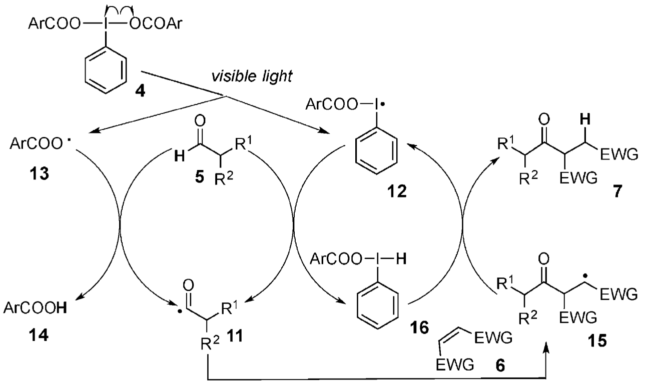
Table 2: Selective hydroacylation of branched aldehydes with electrophilic olefins by the hypervalent iodine(III) catalyst **4e**.[a,b]



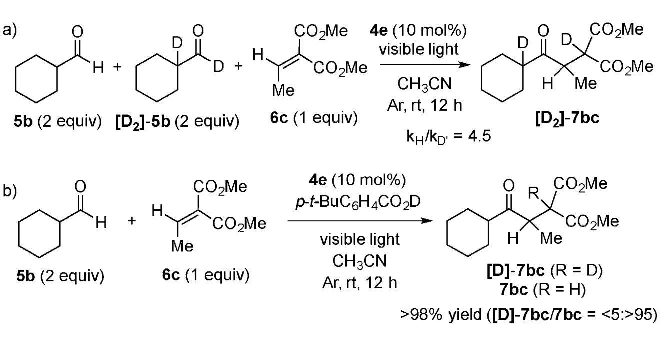
[a] Unless otherwise specified, reactions were conducted in the presence of **4e** (10 mol%), aldehyde **5b–n** (2.4 mmol) and olefin **6b–n** (1.6 mmol) in CH_3CN (1.6 M) under the given reaction conditions to furnish **7b–n** almost exclusively. [b] Yields of isolated **7b–n**. The alkylated products **8b–n** were not detected by ^1H NMR analysis of the crude reaction mixture. [c] Use of **4e** (30 mol%). [d] Use of 0.8 M CH_3CN/H_2O (1:1.5) for 18 h.

thus giving the hydroacylation product **7i** in nearly quantitative yield. Excellent yield of **7j** was obtained, by using diethyl ethoxymethylenemalonate (**6j**; $R^3 = H$; $R^4 = OEt$; $R^5 = R^6 = CO_2Et$), without any of the alkylated product **8j**. The sterically hindered diethyl isopropylidenemalonate (**6k**; $R^3 = R^4 = Me$; $R^5 = R^6 = CO_2Et$) was previously reported to give merely a trace amount of the hydroacylation product **7k**.[8c] To our delight, we obtained the desired **7k** in moderate yield. Here, no alkylated product (**8k**) was observed with this bulky substrate (**6k**) because of the possible steric interactions between the cyclohexyl radical and isopropylidenemalonate. The substrate scope of electrophilic olefins can be extended to those with single electron-withdrawing groups, and give the desired products **7l–n** in good to high yields with excellent selectivities. These results further indicate the superiority of this approach.

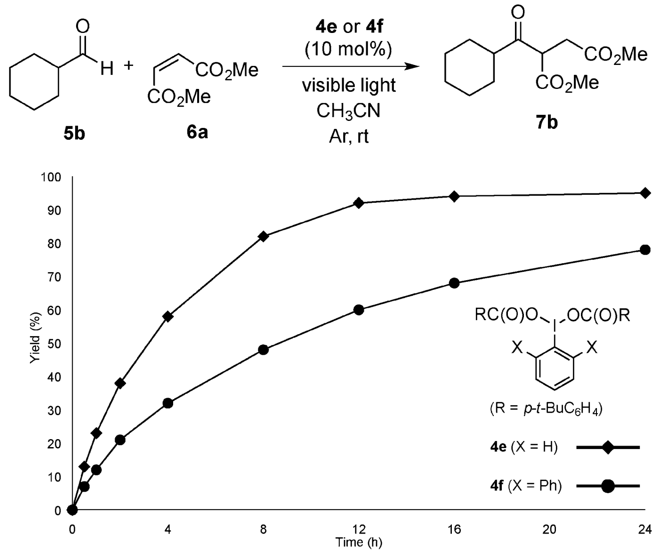
With these results in hand, we propose a reaction mechanism as depicted in Scheme 3. When the reaction of **5a** and **6a** was conducted in the presence of a radical trap, 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO), the TEMPO adduct from the acyl radical **11** [$R^1 = CH(CH_2CH_3)_2$] was isolated with only a trace amount of **7a**.[14] The photochemical decomposition of DIB (**4a**) or PIFA (**4d**) is known to give the iodanyl radical **12** ($Ar = Me$ or CF_3) as well as the acyloxy radical **13** ($Ar = Me$ or CF_3).[10] At this stage, we believe that **12**, rather than **13**, is mainly responsible for generating the acyl radical **11** for the following reasons: 1) In the kinetic isotope experiment using [D_2]-**5b**, the k_H/k_D value was found to be 4.5, thus implying the acyl radical formation to be the rate-determining step (Scheme 4a).[14] 2) When the sterically hindered hypervalent iodine(III) catalyst **4f** was employed, reduction in the reaction progress was observed, thus suggesting that **12** plays an important role in the rate-determining step of the reaction (Scheme 5). Moreover, the rate of reaction was closely correlated with the amount of I(III) catalyst employed (Table 1, entry 10 versus 11). In contrast, **13** may also abstract a hydrogen from the aldehyde to furnish **11** in addition to the acid **14**, which is not utilized for the donation of the hydrogen to the carbon radical **15**.[15] Indeed, the deuterium incorporation into **7** was observed only in trace amounts (< 5%) when p-tBuC$_6$H$_4$COOD was added to the reaction mixture (Scheme 4b). The ability of **15** to abstract hydrogen from the aldehyde **5** is rather low, and thus often requires combined use of auxiliary reducing reagents such as thiols to maintain active chain propagation.[2,16] However, in our catalytic system, we believe that the iodine(III) intermediate **16** can serve as a hydrogen source for **15** to produce final product **7** with regeneration **12** for further use in this catalytic cycle (SCheme 3). In the present selective hydroacylation reaction, the hypervalent iodine(III) catalyst



Scheme 3. Proposed mechanism of hydroacylation reaction catalyzed by **4**.



Scheme 4. Mechanic studies of hydroacylation reaction with the catalyst **4e**.



Scheme 5. Hydroacylation with **4e** and the bulky catalyst **4f**. Unless otherwise specified, reaction of **5b** (0.75 mmol) and **6a** (0.5 mmol) was conducted in the presence of catalyst **4e** or **4f** (10 mol%) in CH_3CN (1.6 M) under Ar at room temperature. Yield was obtained for crude reaction mixture by ^{1}H NMR spectroscopy using 1,1,2,2-tetrachloroethane as an internal standard. The alkylated product **8b** was not obtained under these reaction conditions.

4 does not require a high-energy input to undergo homolysis, and this is the key factor for the origin of superb selectivity toward hydroacylation of branched aldehydes. This low-energy input is responsible for the stability of **11** (R^1 = *sec*-alkyl) in the reaction mixture, thus preventing it from unwanted decarbonylation to produce an alkyl radical (see entries 8 and 9 in Table 1).

In summary, we have succeeded the mild generation of acyl radicals from branched aldehydes by using hypervalent iodine(III) catalysts under visible-light photolysis, and subsequent trapping of such acyl radicals with some electrophilic olefins. Further investigations on more detailed mechanism and synthetic application toward other systems are currently underway in our laboratory.

Experimental Section

Representative procedure (Table 1, entry 10): In a reaction tube containing dimethyl maleate (1.6 mmol), hypervalent iodine(III) catalyst **4e** (0.16 mmol), and 2-ethylbutanal (2.4 mmol) were mixed in dry acetonitrile (1.6 M) under argon atmosphere. The mixture was irradiated by visible light ($\lambda > 400$ nm) at room temperature with stirring for 12 h. Upon completion, acetonitrile was removed under reduced pressure. The crude reaction mixture was purified by flash column chromatography (eluting with *n*-hexane/ethyl acetate = 20:1 to 4:1) to afford a colorless oil (**7a**: 308 mg, 1.26 mmol, 79% yield and **7b**: 11.0 mg, 0.052 mmol, 3% yield); **7a**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 4.11$ (1H, t, $J = 7.1$ Hz), 3.74 (3H, s), 3.68 (3H, s), 2.91 (1H, dd, $J = 17.4$, 7.2 Hz), 2.84 (1H, dd, $J = 17.3$, 7.1 Hz), 2.75–2.67 (1H, m), 1.76–1.62 (2H, m), 1.56–1.39 (2H, m), 0.89 (3H, t, $J = 7.4$ Hz), 0.81 ppm (3H, t, $J = 7.4$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 206.5$, 171.7, 168.8, 54.3, 54.1, 52.6, 52.0, 31.9, 24.2, 22.9, 11.6, 11.3 ppm; **8a**: ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 3.69$ (3H, s), 3.67 (3H, s), 3.01 (1H, dt, $J = 10.8$, 4.1 Hz), 2.74 (1H, dd, $J = 17.0$, 10.8 Hz), 2.33 (1H, dd, $J = 17.0$, 4.0 Hz), 1.61–1.54 (1H, m), 1.40–1.19 (4H, m), 0.91 (3H, t, $J = 7.4$ Hz), 0.88 ppm (3H, t, $J = 7.6$ Hz); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 175.3$, 173.1, 51.8, 51.7, 43.2, 42.9, 32.1, 23.6, 23.3, 11.8, 11.6 ppm.

Received: June 24, 2014

Keywords: aldehydes · hypervalent compounds · iodine · photochemistry · radicals

---

[1] a) C. J. Li, *Chem. Rev.* **1993**, *93*, 2023–2035; b) P. T. Anastas, M. M. Kirchhoff, *Acc. Chem. Res.* **2002**, *35*, 686–694; c) U. M. Lindström, *Chem. Rev.* **2002**, *102*, 2751–2772; d) G. J. Rowlands, *Tetrahedron* **2009**, *65*, 8603–8655; e) G. J. Rowlands, *Tetrahedron* **2010**, *66*, 1593–1636.

[2] For a recent review on acyl radical chemistry, see: C. Chatgilialoglu, D. Crich, M. Komatsu, I. Ryu, *Chem. Rev.* **1999**, *99*, 1991–2069.

[3] For a recent review on radical conjugate addition, see: G. S. C. Srikanth, S. L. Castle, *Tetrahedron* **2005**, *61*, 10377–10441.

[4] a) J. Pfenninger, C. Henberger, W. Graf, *Helv. Chim. Acta* **1980**, *63*, 2328–2337; b) D. Crich, S. M. Fortt, *Tetrahedron* **1989**, *45*, 6581–6593; c) D. L. Boger, R. J. Mathvink, *J. Org. Chem.* **1989**, *54*, 1777–1779; d) K. Haraguchi, H. Tanaka, T. Miyasaka, *Tetrahedron Lett.* **1990**, *31*, 227–230; e) D. L. Boger, R. J. Mathvink, *J. Org. Chem.* **1992**, *57*, 1429–1443; f) C. Chen, D. Crich, A. Papadatos, *J. Am. Chem. Soc.* **1992**, *114*, 8313–8314; g) C. Chen, D. Crich, *Tetrahedron Lett.* **1993**, *34*, 1545–1548; h) D. Crich, C, Chen, J.-T. Hwang, H. Yuan, A. Papadatos, R. I. Walter, *J. Am. Chem. Soc.* **1994**, *116*, 8937–8951; i) J. H. Penn, F. Liu, *J. Org. Chem.* **1994**, *59*, 2608–2612; j) C. Chatgilialoglu, C. Ferreri, M. Lucarini, P. Pedrielli, G. F. Pedulli, *Organometallics* **1995**, *14*, 2672–2676; k) L. Benati, G. Calestani, R. Leardini, M. Minozzi, D. Nanni, P. Spagnolo, S. Strazzari, *Org. Lett.* **2003**, *5*, 1313–1316.

[5] a) I. Ryu, K. Kusano, H. Yamazaki, N. Sonoda, *J. Org. Chem.* **1991**, *56*, 5003–5005; b) I. Ryu, M. Hasegawa, A. Kurihara, A. Ogawa, S. Tsunoi, N. Sonoda, *Synlett* **1993**, 143–145; c) Y. Kishimoto, T. Ikariya, *J. Org. Chem.* **2000**, *65*, 7656–7659; d) I. Ryu, S. Uehara, H. Hirao, T. Fukuyama, *Org. Lett.* **2008**, *10*, 1005–1008; e) I. Ryu, A. Tani, T. Fukuyama, D. Ravelli, M. Fagnoni, A. Albini, *Angew. Chem.* **2011**, *123*, 1909–1912; *Angew. Chem. Int. Ed.* **2011**, *50*, 1869–1872.

[6] a) M. S. Kharasch, W. H. Urry, B. M. Kuderna, *J. Org. Chem.* **1949**, *14*, 248–253; b) B. Fraser-Reid, R. C. Anderson, D. R. Hicks, D. L. Walker, *Can. J. Chem.* **1977**, *55*, 3986–3995; c) C. Chatgilialoglu, L. Lunazzi, D. Macciantelli, G. Placucci, *J. Am. Chem. Soc.* **1984**, *106*, 5252–5256; d) K. Kobayashi, M. Suzuki, H. Takeuchi, A. Konishi, H. Sakurai, H. Suginome, *J. Chem. Soc. Perkin Trans. 1* **1994**, 1099–1104; e) M. Oelgemöller, C. Schiel, J. Mattay, R. Frmhlich, *Eur. J. Org. Chem.* **2002**, 2465–2474.

[7] a) C. Manfrotto, M. Mella, M. Freccero, M. Fagnoni, A. Albini, *J. Org. Chem.* **1999**, *64*, 5024–5028; b) A. M. Cardarelli, M. Fagnoni, M. Mella, A. Albini, *J. Org. Chem.* **2001**, *66*, 7320–7327; c) D. Dondi, I. Caprioli, M. Fagnoni, M. Mella, A. Albini, *Tetrahedron* **2003**, *59*, 947–957; d) S. Esposti, D. Dondi, M. Fagnoni, A. Albini, *Angew. Chem.* **2007**, *119*, 2583–2586; *Angew. Chem. Int. Ed.* **2007**, *46*, 2531–2534; e) S. Protti, D. Ravelli, M. Fagnoni, A. Albini, *Chem. Commun.* **2009**, 7351–7353; f) D. Ravelli, M. Zema, M. Mella, M. Fagnoni, A. Albini, *Org. Biomol. Chem.* **2010**, *8*, 4158–4164.

[8] a) R. J. Fitzmaurice, J. M. Ahern, S. Caddick, *Org. Biomol. Chem.* **2009**, *7*, 235–237; b) V. Chudasama, R. J. Fitzmaurice, J. M. Ahern, S. Caddick, *Chem. Commun.* **2010**, *46*, 133–135;

c) V. Chudasama, R. J. Fitzmaurice, S. Caddick, *Nat. Chem.* **2010**, *2*, 592–596.

[9] For recent reviews, see: a) V. V. Zhdankin, P. J. Stang, *Chem. Rev.* **2002**, *102*, 2523–2584; b) M. Ochiai, V. V. Zhdankin, G. F. Koser, H. Tohma, Y. Kita, *Hypervalent Iodine Chemistry-Modern Developments in Organic Synthesis Topics in Current Chemistry* (Ed.: T. Wirth), Springer, Berlin, **2003**; c) H. Tohma, Y. Kita, *Adv. Synth. Catal.* **2004**, *346*, 111–124; d) T. Wirth, *Angew. Chem.* **2005**, *117*, 3722–3731; *Angew. Chem. Int. Ed.* **2005**, *44*, 3656–3665; e) V. V. Zhdankin, P. J. Stang, *Chem. Rev.* **2008**, *108*, 5299–5358; f) M. Ochiai, *Synlett* **2009**, 159–173; g) T. Dohi, N. Takenaga, A. Goto, H. Fujioka, Y. Kita, *J. Org. Chem.* **2008**, *73*, 7365–7368; h) T. Dohi, Y. Kita, *Chem. Commun.* **2009**, 2073–2085.

[10] a) G. Georgiev, E. Spiridus, A. Varvoglis, *Polym. Bull.* **1985**, *14*, 523–526; b) G. Georgiev, E. Kamenska, G. Karayanidis, I. Siderrou-Karayanidou, A. Varvoglis, *Polym. Bull.* **1987**, *17*, 169–174; c) L. Christov, G. Georgiev, I. Sideridou-Karayanidou, G. Karayanidis, A. Varvoglis, *Polym. Bull.* **1991**, *26*, 617–620; d) G. Georgiev, E. Kamenska, L. Christov, I. Sideridou-Karayanidou, G. Karayanidis, A. Varvoglis, *Eur. Polym. J.* **1991**, *28*, 207–211; e) H. Togo, M. Aoki, M. Yokoyama, *Tetrahedron Lett.* **1991**, *32*, 6559–6562; f) H. Togo, M. Aoki, M. Yokoyama, *Tetrahedron* **1993**, *49*, 8241–8256; g) A. De Mico, R. Maragarita, G. Piancatelly, *Tetrahedron Lett.* **1995**, *36*, 3553–3556.

[11] In a previous report of photocatalysis using TBADT at room temperature, this reaction gave mostly the alkylated product (**7a**/**8a** = 1:2.3, **7a** = 15% yield) after 24 h. The enhanced selectivity was obtained when the reaction was conducted at −20 °C (**7a**/**8a** = 8:1, **7a** = 40% yield). See Ref. [7d].

[12] In a previous report of the aerobic C–H activation at 60 °C, this reaction gave acylated product in 24% yield after 7 days. See Ref. [8c].

[13] See the Supporting Information for characterization of the TEMPO adduct of the acyl radical **11** [$R^1 = CH(CH_2CH_3)_2)$].

[14] Full experimental details are described in the Supporting Information.

[15] Under the given conditions, benzoyl peroxide (BPO) did not catalyze the reaction.

[16] K. Yoshikai, T. Hayama, K. Nishimura, K. Yamada, K. Tomioka, *J. Org. Chem.* **2005**, *70*, 681–683.