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Unexpected conversion of alkyl azides to alkyl iodides and of aryl azides to *N-tert*-butyl anilines

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ABSTRACT

In the presence of *tert*-butyl iodide, alkyl azides are converted into the corresponding iodides at room temperature, whereas, *N-t*-Bu anilines are obtained from aryl azides under the same experimental conditions. A mechanism is proposed to explain this unusual reactivity.

1. Introduction

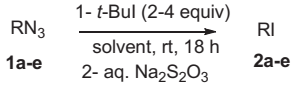
One of the most common methods for the synthesis of primary and secondary alkyl azides is the nucleophilic substitution of the corresponding alkyl halides (generally bromides) with sodium or lithium azide, in various solvents.[1] Only few publications are dealing with the reverse transformation, that is, the generation of an alkyl halide from an alkyl azide. Nitrosation of azidoalkanes with $NO^+BF_4^-$ leads to a mixture of fluoroalkanes, elimination products, and the corresponding aldehydes. Similarly, nitrosation of azidonitriles under the same experimental conditions produces fluoronitriles as the major products.[2] Recently, Benvegnu et al. have observed that, primary azides in position β and γ of ether functions are unexpectedly converted in high yield in chlorinated diethers under usual hydrogenation conditions (H_2, Pd/C), in chlorinated solvents, such as chloroform.[3,4] Finally, the treatment of 6-azido and 4,6-diazido-hexoses by hydrogen bromide in glacial acetic acid was reported to lead to rapid substitution of 6-azides by bromide anion.[5] To our knowledge, no reaction dealing with the direct tranformation of an alkyl azide into the corresponding iodide has ever been described in the literature.

We report in this communication that *tert*-butyl iodide can mediate the conversion of alkyl azides into the corresponding iodides.

2. Results and discussion

The reactions were performed in dichloromethane at room temperature in the presence of 2–4 equiv of *tert*-butyl iodide. The results are reported in Table 1. Primary and secondary azidoalkanes were converted into the corresponding iodides in yields ranging from 41 to 98%. The best yield was observed for the conversion of benzyl azide **1c**. A high yield in **2e** (80%) was similarly reached in

Table 1
Alkyl iodides **2a–e** from the corresponding azides **1a–e**



Entry	Solvent	Substrate		**2a–e** Yield (%)
1	DCM	**1a**	$Ph(CH_2)_3N_3$	56
2[a]	DMF	**1a**	$Ph(CH_2)_3N_3$	—
3	DCM	**1b**	$CyclohexylN_3$	61
4	DCM	**1c**	BnN_3	98
5	DCM	**1d**	*p*-$MePhCH_2N_3$	41
6	DCM	**1e**	$PhO(CH_2)_3N_3$	61
7	Benzene	**1e**	$PhO(CH_2)_3N_3$	80

[a] Compound **1a** was recovered in 95% yield.

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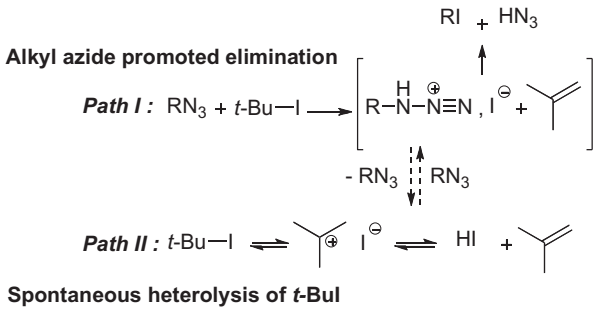
another apolar solvent, i.e., benzene (entry 7). Furthermore, changing DCM for DMF led to almost no conversion of **1a** (entry 2). No reaction at all was observed when *tert*-butyl iodide was replaced by *tert*-butyl bromide or by a secondary alkyl iodide, such as cyclohexyl- or isopropyl-iodide.

The most simple rationale implies that the tertiary iodide plays the role of a source of proton and iodide anion. In the first pathway, the azide would be basic enough in an apolar medium to deprotonate the alkyl iodide. This would produce a protonated azide that would undergo nucleophilic displacement by iodide anion (path I, Scheme 1).



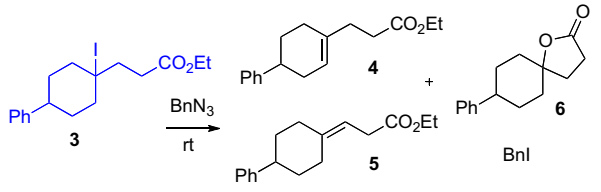
Scheme 1. Proposed mechanism for the formation of RI.

An alternative pathway would involve the spontaneous heterolysis of *tert*-butyl iodide, which would release HI in the reaction medium (path II, Scheme 1). In this hypothesis, the role of the alkyl azide could be either to trap HI or to deprotonate the tertiary carbocation. However, this pathway is unlikely in an apolar aprotic medium. As the reaction of benzyl azide with HI in DCM gave benzyl iodide but in low yield even after 24 h of reaction,[6] we believe that pathway II can be discarded.

Since the involvement of isobutene was difficult to probe, γ-iodoester **3** was prepared according to the methodology developed by Oshima in 60% yield via radical iodide atom transfer process.[7] The behavior of this tertiary iodide in the presence of benzyl azide was highly informative for the understanding of the mechanism.

The results are summarized in Table 2. When the reaction was performed in DCM using a 1:1 ratio of **3** and benzyl azide (entry 1) the elimination products **4** and **5** were obtained in 42% yield (**4**/**5**:25/1). In addition to these alkenes, lactone **6** was isolated in 34% yield. Using 0.5 equiv of benzyl azide and a shorter reaction time gave a similar result (entry 2). In DMF, the elimination products were obtained as the major products in 72% yield (entry 3). Based on NMR, in the presence of an internal probe, benzyl azide was converted to benzyl iodide in 35–40%, respectively (footnotes a and b). However, in the first experiment (entry 1), benzyl iodide was isolated in only 13% yield. Finally, a blank experiment, conducted in the absence of benzyl azide showed that after 5 days, no trace of either elimination products **4**/**5** or lactone **6** could be detected. This observation is in agreement with the alkyl azide playing a crucial role in this process.

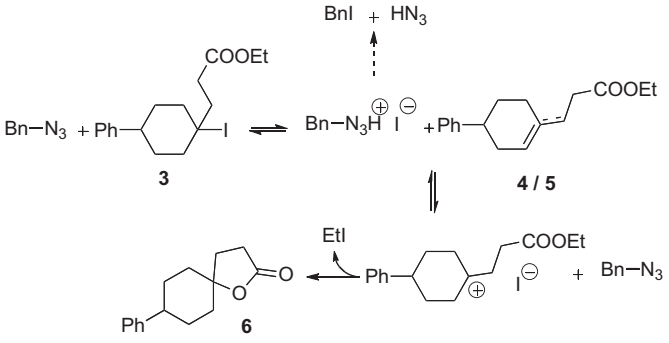
Table 2
Reactivity of tertiary iodide **3**



Entry	Solvent	Time	BnN_3	**4**/**5** Yield (%) (ratio)	**6** Yield (%)	BnI (%)
1	DCM	18 h	1 equiv	42 (25/1)	34	13[a]
2	DCM	12 h	0.5 equiv	38 (25/1)	31	39[b]
3	DMF	7 h	1 equiv	72 (25/1)	6	—[c]
4[d]	DCM	5 days	—	—	—	—

[a] Conversion of benzyl azide to benzyl iodide (35%) was observed based on NMR.
[b] Conversion of benzyl azide to benzyl iodide (40%) was observed based on NMR.
[c] Not measurable.
[d] Almost no conversion.

Based on these results, we proposed the following mechanism (Scheme 2). Since **3** was shown to be stable in DCM in the absence of benzyl azide (Table 2, entry 4), we assumed that path I, starting with the deprotonation of the tertiary iodide by the alkyl azide constitutes the initial step of the reaction. Alkenes **4** and **5** are formed in this step. The azide iodohydrate can evolve through nucleophilic substitution leading to the corresponding iodide. Alternatively it could protonate the alkenes, which would induce the formation of lactone **6** and ethyl iodide. In this hypothesis a substoichiometric amount of benzyl azide would be sufficient to promote the reaction. Indeed, the reaction is still working with 0.5 equiv of benzyl azide (Table 2, entry 2).



Scheme 2. Proposed mechanism with iodide **3**.

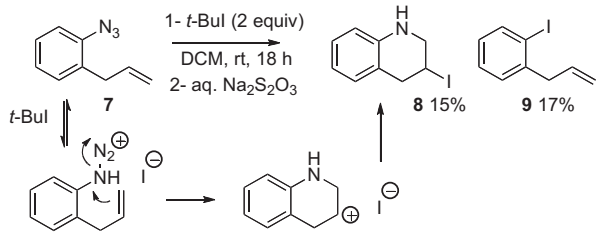
When the reaction was conducted in DMF, lactone **6** was isolated in 6% yield and the proportion of benzyl iodide was not measurable in the crude reaction mixture (Table 2, entry 3). We assumed that in this case, the proton was trapped by DMF (p*Ka*=−1), therefore the alkenes **4**/**5** were isolated as the major products.

This hypothesis can also explain why **1a** was recovered in 95% yield when the reaction was conducted in the presence of *tert*-butyl iodide in DMF (Table 1, entry 2). If the proton is quenched by DMF, *tert*-butyl iodide is consumed to give volatile isobutene whereas the alkyl azide is recovered at the end of the reaction.[8,9]

The reactivity of aryl azides depends strongly on the structure of the starting material.

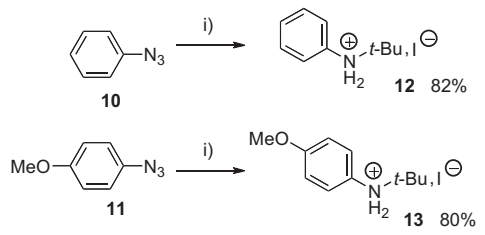
When allyl phenyl azide **7** was reacted with *tert*-butyl iodide, compounds **8** and **9** were isolated in 15% and 17% yields, respectively (Scheme 3). Compared to aliphatic azides, this substrate was less reactive toward protonation, and **7** was recovered in 60% yield. Compound **8** could result from the cyclization of the double bond onto the protonated azide with expulsion of dinitrogen, followed by nucleophilic attack of the iodide anion. A similar mechanism has already been proposed by Rodrigues for the acid-catalyzed cyclization of aryl and vinyl azides.[10] Iodide **9** might result from the formation of an aryl cation.

Simple aryl azides were also tested as substrates to explore the scope and limitation of this process (Scheme 4). The reaction was conducted on phenyl azide **10** in the presence of 4 equiv of *tert*-butyl iodide in DCM. Salt **12** was isolated in 82% yield. The same result was observed when conducting the reaction on *p*-methoxy phenyl azide **11**. In this case, traces amount of *p*-methoxy phenyl

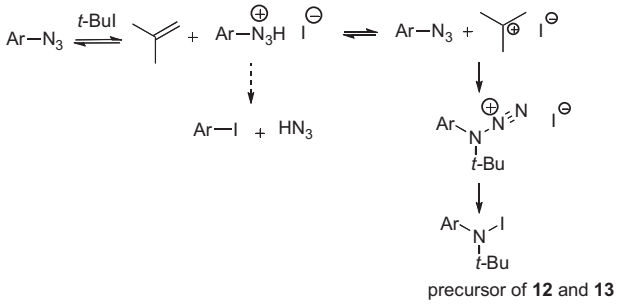


Scheme 3. Reaction of *tert*-butyl iodide with *o*-allyl phenyl azide.

iodide were detected. Again, the detection of aryl iodides in these cases might result from the formation of an aryl cation intermediate (Scheme 5).



Scheme 4. Reaction of *tert*-butyl iodide with aryl azides. (i) *t*-BuI (4 equiv), DCM, RT, 18 h, then solid $Na_2S_2O_3$.



Scheme 5. Proposed mechanism for the formation of **12** and **13**.

The formation of **12** and **13** was rather surprising. We tentatively propose that *N*-*tert*-butyl *N*-aryl iodoamines could be formed through the reaction of aryl azides with *tert*-butyl cation followed by the substitution of N_2 by iodine anion. This intermediate would lead to **12** and **13** under reductive work-up.

3. Conclusion

To conclude, we have shown that, in the presence of *tert*-butyl iodide, alkyl azides are converted into the corresponding iodides at room temperature. A series of experiments argue in favor of the deprotonation of the tertiary iodide by the alkyl azide in the first step. This reaction enables the uncommon transformation of an alkyl azide into the corresponding iodide. Less basic aryl azides show a completely different behavior. They lead directly to *tert*-butyl anilines in good yields.

4. Experimental section

4.1. General

Commercial reagents were used as received. Solvent for reactions (CH_2Cl_2) was filtered over column of dried alumina under a positive pressure of argon or stored on molecular sieves. Dry DMF was obtained from Aldrich. Solvents for extractions and flash column chromatography were of technical grade and were distilled prior to use. NMR spectra were recorded at 300 MHz and 400 MHz (^1H) and 75 MHz and 100 MHz (^{13}C) using $CDCl_3$ as the solvent. Chemical shifts (δ) are reported in parts per million. Signals due to residual protonated solvent or to the deuterated solvent served as the internal standard to calibrate the spectra (^1H NMR, $CHCl_3$, 7.26 ppm; ^{13}C NMR, $CDCl_3$, 77.16 ppm). Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), br (broad). The *J* values are given in hertz. All melting points were uncorrected and were recorded in open capillary tubes using melting points apparatus. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F_{254} plates. Visualization of TLC plates was carried out with one or more of the following methods: 254 nm UV light; dipping in different staining solution: $KMnO_4$ (5 g), Na_2CO_3 (30 g) in H_2O (500 mL); phosphomolybdic acid (25 g), cerium sulfate (10 g), and concd H_2SO_4 in H_2O (940 mL). Sodium sulfate or $MgSO_4$ was used as drying agent. Yields refer to chromatographically and spectroscopically pure compounds. High resolution mass spectra were recorded on a Waters Micromass Autospec Q mass spectrometer and on QStar Elite (Applied Biosystems SCIEX).

4.2. General procedure for azides synthesis

A solution of alkyl bromide (1 equiv) and sodium azide (2.5 equiv) in DMF (0.14 M) was stirred under argon at 80 °C for 18 h. After cooling at room temperature, the reaction mixture was diluted in Et_2O and washed with water (×6). The organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to give the corresponding pure azide without need of any further purification.

*4.2.1. (3-Azido-propyl)-benzene (**1a**).*[11] Reacting (3-bromo-propyl)-benzene (1.5 mL, 9.9 mmol) and sodium azide (1.6 g, 24.6 mmol) in DMF (70 mL) led to (3-azido-propyl)-benzene **1a** (1.6 g, 99%) isolated as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.93 (2H, quint, J=7.0), 2.72 (2H, t, J=7.3), 3.30 (2H, t, J=6.8), 7.17–7.25 (3H, m), 7.28–7.35 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 30.5 (CH_2), 32.9 (CH_2), 50.8 (CH_2), 126.3 (=CH), 128.6 (=CH), 128.7 (=CH), 141.0 (=C).

*4.2.2. Azidocyclohexane (**1b**).*[12] Reacting bromocyclohexane (0.5 mL, 4.0 mmol) and sodium azide (650 mg, 10 mmol) in DMF (60 mL) led to azidocyclohexane **1b** (0.427 g, 85%) isolated as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.11–1.46 (5H, m), 1.50–1.62 (1H, m), 1.68–1.81 (2H, m), 1.85–2.04 (2H, m), 3.24–3.41 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 24.4 (CH_2), 25.5 (CH_2), 31.8 (CH_2), 60.1 (CH).

*4.2.3. Azidomethyl-benzene (**1c**).*[13] Reacting bromomethyl-benzene (1 mL, 8.2 mmol) and sodium azide (1.36 g, 21 mmol) in DMF (60 mL) led to azidomethyl-benzene **1c** (1.08 g, 99%) isolated as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ: 4.35 (2H, s), 7.29–7.46 (5H, m).

*4.2.4. 1-Azidomethyl-4-methyl-benzene (**1d**).*[14] Reacting 1-bromomethyl-4-methyl-benzene (1.5 mL, 8.1 mmol) and sodium azide (1.31 g, 20.2 mmol) in DMF (58 mL) led to 1-azidomethyl-4-methyl-benzene **1d** (0.95 g, 80%) isolated as a yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.37 (3H, s), 4.30 (2H, s), 7.21 (4H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.3 (CH_3), 54.8 (CH_2), 128.40 (=CH), 129.6 (=CH), 132.4 (=C), 138.3 (=C).

*4.2.5. (3-Azido-propoxy)-benzene (**1e**).*[12] Reacting (3-bromo-propoxy)-benzene (1.5 mL, 10.8 mmol) and sodium azide (1.75 g, 26.9 mmol) in DMF (77 mL) led to (3-azido-propoxy)-benzene **1e**

(1.43 g, 75%) isolated as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.07 (2H, quint, J=6.3), 3.53 (2H, t, J=6.5), 4.06 (2H, t, J=6.0), 6.92 (2H, d, J=8.5), 6.98 (1H, t, J=7.3), 7.31 (2H, t, J=7.4). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.9 (CH_2), 48.4 (CH_2), 64.5 (CH_2), 114.7 (=CH), 121.1 (=CH), 129.6 (=CH), 158.8 (=C).

*4.2.6. 1-Azido-2-(prop-2-en-1-yl)benzene (**7**).*[15] Aniline (5 g, 54 mmol), allylbromide (1.1 equiv, 5.2 mL, 60 mmol), K_2CO_3 (1.2 equiv, 8.9 g, 65 mmol) and DMF (110 mL) were stirred at room temperature for 24 h. The reaction was treated with aq NH_4Cl and extracted twice with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$), filtered, and concentrated in vacuo. After purification by flash chromatography on silica gel (100% pentane) *N*-(prop-2-en-1-yl)aniline was isolated as an oil (1.9 g, 26%).[16] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.79 (2H, d, J=5.3), 3.90 (1H, superimposed br s), 5.11–5.40 (2H, m), 5.92–6.02 (1H, m), 6.60–6.77 (3H, m), 7.15–7.23 (2H, m).

To a stirred solution of *N*-(prop-2-en-1-yl)aniline (1.9 g, 14 mmol) in *m*-xylene (30 mL) was added dropwise $BF_3{\cdot}OEt_2$ (48% solution, 1.9 mL, 18 mmol) at −78 °C, and the mixture was stirred for 10 min at room temperature. Then, the reaction mixture was transferred into a micro-autoclave and stirred for 17 h at 190 °C. After cooling to room temperature, the reaction was quenched by the addition of aq NaOH (2 N) and extracted with Et_2O. The combined organic phases were washed with brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. After purification by flash chromatography on silica gel (pentane/ethyl acetate from 100/0 to 90/10) 2-(prop-2-en-1-yl)aniline was isolated as an oil (900 mg, 48%).[17] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.32 (2H, d, J=6.3), 3.60 (2H, br s), 5.06–5.19 (2H, m), 5.97 (1H, ddt, J=17.1, 10.3 and 6.0), 6.80–6.68 (2H, m), 7.12–7.04 (2H, m).

To a suspension of 2-(prop-2-en-1-yl)aniline (900 mg, 6.76 mmol, 1 equiv) in 8.9 mL water were added 2 mL of concentrated HCl. The reaction was cooled to 0 °C. A solution of $NaNO_2$ in 2.2 mL of water (560 mg, 8.11 mmol, 1.2 equiv) was then added. The reaction mixture was stirred for 10 min at 0–5 °C. Sodium azide (527 mg, 8.11 mol, 1.2 equiv) was added portionwise and the mixture was stirred at room temperature for 1 h. The organic layer was washed successively with water, brine and dried over $MgSO_4$ to give 1-azido-2-(prop-2-en-1-yl)benzene **6** (950 mg, 88%) isolated as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.34 (2H, d, J=6.5), 5.05 (2H, m), 5.94 (1H, ddt, J=16.8, 10.3 and 6.5) 7.06–7.20 (3H, m), 7.24–7.30 (1H, m).

*4.2.7. Azidobenzene (**10**).*[13] To a suspension of aniline (2 g, 21 mmol, 1 equiv) in 27.6 mL of water were added 6.3 mL of concentrated HCl. The reaction was cooled to 0 °C and aqueous solution of $NaNO_2$ in 6.9 mL of water was added (1.78 g, 26 mmol, 1.2 equiv). The reaction mixture was stirred for 10 min at 0–5 °C. Sodium azide (1.67 g, 26 mmol, 1.2 equiv) was added portionwise and the mixture was stirred at room temperature for 1 h. The reaction was diluted in ethyl acetate. The organic layer was washed successively with water, brine and dried over $MgSO_4$ to give azidobenzene **10** (1.7 g, 68%) isolated as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.02–7.07 (2H, m), 7.13–7.19 (1H, m), 7.33–7.40 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 119.2 (=CH), 125.0 (=CH), 129.9 (=CH), 140.1 (=C).

*4.2.8. 1-Azido-4-methoxybenzene (**11**).*[18] To a suspension of *p*-anisidine (2 g, 18 mmol, 1 equiv) in 23.6 mL of water were added 5.4 mL of concentrated HCl. The reaction was cooled to 0 °C and aqueous solution of $NaNO_2$ in 5.7 mL of water was added (1.49 g, 22 mmol, 1.2 equiv). The reaction mixture was stirred for 10 min at 0–5 °C. Sodium azide (1.40 g, 22 mmol, 1.2 equiv) was added portionwise and the mixture was stirred at room temperature for 1 h. The reaction was diluted in ethyl acetate. The organic layer was washed successively with water, brine and dried over $MgSO_4$ to give 1-azido-4-methoxybenzene **12** (2.2 g, 82%) isolated as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.80 (3H, s), 6.89 (2H, d, J=9.0), 6.96 (2H, d, J=9.0). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 55.7 (CH_3), 115.3 (=CH), 120.1 (=CH), 132.5 (=C), 157.1 (=C).

4.3. General procedure for the conversion of azides into iodides

To a solution of alkyl azide (1 equiv) 0.2 M in dichloromethane were added at room temperature 2–4 equiv of *tert*-BuI under an argon atmosphere. After stirring for 18 h at room temperature, the reaction mixture was washed with saturated $Na_2S_2O_4$ and the layers were separated. The organic phase was dried ($MgSO_4$), filtered, and concentrated in vacuo. Flash column chromatography on silica gel using pentane as the eluent afforded the corresponding iodide.

*4.3.1. (3-Iodo-propyl)-benzene (**2a**).*[19] Reacting (3-azido-propyl)-benzene (50 mg, 0.31 mmol) and *tert*-BuI (80 μL, 0.67 mmol) in CH_2Cl_2 (1.6 mL) gave (3-iodo-propyl)-benzene **2a** (43 mg, 56%) isolated as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.14 (2H, quint, J=7.0), 2.74 (2H, t, J=7.0), 3.18 (2H, t, J=6.8), 7.13–7.25 (3H, m), 7.27–7.37 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 6.5 (CH_2I), 35.0 (CH_2), 36.3 (CH_2), 126.3 (=CH), 128.6 (=CH), 128.7 (=CH), 140.5 (=C).

*4.3.2. Iodocyclohexane (**2b**).*[20] Reacting azidocyclohexane (50 mg, 0.40 mmol) and *tert*-BuI (100 μL, 1.84 mmol) in CH_2Cl_2 (2 mL) gave iodocyclohexane **2b** (51 mg, 61%) isolated as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.20–1.40 (3H, m), 1.50–1.78 (3H, m), 1.82–2.06 (2H, m), 2.08–2.25 (2H, m), 4.36 (1H, tt, J=3.6 and 9.5).

*4.3.3. Iodomethyl-benzene (**2c**).*[20] Reacting azidomethyl-benzene (50 mg, 0.38 mmol) and *tert*-BuI (90 μL, 0.76 mmol) in CH_2Cl_2 (2 mL) gave iodomethyl-benzene **2c** (82 mg, 98%) isolated as an oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.47 (2H, s), 7.22–7.45 (5H, m).

*4.3.4. 1-Iodomethyl-4-methyl-benzene (**2d**).*[21] Reacting 1-azidomethyl-4-methyl-benzene (100 mg, 0.68 mmol) and *tert*-BuI (324 μL, 2.72 mmol) in CH_2Cl_2 (3.4 mL) gave 1-iodomethyl-4-methyl-benzene **2d** (65 mg, 41%) isolated as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.31 (3H, s), 4.46 (2H, s), 7.10 (2H, d, J=8.0), 7.28 (1H, d, J=8.0). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 6.4 (CH_2I), 21.5 (CH_3), 128.9 (=CH), 129.8 (=CH), 136.5 (=C), 138.1 (=C).

*4.3.5. (3-Iodo-propoxy)-benzene (**2e**).*[22] Reacting (3-azido-propoxy)-benzene (100 mg, 0.56 mmol) and *tert*-BuI (269 μL, 2.26 mmol) in CH_2Cl_2 (2.8 mL) gave (3-iodo-propoxy)-benzene **2e** (90 mg, 61%) isolated as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.29 (2H, quint, J=6.3), 3.38 (2H, t, J=6.8), 4.05 (2H, t, J=5.8), 6.92 (2H, d, J=8.0), 6.98 (1H, t, J=7.3), 7.28 (2H, t, J=8.3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 2.7 (CH_2I), 33.2 (CH_2), 67.3 (CH_2), 114.7 (=CH), 121.1 (=CH), 129.6 (=CH), 158.8 (=C).

4.3.6. N-tert-Butylanilinium iodide (12). To a solution of azidobenzene **10** (100 mg, 0.84 mmol, 1 equiv) 0.2 M in dichloromethane were added at room temperature 4 equiv of *tert*-BuI (400 μL, 3.36 mmol) under an argon atmosphere. After stirring for 18 h at room temperature, the reaction mixture was treated with solid $Na_2S_2O_4$, the mixture was filtered, and concentrated in vacuo to give **12** (190 mg, 82%). Mp: 170–172 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.38 (9H, s), 7.20–7.25 (1H, m), 7.26–7.33 (2H, m), 7.42–7.50 (2H, m), 8.55 (2H, br s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.9 (CH_3), 61.5 (C), 124.8 (=CH), 127.7 (=CH), 129.2 (=CH), 133.5 (=C). HRMS (ESI):

m/*z*: calcd for [M^+] $C_{10}H_{16}N^+$: 150.1277; found: 150.1278. MS (ESI): *m*/*e*: 427.2 [(MI)C^+] and 704.2 [$(MI)_2C^+$].

*4.3.7. N-tert-Butyl-4-methoxyanilinium iodide (**12**).* To a solution of 1-azido-4-methoxybenzene **11** (100 mg, 0.67 mmol, 1 equiv) 0.2 M in dichloromethane were added at 30 °C 4 equiv of *tert*-BuI (319 μL, 2.68 mmol) under an argon atmosphere. After stirring for 18 h at room temperature, the reaction mixture was treated with solid $Na_2S_2O_4$, the mixture was filtered, and concentrated in vacuo to give **13** (165 mg, 80%). Mp: 165–167 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.47 (9H, s), 3.80 (3H, s), 6.85 (2H, d, *J*=9.0), 7.60 (2H, d, *J*=9.0), 9.93 (2H, br s). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.3 (CH_3), 55.6 (CH_3), 63.6 (C), 114.5 (=CH), 122.9 (=C), 127.8 (=CH), 160.4 (=C). HRMS (ESI): *m*/*z*: calcd for [M^+] $C_{11}H_{18}NO^+$: 180.1383; found: 180.1383. MS (ESI): *m*/*e*: 487.1 [(MI)C^+].

*4.3.8. 3-Iodo-1,2,3,4-tetrahydriquinoline (**8**) and 1-iodo-2-(prop-2-en-1-yl)benzene (**9**).*[23] To a solution of 1-azido-2-(prop-2-en-1-yl) benzene **7** (100 mg, 0.63 mmol, 1 equiv) 0.2 M in dichloromethane were added at room temperature 4 equiv of *tert*-BuI (300 μL, 2.51 mmol) under an argon atmosphere. After stirring for 18 h at room temperature, the reaction mixture was washed with $Na_2S_2O_4$ and the layers were separated. The organic phase was dried ($MgSO_4$), filtered, and concentrated in vacuo. Flash column chromatography on silica gel (pentane/ethyl acetate from 100/0 to 80/20) afforded to **7** in 60% (60 mg), **9** in 17% (26 mg)[24] and **8** in 16% (25 mg).

*4.3.8.1. 3-Iodo-1,2,3,4-tetrahydriquinoline (**8**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.55 (1H, s), 2.91 (1H, dd, *J*=14.3 and 10.0), 3.49 (1H, dd, *J*=14.3 and 4.3), 3.73 (1H, t, *J*=10.0), 4.05 (1H, dd, *J*=10.0 and 3.9), 4.57 (1H, tt, *J*=10.0 and 4.0), 7.07–7.40 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.4 (CH_2), 31.7 (CH), 42.1 (CH_2), 118.4 (=CH), 124.8 (=CH), 128.8 (=CH), 130.4 (=C), 131.7 (=CH), 138.5 (=C). HRMS (ESI): *m*/*z*: calcd for [MH^+] $C_9H_{11}IN$: 259.9931; found: 259.9932.

*4.3.8.2. 1-Iodo-2-(prop-2-en-1-yl)benzene (**9**).*[23] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.49 (2H, d, *J*=6.5), 5.08 (1H, dq, *J*=17.1 and 1.8), 5.14 (1H, dq, *J*=10.0 and 1.5), 5.96 (1H, ddt, *J*=17.1, 10.0 and 6.5), 6.85–6.96 (1H, m), 7.18–7.24 (1H, m), 7.27–67.33 (1H, m), 7.79–7.88 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 45.2 (CH_2), 101.0 (=C), 116.9 ($=CH_2$), 128.2 (=CH), 128.6 (=CH), 129.9 (=CH), 135.9 (=CH), 139.7 (=CH), 142.9 (=C).

4.4. Synthesis and reactivity of 3

*4.4.1. Ethyl 3-(1-iodo-4-phenylcyclohexyl) propanoate (**3**).*[7a] Potassium *tert*-butoxide (13.5 g, 120 mmol) and Ph_3PCH_3Br (43.0 g, 120 mmol) were refluxed in Et_2O during 30 min. A solution of the 4-phenyl-cyclohexanone (14.0 g, 80 mmol) in Et_2O (400 mL) was cautiously added via syringe and the reaction mixture was refluxed for another 60 min. The yellow suspension was cooled down and washed with H_2O, dried with $MgSO_4$. Purification by FC (cyclohexane/^{t}BuOMe 30:1) provided 4-methylene-1-phenyl-cyclohexane **S1** (13.7 g, 79 mmol, 99%) as a colorless oil.[25] ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.51–1.65 (2H, m), 1.99–2.04 (2H, m), 2.17–2.27 (2H, m), 2.42–2.48 (2H, m), 2.65–2.75 (1H, m), 4.71 (2H, s), 7.18–7.35 (5H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 35.1 (CH_2), 35.5 (CH_2), 44.1 (CH), 107.4 ($=CH_2$), 126.0 (=CH), 126.8 (=CH), 128.3 (=CH), 146.8 (=C), 148.7 (=C).

To a stirred solution of olefin **S1** (861 mg, 5 mmol) and ethyl iodoacetate (1.1 g, 5 mmol) in benzene (20 mL), triethylborane (500 μL, 0.5 mmol, 1 M in hexane) was added (syringe has to be immersed to the reaction mixture). Reaction mixture was stirred under aerobic condition at room temperature for 6 h. Reaction mixture was washed with saturated Na_2CO_3, organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the crude product. Purification by FC (pentane/Et_2O 19:1) gave the major diastereomer of ethyl 3-(1-iodo-4-phenylcyclohexyl) propanoate **3** (917 mg, 2.3 mmol) in 46% yield. Light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.07–1.20 (2H, m), 1.29 (3H, t, *J*=7.2), 1.85–1.91 (2H, m), 1.99–2.15 (2H, m), 2.19–2.27 (4H, m), 2.53 (1H, tt, *J*=12.2 and 3.8), 2.68–2.75 (2H, m), 4.17 (2H, q, *J*=7.2), 7.18–7.35 (5H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.3 (CH_3), 32.2 (CH_2), 32.9 (CH_2), 43.6 (CH_2), 43.7 (CH_2), 44.4 (CH), 60.7 (CH_2), 64.3 (C), 126.3 (=CH), 127.0 (=CH), 128.5 (=CH), 146.4 (=C), 173.2 (C=O). ESI-HRMS for [MH^+] $C_{17}H_{24}IO_2$: calcd 387.0815; found 387.0830.

*4.4.2. Ethyl 3-(4-phenylcyclohex-1-enyl)propanoate (**4** and **5**).* Benzyl azide **1c** (77 mg, 0.6 mmol) was added to a stirred solution of γ-iodoester **3** (226 mg, 0.6 mmol) in DMF (2 mL) and the reaction mixture was stirred for 7 h at room temperature. The mixture was diluted with H_2O and extracted with Et_2O, combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified under pressure by flash chromatography (pentane/ether 40:1), affording a mixture of the two regioisomers **4** and **5** (110 mg, 72%, ratio 25:1) as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.30 (3H, t, *J*=7.2), 1.72–1.87 (1H, m), 1.19–2.38 (7H, m), 2.25 (2H, m), 2.73–2.82 (1H, m), 4.17 (2H, q, *J*=7.2), 5.54–5.56 (1H, m), 7.19–7.35 (5H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.4 (CH_3), 29.0 (CH_2), 30.1 (CH_2), 32.7 (CH_2), 33.0 (CH_2), 33.5 (CH_2), 40.1 (CH), 60.3 (CH_2), 121.3 (=CH), 126.1 (=CH), 126.9 (=CH), 128.4 (=CH), 136.2 (=C), 147.1 (=C), 173.5 (C=O). ESI-HRMS for [MH^+] $C_{17}H_{23}O_2$: calcd 259.1693; found 259.1688.

*4.4.3. 8-Phenyl-1-oxaspiro[4.5]decan-2-one (**6**).* Benzyl azide **1c** (25 mg, 0.2 mmol) was added to a stirred solution of γ-iodoester **3** (145 mg, 0.4 mmol) in DCM (2 mL) and the mixture was stirred for 12 h at room temperature. The mixture was diluted with DCM and washed with H_2O, combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (pentane/ether 40:1), affording a mixture of two diastereomers of compound **6** (27 mg, 31%) as colorless crystalline solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.50–1.70 (2H, m), 1.78–2.07 (6H, m), 2.18 (2H, t, *J*=8.3), 2.54–2.66 (3H, m), 7.53–7.19 (5H, m). *Major diastereomer* ^{13}C NMR (75 MHz, $CDCl_3$) δ: 28.7 (CH_2), 30.6 (CH_2), 30.7 (CH_2), 36.8 (CH_2), 42.7 (CH), 86.6 (C), 126.5 (=CH), 126.8 (=CH), 128.6 (=CH), 145.6 (=C), 176.5 (C=O). *Minor diastereomer*, characteristic signals, ^{13}C NMR (75 MHz, $CDCl_3$) δ: 29.9 (CH_2), 34.3 (CH_2), 37.4 (CH_2), 43.5 (CH), 85.1 (C), 126.3 (=CH), 127.0 (=CH), 128.5 (=CH), 146.5 (=C), 176.8 (C=O). ESI-HRMS for [MNa^+] $C_{15}H_{18}NaO_2$: calcd 253.1189; found 253.1198.

Supplementary data

Electronic Supplementary data (ESI) available: ^{1}H and ^{13}C NMR spectrum for all new compounds. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2012.09.066.

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