Direct Bromination and Iodination of Non-Activated Alkanes by Hypohalite Reagents

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Dedicated to Bernd Giese on the occasion of his 65th birthday

Abstract: The direct functionalisation of alkanes through bromination and iodination has been successfully achieved. The combination of stoichiometric mixtures of elemental halogen and sodium alkoxides leads to the formation of alkyl hypobromites and hypoiodites as reagents. The halogenation occurs without external photostimulation under thermal reaction conditions.

Key words: alkanes, halogenation, hypobromites, hypoiodites

There are various methods known for the functionalisation and manipulation of non-activated C–H bonds, but many of them are still lacking the desired control and selectivity. Highly reactive reagents are necessary to perform such transformations, such as carbenes,[1] superacids,[2] free radicals,[3] or transition metals.[4] The strong reaction conditions required by these reagents might be incompatible with other functional groups and also skeletal rearrangements can occur.

The halogenation of alkanes is particularly interesting. Hydrocarbons are cheap and abundant starting materials, which are used for the direct synthesis of haloalkanes being valuable and useful building blocks in synthesis.

The iodination of alkanes, unlike bromination and chlorination, is thermodynamically forbidden,[5] with an overall positive enthalpy of 20–30 kcal/mol. Recently, new methodologies have been established for such transformations. For example, the discovery of the first ionic iodination of alkanes by superelectrophilic tetrahalomethane–aluminium triiodide complexes at –20 °C,[6] the first application of the Suárez reagent, a combination of iodine and (diacetoxyiodo)benzene, for a carbon-hydrogen bond activation in the synthesis of monoiodoalkanes or 1-acetoxy-2-iodocycloalkanes,[7] and the radical monoiodination of alkanes by mixtures of tetraiodomethane or iodoform with powdered NaOH at room temperature.[8]

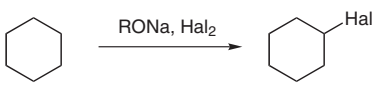
Alkyl hypohalites are positive halogen carrier reagents which have found extensive application for the activation of alkanes and other non-activated C–H bonds. *tert*-Butyl hypochlorite is a stable compound in the dark and easily prepared by reaction of *t*-BuOH with chlorine in aqueous NaOH.[9] It has promising chlorinating properties for non-activated allylic[10] and benzylic positions and for alkanes.[11] The photolysis and thermolysis of alkyl hypochlorites, derived from alcohols with hypochlorous acid, has been extensively used for the preparation of δ-chlorohydrins, tetrahydrofuranes[12] and spiro ethers.[13]

tert-Butyl hypobromite has been successfully prepared by reaction of *t*-BuOH with hypobromous acid in trichlorofluoromethane and used for the radical bromination of alkanes and alkenes such as cyclohexene to give 3-bromocyclohexene, a reaction which occurs photochemically in a few minutes at room temperature.[14]

The unstable *tert*-butyl hypoiodite has only been generated in situ from reaction of mercury iodide and *tert*-butyl hypochlorite but found to be a promising iodinating reagent for the functionalisation of alkanes[15] and cubane skeletons[16] when irradiated in Freon-113 as inert solvent. One of the first applications of organic hypoiodites was in steroid chemistry. Barton[17] used *tert*-butyl hypoiodite, prepared from *tert*-butyl hypochlorite or from potassium *tert*-butoxide and iodine, as a reagent to prepare steroid hypoiodites from the corresponding alcohols. These were used as intermediates in a photochemical intramolecular hydrogen abstraction, followed by iodination and subsequent ring closure of the 1,5-iodoalcohols to tetrahydrofurans or spiroketals.[18] Other hypoiodites can also be prepared from heavy metal salts [$Pb(OAc)_4$, $Hg(OAc)_2$, AgOAc, HgO] in combination with iodine to generate I_2O that leads to hypoiodite formation in situ.[19]

We have recently reported the in situ generation of *tert*-butyl hypoiodite for an efficient iodination of various alkanes.[20] We now describe an expansion of these studies towards bromination and discuss the observed selectivities in more detail (Scheme 1). We reported the formation of iodocyclohexane by iodination of cyclohexane with iodine and sodium *tert*-butoxide, which implied the generation of the corresponding hypoiodite intermediate.

Other alkoxides seem to be less efficient in the iodination which apparently only proceeds with tertiary alkoxides. We show that the addition of small amounts of bromine (20 mol%) can improve reproducibility and yields. These



1 Hal = I
2 Hal = Br

Scheme 1 Iodination and bromination of cyclohexane

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results are shown in Table 1, where the yield of iodocyclohexane **1** could be improved from 84% to 94% (entry 4). Although 20 mol% bromine are present, bromocyclohexane **2** is not isolated at all in this reaction and no traces could be found by GC analysis. A possible conversion of initially formed **2** to **1** under the reaction conditions is not taking place: After the addition of small amounts of **2** (0.2 equiv) to the reaction the crude product was found to be a mixture of **1** and **2**.

However, the addition of only 0.1 equivalents of an alcohol to the iodination with iodine and sodium *tert*-butoxide, completely stops the iodination process. Only if additional bromine is present, the iodination takes place. In the presence of 0.2 equivalents of alcohol (MeOH, EtOH, *t*-BuOH) and 0.2 equivalents of bromine the reaction yields only **1** in up to 65%.

Table 1 Iodination and Bromination of Cyclohexane

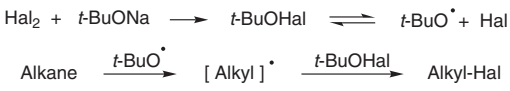
Entry	RONa	Hal_2: I_2 **1**, yield (%)	Hal_2: I_2 + 0.2 equiv Br_2 **1**, yield (%)	Hal_2: Br_2 **2**, yield (%)
1	–	0	–	86
2	MeONa	0	0	21
3	EtONa	1	1	60
4	*tert*-BuONa	84	94	100
5	$EtMe_2CONa$	70	72	50

Conditions: Addition of 1 equiv of alkoxide to a 0.1 M solution of 1 equiv Hal_2 in cyclohexane, then stirring at 40 °C for 15 h.

The radical bromination of cyclohexane is known.[5] Upon addition of primary alkoxides a decreased yield of bromocyclohexane **2** was observed in the bromination of cyclohexane. The primary alkyl hypobromites formed are obviously less efficient for hydrogen abstraction (Table 1, entries 2 and 3) than bromine itself (Table 1, entry 1). Only with *tert*-butyl hypobromite an even higher yield than with elemental bromine was observed (Table 1, entry 4).

The reaction proceeds in the absence of external photostimulation under thermal conditions. Bromination and iodination of toluene occur at the side chain and not on the aromatic nucleus, which is indicative of the radical nature of the process.

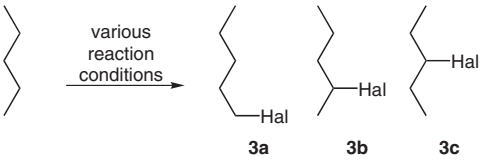
As shown in Scheme 2, the *tert*-butoxyl radical is formed by homolysis of the corresponding *tert*-butyl hypohalite. It has been identified as the free radical chain carrier and hydrogen abstracting species by comparing its relative reactivities with primary and secondary hydrogen atoms



Scheme 2 Generation of *tert*-butoxyl radicals as hydrogen abstracting species for alkanes

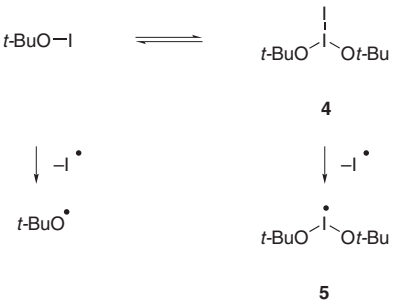
with the values described in the literature for halogen and alkoxyl radicals.

To establish the relative reactivities of the *tert*-butyl hypohalites towards primary and secondary hydrogen abstraction, we investigated the reaction with pentane in detail. A reaction at one of the primary hydrogen atoms will lead to 1-halopentane (**3a**), whereas an abstraction of a secondary hydrogen will lead to 2-halopentane (**3b**) or 3-halopentane (**3c**) (Scheme 3). A comparison to ratios obtained in other radical reactions as described in literature is possible and these references are included in Table 2.



Scheme 3 Halogenation of pentane

In Table 2 the results of the halogenation of pentane are compared with some reactions described in literature. The identification of the reactive radicals operating in these reactions is complicated because other reactive species might be involved as shown in Scheme 4.



Scheme 4 Radicals derived from *tert*-butyl hypoiodite

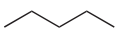
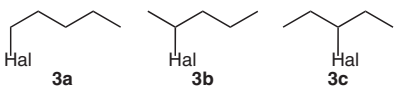
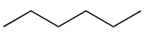
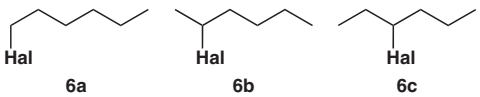
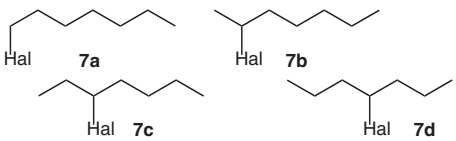
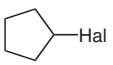
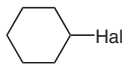
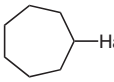
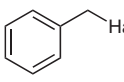
The analysis of the reactivities towards the abstraction of primary and secondary hydrogen atoms suggests that the formation of *tert*-butyl hypoiodite using *tert*-butyl hypochlorite and mercury iodide (Table 2, entry 10) which can involve dimerisation to molecules such as **4**. The reactive species might be radical **5** showing comparable selectivities than the radical derived from (dichloroiodo)benzene (Table 2, entry 3). On the basis of this selectivity observed for the *tert*-butoxyl radical derived from *tert*-butyl hypoiodite, the existence of hypervalent species of type **4** and radicals **5** was postulated. The unimolecular decomposition of the *tert*-butyl radical into acetone and a methyl radical is known but does not compete with the fast abstraction of hydrogen atoms from alkanes.[25] The selectivities found in reactions described in Table 2, entries 2, 8, 11 and 13 involve *tert*-butoxyl radicals and are comparable. The radical obtained from the alkoxide of 2-methyl-2-butanol shows similar reactivities to the *tert*-butoxyl radical (Table 2, entries 12 and 14) whereas in the reaction with only bromine the selectivity (1:19) might in-

Table 2 Halogenation of Pentane

Entry	Reagents/Temp	Ratio **3a**:**3b**:**3c**	Relative reactivities Primary:Secondary hydrogen atoms	Yield (%)	Reference
1	Cl_2, 40 °C		1:4		21
2	*t*-BuOCl, 40 °C		1:8		22
3	$PhICl_2$, 40 °C		1:21		23
4	Br_2, 40 °C	1:189:51	1:240	85	
5	Br_2, 80 °C		1:220		24
6	Br_2, MeONa	1:41:12	1:53	53	
7	Br_2, EtONa	1:190:52	1:242	53	
8	Br_2, *t*-BuONa	1:6:4	1:9	61	
9	Br_2, $EtMe_2CONa$	1:11.7:7.9	1:19	80	
10	*t*-BuOCl, HgI_2	[a]	1:29	71	12
11	I_2, *t*-BuONa	1:5:3	1:8	61	
12	I_2, $EtMe_2CONa$	1:8.2:3.1	1:11.3	37	
13	I_2, Br_2, *t*-BuONa	1:6.7:2.7	1:9.4	94	
14	I_2, Br_2, $EtMe_2CONa$	1:3:1	1:4	50	

[a] Ratio based on the reaction with *n*-butane (1-iodobutane:2-iodobutane = 1:29).

Table 3 Yields of Reaction of Alkanes with Alkyl Hypobromites

Entry	Substrate	Products	Yield (%) (Hal = Br)	Yield (Hal = I)
1		 Hal **3a** Hal **3b** Hal **3c**	61 (**3a**:**3b**:**3c** = 1:10.4:3.7)	94 (**3a**:**3b**:**3c** = 1:6.7:2.7)
2		 **Hal** **6a** **Hal** **6b** **Hal** **6c**	80 (**6a**:**6b**:**6c** = 1:11.8:7.8)	90 (**6a**:**6b**:**6c** = 1:5:4)
3		 Hal **7a** Hal **7b** Hal **7c** Hal **7d**	59 (**7a**:**7b**:**7c**:**7d** = 1:10.1:6.5:3.5)	70 (**7a**:**7b**:**7c**:**7d** = 1:8.7:5.9:2.4)
4		 Hal **8**	Quant.	65
5		 Hal **9**	Quant.	94
6		 Hal **10**	60	84
7		 Hal **11**	Quant.	40

dicate an involvement of a hypervalent radical of type **5** or some free bromine reacting independently with pentane.

The regioselectivity in the iodination of linear alkanes with stoichiometric mixtures of iodine and sodium *tert*-butoxide implies the in situ formation of alkoxide radicals, which act as the hydrogen abstracting species and as

the radical chain carrier species of the halogenation. The formation of alkyl hypoiodites from such reagent mixtures is supported by the fact that similar regioselectivities have been reported for the chlorination of linear alkanes by *tert*-butyl hypochlorite as chlorinating reagent.[21]

The regioselectivities for the hydrogen abstraction in the reaction of alkanes with alkyl hypobromites generated from stoichiometric mixtures of bromine and tertiary alkoxides as shown in Tables 2 and 3 are similar to regioselectivities reported for alkoxy radicals and different from the selectivities reported for bromine radicals (Table 2, entries 4 and 5). Therefore, the mechanism involves the homolysis of alkyl hypohalites, but seems to be restricted to tertiary alkyl derivatives. There is no trace of iodoalkanes when primary alkoxides are used for hypoiodite formation, and bromoalkanes are also formed in lower yields when primary alkoxides are used. This indicates a thermodynamically unfavorable formation, homolysis or halogenation of alkanes with primary alkyl hypohalites.

As mentioned above, a remarkable effect on reproducibility and yields was observed in the iodination of alkanes when sub-stoichiometric amounts of bromine were added to the reaction. The presence of bromine seems to improve the radical initiation step because of the more favorable energetic balance of the formation and homolysis of *tert*-butyl hypobromite than of *tert*-butyl hypoiodite. Mixed hypervalent species of type **4** might be involved as well.

As a hydrogen abstracting species, the *tert*-butoxyl radical was found to exhibit modest selectivities. A general comparison for alkanes showed a selectivity of approximately 1:14:40 for primary–secondary–tertiary hydrogen atoms. This selectivity roughly reflects the strength of the corresponding C–H bonds, although only for substrates with hydrogen–carbon bond dissociation energies of larger than ca. 92 kcal/mol normal reactivity trends are observed. Interestingly, benzylic C–H bonds with about 10 kcal/mol difference in bond strength to aliphatic C–H bonds are comparable in reactivity. A recent analysis of data on the hydrogen abstraction with *tert*-butoxyl radicals from hydrocarbons indicates that most of these reactions in solution at room temperature are entropy-controlled.[26] One of the few examples of the solvent polarity having a significant effect on the rate of radical reactions is the increase of the relative rate β-C–C vs. C–H abstraction in more polar solvents.[27]

In conclusion, we have developed a metal-free process for the direct iodination and bromination of alkanes using *tert*-butyl hypohalites as cheap and efficient reagents. The procedures described here are very simple and can be performed without prior purification of the solvents.

^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker DPX machines; $CDCl_3$ was used as solvent and as internal reference (δ = 7.26/77.0) in all the spectra; coupling constants *J* are given in Hz. The NMR spectra for 3- and 4-bromoheptane and 2-, 3- and 4-iodoheptane could not be unambiguously assigned from the NMR spectra available and are not included. All reagents were purchased as ACS grade and used without any further purification.

GC analysis was performed on a Varian 3900 GC apparatus using a Varian Factor FOUR Capillary Column VF-1ms 15 m × 0.25 mm ID DF = 0.25. The retention times indicated with each compound are referring to the temperature programme used for the analysis (from 50 °C to 150 °C with 3 °C/min). t_R (1-Bromopentane) = 6.24 min, t_R (2-bromopentane) = 4.48 min, t_R (3-bromopentane) = 4.62 min, t_R (1-iodopentane) = 8.85 min, t_R (2-iodopentane) = 6.30 min, t_R (3-iodopentane) = 6.74 min, t_R (1-bromohexane) = 8.49 min, t_R (2-bromohexane) = 6.92 min, t_R (3-bromohexane) = 7.10 min, t_R (1-iodohexane) = 11.11 min, t_R (2-iodohexane) = 8.74 min, t_R (3-iodohexane) = 9.30 min, t_R (1-bromoheptane) = 9.96 min, t_R (2-bromoheptane) = 8.11 min, t_R (3-bromoheptane) = 8.04 min, t_R (4-bromoheptane) = 7.71 min, t_R (1-iodoheptane) = 17.58 min, t_R (2-iodoheptane) = 12.71 min, t_R (3-iodoheptane) = 12.21 min, t_R (4-iodoheptane) = 10.17 min, t_R (bromocylopentane) = 4.65 min, t_R (iodocyclopentane) = 10.90 min, t_R (bromocyclohexane) = 12.46, t_R (iodocyclohexane) = 22.99, t_R (bromocycloheptane) = 19.16 min, t_R (iodocycloheptane) = 25.39 min, t_R (benzyl bromide) = 19.30 min, t_R (benzyl iodide) = 20.58 min.

Iodocyclohexane; Typical Procedure

Iodine (635 mg, 2.5 mmol) and Br_2 (80 mg, 25.6 μL, 0.5 mmol) were dissolved in cyclohexane (20 mL, 185 mmol) and *t*-BuONa (288 mg, 3 mmol) was added. The suspension was stirred at 40 °C for 15 h. The mixture was washed with 1% aq $Na_2S_2O_3$ (30 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue distilled to yield iodocyclohexane **9** (Hal = I) in 94% yield (493 mg) as a light yellow liquid.

1-Bromopentane (3a; Hal = Br)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (m, 3 H, CH_3, H-5), 1.30–1.50 (m, CH_2, 4 H), 1.85 (m, 2 H, CH_2, H-2), 3.40 (m, 2 H, CH_2Br).[28]

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (C-5), 22.0 (C-4), 30.5 (C-3), 32.7 (C-2), 33.7 (C-1).[29]

2-Bromopentane (3b; Hal = Br)[30]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (t, 3 H, *J* = 7.2 Hz, CH_3, H-5), 1.44 (m, 2 H, CH_2), 1.66 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.75 (m, 2 H, CH_2), 4.06 (m, 1 H, CHBr).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.4 (C-5), 21.0 (C-4), 26.4 (C-3), 43.2 (C-1), 51.6 (C-2).

3-Bromopentane (3c; Hal = Br)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.02 (t, *J* = 7.3 Hz, 6 H, CH_3), 1.81 (m, 4 H, CH_2), 3.86 (m, 1 H, CHBr).[31]

^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.1 (C-3), 31.8 (C-2), 61.0 (C-1).[32]

1-Iodopentane 3a (Hal = I)[33]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (m, 3 H, CH_3, H-5), 1.34 (m, 2 H, CH_2, H-4), 1.43 (m, 2 H, CH_2, H-3), 1.81 (m, 2 H, CH_2), 3.12 (t, *J* = 7.06 Hz, 2 H, CH_2I).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.4 (C-1), 14.1 (C-5), 21.6 (C-4), 32.6 (C-3), 33.5 (C-2).

2-Iodopentane (3b; Hal = I)[32]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.32 (m, 2 H, CH_2, H-4), 1.75 (m, 2 H, CH_2, H-3), 1.86 (d, *J* = 7.8 Hz, 3 H, CH_3, H-1), 4.14 (m, 1 H, CHI).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.1 (C-5), 22.9 (C-4), 28.9 (C-1), 30.4 (C-2), 44.9 (C-3).

3-Iodopentane (3c; Hal = I)[31,34]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.2 Hz, 6 H, CH_3), 1.80 (m, 4 H, CH_2), 4.01 (m, 1 H, CHI).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (C-3), 44.7 (C-1), 44.7 (C-2).

1-Bromohexane (6a; Hal = Br)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (m, 3 H, CH_3, H-6), 1.30 (m, 4 H, CH_2, H-4, H-5), 1.41 (m, 2 H, CH_2, H-3), 1.82 (m, 2 H, CH_2, H-2), 3.34 (t, *J* = 6.9 Hz, 2 H, CH_2I).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (C-6), 22.6 (C-5), 27.8 (C-3), 30.9 (C-4), 32.8 (C-2), 33.7 (C-1).

2-Bromohexane (6b; Hal = Br)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (m, 3 H, CH_3, H-6), 1.35 (m, 2 H, CH_2, H-5), 1.37 (m, 1 H, CH_2, H-4), 1.50 (m, 1 H, CH_2, H-4), 1.70 (d, *J* = 6.9 Hz, 3 H, CH_3, H-1), 1.78 (m, 2 H, CH_2, H-3), 4.08 (m, 1 H, CHBr, H-2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0 (C-6), 22.1 (C-5), 26.4 (C-1), 29.9 (C-4), 40.8 (C-3), 51.9 (C-2).[32]

3-Bromohexane (6c; Hal = Br)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (m, 3 H, CH_3, H-6), 0.99 (m, 3 H, CH_3, H-1), 1.30 (m, 2 H, CH_2, H-5), 1.74 (m, 4 H, CH_2, H-2, H-4), 3.95 (m, 1 H, CHBr, H-3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.1 (C-1), 13.5 (C-6), 20.8 (C-5), 32.2 (C-2), 40.8 (C-4), 60.4 (C-3).[32]

1-Iodohexane (6a; Hal = I)[35]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (m, 3 H, CH_3), 1.29 (m, 6 H, CH_2, H-3–H-5), 1.82 (m, 2 H, CH_2, H-2), 3.18 (t, *J* = 7.1 Hz, 2 H, CH_2I).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.1 (C-1), 14.0 (C-6), 22.5 (C-5), 30.2 (C-3), 30.7 (C-4), 33.6 (C-2).

2-Iodohexane (6b; Hal = I)[32]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (m, 3 H, CH_3, H-6), 1.25 (s, 2 H, CH_2, H-5), 1.39 (m, 1 H, CH_2), 1.49 (m, 1 H, CH_2), 1.79 (s, CH_2, 2 H, H-3), 1.85 (d, *J* = 6.8 Hz, 3 H, H-1), 4.15 (m, 1 H, CHBr, H-2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9 (C-6), 21.9 (C-5), 28.9 (C-1), 30.2 (C-2), 31.9 (C-4), 42.7 (C-3).

3-Iodohexane 6c (Hal = I)[32]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85 (m, 3 H, CH_3, H-6), 0.98 (t, *J* = 7.2 Hz, 3 H, CH_3, H-1), 1.30 (s, 2 H, CH_2, H-5), 1.81 (s, 4 H, CH_2, H-2, H-4), 4.05 (m, 1 H, CHBr, H-3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.2 (C-6), 14.1 (C-1), 22.8 (C-6), 33.8 (C-2), 41.7 (C-3), 42.4 (C-4).

1-Bromoheptane (7a; Hal = Br)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 6.4 Hz, 3 H, CH_3, H-7), 1.24 (m, 6 H, CH_2, H-4–H-6), 1.34 (m, 2 H, CH_2, H-3), 1.78 (m, 2 H, CH_2, H-2), 3.34 (t, *J* = 7.5 Hz, 2 H, CH_2Br, H-1).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (C-7), 22.7 (C-6), 28.2 (C-5), 28.5 (C-4), 31.7 (C-3), 33.0 (C-2), 33.8 (C-1).

2-Bromoheptane (7b; Hal = Br)
^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.84 (m, 3 H, CH_3, H-7), 1.25 (m, 4 H, CH_2), 1.35 (m, 1 H), 1.45 (m, 1 H), 2.06 (d, *J* = 6.6 Hz, 3 H, CH_3, H-1), 2.20 (m, 2 H), 4.09 (m, 1 H, CHBr, H-2).

1-Iodoheptane (7a; Hal = I)[36]
^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 6.9 Hz, 3 H, CH_3, H-7), 1.33 (m, 6 H, CH_2), 1.39 (m, 2 H), 1.84 (m, 2 H, H-2), 3.21 (t, *J* = 7.1 Hz, 2 H, CH_2I).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 7.4, 14.1, 22.6, 28.3, 30.5, 31.6, 33.6.

Bromocyclopentane (8; Hal = Br)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60 (s, 2 H), 1.81 (s, 2 H), 2.05 (s, 4 H, H-2), 4.41 (m, 1 H, CHBr).

^{13}C NMR (75 MHz, $CDCl_3$): 23.2 (C-3), 37.8 (C-2), 53.8 (C-1).

Iodocyclopentane (8; Hal = I)[31,37]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.57 (m, 2 H, CH_2), 1.76 (m, 2 H, CH_2), 1.99 (m, 4 H, CH_2), 4.29 (m, 1 H, CHI).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.9 (C-3), 28.7 (C-1), 39.8 (C-2).

Bromocyclohexane (9; Hal = Br)[31,37]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 3 H), 1.60 (s, 1 H), 1.75 (s, 4 H), 2.15 (s, 2 H), 4.16 (m, 1 H, CHBr).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.1 (C-4), 25.9 (C-3), 37.5 (C-2), 53.6 (C-1).

Iodocyclohexane (9; Hal = I)[31]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (m, 3 H), 1.60 (m, 3 H), 1.91 (m, 2 H, CH_2), 2.11 (m, 2 H, CH_2), 4.28 (m, 1 H, CHI).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.2 (C-4), 27.3 (C-3), 35.5 (C-1), 39.6 (C-2).

Bromocycloheptane (10; Hal = Br)
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (m, 2 H, H-3), 1.52 (m, 4 H, H-4), 1.70 (m, 2 H, H-3), 2.15 (m, 2 H, H-2), 2.45 (m, 2 H, H-2), 4.25 (m, 1 H, CHBr).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.4 (C-4), 28.9 (C-3), 41.2 (C-2), 58.0 (C-1).

Iodocycloheptane (10; Hal = I)[38]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (s, 8 H), 2.25 (m, 4 H), 4.42 (m, 1 H, CHI).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.0 (C-2), 27.4 (C-3), 36.3 (C-1), 42.0 (C-4).

Benzyl Bromide (11; Hal = Br)[36]
^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.37 (s, 2 H, CH_2Br), 7.14–7.28 (m, 5 H, Ar-H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 33.7, 128.5, 128.9, 129.9, 137.9.

Benzyl Iodide (11; Hal = I)[39]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.39 (s, 2 H, CH_2I), 7.15–7.31 (m, 5 H, Ar-H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 5.8 (CH_2I), 127.7, 128.5, 128.6, 139.5.

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