JOC The Journal of Organic Chemistry

Article

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Aliphatic C−H Bond Iodination by a *N*-Iodoamide and Isolation of an Elusive *N*-Amidyl Radical

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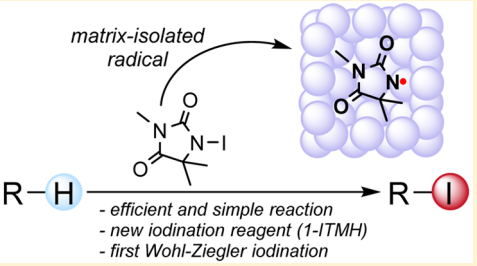
Supporting Information

ABSTRACT: Contrary to C−H chlorination and bromination, the direct iodination of alkanes represents a great challenge. We reveal a new *N*-iodoamide that is capable of a direct and efficient C−H bond iodination of various cyclic and acyclic alkanes providing iodoalkanes in good yields. This is the first use of *N*-iodoamide for C−H bond iodination. The method also works well for benzylic C−H bonds, thereby constituting the missing version of the Wohl−Ziegler iodination reaction. Mechanistic details were elucidated by DFT computations, and the N-centered radical derived from the used *N*-iodoamide, which is the key intermediate in this process, was matrix-isolated in a solid argon matrix and characterized by UV−vis as well as IR spectroscopy.



INTRODUCTION

Alkyl halides are some of the most important starting materials in synthetic chemistry. Among them, alkyl iodides are especially valuable as substrates for subsequent functionalizations, as they possess the weakest carbon−halogen bonds. The most attractive synthetic route to these compounds is the direct C−H bond functionalization of unactivated hydrocarbons. While direct halogenations with molecular fluorine through bromine are well established, the corresponding iodination is thermodynamically unfavorable.[4] Moreover, iodine−carbon bonds can be easily cleaved thermally or photochemically, which puts substantial limitations on the reaction conditions for direct C−H bond iodinations.[5]

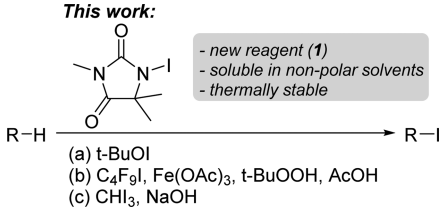
Several methods for the direct C−H bond iodination are based on the use of strongly electrophilic radicals instead of I-radicals.[6−11] A serious limitation in the reaction with iodine is that the formed hydrogen iodide can reduce alkyl iodides back to the corresponding alkanes because there is a significant driving force for the formation of a strong bond between hydrogen and its radical abstractor. The most significant iodination methods known to date are presented in Scheme 1.

The first radical iodination method and its modifications employed *tert*-butyl hypoiodite (Scheme 1a), which is highly unstable and must be prepared *in situ*.[10] In an alternative approach the propensity of perfluoroalkyl radicals for hydrogen atom abstraction from hydrocarbons[12] was utilized.[13] The reaction conditions require a mixture of the *tert*-butyl hydroperoxide/iron(III) redox system and perfluoroalkyl iodide in hot acetic acid (Scheme 1b).

One of us developed a method in which the direct iodination of alkanes is achieved in the absence of strong oxidating agents. Thus, aliphatic hydrocarbons are converted to the corresponding iodoalkanes upon reaction with CHI_3 (which provides the chain carrier species CI_4 next to CH_2I_2 via disproportionation *in situ*) and solid sodium hydroxide in a heterogeneous two-phase system (Scheme 1c).[14−16] While this reaction is useful and operationally very simple and broadly applicable to alkanes, iodination of benzylic positions (Wohl−Ziegler reaction) proved unsuccessful. As such, methods for the direct C−H iodination are still rare,[17] and the development of efficient synthetic approaches represents a formidable challenge.

In this paper we describe a novel, efficient, and operationally convenient method for the iodination of hydrocarbons with the single new reagent 1-iodo-3,5,5-trimethylhydantoin (1-ITMH, **1**),[18] which is the only *N*-iodoamide that effectively enabled this transformation. Remarkably, while the direct chlorination or bromination of alkanes by *N*-bromo or chloro amides are well-documented,[19−21] the corresponding C−H iodination has *not* been reported. Reagent **1**, which fills this missing link, behaves as both a powerful radical initiator and an iodine donor. Our reagent can readily be prepared and, contrary to some other iodoamides (e.g., 1,3-diiodo-5,5-dimethylhydantoin (DIH, **3**)), is quite stable and shows good solubility in organic solvents. Reagent **1** is

Scheme 1. Existing Iodination Methods (a−c), and the Approach Pursued in This Work



Received: March 8, 2017
Published: May 8, 2017

DOI: 10.1021/acs.joc.7b00557
J. Org. Chem. 2017, 82, 7093−7100

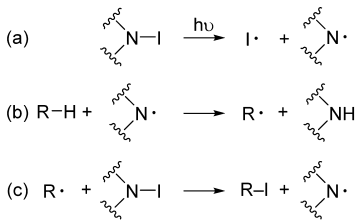
capable of iodinating the C−H bonds in various cyclic and acyclic alkanes. Moreover, **1** allows the direct conversion of benzylic C−H bonds to the benzyl iodides, thus, accomplishing the missing iodine version of the well-known Wohl−Ziegler reaction. Our mechanistic and spectroscopic studies support the formation of a N-centered radical derived from **1** as the key species in this process. This hitherto elusive N-amidyl radical was isolated in an argon matrix and characterized by IR and UV analyses.

RESULTS AND DISCUSSION

Recently, we developed an efficient iododecarboxylation utilizing DIH or NIS as both the radical initiator and the iodine source.[22] It was assumed that the *in situ* formed N-centered radical homolytically cleaves the strong O−H bond of the carboxylic acid group (BDE(AcO−H)) = 112.0 kcal mol^{-1};[1] BDE = bond dissociation energy) as a key step in the reaction. We sought to apply this idea to the radical iodination of alkanes with N−I amides, as the average BDEs for their C−H bonds are similar to those of O−H-bonds in carboxylic acids [BDE(C−H)$_{avg}$ = 98.7 kcal mol^{-1}].[1]

A plausible radical chain reaction is depicted in Scheme 2. Presumably, the thermodynamic driving force for this process

Scheme 2. A Proposed Mechanistic Pathway and Relevant Bond Dissociation Energies



#	Bond type	BDE$_{(avg.)}$ kcal mol^{-1}
1	C–H (sp^3)	98.7[1]
2	C–I (sp^3)	56.5[1]
3	N–I (NIS)	56.8[2]
4	N–I (1-ITMH, **1**)	43.5[a]
5	N–I (3-ITMH)	54.6[a]
6	N–H (succinimide)	118.0[3]

[a]Computed at M06-2X/6-311G(d,p).

is the weaker N−I bond in the iodo-amide as compared to the newly formed C−I bond of the product. Contrary to NCS, NBS, and their derivatives, the BDE in NIS is not compensated for by the formation of the alkyl iodide. Indeed, our attempts to iodinate cyclohexane with NIS resulted in a very low yield of the desired product (Scheme 3, entry 1). In an attempt to overcome this problem, we searched for an iodoamide with an N−I BDE lower than that in NIS. We proposed that DIH could be a good candidate for this reaction since its N−I BDEs are considerably lower (38.1 kcal mol^{-1} for N^1 and 48.7 kcal mol^{-1} for N^3).[2] However, DIH proved inefficient for the iodination of cyclohexane furnishing low conversion (entry 2), which can be rationalized by its low solubility.[23] An attempt to perform this reaction in polar solvents such as acetonitrile resulted in no product formation. In looking for a new reagent that could perform an efficient iodination in nonpolar solvents (e.g., alkanes) we decided to create a more soluble derivative of DIH by replacing the iodine on the N3 atom by a methyl group to reduce the molecule's overall polarity. Hence, we synthesized novel N−I amide **1**, which, indeed, exhibits much better solubility in alkanes as compared to DIH.

Importantly, our DFT computations reveal that **1** possesses a relatively weak N−I bond of only 43 kcal mol^{-1} (Scheme 2). Moreover, differential scanning calorimetry analysis shows the significant thermal stability of **1**.[18] Its counterpart, 3-ITMH (BDE (N−I) = 54.6 kcal mol^{-1}), was also prepared for comparison (vide infra).[18]

Gratifyingly, when **1** was irradiated in neat refluxing cyclohexane with a 3 W white LED lamp (λ = 400−800 nm) under a N_2 atmosphere, the desired iodocyclohexane was obtained in 86% yield after 2 h (Scheme 3, entry 7). As expected, 3-ITMH was much less active in this reaction and provided as poor a result as NIS (entry 6). Other commonly used N−I amides were more inferior compared to **1** in this iodination process (entries 1−6).

After identifying **1** as an efficient reagent for C−H iodination, we determined the key factors of this reaction. The main conclusions are as follows: (1) irradiation is necessary; carrying out the reaction in the dark results in almost no product (entry 9); (2) the process can be carried out under aerobic conditions with no significant decrease in yield (compare entries 7 and 8); (3) addition of large quantities of water leads to inferior results, due to hydrolysis of the N−I bond in **1** (entry 10);[24] (4) performing this process in solvents other than the neat alkane furnishes reduced yields.

We were pleased to find that numerous alkanes undergo efficient C−H iodination with our reagent under optimized conditions (Table 1). Thus, cycloalkanes can be selectively converted to their corresponding monoiodo derivatives in good yields within relatively short reaction times (entries 1−5). Acyclic alkanes and haloalkanes also undergo smooth iodination resulting in a mixture of iodoalkanes, which is typical for radical halogenations (entries 6−8).

Notably, benzylic C−H bonds also can be iodinated with **1**. While bromination or chlorination of these bonds with NBS or NCS in CCl_4 represents the well-known Wohl−Ziegler reaction, the analogous process with NIS is not possible due to its endergonicity (BDEs in kcal mol^{-1} of N−I(NIS) = 61.9, $PhCH_2$−I = 46.7).[1−3] As such, our process constitutes the missing iodine version of the Wohl−Ziegler reaction that allows the direct preparation of benzyl iodides with a simple *N*-haloamide.

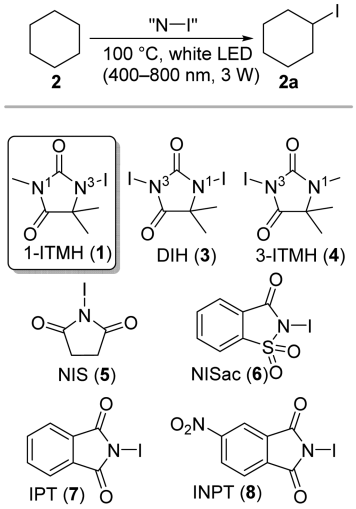
While performing this reaction under our optimized conditions for benzylic C−H bonds (see Supporting Information), we found that the method is broadly applicable to a range of substrates displaying different electronic and steric properties (Table 2). The target iodides were obtained in moderate to good yields within 3 h. Even in the case of mesitylene, where the aromatic ring is strongly activated toward electrophilic aromatic substitution, the benzylic C−H iodination product was obtained in 45% yield (entry 5), together with 41% of 2-iodo-1,3,5-trimethylbenzene.

Note that the isolation of benzylic iodination products from benzene solution proved to be challenging. Organic iodides are frequently not the final targets and are used in synthesis as substrates for further functionalization via facile nucleophilic displacement of the iodide group. Therefore, the organic iodides can be converted in situ to the desired compounds followed by isolation. We exemplified this scenario by in situ conversion of benzyl iodides, obtained by our method, to the corresponding benzyl benzoates via facile reaction with tetrabutylammonium benzoate (Table 2). We were pleased to find that these organic benzoates can be easily isolated from these reaction mixtures by column chromatography with only a slight decrease in product yield.

We addressed the mechanistic features of this process as well as the properties of **1** both experimentally and computationally.

DOI: 10.1021/acs.joc.7b00557
J. Org. Chem. 2017, 82, 7093−7100

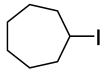
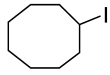
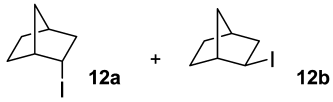
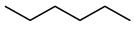
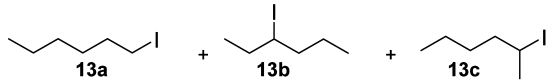
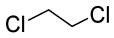
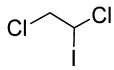
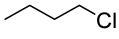
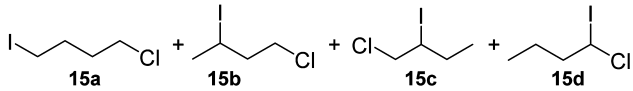
Scheme 3. Optimization of the Reaction Conditions



#	Conditions	"N–I"	Yield %[a,b] 1 h	2 h
1	neat	5	3	4
2	neat	3	9	10
3	neat	7	4	4
4	neat	8	0	0
5	neat	6	8	11
6	neat	4	1	1
7	neat	1	86	86
8	neat – air	1	85	81
9	neat – dark	1	-	8
10	neat – H_2O[c]	1	17	25
11	CCl_4	1	58	56
12	PhH	1	45	46
13	PhCl	1	33	33
14	PhF	1	41	40
15	$PhCF_3$	1	48	44
16	CH_2Cl_2	1	9	9
17	DCE	1	0	3

[a]GC yield. [b]Yields are calculated with respect to *N*-iodoamide. [c]10% mol H_2O relative to **1**.

Table 1. Iodination of Some Aliphatic Hydrocarbons with 1[a]

#	Substrate		Time [h]	Product(s)	Yield %[b]
1		**9**	2	 **9a**	60[c,f]
2		**2**	1	 **2a**	62
3		**10**	1	 **10a**	60
4		**11**	1	 **11a**	73
5		**12**	1	 **12a** + **12b**	32[c,f,g,h] *dr* 31:69
6		**13**	2	 **13a** + **13b** + **13c**	70[c,f,g] 7:35:58
7		**14**	24	 **14a**	59[d]
8		**15**	2	 **15a** + **15b** + **15c** + **15d**	48[c,e] 9:42:22:27

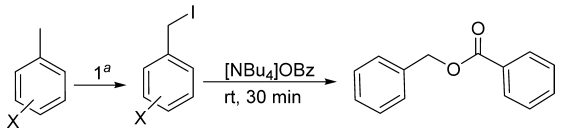
[a]Reaction conditions: neat, 100 °C, white LED irradiation (400–800 nm, 3 W). [b]Yields are calculated with respect to 1-ITMH. [c]GC yield. [d]Reaction performed with a 250 W incandescent light bulb. [e]Isomer ratio determined by GC. [f]Isomer ratio determined by ^{1}H NMR spectroscopy. [g]Reaction performed in a closed tube. [h]Reaction in a mixture of substrate with $PhCF_3$ in a 1:1 ratio.

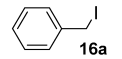
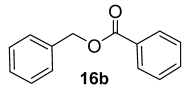
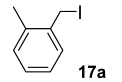
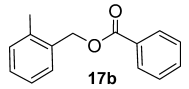
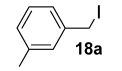
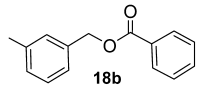
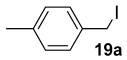
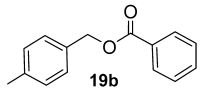
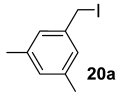
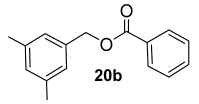
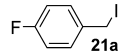
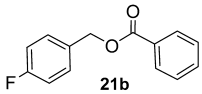
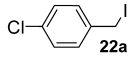
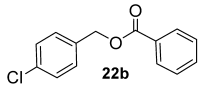
We assumed that, owing to its relatively weak N—Hal bond, **1** readily undergoes N—I bond homolysis[25,26] in the first step of the mechanism (Scheme 2). This leads to formation of an elusive N-centered radical, which represents a key species for understanding the iodination reaction described above. We attempted to isolate such species to examine the feasibility of its formation and to understand the nature of such N-centered radicals.

Hioe et al.[27] computed the radical stabilization energies (RSE) for various N-centered radicals and demonstrated that the attachment of a carbonyl group to the amino radical significantly destabilizes such species and makes them much more reactive.

DOI: 10.1021/acs.joc.7b00557
J. Org. Chem. 2017, 82, 7093–7100

Table 2. Iodine Version of the Wohl–Ziegler Reaction



#	Iodide	Yield %[b]	Ester	Yield %[c]
1	 16a	42	 16b	39
2	 17a	63	 17b	58
3	 18a	54	 18b	51
4	 19a	66[d]	 19b	56
5	 20a	45[e]	 20b	37
6	 21a	47	 21b	40
7	 22a	45	 22b	39

[a]Reaction conditions: benzene, 120 °C, white LED irradiation (3 W, white LED, 400–800 nm), 3 h. [b]GC yield. [c]Yield of isolated product. [d]In addition 16% of 1-iodo-2,4-dimethylbenzene formed. [e]In addition, 41% of 2-iodo-1,3,5-trimethylbenzene formed.

The addition of a second carbonyl group next to the radical center increases the destabilizing effect by reduction of the resonance interactions between the carbonyl group and the nitrogen lone pair.

The matrix isolated ESR spectra of the succinimidyl and phthalimidyl as well as the 1,8-naphthalimidyI radicals in argon matrices have been reported.[28,29] The succinimidyl radical and its alkylated analogues have been known to exist in thermodynamic equilibrium with their ring-opened isomers.[30] Many theoretical investigations concerning the σ versus π character of the succinimidyl radical have been reported.[30,31] According to recent G3B3 computations, the succinimidyl radical prefers a σ rather than a π ground state, in which the nitrogen lone pair of electrons is localized in a π molecular orbital.[27]

We aimed at generating and spectroscopically identifying the N-centered radical **23**, derived from **1**, under photochemical and thermal conditions. For this goal, we matrix isolated **23** via high-vacuum flash pyrolysis of **1** in argon at 10 K. The infrared spectrum of **1** isolated in a solid argon matrix at 10 K is presented in Figure 1; the agreement between the experimental and computed spectrum is very good. The matrix containing **1** was irradiated with monochromatic UV light tuned to specific wavelengths. Irradiation of the matrix (λ > 366 nm) induced no changes. However, irradiation at λ = 366 nm resulted in a decrease of all IR absorptions assigned to **1** and in the formation of new bands at around 2350–2250 cm^{-1} that were attributed to the decomposition products **27** and **28** (Figure 1b).

Formation of such isocyanate products could not be ruled out by comparison with literature data and computed spectra.[32] Therefore, a detailed computational analysis was undertaken to shed some light onto the mechanism of the formation of **27** and **28** starting from radical **23** (Figure 2).

Although it is not clear if this is a photochemical or a hot ground state reaction, only ground state reactions were investigated. We suggest that the elusive radical **23**, formed by N–I homolysis of **1**, can decompose through several pathways. The first reaction path implies the cleavage of the C–N bond in **23** to produce radical **24** via **TS1** (Figure 2). The barrier is 24.5 kcal mol^{-1} (including the zero-point vibrational energy correction, ZPVE, denoted as ΔH_0). The other pathway for producing **27** and **28** proceeds through radical **25**, which forms from **23** via **TS2** ($\Delta H_0^{\ddagger}$ = 29.9 kcal mol^{-1}). Subsequent C–C bond fission to **27** and **28** is accompanied by an activation barrier (**TS4**) of 35.7 kcal mol^{-1}. The rearrangement of **23** to **26** is also endothermic by +13.4 kcal mol^{-1} with an activation barrier

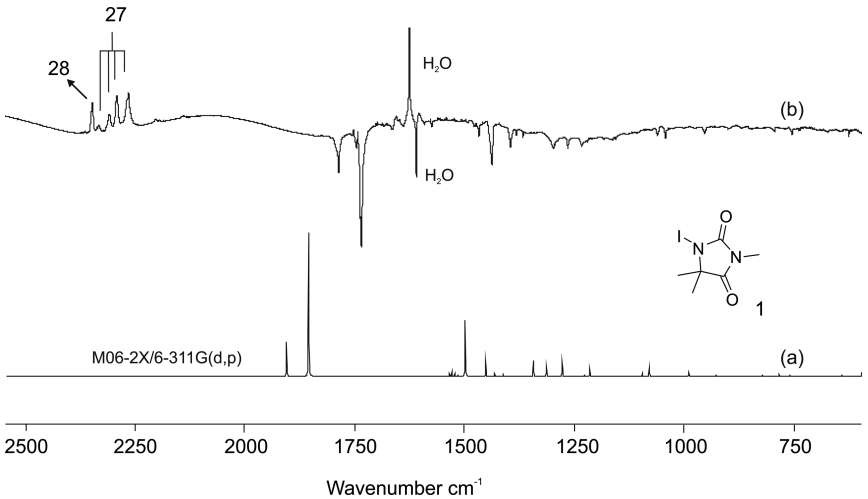


Figure 1. (a) IR spectrum of 1-ITMH computed at the M06-2X/6-311++G(2p,2d) level of theory. (b) IR difference spectra showing the photochemistry of 1-ITMH upon irradiation with λ = 366 nm in argon at 10 K. Bands pointing downward assigned to 1-ITMH disappear and bands pointing upward assigned 27 and 26 appear after 20 min irradiation time.

DOI: 10.1021/acs.joc.7b00557
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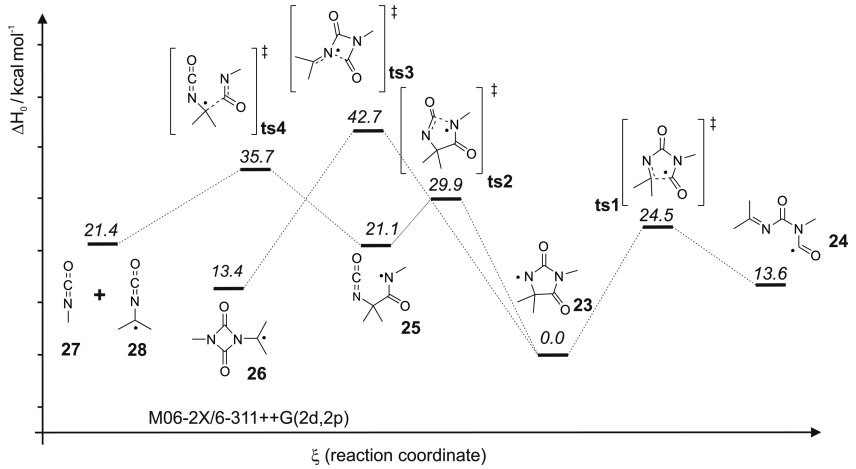

Figure 2. Energy profile (ΔH_0) in kcal mol^{-1} of the reactions of radical **23** at the M06-2X/6-311++G(2d,2p) level of theory.

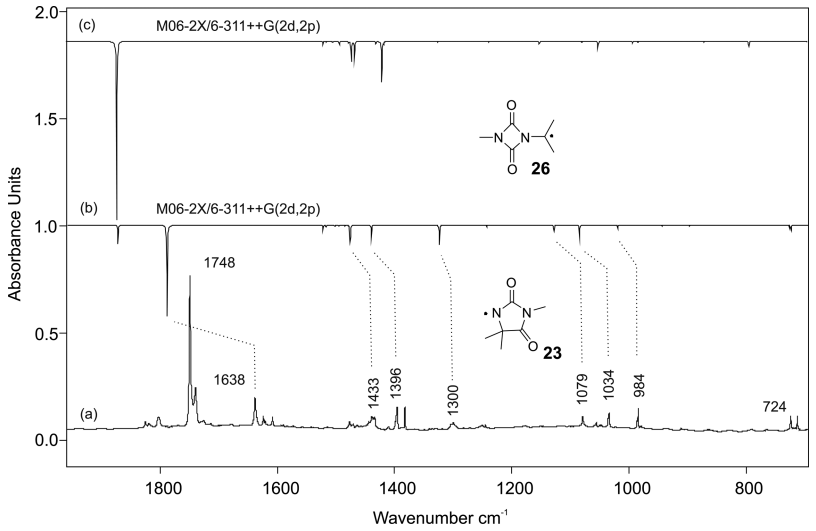

Figure 3. IR spectra showing the products of the FVP of **1** in argon with subsequent trapping in an argon matrix at 10 K: (a) Spectrum obtained after FVP at 700 °C; (b) Spectrum of **23** computed at M06-2X/6-311++G(2d,2p); (c) Spectrum of **26** computed at M06-2X/6-311++G(2d,2p).

of 42.7 kcal mol^{-1}, respectively (M06-2X/6-311++G(2d,2p), $\Delta H_0^{\ddagger}$). However, radical **23** was not observed in our matrix isolation experiments *under photochemical conditions* and we turned our attention to the thermal generation of **23**.

Gratifyingly, radical **23** can be generated by flash vacuum pyrolysis (FVP) of **1** at 700 °C with subsequent trapping of the products in solid argon at 10 K (Figure 3a). The second equally prominent product formed under these conditions is radical **26**, obtained from **23** by rearrangement via **TS3** (Figure 3) in the gas phase. The computed spectrum of **23** reproduces the experimental spectrum obtained after FVP experiments well. The most intense band due to the C═O stretch was observed at 1635 cm^{-1}, which is in good agreement with the unscaled computed value (1788 cm^{-1}). With the aid of the computations, the additional intense IR bands of medium intensity at 1433, 1396, 1300, 1079, 1034, and 984 cm^{-1} could be assigned to the radical **23** (Table S2). In addition, the strongest absorption at 1748 cm^{-1} is attributed to the C═O stretching vibration in **26**, which is in agreement with its computed IR spectrum (1871 cm^{-1}, Figure 3c). Moreover, UV irradiation (λ = 366 nm) of the matrix containing **23** results in the complete disappearance of all its bands and the simultaneous appearance of a new set of bands in the region 2350−2250 cm^{-1} indicating complete destruction of the five-membered ring.

Figure 4 shows the matrix isolated UV/vis absorption spectrum of **23** recorded in the 250−800 nm range. The spectrum reveals a strong absorption band located at λ_{max} = 374 nm. The absorption band of **23** observed experimentally is in good agreement with the computed (TD-M06-2X/6-311++G(2d,2p) value at λ_{max} = 393 nm (f = 0.0234). Upon photolysis using 312 nm light, the broad absorption at 373 nm disappeared.

According to UM06-2X/6-311++G(2d,2p) computations, radical **23** displays a C_s point group with a $^2A''$ electronic ground state. This formally corresponds to the odd electron being localized in the nitrogen p orbital perpendicular to the plane, i.e., in conjugation with the π-system. However, a hypothetical isodesmic reaction of the 1-IMTH radical with ammonia at 298.15 K (below) gives a thermoneutral reaction enthalpy (ΔH_{298}) at (U)M06-2X/6-311++G(2d,2p) of only 0.1 kcal mol^{-1}. The stabilization of **23** apparently derives through hyperconjugative interactions of the unpaired spin with adjacent C−C bonds, which compensates for the potentially destabilizing effect of the adjacent carbonyl group.

In summary, we established a novel facile and efficient method for the synthesis of iodoalkanes via direct C−H bond iodination with the new iodoamide **1**. While other N−I amides proved inefficient in this process, this iodination fills the "missing link" in

DOI: 10.1021/acs.joc.7b00557
J. Org. Chem. 2017, 82, 7093−7100

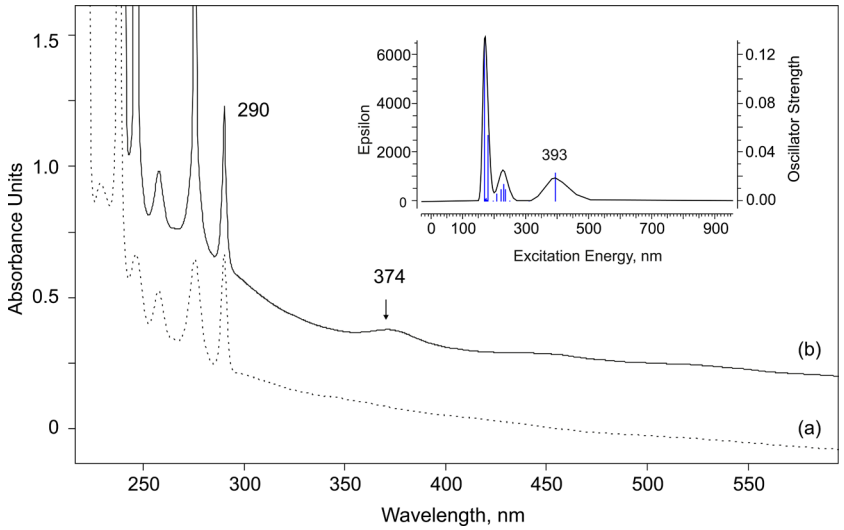

Figure 4. (a) UV/vis spectrum of **1** in an argon matrix at 10 K. (b) UV/vis spectrum obtained after FVP at 700 °C, indicative of radical **23**. Inset: TD-M06-2X/6-311+G(2d,2p) computed UV/vis spectrum of **23**.

C−H halogenations utilizing N−Hal compounds. A substantial advantage of this approach is the facile preparation of the new iodination reagent, its solubility in nonpolar solvents, and its thermal stability. Our mechanistic studies led to the isolation and first IR- and UV-spectroscopic characterization of the elusive N-radical derived from **1**, which represents the key species of this process.

EXPERIMENTAL SECTION

General Information. *Reagents.* All reagents and solvents were purchased from Sigma-Aldrich a part of Merck, Alfa Aesar, and Acros Organics unless specified otherwise and used without further purification.

Techniques. All reactions were performed under a nitrogen atmosphere. Yields of isolated product refer to products with more than 95% purity by ^{1}H NMR. Flash column chromatography was performed employing 63−200 μm silica gel 60 according to standard techniques.[33]

Analytical Methods. GC analyses were performed on a Shimadzu GC-2010 gas chromatography instrument with flame ionization detector (FID) using a 30 m × 0.25 mm Quadrex capillary column with methyl 5% phenyl silicone stationary phase, 0.25 μm film thickness. For TLC analysis, Merck precoated TLC plates (silica gel 60 F-254 on glass plates, 0.25 mm) were used. NMR spectra were recorded on a Bruker AV-400 (^{1}H/^{13}C/^{19}F at 400/100/376 MHz). For ^{1}H and ^{13}C NMR, a residual solvent peak was used as an internal standard. For ^{19}F NMR spectra, the signal of C_6F_6 (δ −164.9 ppm) was used as an internal standard.

Matrix Apparatus Design. For the matrix isolation studies, we used an APD Cryogenics HC-2 cryostat with a closed-cycle refrigerator system, equipped with an inner CsI window for IR measurements. Spectra were recorded with a Bruker IFS 55 FT-IR spectrometer with a spectral range of 4500−400 cm^{-1} and a resolution of 0.7 cm^{-1}, and UV/vis spectra were recorded with a JASCO V-670 spectrophotometer. For the combination of high-vacuum flash pyrolysis with matrix isolation, we employed a small, home-built, water-cooled oven, which was directly connected to the vacuum shroud of the cryostat. The pyrolysis zone consisted of an empty quartz tube with an inner diameter of 8 mm, which was resistively heated over a length of 50 mm by a coaxial wire. The temperature was monitored with a NiCr−Ni thermocouple. 1-Iodo-3,5,5-trimethylhydantoin (1-ITMH, **1**) was evaporated (60 °C) from a storage bulb into the quartz pyrolysis tube. At a distance of approximately 50 mm, all pyrolysis products were co-condensed with a large excess of argon (typically 60−120 mbar from a 2000 mL storage bulb) on the surface of the matrix window at 11 K. Several experiments with pyrolysis temperatures ranging from 600 to 960 °C were performed in order to determine the optimal pyrolysis conditions. A high-pressure mercury lamp (HBO 200, Osram) with a monochromator (Bausch & Lomb) was used for irradiation.

Computations. All geometries were optimized and characterized as minima or transition structures by means of analytical harmonic vibrational frequency computations at the M06-2X/6-311++G(2d,2p) level of theory (for more details, refer to the Supporting Information).[34−37] All computations were performed with the Gaussian09 program.[38]

Preparation of N-Iodoamides:[18] *1-Iodo-3,5,5-trimethylhydantoin (1-ITMH, **1**).* A mixture of 3,5,5-trimethylhydantoin (1.0 g, 7 mmol), $PhI(OAc)_2$ (1.36 g, 4.22 mmol), I_2 (1.17 g, 4.57 mmol), and cyclohexane (20 mL) was stirred at rt for 40 h and then cooled to 0 °C, and stirring continued for an additional hour. The precipitated solid was filtered, washed on the filter with cold cyclohexane, and dried in vacuo to give 1.64 g (88%) of crystalline 1-ITMH; mp 198−199 °C (dec); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.07 (s, 3H, CH_3), 1.24 (s, 6H, 2 CH_3) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.1, 156.1, 65.5, 26.4, 24.6 ppm; HRMS (ESI-TOF) m/z: $(M + H)^+$ calcd for $C_6H_{10}N_2O_2I$ 268.9787, found 268.9773.

*3-Iodo-1,5,5-trimethylhydantoin (3-ITMH, **4**).* A mixture of 1,5,5-trimethylhydantoin (1.0 g, 7.0 mmol), $PhI(OAc)_2$ (1.4 g, 4.2 mmol), I_2 (1.2 g, 4.6 mmol), and MeCN (10 mL) was stirred at rt for 5 h and then concentrated in vacuo. CCl_4 (10 mL) was added to the residue, and the obtained mixture was stirred for 15 min at rt and 1 h at 0 to 5 °C. The precipitated solid was filtered, washed on the filter with cold CCl_4, and dried in vacuo to give 1.84 g (98%) of crystalline 3-ITMH; mp 213−4 °C (dec); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.95 (s, 3H), 1.39 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.6, 154.4, 64.2, 26.0, 22.9 ppm; HRMS (ESI-TOF) m/z: $(M + H)^+$ calcd for $C_6H_{10}N_2O_2I$ 268.9787, found 268.9795.

*N-Iodophthalimide (**7**).* A mixture of phthalimide (1.00 g, 6.8 mmol), $PhI(OAc)_2$ (1.31 g, 4.1 mmol), I_2 (1.12 g, 4.4 mmol), and MeCN (25 mL) was stirred for 6 h, at rt, and concentrated in vacuo. CCl_4 (25 mL) was added to the residue, and the obtained mixture was stirred for 15 min at rt and 1 h at 0 to 5 °C. The precipitated solid was filtered, washed on the filter with cold CCl_4, and dried in vacuo to give 1.80 g (97%) of *N*-iodophthalimide as an off-white powder. ^{1}H NMR (DMSO-d_6, 100 MHz) δ 7.82−7.72 (m, 4H) ppm; ^{13}C NMR (DMSO-d_6, 100 MHz) δ 170.7, 133.8, 132.8, 122.8 ppm.

*N-Iodo-4-nitrophthalimide (**8**).* A mixture of 4-nitrophthalimide (0.40 g, 2.08 mmol), $PhI(OAc)_2$ (0.40 g, 1.25 mmol), I_2 (0.34 g, 1.35 mmol), and MeCN (10 mL) was stirred (4 h) at rt and concentrated in vacuo. CCl_4 (10 mL) was added to the residue, and the obtained mixture was stirred for 15 min at rt and 1 h at 0 to 5 °C. The precipitated solid was filtered off, washed on the filter with cold CCl_4, and dried in vacuo to give 0.63 g (100%) of *N*-iodo-4-nitrophthalimide. ^{1}H NMR (CD_3CN,

DOI: 10.1021/acs.joc.7b00557
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400 MHz) δ 8.51 (d, J = 8.8 Hz, 1H), 8.47 (s, 1H) 7.97 (d, J = 8.6 Hz, 1H) ppm; ^{13}C NMR (CD_3CN, 100 MHz) δ 169.3, 168.9, 152.3, 138.4, 135.1, 130.0, 125.3, 119.0 ppm; HRMS (APCI-QTOF) m/z: $(M + H_2O)^+$ calcd for $C_8H_5IN_2O_5$ 335.9243, found 335.92.40.

Preparation of 3,5,5-Trimethylhydantoin. A mixture of 5,5-dimethylhydantoin (12.8 g, 100 mmol), MeI (21.3 g, 150 mmol), K_2CO_3 (20.7 g, 150 mmol), and acetone (200 mL) was stirred for 16 h, at rt, and concentrated in vacuo. An aqueous solution of the residue was extracted with CH_2Cl_2 (3 × 50 mL). Combined organic extracts were washed with water (50 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to give 11.8 g (83%) of 3,5,5-trimethylhydantoin. ^{1}H NMR δ ($CDCl_3$, 400 MHz) 6.49 (br s, 1H), 3.00 (s, 3H, CH_3), 1.43 (s, 6H, 2 CH_3) ppm. ^{13}C NMR δ ($CDCl_3$, 100 MHz) 177.6, 157.0, 59.0, 25.1, 24.7 ppm.

General Procedure for Iodination of Alkanes. 1-Iodo-3,5,5-trimethylhydantoin (1-ITMH) (0.125g, 0.466 mmol) and 5 mL of alkane were stirred at 100 °C under 3 W white LED lamp irradiation. Then the reaction mixture was washed with 1 M aq Na_2SO_3, dried over Na_2SO_4, and filtered. The solvent was removed by distillation, and the residue was purified by chromatography on silica gel (eluent: pentane). The experimental results are presented in Table1.

*Iodocyclohexane (**2a**).*[9] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.35 (m, 1H), 2.13 (m, 2H), 1.93−1.99 (m, 2H), 1.60−1.70 (m, 3H), 1.30−1.40 (m, 3H) ppm; (^{13}C NMR $CDCl_3$, 100 MHz) δ 39.7, 32.8, 27.4, 25.3 ppm; HRMS (APCI-QTOF) m/z: $(M)^+$ calcd for $C_6H_{11}I$ 209.9906, found 209.9900.

*Iodocycloheptane (**10a**):*[9] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.48 (m, 1H), 2.24−2.30 (m, 2H), 2.10−2.20 (m, 2H), 1.52−1.64 (m, 6H), 1.38−1.50 (m, 2H) ppm; (^{13}C NMR $CDCl_3$, 100 MHz) δ 41.9, 36.0, 27.3, 27.0 ppm; HRMS (ESI-TOF) m/z: $(M - H)^-$ calcd for $C_7H_{12}I$ 222.9984, found 222.9982.

*Iodocyclooctane (**11a**):*[39] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.57 (m, 1H), 2.20−2.23 (m, 4H), 1.40−1.70 (m, 10H) ppm; (^{13}C NMR $CDCl_3$, 100 MHz) δ 38.2, 37.9, 27.5, 26.7, 25.2 ppm; HRMS (ESI-TOF) m/z: $(M + H)^+$ 239.0267, $C_8H_{16}I$ calcd mass 239.0297.

*1,2-Dichloro-1-iodoethane (**14a**).* ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.71 (dd, J = 8.3, 4.8 Hz, 1H), 4.16 (dd, J = 12.0, 4.8 Hz, 1H), 4.03 (dd, J = 12.0, 8.3 Hz, 1H) ppm; (^{13}C NMR $CDCl_3$, 100 MHz) δ 53.0, 25.7 ppm; HRMS (ESI-TOF) m/z: $(M)^+$ calcd for $C_2H_3Cl_2I$ 223.8650, found 223.8650.

General Procedure for Iodination of Methylarenes. A mixture of methylarene $ArCH_3$ (1 mL), benzene (4 mL), and 1-ITMH (0.10 g, 0.73 mmol) was stirred at 120 °C under 3 W white LED lamp irradiation over 3 h. The reaction mixture was analyzed by GC. The experimental results are presented in Table 2.

General Procedure for Synthesis of Benzyl Benzoate Derivatives (ArCH_2OBz). A mixture of methylarene $ArCH_3$ (7 mL), benzene (28 mL), and 1-ITMH (0.7 g, 2.61 mmol) was stirred and heated at 120 °C, under 3 W white LED lamp irradiation. After 3 h the reaction was cooled to the room temperature and tetrabutylammonium benzoate [NBu_4]OBz (0.95 g, 2.61 mmol) was added. After 0.5 h the mixture was concentrated under reduced pressure, and desired compound was purified by silica gel chromatography (eluent: gradient CH_2Cl_2/hexane). The experimental results are presented in Table 2.

*Benzyl Benzoate (**16b**):*[40] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.07 (m, 2H), 7.56 (m, 1H), 7.49−7.32 (m, 7H), 5.37 (s, 2H); (^{13}C NMR $CDCl_3$, 100 MHz) δ 166.4, 136.1, 133.0, 130.2, 129.7, 128.6, 128.4, 128.3, 128.2, 66.7 ppm.

*2-Methylbenzyl Benzoate (**17b**):*[41] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.07 (m, 2H), 7.56 (m, 1H), 7.43 (m, 3H), 7.2−7.3 (m, 4H), 5.38 (s, 2H), 2.42 (s, 3H); (^{13}C NMR $CDCl_3$, 100 MHz) δ 166.1, 136.9, 133.9, 132.9, 130.3, 130.1, 129.5, 129.1, 128.4, 128.3, 125.9, 65.0, 18.8 ppm.

*3-Methylbenzyl Benzoate (**18b**):*[41] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.1 (m, 2H), 7.56 (m, 1H), 7.44 (m, 2H), 7.28 (m, 3H), 7.17 (m, 1H), 5.34 (s, 2H), 2.38 (s, 3H); (^{13}C NMR $CDCl_3$, 100 MHz) δ 166.2, 138.1, 135.9, 132.9, 130.1, 129.6, 128.9, 128.4, 128.3, 125.2, 66.6, 21.3 ppm.

*4-Methylbenzyl Benzoate (**19b**):*[41] ^{1}H NMR δ ($CDCl_3$, 400 MHz) 8.24 (m, 2H), 7.63 (m, 1H), 7.55−7.47 (m, 4H), 7.32 (m, 2H), 5.48 (s, 2H), 2.49 (s, 3H); (^{13}C NMR $CDCl_3$, 100 MHz) δ 166.2, 137.8, 133.0, 132.8, 130.2, 129.6, 129.1, 128.23, 128.20, 66.5, 21.1 ppm.

*3,5-Dimethylbenzyl Benzoate (**20b**):*[42] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.1 (m, 2H), 7.56 (m, 1H), 7.43 (m, 2H), 7.1 (s, 2H), 6.98 (s, 1H), 5.3 (s, 2H), 2.4 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.4, 138.2, 135.9, 133.0, 129.9, 129.7, 128.3, 126.1, 66.8, 21.3 ppm.

*4-Fluorobenzyl Benzoate (**21b**):*[41] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.06 (m, 2H), 7.57 (m, 1H), 7.44 (m, 4H), 7.07 (m, 2H), 5.32 (s, 2H); (^{13}C NMR $CDCl_3$, 100 MHz) δ 166.2, 162.6 (d, J = 246.8 Hz), 133.1, 131.9 (d, J = 3.3 Hz), 130.2 (d, J = 8.4 Hz), 130.0, 129.6, 128.4, 115.4 (d, J = 21.7 Hz), 65.9; ^{19}F ($CDCl_3$, 376 MHz) δ −116.6 ppm.

*4-Chlorobenzyl Benzoate (**22b**):*[41] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05 (m, 2H), 7.58 (m, 1H), 7.47 (m, 2H), 7.43−7.35 (m, 4H), 5.32 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.3, 134.6, 134.1, 133.2, 129.9, 129.7, 129.6, 128.8, 128.4, 65.8 ppm.

Preparation of GC Standards. Preparation of Alkyl Iodides from Alcohols Was Performed via a Known Procedure:[39] *2-Iodohexane (**13c**).*[9] Prepared from 2-hexanol in 64% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.15 (m, 1H), 1.88 (d, J = 6.9 Hz, 3H), 1.76−1.85 (m, 1H), 1.54−1.62 (m, 1H), 1.23−1.46 (m, 4H), 0.88 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 42.7, 31.9, 30.5, 29.0, 21.9, 14.0 ppm.

*3-Iodohexane (**13b**).*[9] Prepared from 3-hexanol in 67% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.06 (m, 1H), 1.70−1.90 (m, 3H), 1.47−1.66 (m, 2H), 1.30−1.43 (m, 1H), 0.98 (t, J = 7.2 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 42.4, 42.0, 33.8, 22.8, 14.2, 13.3 ppm.

*1-Chloro-2-iodobutane (**15c**).* Prepared from 1-chlorobutan-2-ol in 37% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.15−4.24 (m, 1H), 4.03 (dd, J = 11.1, 4.5 Hz, 1H), 3.80 (dd, J = 11.1, 10.3 Hz, 1H), 1.95−2.10 (m, 1H), 1.70−1.84 (m, 1H), 1.04 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 49.5, 35.4, 29.7, 13.3 ppm; HRMS (ESI-TOF) m/z: $(M - H)^-$ calcd for C_4H_7ICl 216.9281, found 216.9269.

*1-Chloro-3-iodobutane (**15b**).* Prepared from 4-chlorobutan-2-ol in 61% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.30−4.40 (m, 1H), 3.55−3.75 (m, 2H), 2.20−2.30 (m, 1H), 1.90−2.00 (m, 2H), 1.97 (d, J = 6.9 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 44.9, 44.8, 28.8, 25.3 ppm.

Preparation of Alkyl Iodides from Carboxylic Acids Was Performed by Known Procedure:[22] *1-Chloro-1-iodobutane (**15d**).* Prepared from 2-chloropentanoic acid in 60% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.77 (t, J = 6.3 Hz, 1H), 2.67 (m, 2H), 1.56 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 48.6, 30.4, 22.2, 12.7 ppm; HRMS (ESI-TOF) m/z: $(M - H)^-$ calcd for C_4H_7ICl 216.9281, found 216.9269.

*Mixture of 2-exo- (63%) and 2-endo- (37%) Iodonorbornanes (**12a, 12b**).* Prepared from 2-*endo*-norbornanecarboxylic acid in 30% yield. 2-*exo*-Iodonorbornane:[43] ^{1}H NMR ($CDCl_3$, 400 MHz) (*diagnostic signal*) δ 3.97 ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 48.1, 45.3, 38.1, 36.44, 30.5, 28.9, 28.5 ppm. 2-*endo*-Iodonorbornane:[43] ^{1}H NMR ($CDCl_3$, 400 MHz) (*diagnostic signal*) δ 4.20 ppm. ^{13}C NMR ($CDCl_3$, 100 MHz) δ 44.9, 43.4, 37.0, 36.37, 32.6, 29.7, 28.6 ppm.

Preparation of Benzyl Iodides from Benzyl Chlorides or Bromides Was Performed by Known Procedure:[44] *2-Methylbenzyl Iodide (**17a**).*[7] Prepared from 2-methylbenzyl chloride in 81% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29 (m, 1H), 7.21−7.11 (m, 3H), 4.45 (s, 2H), 2.34 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 136.9, 136.6, 130.9, 129.4, 128.4, 126.5, 19.0, 5.3 ppm.

*3-Methylbenzyl Iodide (**18a**).*[7] Prepared from 3-methylbenzyl bromide in 76% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.19−7.17 (m, 3H), 7.05 (m, 1H), 4.43 (s, 2H), 2.33 (s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.2, 138.5, 129.5, 128.79, 128.78, 125.9, 21.4, 6.1 ppm.

*4-Methylbenzyl Iodide (**19a**).*[7] Prepared from 4-methylbenzyl chloride with 80% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.16 (d, J = 8.0 Hz, 2H), 7.00 (d, J = 7.9 Hz, 2H), 4.34 (s, 2H), 2.2 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.8, 136.4, 129.6, 128.7, 21.3, 6.3 ppm.

*4-Chlorobenzyl Iodide (**22a**).*[7] Prepared from 4-chlorobenzyl chloride acid in 85% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.22 (d, J = 8.5 Hz, 2H), 7.18 (d, J = 8.5 Hz, 2H), 4.33 (s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.0, 133.7, 130.2, 129.1, 4.3 ppm.

*4-Fluorobenzyl Iodide (**21a**).*[45] Prepared from 4-fluorobenzyl chloride in 92% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35 (dd, J = 8.6, 5.3 Hz, 2H), 6.98 (dd, J = 8.6, 8.6 Hz, 2H), 4.44 (s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.2 (d, J = 248 Hz), 135.3 (d, J = 3 Hz),

DOI: 10.1021/acs.joc.7b00557
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130.6 (d, J = 8 Hz), 115.9 (d, J = 22 Hz), 4.7 ppm; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −116.7 ppm; HRMS (APSI-QTOF) m/z: $(M + K)^-$ calcd for C_7H_5FKI 273.9057, found 273.9039.

Preparation of 4-Chlorobutan-2-ol. $SOCl_2$ (0.43 mL, 6.0 mmol) was added dropwise to a stirred mixture of 4-hydroxybutan-2-one (0.50 g, 5.7 mmol), DMF (one drop), and CH_2Cl_2 (5 mL). The obtained mixture was stirred overnight at rt and then treated with saturated aqueous solution of NH_4Cl. The organic fraction was dried with Na_2SO_4 and concentrated in vacuo. $NaBH_4$ (0.43 g, 11.4 mmol) was added by small portions to a stirred solution of the residue in MeOH (5 mL) at 0 °C, and the mixture was stirred (1 h) at rt. Water was added to the stirred mixture, and the product was extracted with Et_2O. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by chromatography on silica gel (eluent: gradient CH_2Cl_2/pentane) to give 0.45 g (73% yield) of 4-chlorobutan-2-ol.

4-Chlorobutan-2-ol.[46] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.05 (m, 1H), 3.67 (m, 2H), 1.88 (m, 2H), 1.24 (d, J = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 64.8, 41.8, 41.3, 23.3 ppm.

Preparation of 1-Chlorobutan-2-ol. The reaction was performed via a known procedure[47] from 1,2-epoxybutane giving a 20% of corresponding 1-chlorobutan-2-ol.

1-Chlorobutan-2-ol.[48] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.68 (m, 1H), 3.58 (dd, J = 11.1, 3.5 Hz, 1H), 3.44 (dd, J = 11.1, 6.8 Hz, 1H), 2.73 (s, 1H), 1.53 (m, 2H), 0.93 (t, J = 7.5 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 72.75, 49.9, 27.2, 9.9 ppm.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00557.

Spectra of new compounds (^{1}H, ^{13}C, and ^{19}F NMR), tabulated geometric structure data and electronic energies and reaction optimization conditions for *p*-xylene (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was supported by a grant from the German−Israeli Project Cooperation (DIP, Schr 597/19-1) between M.G. and P.R.S.

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DOI: 10.1021/acs.joc.7b00557
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