catalysts

MDPI

Article

Direct Cross-Coupling of Alcohols with *O*-Nucleophiles Mediated by *N*-Iodosuccinimide as a Precatalyst under Mild Reaction Conditions

Njomza Ajvazi [1,2,*] and Stojan Stavber [1,3]

[1] Jožef Stefan International Postgraduate School, Jamova 39, 1000 Ljubljana, Slovenia; stojan.stavber@ijs.si
[2] Alma Mater Europaea Campus College "REZONANCA", 10000 Pristina, Kosovo
[3] Jožef Stefan Institute, Jamova 39, 1000 Ljubljana, Slovenia
* Correspondence: njomza.ajvazi@rezonanca-rks.com; Tel.: +383-44-258-553

Abstract: We report *N*-iodosuccinimide as the most efficient and selective precatalyst among the *N*-halosuccinimides for dehydrative *O*-alkylation reactions between various alcohols under high-substrate concentration reaction conditions. The protocol is non-metal, one-pot, selective, and easily scalable, with excellent yields; enhancing the green chemical profiles of these transformations.

Keywords: alcohols; *N*-iodosuccinimide; cross-coupling; etherification; green chemistry

Citation: Ajvazi, N.; Stavber, S. Direct Cross-Coupling of Alcohols with *O*-Nucleophiles Mediated by *N*-Iodosuccinimide as a Precatalyst under Mild Reaction Conditions. *Catalysts* **2021**, *11*, 858. https://doi.org/10.3390/catal11070858

Academic Editors: Monica Trif, Anis Hamzah Fakeeha, Alexandru Rusu and Santosh Kumar

Received: 11 June 2021
Accepted: 14 July 2021
Published: 17 July 2021

1. Introduction

The C–O bond construction is one of the significant implements in organic synthesis since it provides access to the production of cosmetics, fragrances, pharmaceuticals, and dyestuffs [1]. Since alcohols are inexpensive and could effectively serve as alkylating agents, their direct cross-coupling with *O*-nucleophiles could be a very desirable strategy for avoiding an additional synthetic step for coupling reactions.

Activation of alcohols for nucleophilic substitution using a substoichiometric amount of different catalysts, such as metal ions: [RuCp(o-EtOdppe)](OTs), $CuBr_2$, $NaAuCl_4$, Brønsted, or Lewis acids (hypervalent [bis(trifluoroacetoxy)iodo]benzene catalyst has been found to function as a Lewis acid) or other supporters such as organohalides or molecular iodine in the presence of solvents has been touched on by some reviews [2–10] and recently developed reports [11–14]. However, the requirement for toxic and costly reagents, environmentally inappropriate solvents, multiple synthetic steps, and high temperatures make such a synthetic protocol less desirable from a sustainability perspective. Therefore, these disadvantages have challenged chemists to invent and develop novel methods for direct dehydrative C–O coupling, using alcohols as electrophiles under environmentally benign conditions.

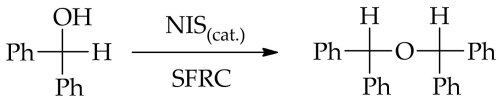
We previously reported the role of *N*-halosuccinimides (NXSs) (chloro, bromo, or iodo) as the mediator for the direct conversion of a hydroxyl group, forming new C–C or C-heteroatom bonds. *N*-iodosuccinimide (NIS) was the most efficient and selective mediator among the NXSs [15].

With our continuous research work on improving and developing greener protocols [16–19], we now report the expanding role of NIS as a commercially available, metal-free, and easy-to-handle precatalyst for direct dehydrative *O*-alkylation reactions between various alcohols under high-substrate concentration reaction conditions (HCRC), and leading to a practical, efficient, selective, and easily scalable method.

A high-concentration reaction condition in our case is defined as a concentration where less than 0.2 mL of solvent/mmol of substrate and reagent was used.

2. Results and Discussion

We began our investigations by using diphenylmethanol **1** with NIS as the precatalyst under solvent-free reaction conditions (SFRC), where the dimerization process was observed (Scheme 1), resulting in the formation of symmetric ether **2** (entry 1, Table 1). For the transformation of diphenylmethanol **1** without NIS, in the presence of MeOH **3** under HCRC, no conversion of the starting material was observed [15].



1 **2**

Scheme 1. The conversion of diphenylmethanol **1** mediated by NIS under SFRC.

Table 1. The effect of the loading of NIS on the conversion of diphenylmethanol **1** under SFRC [a].

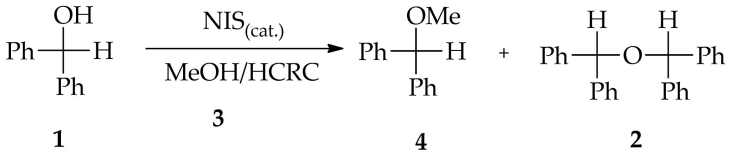
Entry	NIS (mol %)	Conv. [b] (%) of 1	Yield [c] (%) 2
1	0.5	79	78 [d]
2	1	90	89 [d]
3	2	100	100

[a] Reaction conditions: diphenylmethanol **1** (0.5 mmol), 70–75 °C, 3.5 h. [b,c] Determined by ^{1}H NMR spectroscopy. [d] Benzophenone 1%.

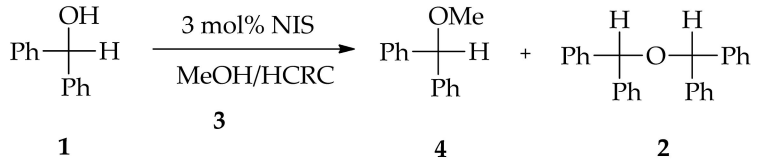
The effect of NIS loading for the reaction of diphenylmethanol **1** in the absence of a nucleophile source under SFRC was examined, and the results are presented in Table 1, and in Supplementary Materials To increase the yield of the product, different concentrations of the precatalyst were used. Employing 0.5 mol% of the precatalyst, the formation of the corresponding product **2** with good yield was observed, accompanied by a trace of oxidized alcohol (entry 1). By increasing the precatalyst loading to 1 mol%, we observed the high conversion of the starting material **1** into the corresponding product **2**, accompanied by a trace of oxidized alcohol (entry 2). We found that for the quantitative conversion of the starting material **1** to the dimeric ether **2**, 2 mol% of the precatalyst was effective (entry 3).

Furthermore, we continued our investigations by heating diphenylmethanol **1** with methanol (MeOH) **3** mediated by NIS under HCRC, affording the corresponding ether **4** in excellent yield [15]. (Scheme 1).

In searching for the optimal reaction conditions, different parameters, such as loading of the NIS as the mediator and temperature for the reaction of diphenylmethanol **1** with MeOH **3** under HCRC (Schemes 2 and 3), were first examined, and the results are presented in the Tables 2 and 3 and in Supplementary Materials. To determine the effectiveness of the NIS as the mediator, different concentrations of the precatalyst were employed. In the reaction of diphenylmethanol **1** with MeOH **3** using 0.5 mol% of the precatalyst, the formation of the corresponding product **4** in good yield and accompanied by a small amount of symmetric ether **2** was observed (entry 1). By increasing the precatalyst loading to 1 mol%, quantitative conversion of the starting material **1** into the corresponding product **4** was noticed, accompanied by a small amount of dimeric ether **2** (entry 2). Similar results were achieved when the precatalyst loading was increased up to 2 mol% (entry 3). An improvement of 100% yield, without forming the dimeric ether was attained by increasing the precatalyst loading up to 3 mol% (entry 4).



Scheme 2. The conversion of diphenylmethanol **1** in the presence of MeOH **3** mediated by NIS under HCRC.



Scheme 3. The conversion of diphenylmethanol **1** in the presence of MeOH **3** mediated by NIS under HCRC.

Table 2. The effect of the loading of NIS on the conversion of diphenylmethanol **1** with MeOH **3** under HCRC [a].

Entry	NIS (mol %)	Conv. [b] (%) of 1	Relative Distribution [c] (%)	
			4	**2**
1	0.5	83	78	5
2	1	100	94	6
3	2	100	95	5
4	3	100	100	/

[a] Reaction conditions: diphenylmethanol **1** (0.5 mmol), MeOH **3** (1 mmol), 70–75 °C, 6 h. [b] Determined by ^{1}H NMR spectroscopy. [c] Yields calculated relative to alcohol **1**.

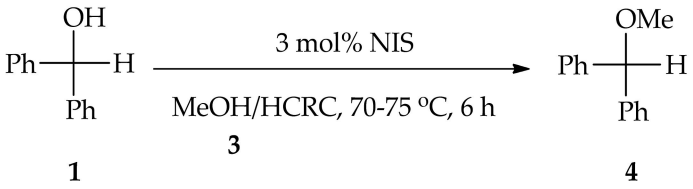
Table 3. The catalytic effect of NIS on the conversion of diphenylmethanol **1** with MeOH **3** based on the temperature under HCRC [a].

Entry	T(°C)	Conv. [b] (%) of 1	Relative Distribution [c] (%)	
			4	**2**
1	rt	/	/	/
2	40–45	26	23	3
3	50–55	61	56	5
4	60–65	86	81	3 [d]
5	70–75	100	100	/

[a] Reaction conditions: diphenylmethanol **1** (0.5 mmol), MeOH 3 (1 mmol), 6 h. [b] Determined by ^{1}H NMR spectroscopy. [c] Yields calculated relative to alcohol **1**. [d] Benzophenone 2%. rt—room temperature.

The effect of temperature on the course of the reaction was examined by the reaction of diphenylmethanol **1** with MeOH **3** mediated by NIS under HCRC. When the reaction was carried out at room temperature, no transformation took place (entry 1). When the reaction was performed at 40–45 °C, the desired product **4** in low yield and a small amount of dimeric ether **2** were obtained (entry 2). An increase of reaction temperature up to 50–55 °C provided the corresponding product **4** in moderate yield, accompanied by a small amount of symmetric ether **2** (entry 3). Further optimization revealed that the reaction could be performed smoothly by raising the temperature to 60–65 °C. An improvement by 100% yield without forming the symmetric ether was attained by increasing the reaction temperature to 70–75 °C.

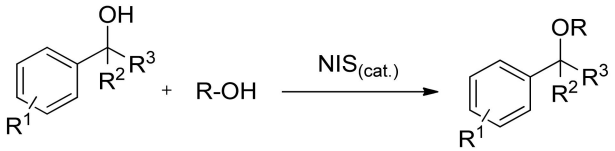
Screening on precatalyst loading and reaction temperature showed that 3 mol% NIS, 70–75 °C, and 6 h were the best conditions ensuring complete conversion of **1** into the corresponding ether **4** (Scheme 4).



1 **4**

Scheme 4. Optimal reaction conditions for the conversion of diphenylmethanol **1** into the (methoxymethylene)dibenzene **4** mediated by NIS under HCRC.

Encouraged by these promising results, we applied the obtained optimal reaction conditions to direct dehydrative *O*-alkylation reactions between different alcohols mediated by NIS under HCRC (Scheme 5), and the results are collected in Table 4.



Scheme 5. Transformation of benzyl and tertiary alkyl alcohols with alkyl alcohols mediated by NIS under SFRC, under HCRC or in solution.

Table 4. Transformation of benzyl and tertiary alkyl alcohols with alkyl alcohols mediated by NIS under SFRC, under HCRC or in solution [a].

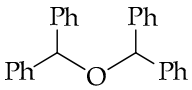
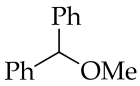
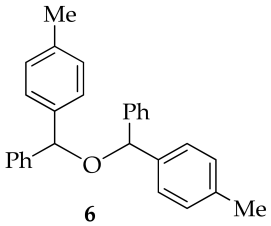
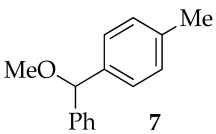
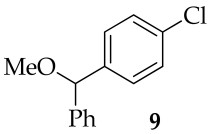
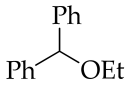
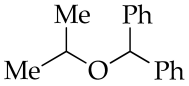
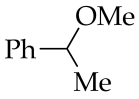
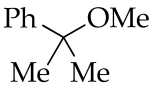
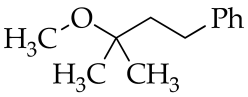
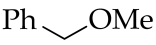
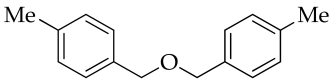
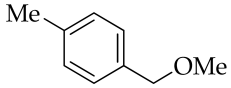
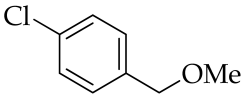
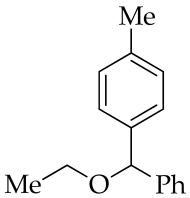
Entry	R^1, R^2, R^3	R–OH, Time (h)	Product	Conversion [b] (%) (Yield [c] (%))
1 [g]	$R^1 = R^2 = H$, $R^3 = Ph$ **1**	/ (3.5)	 **2**	100 "(99) [15]"
2	$R^1 = R^2 = H$, $R^3 = Ph$ **1**	MeOH **3** (6)	 **4**	100
3 [g]	$R^1 = Me$, $R^2 = H$, $R^3 = Ph$ **5**	/ (4.5)	 **6**	100 (99)
4	$R^1 = Me$, $R^2 = H$, $R^3 = Ph$ **5**	MeOH **3** (6)	 **7**	100 [d] (90)
5	$R^1 = Cl$, $R^2 = H$, $R^3 = Ph$ **8**	MeOH **3** (24)	 **9**	100 (99)

Table 4. *Cont.*

Entry	R^1, R^2, R^3	R–OH, Time (h)	Product	Conversion [b] (%) (Yield [c] (%))
6	$R^1 = R^2 = H$, $R^3 = Ph$ **1**	EtOH **10** (24)	 **11**	100 [d] (89)
7	$R^1 = R^2 = H$, $R^3 = Ph$ **1**	*i*PrOH **12** (24)	 **13**	100 [d] (88)
8	$R^1 = R^2 = H$, $R^3 = Me$ **14**	MeOH **3** (24)	 **15**	67 [e] "(61) [f] [15]"
9	$R^1 = H$, $R^2 = R^3 = Me$ **16**	MeOH **3** (24)	 **17**	93 "(90) [15]"
10	$C_6H_5(CH_2)_2C(CH_3)_2$ **18**	MeOH **3** (24)	 **19**	74 "(64) [15]"
11	$R^1 = R^2 = R^3 = H$ **20**	MeOH **3** (24)	 **21**	"2 [e] [15]" -
12 [g]	$R^1 = Me$, $R^2 = R^3 = H$ **22**	/ (24)	 **23**	100 (99)
13	$R^1 = Me$, $R^2 = R^3 = H$ **22**	MeOH **3** (24)	 **24**	10 [d]
14	$R^1 = Cl$, $R^2 = R^3 = H$ **25**	MeOH **3** (24)	 **26**	-
15	$R^1 = Me$, $R^2 = H$, $R^3 =$ Ph **5**	TMSOEt **27** (24)	 **28**	100 [e] "(89) [15]"

[a] Reaction conditions: alcohol (0.5 mmol), NIS (2–10 mol %), MeOH, EtOH, *i*PrOH, or TMSOEt (0.55 mmol-1 mL), 50–85 °C, 3.5–24 h. [b] Determined by ^{1}H NMR spectroscopy. [c] Isolated yields. [d] Oxidized alcohol and dimeric ether 4–6%. [e] Oxidized alcohol 2–9%. [f] Specific rotation [α] = +15°. [g] Reactions was performed under SFRC.

Effective transformation with MeOH **3**, mediated by NIS, was observed in the reaction with additional derivatives of diphenylmethanol bearing EDG or EWG on the aromatic rings affording the corresponding products in excellent yields. We checked the reaction of phenyl(*p*-tolyl)methanol **5** with NIS as the mediator, in the absence or in the presence of MeOH, wherein in both cases we established the quantitative formation of the dimeric ether **6** (entry 3, Table 4) or the corresponding ether **7** (entry 4, Table 4). Etherification of (4-chlorophenyl)(phenyl)methanol **8** with MeOH **3**, mediated by NIS under HCRC, provided the corresponding product **9** in excellent yield (entry 5, Table 4).

Furthermore, we performed the reaction of diphenylmethanol **1** catalyzed by NIS, in the presence of EtOH **10**, under HCRC, which efficiently and successfully resulted in the formation of the corresponding ether **11**, accompanied by a small amount of dimeric ether **2** and oxidized alcohol (entry 6, Table 4). The transformation of diphenylmethanol **1** catalyzed by NIS in isopropyl solution (*i*-PrOH) **12**, provided the corresponding ether **13** in high yield, accompanied by a small amount of oxidized alcohol (entry 7, Table 4).

The effective and selective transformation was observed in the reaction with tertiary benzyl and alkyl alcohols. 2-Phenylpropan-2-ol **16** was readily mediated by NIS under HCRC to afford quantitative yields of target ether **17** in methanol solution [15] (entry 9, Table 4). α,α-dimethylbenzenepropanol **18** catalyzed by NIS, in the presence of MeOH **3** under HCRC was successfully converted into their corresponding ether **19** [15] (entry 10, Table 4).

In the case of 1,1-diphenylethanol in the presence of a substoichiometric amount of NIS (0.5 mol% NIS, 70–75 °C, 24 h) under SFRC, 1,1-diphenylethene in the quantitative yield was observed, while in the presence of MeOH, EtOH, and *i*-PrOH increasing the amount of NIS up to 5 mol%, under HCRC, the formation of the corresponding alkene in high yield, accompanied by the formation of benzophenone (12–30%) was observed. We further investigated reactions of primary benzyl alcohols bearing EWG and EDG on the aromatic ring with MeOH under HCRC. In the case of primary unsubstituted benzyl alcohol **20**, in the presence of MeOH, mediated by NIS, and under HCRC, only a trace amount of benzaldehyde was observed [15] (entry 11, Table 4). The transformation of 4-methylbenzyl alcohol **22** catalyzed by NIS in the absence of MeOH, under SFRC, was efficiently and selectively converted into the dimeric ether **23** (entry 12, Table 4). Etherification of 4-methylbenzyl alcohol **22** with MeOH under HCRC or in solution, using NIS as the precatalyst was not efficient (entry 13, Table 4). 4-chlorobenzyl alcohol **25** in the presence of MeOH, mediated by NIS was unable to undergo conversion (entry 14, Table 4).

Furthermore, we performed the reaction of phenyl(*p*-tolyl)methanol **5** with NIS as the mediator in the presence of ethoxytrimethylsilane (TMSOEt) **26** as the nucleophile source, where the ethoxy functional group was introduced efficiently into the organic molecule **27** [15], (entry 15, Table 4).

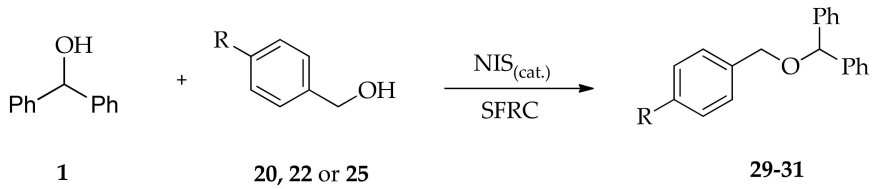
Additionally, to verify the synthetic value of the reported procedure, synthesis of (methoxymethylene)dibenzene **4** was accomplished at 10 mmol scale with high yield.

It was reported that the I–N bond of NIS as a precatalyst was activated by its reaction with the addition of alcohol. Consequently, it seems possible that transient halogen bonding could be necessary for the catalytic activity of NIS. Based on all the presented results, a potential explanation indicates the formation of HOI from the decomposition of NIS as the precatalyst by its reaction with the addition of alcohol [20–23]. The halogen bonding adducts are not the activated species. Instead, halonium (X^+) transfer will generate the intermediate resulting succinimide anion and HOI, promoting the etherification reaction.

HOI decomposes, forming I_2 and HIO_3. Iodine is well known for forming HOI and HI in aqueous reaction media, providing the regeneration of HOI for further activity as a catalyst. It could be seen that the formation of water through the etherification reaction as the only by-product of the reaction could accelerate the reaction. The assumption that NIS was a precatalyst providing HOI, I_2, and protons during the system, which could correspond to nucleophilic substitution acceleration, was indicated to be reasonable [15,18]. To get insight into the precatalyst's thermal stability, thermal gravimetric analysis (TGA)

on the NIS was accomplished. It was observed that degradation of the NIS did not occur at 25–200 °C [15].

To further extend this etherification protocol's scope, we studied the impact of NIS as the precatalyst for direct etherification of diphenylmethanol **1** with primary benzyl alcohols bearing an electron-withdrawing, as well as electron-donating, substituent on the aromatic ring under SFRC (Scheme 6). The results are collected in Table 5. Direct etherification of diphenylmethanol **1** with unsubstituted benzyl alcohol **20** was carried out using NIS as the precatalyst under SFRC, leading to the corresponding ether **29** in high yield. In contrast, a small amount of oxidized alcohol and aldehyde were detected as side products (entry 1, Table 5). In the case of the reaction of diphenylmethanol **1** with 4-methylbenzyl alcohol **22** using NIS as the precatalyst under SFRC, the formation of the corresponding ether **30** in good yield, with a small amount of oxidized alcohol and dimeric ether **2** as side products (entry 2, Table 5), was detected. In the case of the reaction of diphenylmethanol **1** with 4-chlorobenzyl alcohol **25**, mediated by NIS under SFRC, we observed the quantitative conversion of the starting material **1** into the corresponding ether **31**, accompanied by a small amount of oxidized alcohol (entry 3, Table 5).



1 **20, 22** or **25** **29-31**

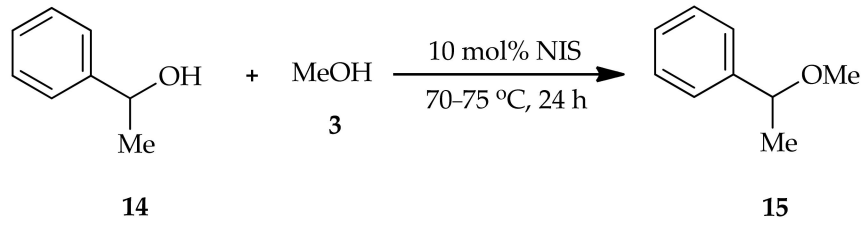
Scheme 6. Direct etherification of diphenylmethanol **1** with primary benzyl alcohols **20**, **22,** and **25**, mediated by NIS under SFRC.

Table 5. Direct etherification of diphenylmethanol **1** with primary benzyl alcohols **20**, **22**, and **25**, mediated by NIS under SFRC [a].

Entry.	R	Conversion. [b] (%) of 1 (Yield [c] (%))
1	H	100 [d] (88)
2	4-Me	96 [e] (73)
3	4-Cl	100 [d] (90)

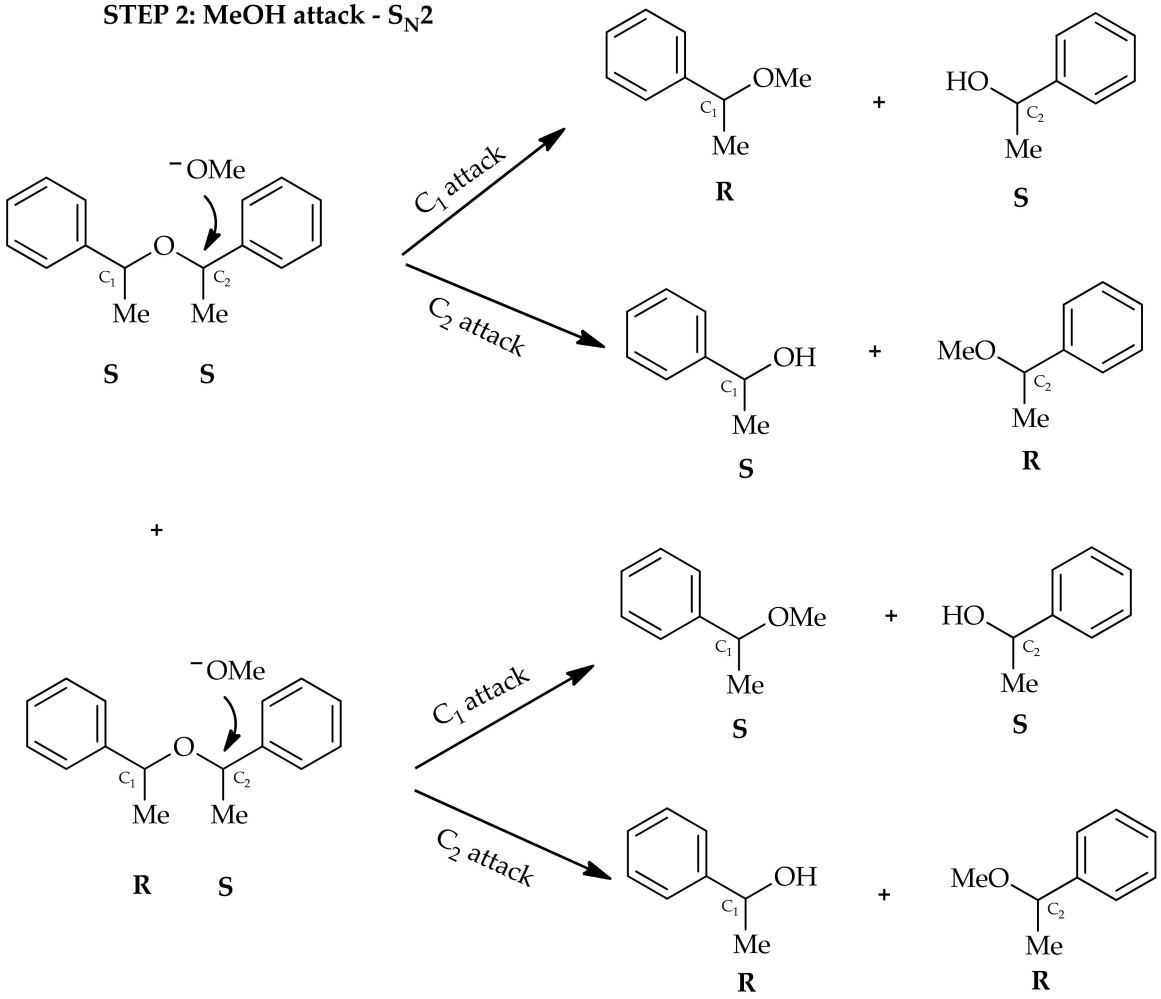
[a] Reaction conditions: Diphenylmethanol **1** (0.5 mmol), primary benzyl alcohols **20**, **22**, and **25** (0.65 mmol), NIS (6–10 mol%), 70–75 °C, 24 h. [b] Determined by ^{1}H NMR spectroscopy. [c] Yields calculated relative to alcohol **1**. Values in parentheses are isolated yields. [d] Oxidized alcohol and aldehyde 6–10%. [e] Oxidized alcohol and dimeric ether 18%.

We previously presented the stereochemical pathway of the etherification between (S)-(−)-1-phenylethanol **14** and MeOH **3**, mediated by NIS, affording the corresponding ether **15** in moderate yield (entry 8, Table 4) and accompanied by a small amount of oxidized alcohol. The specific rotation of pure product **15** provided the value [α] = +15°, disclosing that we are not dealing with totally S_N1 or S_N2 cases but with the combination of both. It could be seen that the dimerization process is the S_N1 and the final etherification is the S_N2 mechanism, (Scheme 7).



STEP 1: Ether formation - S_N1

STEP 2: MeOH attack - S_N2



Scheme 7. Plausible reaction mechanism.

3. Materials and Methods

Chemicals used for synthetic methods were provided from commercial resources (Sigma Aldrich, St. Louis, MO, USA; Merck, Darmstadt, Germany; Fluka, Seelze, Germany). Reactions were observed by thin-layer chromatography (mobile phase: dichloromethane/hexane 9:1) with silica gel coated plates (Silica gel/TLC cards; DC-Alufolien-Kieselgel, Sigma Aldrich, St. Louis, MO, USA), and detected by UV (Camag, Muttenz, Switzerland) lamp (254 nm). Column chromatography (CC) was performed using silica gel Kieselgel 60 (Fluka, Sigma-Aldrich, St. Louis, MO, USA, particle size: 0.063–0.200 mm). Using a Varian INOVA 300 NMR, Ljubljana, Slovenia instrument, ^{1}H and ^{13}C NMR spectra were recorded using $CDCl_3$ as the solvent with $SiMe_4$ (TMS) as an internal reference. Melting points were measured using Buchi-Melting Point M-560 equipment, BUCHI Switzerland.

General procedure for etherification of alcohols mediated by NIS on half mmol scale: A mixture of benzyl alcohol (0.5 mmol), and *N*-iodosuccinimide as a mediator (3–10 mol%), which had been powdered in a mortar in the case of solid-state reactants, was placed in a 4 mL screw-capped vial, followed by adding liquid component alkyl alcohol (1 mmol-1 mL) and heated to 70–75 °C for 6 h–24 h. TLC detected the progress of the reaction mixture. After cooling down to room temperature the mixture was diluted with ethyl acetate (15 mL), washed thoroughly with $Na_2S_2O_3$ (2 × 3 mL), $NaHCO_3$ (2 × 3 mL), and distilled water (2 × 5 mL), and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure, and the crude reaction mixture obtained was determined by ^{1}H NMR.

The scale-up procedure for the synthesis of (Methoxymethylene)dibenzene **4** with MeOH **3**, mediated by NIS: A mixture of diphenylmethanol **1** (10 mmol, 2.2425 g), 3 mol% NIS (67.5 mg, 0.3 mol), which had been previously powdered in a mortar, was transferred to a 20 mL screw-capped glass scintillation vial, MeOH **3** (20 mmol, (800 µL) was added, and heated at 70–75 °C for 6 h. TLC followed the progress of the reaction mixture. Upon completion of the reaction, the mixture was cooled to room temperature. Finally, the crude reaction mixture was purified by column chromatography to obtain a pure product in excellent yield (colorless oil, 2.1725 g, and 90%).

4. Conclusions

In conclusion, we have presented an efficient, selective, one-pot, metal-free methodology for direct C–O bond formation from readily available alcohols, using NIS as a metal-free and easy-to-handle precatalyst under HCRC. In the case of 1,1-diphenylethanol mediated by NIS under SFRC, dehydration resulting in 1,1-diphenylethene was observed, while phenyl-substituted primary and secondary alcohols under the same conditions gave dimeric ethers. Phenyl-substituted primary, secondary, and tertiary alcohols under HCRC gave alkyl ethers, while under the same conditions 1,1-diphenylethanol gave 1,1-diphenylethene. The large scale synthesis of methoxymethylene)dibenzene **4** was performed, with excellent yield. Moreover, etherification could also be achieved by cross coupling two different benzyl alcohols and mediated by NIS as the precatalyst under SFRC.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/catal11070858/s1, General Information, Optimisation of Reaction Conditions, Scheme S1. The conversion of diphenylmethanol 1 mediated by NIS under SFRC, Figure S1: The effect of loading of NIS on the conversion of diphenylmethanol **1** under SFRC, Scheme S2. The conversion of diphenylmethanol 1 in the presence of MeOH 3 mediated by NIS under HCRC, Figure S2: The effect of loading of NIS on the conversion of diphenylmethanol **1** with MeOH **3** under HCRC, Scheme S3. The conversion of diphenylmethanol 1 in the presence of MeOH 3 mediated by NIS under HCRC, Figure S3: The catalytic effect of NIS on the conversion of diphenylmethanol **1** with MeOH **3** based on temperature, under HCRC, Characterization Data of Isolated Final Products, Measurements of Specific Rotation, ^{1}H NMR and ^{13}C NMR Spectra of Isolated Final Products, Figure S4. ^{1}H NMR and ^{13}C NMR spectra for (methoxymethylene)dibenzene (**4**), Figure S5: ^{1}H NMR and ^{13}C NMR spectra for (±) 4,4′-(oxybis(phenylmethylene))bis(methylbenzene) (**6**), Figure S6: ^{1}H NMR and ^{13}C NMR spectra for (±) 1-(methoxy(phenyl)methyl)-4-methylbenzene (**7**), Figure S7: ^{1}H NMR and ^{13}C NMR spectra for 1-chloro-4-(methoxy(phenyl)methyl)benzene (**9**), Figure S8: ^{1}H NMR and ^{13}C NMR spectra for (ethoxymethylene)dibenzene (**11**), Figure S9: ^{1}H NMR and ^{13}C NMR spectra for isopropoxydiphenylmethane (**13**), Figure S10: ^{1}H NMR and ^{13}C NMR spectra for 4,4′-(oxybis(methylene))bis(methylbenzene) (**23**), Figure S11: ^{1}H NMR and ^{13}C NMR spectra for ((benzyloxy)methylene)dibenzene (**29**), Figure S12: ^{1}H NMR and ^{13}C NMR spectra for (((4-methylbenzyl)oxy)methylene)dibenzene (**30**), Figure S13: ^{1}H NMR and ^{13}C NMR spectra for (((4-chlorobenzyl)oxy)methylene)dibenzene (**31**), Figure S14: Thermal Gravimetric (TG) analysis of the NIS. References [24–33] are cited in the Supplementary Materials.

Author Contributions: Conceptualization, S.S.; formal analysis, N.A. and S.S.; Investigation, N.A. and S.S.; methodology, N.A. and S.S.; writing—original draft, N.A. and S.S.; writing—review and editing, N.A. and S.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Slovene Human Resources Development and Scholarship Fund (contract: 11011-9/2011), Slovenian Research Agency (contract: Programme P1-0134).

Data Availability Statement: The data presented in this study are available in the Supplementary Materials.

Acknowledgments: The authors are grateful to the Slovenian NMR Centre at the National Institute of Chemistry, Ljubljana, Slovenia, U. Grošelj for the specific rotation measurements, P. Bukovec for the TGA analysis of *N*-iodosuccinimide.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References

1. Fuhrmann, E.; Talbiersky, J. Synthesis of Alkyl Aryl Ethers by Catalytic Williamson Ether Synthesis with Weak Alkylation Agents. *Org. Process Res. Dev.* **2005**, *9*, 206–211. [CrossRef]
2. Emer, E.; Sinisi, R.; Capdevila, M.G.; Petruzziello, D.; De Vincentiis, F.; Cozzi, P.G. Direct Nucleophilic SN1-Type Reactions of Alcohols. *Eur. J. Org. Chem.* **2011**, *2011*, 647–666. [CrossRef]
3. Kumar, R.; Van der Eycken, E.V. Recent approaches for C-C bond formation via direct dehydrative coupling strategies. *Chem. Soc. Rev.* **2013**, *42*, 1121–1146. [CrossRef] [PubMed]
4. Jiang, D.; He, T.; Ma, L.; Wang, Z. Recent developments in Ritter reaction. *RSC Adv.* **2014**, *4*, 64936–64946. [CrossRef]
5. Chen, L.; Yin, X.-P.; Wang, C.-H.; Zhou, J. Catalytic functionalization of tertiary alcohols to fully substituted carbon centres. *Org. Biomol. Chem.* **2014**, *12*, 6033–6048. [CrossRef]
6. Chaskar, A.; Murugan, K. Direct allylation of alcohols using allyltrimethylsilane: A move towards an economical and ecological protocol for C-C bond formation. *Catal. Sci. Technol.* **2014**, *4*, 1852–1868. [CrossRef]
7. Uchuskin, M.G.; Makarov, A.S.; Butin, A.V. Catalytic Alkylation of Furans by π-Activated Alcohols (Review). *Chem. Heterocycl. Compd.* **2014**, *50*, 791–806. [CrossRef]
8. Shang, X.; Liu, Z.-Q. Iron-Catalyzed Alkylation of Alkenes and Alkynes Using Alcohols as the Alkylating Reagent. *Synthesis* **2015**, *47*, 1706–1708. [CrossRef]
9. Dryzhakov, M.; Richmond, E.; Moran, J. Recent Advances in Direct Catalytic Dehydrative Substitution of Alcohols. *Synthesis* **2016**, *48*, 935–959.
10. Ajvazi, N.; Stavber, S. Alcohols in direct carbon-carbon and carbon-heteroatom bond-forming reactions: Recent advances. *Arkivoc* **2018**, *2018*, 288–329. [CrossRef]
11. Xu, Q.; Xie, H.; Chen, P.; Yu, L.; Chen, J.; Hu, X. Organohalide-catalyzed dehydrative O-alkylation between alcohols: A facile etherification method for aliphatic ether synthesis. *Green Chem.* **2015**, *17*, 2774–2779. [CrossRef]
12. Veenboer, R.M.P.; Nolan, S.P. Gold(i)-catalysed dehydrative formation of ethers from benzylic alcohols and phenols. *Green Chem.* **2015**, *17*, 3819–3825. [CrossRef]
13. Demchuk, O.M.; Jasiński, R.; Formela, A. The Halogen-Less Catalytic Transition Metal-Mediated Cross-Coupling Reactions: A Sustainable Alternative for Utilisation of Organohalides. In *Chemistry beyond Chlorine*; Springer: Cham, Switzerland, 2016; pp. 17–94.
14. Böldl, M.; Fleischer, I. Dehydrative Coupling of Benzylic Alcohols Catalyzed by Brønsted Acid/Lewis Base. *Eur. J. Org. Chem.* **2019**, *2019*, 5856–5861. [CrossRef]
15. Ajvazi, N.; Stavber, S. N-Halosuccinimides as Precatalysts for C-, N-, O-, and X-Nucleophilic Substitution Reactions of Alcohols under Mild Reaction Conditions. *Catalysts* **2020**, *10*, 460. [CrossRef]
16. Stavber, G.; Iskra, J.; Zupan, M.; Stavber, S. Aerobic oxidative iodination of ketones catalysed by sodium nitrite "on water" or in a micelle-based aqueous system. *Green Chem.* **2009**, *11*, 1262–1267. [CrossRef]
17. Stavber, G.; Stavber, S. Towards Greener Fluorine Organic Chemistry: Direct Electrophilic Fluorination of Carbonyl Compounds in Water and Under Solvent-Free Reaction Conditions. *Adv. Synth. Catal.* **2010**, *352*, 2838–2846. [CrossRef]
18. Čebular, K.; Božić, B.Đ.; Stavber, S. 1,3-Dibromo-5,5-dimethylhydantoin as a Precatalyst for Activation of Carbonyl Functionality. *Molecules* **2019**, *24*, 2608. [CrossRef]
19. Ajvazi, N.; Stavber, S. N-Iodosuccinimide as a Precatalyst for Direct Cross-Coupling of Alcohols with C-Nucleophiles under Solvent-Free Reaction Conditions. *Catalysts* **2020**, *10*, 850. [CrossRef]
20. Bulfield, D.; Huber, S.M. Halogen Bonding in Organic Synthesis and Organocatalysis. *Chem. Eur. J.* **2016**, *22*, 14434–14450. [CrossRef]
21. Breugst, M.; Von der Heiden, D. Mechanisms in Iodine Catalysis. *Chem. Eur. J.* **2018**, *24*, 9187–9199. [CrossRef]
22. Clark, T.; Hennemann, M.; Murray, J.S.; Politzer, P. Halogen bonding: The σ-hole. *J. Mol. Model.* **2006**, *13*, 291–296. [CrossRef] [PubMed]
23. Politzer, P.; Murray, J.S.; Clark, T. Halogen bonding: An electrostatically-driven highly directional noncovalent interaction. *Phys. Chem. Chem. Phys.* **2010**, *12*, 7748–7757. [CrossRef]

24. Yoshiharu, O.; Yoshihiro, N.; Makoto, Y.; Akio, B. InI_3/Me_3SiI-catalyzed Direct Alkylation of Enol Acetates Using Alkyl Acetates or Alkyl Ethers. *Chem. Lett* **2011**, *40*, 1223–1255.
25. Das, T.; Chakraborty, A.; Sarkar, A. Solvent control of product diversity in palladium-catalyzed addition of arylboronic acid to aryl aldehydes. *Tetrahedron Lett.* **2014**, *55*, 5174–5178. [CrossRef]
26. Arendt, K.M.; Doyle, A.G. Dialkyl Ether Formation by Nickel-Catalyzed Cross-Coupling of Acetals and Aryl Iodides. *Angew. Chem. Int. Ed.* **2015**, *54*, 9876–9880. [CrossRef] [PubMed]
27. Muramatsu, W.; Nakano, K.; Li, C.-J. Simple and Direct sp3C–H Bond Arylation of Tetrahydroisoquinolines and Isochromans via 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone Oxidation under Mild Conditions. *Org. Lett.* **2013**, *15*, 3650–3653. [CrossRef] [PubMed]
28. Garcia, M.A.; García-Muñoz, Ángel; Pena, J.A.; Trujillo-Reyes, J.; Morales-Luckie, R.A.; Ávalos-Borja, M.; Vilchis-Néstor, A.R.; Sánchez-Mendieta, V.; Corona, D.; Cuevas-Yanez, E. Carbenoid Etherifications Catalyzed by "Green" Silver Nanoparticles and Iron-Copper Nanoparticles. *Lett. Org. Chem.* **2012**, *9*, 2–6. [CrossRef]
29. Leino, R.; Savela, R. Synthesis of Ethers from Carbonyl Compounds by Reductive Etherification Catalyzed by Iron(III) and Silyl Chloride. *Synth.* **2015**, *47*, 1749–1760. [CrossRef]
30. Howard, K.T.; Duffy, B.C.; Linaburga, M.R.; Chisholm, J. Formation of DPM ethers using O-diphenylmethyl trichloroacetimidate under thermal conditions. *Org. Biomol. Chem.* **2016**, *14*, 1623–1628. [CrossRef]
31. Stanescu, M.A.; Varma, R.S. Nafion-catalyzed preparation of benzhydryl ethers. *Tetrahedron Lett.* **2002**, *43*, 7307–7309. [CrossRef]
32. Dehmlow, E.V.; Sleegers, A. Applications of phase transfer catalysis. 39. Do simple optically active phase-transfer agents catalyze enantioselective ether formation? *J. Org. Chem.* **1988**, *53*, 3875–3877. [CrossRef]
33. Diem, M.J.; Burow, D.F.; Fry, J.L. Oxonium salt alkylation of structurally and optically labile alcohols. *J. Org. Chem.* **1977**, *42*, 1801–1802. [CrossRef]