Cluster

Visible-Light-Mediated Z-Stereoselective Monoalkylation of β,β-Dichlorostyrenes by Photoredox/Nickel Dual Catalysis

Α

Mehdi Abdellaoui Alexandre Millanvois Etienne Levernier Cyril Ollivier*[®] Louis Fensterbank*[®]

Institut Parisien de Chimie Moléculaire, Sorbonne Université, UMR CNRS 8232, 4 Place Jussieu, Paris Cedex 05, France cyril.ollivier@sorbonne-universite.fr louis.fensterbank@sorbonne-universite.fr Published as part of the Cluster Modern Nickel-Catalyzed Reactions



Received: 18.12.2020 Accepted after revision: 26.01.2021 Published online: 27.01.2021 DOI: 10.1055/a-1374-9384; Art ID: St-2020-k0632-c

Abstract Metal-catalyzed alkylation of 1,1-dihalovinyl moiety commonly suffers from both a lack of stereoselectivity and the overreaction leading to the dialkylation product. The methodology described herein features a new pathway to alkylate stereoselectively β , β -dichlorostyryl substrates to provide the Z-trisubstituted olefin only with fair to good yields. This cross-coupling reaction bears on the smooth and photoinduced formation of a C-centered radical that engages in a nickel-catalyzed organometallic cycle to form the key C_{sp2}–C_{sp3} bond.

Key words cross-coupling, stereoselective alkylation, radical, dichlorostyrenes, bis(catecholato)silicates, dual catalysis, counterion, nickel

The substitution of the carbon–chlorine bond of $\beta_i\beta$ -dichlorostyryl derivatives^{1,2} was firstly approached by Minato and Tamao^{3,4} who developed a palladium-catalyzed arylation that advantageously provided the Z-monoarylated product (Scheme 1, eq. a). Later, Negishi and co-workers developed a palladium-catalyzed alkynylation^{5,6} employing zinc acetylides as nucleophilic partners to afford the Z-monosubstituted products with high yields and stereoselectively (Scheme 1, eq. b). However, the formation of the side dialkynylated product remains the main weakness of this methodology. Concerning the alkylation attempts of $\beta_i\beta_j$ -dichlorostyryl substrates, they also suffered from overreaction and the disubstituted products were often observed.^{7,8} An alternative was considered by Figadère and Alami and consisted in the iron-catalyzed version of the Kumada cross-coupling but the formation of the dialkylated compound remained competitive (Scheme 1, eq. c).9 It was not until the work of Roulland and co-workers¹⁰ that a promising answer to the problem of a stereoselective monoalkylation was provided. Indeed, Roulland designed a Suzuki-type reaction with 9-BBN alkyl boranes that relies on the use of a bidentate phosphine ligand for palladium with a large bite angle to achieve the monoalkylation with high stereoselectivity and in excellent yields. However, once again, they observed traces of the *E*-stereoisomer and/or of the dialkylated side product that proved difficult to separate (Scheme 1, eq. d).





Scheme 1 Literature on metal-catalyzed arylation, alkynylation, and alkylation of β , β -dichlorostyrenes

M. Abdellaoui et al.

In contrast, to the best of our knowledge, nickel-catalyzed monoalkylation of such electrophiles has not yet been reported in the literature. Indeed, the closest example was the enantioselective alkylation of (Z)- β -bromo-styryl derivatives developed by Reisman¹¹ to afford the *Z*-trisubstituted alkenes with retention of the stereochemistry of the double bond. However, this methodology did not involve the substitution of dihalogenated styryl derivatives.

Considering those elements and based on our continuing interest in photoredox catalysis¹²⁻¹⁵ and in photoredox/Ni dual catalysis,¹⁶⁻²⁰ we considered involving bis(catecholato)silicates in a photoredox/Ni-catalyzed vinylation reaction.²¹ Indeed, thanks to their low oxidation potential (between 0.3 and 0.9 V vs SCE) bis(catecholato)silicates are known as efficient radical precursors.²² Their uses in dual catalysis were investigated by our group^{22,23} and the group of Molander for the alkylation of aryl and alkenyl halides.^{24,25} To illustrate the versatility of this methodology, our group also investigated the C_{sp3}-C_{sp3} bond formation,²⁶ the formation of ketones through cross-coupling with acyl chlorides,²⁷ and the alkylation of alkenyl halides including one preliminary example of alkylation of *p*-methoxy $\beta_i\beta_j$ -dichlorostyrene.²⁸ We wished to further investigate this valuable transformation and examined the reactivity of various dichlorostyryl substrates 1 towards silicates 2 to furnish cross-coupling (Z)-styrylchloride products **3** (Scheme 1, eq. e).²⁹

[18-C-6]-Potassium silicates **2a** (R = Bn), **2b** (R = $-(CH_2)_2OAc$), **2c** (R = cyclohexyl), and **2d** (R = $-CH_2NHPh$) were prepared as in previously described procedures.^{22,30} At the occasion of this study, we also introduced the previously unknown sodium silicates **2-Na** since they could result in altered reactivity. Sodium salts as additives have indeed resulted in optimized reactivity in some nickel-catalyzed cross-coupling reactions.^{11,31}

Sodium silicates **2-Na** were prepared as previously for potassium silicates (Scheme 2).²² The desired alkoxysilane is reacted with catechol (2 equiv.) and with 1 equiv. of sodium methoxide in methanol. 15-Crown-5 (1 equiv.) can also be added in the reaction mixture to provide sodium silicates **2'**. Gram quantities of **2a-Na** (55% yield), **2b-Na** (64%),



and **2c-Na** (55%) were obtained. Similarly, 15-C-5-chelated sodium silicates **2a'** were isolated in 45% yield. All these sodium silicates can be kept several months without degradation if stored under air- and moisture-free conditions.

Suitable crystals of the sodium bis(catecholato)benzyl silicate **2a-Na** were obtained by vapor diffusion using an acetone/diethyl ether mixture (Figure 1). [$C_{22}H_{21}NaO_5Si$] crystallized in a tetragonal crystal system with a = 19.0046(7) Å, b = 19.0046(7) Å, c = 11.5788(5) Å, $\alpha = \beta = \gamma = 90^{\circ}$ (Z = 8).³² Sodium ions are coordinated to one oxygen atom of four catechol ligands and one acetone molecule completes the coordination sphere. The O_{1-5} -Na₁ bond lengths are spanning from 2.288(3) Å to 2.355(2) Å. Finally, an intramolecular π -cation interaction between the centroid of the benzyl and Na₁ can be observed with a distance of 3.2712(9) Å.



Figure 1 X-ray crystal structure of **2a-Na**, thermal ellipsoids are drawn at 50% probability level. Hydrogen atoms are omitted for clarity. Dashed lines denote bonds between neighboring silicates.

The Si coordination of 2a-Na can be described as a slightly distorted square pyramid (SP) structure with the benzyl group occupying the apical site (Si-C₁₃ bond length = 1.879(2) Å). The four basal positions are occupied by the two oxygen atoms of two catechol ligands. We can notice that the Si atom is located just a little above the plane defined by these fourth atoms (distance Si-plane centroid = 0.4517(6) Å). For **2a-Na**, the dihedral angle method permits to calculate a displacement of 89.3% (TBP → SP, TBP: trigonal bipyramidal).³³ This is also underlined by the close values of all the 4 basal bond Si-O distances from 1.735(2) to 1.759(2) Å. Compared to an idealized SP with four angles of 86°, a slight distortion is observed with angle deviations from -2.5° to 2.1°. Interestingly, **2a-Na** forms a polymeric assembly along the *c*-axis that originates from multiple interactions between Na and oxygen atoms of the catechols of two silicates (see Supporting Information). Sodium cyclohexyl silicate 2c-Na also crystallized, and an XRD structure

с

M. Abdellaoui et al.

analysis was obtained³⁴ and proved to be very similar to the corresponding potassium one.²²

Finally, oxidation potentials of sodium silicates were determined by cyclic voltammetry and proved consistent with the low values we already observed for the potassium ones²² i.e., $E_{ox} = +0.77$ V vs SCE for **2a-Na**, +0.88 V for **2b-Na**, and +0.81 V for **2c-Na**.

All β , β -dichlorostyrenes **1** were synthesized by a common Corey–Fuchs–Ramirez olefination from the corresponding aldehydes³⁵ and were obtained with good yields. For our catalytic system, we considered the same as in our previous studies,²⁸ namely nickel(II)-dme in the presence of 2,6-di-*tert*-butyl bipyridine as catalytic system and 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene (4CzIPN)³⁶ as photocatalyst. 4CzIPN is endowed with a very high reduction potential after photoexcitation (+1.59 V vs SCE)³⁷ and a long-lived excited state (5.1 µs) which enables the efficient oxidation of the silicate ($E_{ox} < 0.9$ V vs SCE) to afford the corresponding C-centered radical.

We first concentrated on the cross-coupling of 1-vinylnaphthalene derivatives **1a** as electrophiles with benzyl silicates **2a** (see Table 1). We began our investigation by delineating the range of dihalogenostyrenes that could handle this approach (Table 1, entries 1–3). The difluorinated reagent **1a-F** did not react despite the presence of silicon on the radical precursor likely to establish a strong interaction with a fluoride. In contrast, the dibrominated reagent **1a-Br** led in our conditions to a complex mixture in which only a marginal amount of monoalkylated was detected. Interestingly, only the presumably less reactive dichlorinated substrate **1a** positively reacted in this dual catalysis reaction (44% of adduct **3aa**) and was then chosen as model substrate for the optimization of the reaction conditions. To our delight, the alkylation occurred selectively without any

signed by analogy with subsequent findings (vide infra). We then examined the effect of the cation in this reaction. No improvement of yield was observed from free potassium silicate 2a-K (39% of 3a, entry 4), sodium silicates with 15-C-5 (2a', 39%, entry 5) or without 15-C-5 (2a-Na, 42%, entry 6). Nevertheless, the fact that the plain sodium silicate 2a-Na could be engaged successfully opened interesting perspectives. Focusing on silicate 2a, we then investigated other possibilities to increase the yield of 3aa (Table 1). While doubling the loading in silicate (entry 7) or its concentration (entry 8) did not have a significant impact on the yield, a longer reaction time (72 h) with double amount of 2a provided the best yield of 3a (70%, entry 10). We also checked that nickel catalysis was necessary for this transformation: no radical addition – β -elimination of a chlorine radical takes place²² to deliver **3aa** (entry 11)

formation of side products such as the dialkylated product

or the E-stereoisomer. The Z-stereochemistry of 3aa was as-

Table T	Optimization of the Cross-Coupling Reaction	
		4C7IPN (1 mol%)

Table 1 Optimization of the Cross-Coupling Reaction

	1a	a-X 2a	rt	3aa	
Entry	Reaction time (h)	Х	[Si] counterion Y	Silicate (equiv.)	Yield of 3aa (%) ^a
1	48	F, 1a-F	K[18-C-6], 2a	1.5	NR ^b
2	48	Br, 1a-Br	K[18-C-6], 2a	1.5	mixture
3	48	Cl, 1a	K[18-C-6], 2a	1.5	44
4	48	Cl, 1a	K, 2a-K	1.5	39
5	48	Cl, 1a	Na[15-C-5], 2a '	1.5	39
6	48	Cl, 1a	Na, 2a-Na	1.5	42
7	48	Cl, 1a	K[18-C-6], 2a	3	47
8 ^c	48	Cl, 1a	K[18-C-6], 2a	3	51
9	72	Cl, 1a	K[18-C-6], 2a	1.5	50
10	72	Cl, 1a	K[18-C-6], 2a	3	70
11 ^d	48	Cl, 1a	K[18-C-6], 2a	1.5	0

iCl₂·dme (2 mol%)

^a NMR yield was determined using 1,3,5-trimethoxybenzene as internal standard.

^b NR: no reaction detected.

^c Variation of the concentration (0.1–0.2 M)

^d Reaction performed without nickel catalyst.

M. Abdellaoui et al.

Based on all the results from Table 1, the standard conditions (48 h and 1.5 equiv. of silicate) appear to be a good compromise in terms of reaction time and cost to reach a decent yield in this cross-coupling reaction. Subsequently, we engaged under those conditions various [18-C-6]-potassium and sodium silicates **2** and **2-Na** with β , β -dichlorostyrenes **1** under the Ni/4CzIPN dual catalysis conditions to explore the scope of this reactivity (Scheme 2).

The results of Scheme 3 illustrate a certain versatility of this cross-coupling reaction between the *gem*-dichlorostyryl precursors **1** and the silicates **2**. Indeed, the reaction occurs with an alkyl silicate (primary and secondary), a benzylic one, and even the α -methyl-anilino-silicate with various dichlorostyrenes **1**, and provides previously unknown coupling products with fair to good yields. In some cases, the use of the sodium silicates **2-Na** compared to the potassium ones **2** proved more rewarding in terms of yields for coupling products **3** (products **3ab** and **3bc**). The coupling does not depend on the electron-withdrawing or electron-donating character of the substituent of the dichlorostyrene. Indeed, substrates that own a methoxy group or a trifluoromethyl group in *para* position react similarly with the



Scheme 3 Reaction of *gem*-dichlorostyrenes **1** with various silicates **2** (isolated yieds). *Reagents and conditions*: **1** (1 equiv), **2** (1.5 equiv), 4CzIPN (1 mol%), NiCl₂·dme/dtbbpy (2 mol%), rt for 48 h. ^a NMR yield was determined using 1,3,5-trimethoxybenzene as internal standard. ^b See also ref. 28. ^c NR: no reaction detected, starting material was recovered.

primary alkyl acetoxypropyl radical (**2b**) or the more nucleophilic α -methyl-aniline one (**2d**) (Scheme 3).

Of note, the more sensitive precursors, piperonal and nitro substrates failed to give any adducts (**3fb** and **3gb**) and it is also important to specify that only the *Z*-isomer, as determined by NOESY experiments, of each adduct **3** was isolated and that no dialkylation product was observed. In the reactions of amino silicate **2d**, some (*Z*)-chlorostyrene was formed as side product in 15–20% yield that was highly suggestive of a protodenickelation based on the proposed mechanism of Scheme 4.



Scheme 4 Plausible mechanism for the cross-coupling reaction

Because we know that nickel is necessary in these reactions to obtain products 3 and based on the literature mechanism proposals of related Ni/photoredox dual catalysis reactions, ^{18-20,38} it appears reasonable to invoke the trapping by nickel of a C-centered radical originating from the photoinduced oxidation of the silicates 2. The nickel intermediate that would be involved is the nickel(II) complex I that originates from the oxidative addition into the C-Cl bond of the substrates 1 (Scheme 4). The observed Z-selectivity might be ascribed to the presence of the bidentate ligand on nickel that would generate a significant steric hindrance around the metallic center and that possibly orients the oxidative addition on the more accessible C-Cl bond, with no aryl group in syn. Even though the effect of the bulkiness around the metallic center seems clear, the insensitivity of the coupling to the substituent on the aryl moiety might appear strange but is reminiscent of previous findings in arylative couplings.^{23,24} This would be consistent with a radical addition on nickel(II) that is rather insensitive to electronic effects.³⁹⁻⁴² The resulting nickel(III) complex II then undergoes reductive elimination to provide products **3** and a nickel(I) salt that would be reduced by the photoredox cycle to Ni(0).

Based on the clean but inefficient conversion of some of these reactions, we also wished to explore other conditions to run them. Notably we used an in-house flow setting^{43,44} (see the Supporting Information for details) in order to re-

Е

Synlett

M. Abdellaoui et al.

Cluster

duce the reaction times. We tested silicate **2c** and naphthyl electrophile **1a** as a model reaction based on its efficiency in batch after 48 h of irradiation (70% of **3ac**, Scheme 3). Interestingly, within a residence time of 50 min, we reached 32% yield in **3ac** and 50% within 90 min (Scheme 5). Therefore, the flow conditions open promising perspectives for this methodology.



Finally, we investigated the possibility of the postfunctionalization of the alkylated adducts **3** by using our methodology. We engaged different monoalkylated products **3** with silicates **2** (**3bb** with benzyl silicate and **3bd** with acetoxypropyl silicate) and we only recovered the starting material after 2 days of irradiation. All in all, this absence of reactivity confirms that our methodology is inoperative to achieve the substitution of the two C–Cl bonds. Nevertheless, Roulland's and Tamao's works showed that the postfunctionalization of the monosubstituted product was effective by engaging them in their palladium-catalyzed alkylation or arylation sequences.^{2,3}

To conclude, we have developed an innovative way to alkylate gem-dichlorostyrenes with fair to good yields. Contrary to most of the previous methodologies employing palladium catalysts, this cross-coupling reaction advantageously combines the earth-abundant nickel metal with a cheap organic dye to achieve smoothly the substitution at room temperature (where all the previous methods mentioned are performed under reflux). Furthermore, the main advantages of this reaction are its total Z-stereoselectivity and the absence of overreaction to widen the scope of this methodology. Otherwise, one of the aims of the study was the approach of the silicate's counterion and its effect on the photoredox catalysis. The second interest of this study is the introduction of sodium silicates 2-Na that improves the atom economy compared to the [18-C-6]-chelated potassium silicate analogues 2. If this work provided interesting and promising insights, the influence of the counterion remains nonexhaustive and will be pursued by our group.

Funding Information

The authors thank the Agence Nationale de la Recherche (Grant No. ANR-17-CE07-0018, HyperSilight (PhD grant to EL)), the Centre National de la Recherche Scientifique (CNRS), and Sorbonne Université for financial support.

Acknowledgment

We are grateful to J. Forté, G. Gontard and Lise-Marie Chamoreau for X-ray diffraction analyses and helpful discussions.

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-1374-9384.

References and Notes

- (1) Chelucci, G. Chem. Rev. 2012, 112, 1344.
- (2) Arthuis, M.; Lecup, A.; Roulland, E. Chem. Commun. 2010, 46, 7810.
- (3) Minato, A.; Suzuki, K.; Tamao, K. A. J. Am. Chem. Soc. **1987**, 109, 1257.
- (4) Minato, A. J. Org. Chem. 1991, 56, 4052.
- (5) Shi, J.; Zeng, X.; Negishi, E. Org. Lett. 2003, 5, 1825.
- (6) Negishi, E.; Shi, J.; Zeng, X. Tetrahedron 2005, 61, 9886.
- (7) Andrei, D.; Wnuk, S. F. J. Org. Chem. 2006, 71, 405.
- (8) Tan, Z.; Negishi, E. Angew. Chem. Int. Ed. 2006, 45, 762.
- (9) Dos Santos, M.; Franck, X.; Hocquemiller, R.; Figadère, B.; Peyrat, J.-F.; Provot, O.; Brion, J.-D.; Alami, M. Synlett 2004, 2697.
- (10) Liron, F.; Fosse, C.; Pernolet, A.; Roulland, E. J. Org. Chem. **2007**, 72, 2220.
- (11) DeLano, T. J.; Reisman, S. E. ACS Catal. 2019, 9, 6751.
- (12) McAtee, R. C.; McClain, E. J.; Stephenson, C. R. J. *Trends Chem.* **2019**, *1*, 111.
- (13) Marzo, L.; Pagire, S. K.; Reiser, O.; König, B. Angew. Chem. Int. Ed. 2018, 57, 10034.
- (14) Crespi, S.; Fagnoni, M. Chem. Rev. 2020, 120, 9790.
- (15) Xuan, J.; Zang, Z.-G.; Xiao, W.-J. Angew. Chem. Int. Ed. 2015, 54, 15632.
- (16) Levin, M. D.; Kim, S.; Toste, F. D. ACS Cent. Sci. 2016, 2, 293.
- (17) Hopkinson, M. N.; Sahoo, B.; Li, J.-L.; Glorius, F. Chem. Eur. J. 2014, 20, 3874.
- (18) Nacsa, E. D.; MacMillan, D. W. C. Org. React. 2019, 471.
- (19) Skubi, K. L.; Blum, T. R.; Yoon, T. P. Chem. Rev. 2016, 116, 10035.
- (20) Tellis, J. C.; Kelly, C. B.; Primer, D. N.; Jouffroy, M.; Patel, N. R.; Molander, G. A. Acc. Chem. Res. 2016, 49, 1429.
- (21) Goddard, J.-P.; Ollivier, C.; Fensterbank, L. Acc. Chem. Res. 2016, 49, 1924.
- (22) Corcé, V.; Chamoreau, L. M.; Derat, E.; Goddard, J.-P.; Ollivier, C.; Fensterbank, L. Angew. Chem. Int. Ed. 2015, 54, 11414.
- (23) Lévêque, C.; Chenneberg, L.; Corcé, V.; Goddard, J.-P.; Ollivier, C.; Fensterbank, L. Org. Chem. Front. **2016**, 3, 462.
- (24) Jouffroy, M.; Primer, D. N.; Molander, G. A. J. Am. Chem. Soc. 2016, 138, 475.
- (25) Patel, N. R.; Kelly, C. B.; Jouffroy, M.; Molander, G. A. Org. Lett. 2016, 18, 764.
- (26) Lévêque, C.; Corcé, V.; Chenneberg, L.; Ollivier, C.; Fensterbank, L. Eur. J. Org. Chem. 2017, 2118.

Syn lett

M. Abdellaoui et al.

- (27) Levernier, E.; Corcé, V.; Rakotoarison, L.-M.; Smith, A.; Zhang, M.; Ognier, S.; Tatoulian, M.; Ollivier, C.; Fensterbank, L. Org. *Chem. Front.* **2019**, *6*, 1378.
- (28) Lévêque, C.; Chenneberg, L.; Corcé, V.; Ollivier, C.; Fensterbank, L. Chem. Commun. 2016, 52, 9877.
- (29) For a recent access to vinylchlorides, see: Adak, T.; Hoffmann, M.; Witzel, S.; Rudolph, M.; Dreuw, A.; Hashmi, A. S. K. *Chem. Eur. J.* **2020**, *26*, 15573.
- (30) Corcé, V.; Lévêque, C.; Ollivier, C.; Fensterbank, L. In Science of Synthesis: Photocatalysis in Organic Synthesis; König, B., Ed.; Thieme: Stuttgart, 2019, 427–466.
- (31) Prinsell, M. R.; Everson, D. A.; Weix, D. J. Chem. Commun. 2010, 46, 573.
- (32) CCDC 2048159 contains the supplementary crystallographic data for compound **2a-Na**. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.
- (33) Holmes R. R., Deiters J. A.; Phosphorus, Sulfur Silicon Relat. Elem.; 1995, 98: 105.
- (34) CCDC 2050302 contains the supplementary crystallographic data for compound **2c-Na**. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

- (35) Burton, G.; Elder, J. S.; Fell, S. C. M.; Stachulski, A. V. *Tetrahedron Lett.* **1988**, *29*, 3003.
- (36) Shang, T.-Y.; Lu, L.-H.; Cao, Z.; Liu, Y.; He, W.-M.; Yu, B. *Chem. Commun.* **2019**, *55*, 5408.
- (37) Le Vaillant, F.; Garreau, M.; Nicolai, S.; Gryn'ova, G.; Corminboeuf, C.; Waser, J. *Chem. Sci.* **2018**, 9, 5883.
- (38) Tasker, S. Z.; Jamison, T. F. J. Am. Chem. Soc. 2015, 137, 9531.
- (39) Durandetti, M.; Nédélec, J.-Y.; Périchon, J. J. Org. Chem. **1996**, 61, 1748.
- (40) Weix, D. J. Acc. Chem. Res. 2015, 48, 1767.
- (41) Richmond, E.; Moran, J. Synthesis 2018, 50, 499.
- (42) (a) Lévêque, C.; Ollivier, C.; Fensterbank, L. In Nickel Catalysis in Organic Synthesis; Ogoshi, S., Ed.; Wiley-VCH: Weinheim, 2020, 151–181. (b) Goldfogel, M. J.; Huang, L.; Weix, D. J. In Nickel Catalysis in Organic Synthesis; Ogoshi, S., Ed.; Wiley-VCH: Weinheim, 2020, 183–222.
- (43) Cambié, D.; Bottecchia, C.; Straathof, N. J. W.; Hessel, V.; Noël, T. *Chem. Rev.* **2016**, *116*, 10276.
- (44) Garlets, Z. J.; Nguyen, J. D.; Stephenson, C. R. J. *Isr. J. Chem.* **2014**, *54*, 351.