Mechanosynthesis of Noels-type NHC−Ruthenium Complexes and Applications in Ring-Opening Metathesis Polymerization

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ABSTRACT: The use of ball mills enabled the efficient mechanosynthesis of a variety of *N*-aryl,*N*-alkyl imidazolium salts and of corresponding NHC silver(I) complexes. Transmetalation with ruthenium via mechanochemistry allowed the rapid access (from 1.5 min to 1 h) to complexes having a similar structure to Noels-type precatalysts. Evaluation of the complexes in the ring-opening metathesis polymerization of norbornene in different solvent, including nontoxic ones, showed a high catalytic activity for one of them, comparable to that of the Noels catalyst.
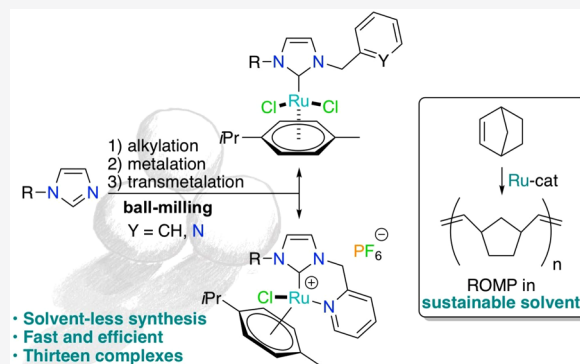
Since its discovery, olefin metathesis has become an important chemical transformation in the academic as well as in the industrial world.[1] In particular, ring-opening metathesis polymerization (ROMP) finds applications in the synthesis of useful polymer materials such as poly(norbornene) or poly(dicyclopentadiene).[2] In regards to this reaction, the ruthenium−arene complex [RuCl₂(p-cymene)(IMes)] (IMes = 1,3-bis(mesityl)imidazol-2-ylidene), also known as Noels' catalyst, was found to be highly active.[3] Although benzylidene Grubbs-like complexes are still under intensive study in order to develop a universal catalyst, Noels' type complexes have less been investigated. Thus, we describe herein the mechanosynthesis of analogs of Noels-like complexes through alkylation of *N*-arylimidazoles, silver metalation, and transmetalation in a ball mill, as well as their evaluation in ROMP of norbornene (NB). Mechanochemistry, including ball mills and reactive extrusion, was recognized in 2019 by IUPAC as an innovation that will change the world.[4] This technology allows the avoidance of solvent in the reaction mixture, thus reducing the environmental impact of the reaction, and generally permits an increase of the reaction speed compared to solution-based methods.[5] Additionally, it permits the synthesis of compounds inaccessible by other means.[6] Of note, ball-milling was recently used for the synthesis of second- and third-generation Grubbs- and Hoveyda-like complexes through a solvent-free carbene addition reaction.[7] We thus desired to take advantage of our expertise in the preparation of metal complexes via ball-milling[8] for the synthesis of Noels-type olefin metathesis catalysts.[5b]

On the basis of our experience on the formation of *N*,*N*-dialkylimidazolium salts,[8e] alkylation of *N*-mesityl- and *N*-(2,6-
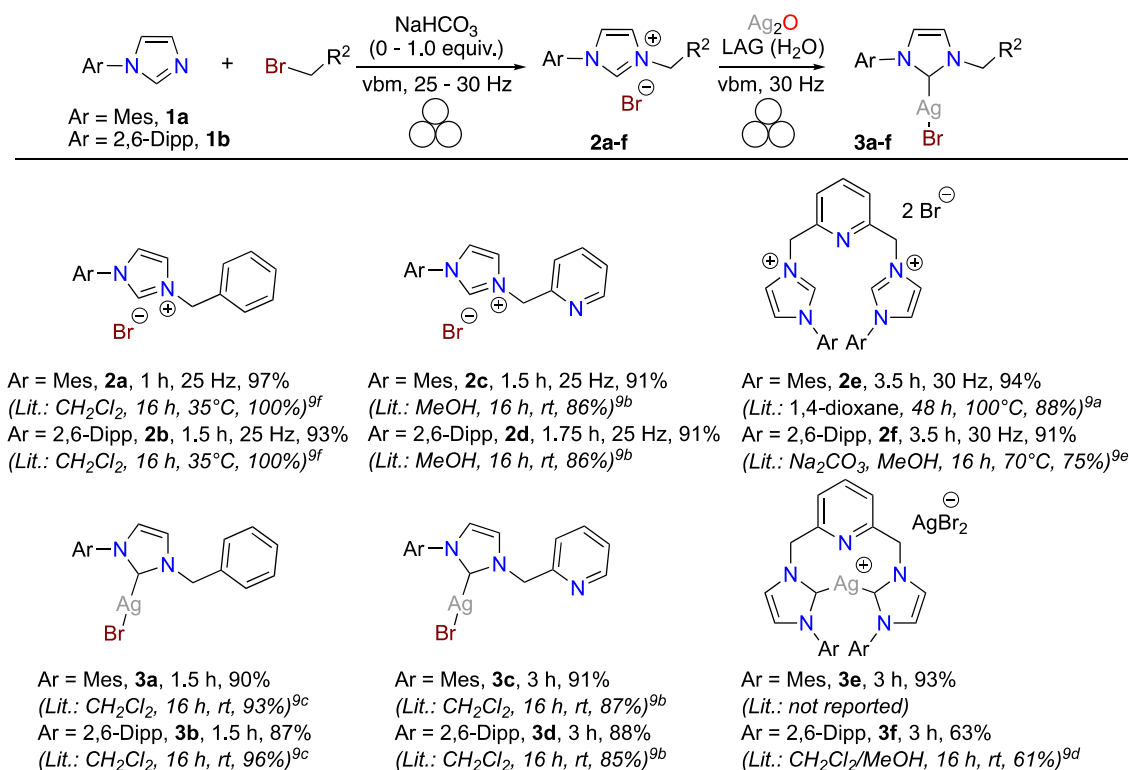
diisopropylphenyl) imidazole was examined in a ball mill (Scheme 1). In a vibratory ball mill (vbm), milling *N*-arylimidazoles at 25 Hz with benzyl bromide in a PTFE jar with a 1 cm diameter stainless-steel ball allowed us to obtain full conversion into corresponding imidazolium salts **2a** and **2b**, respectively, in less than 1.5 h. No purification was required, and a simple extraction and filtration over Celite furnished the pure compounds in 97 and 93% yield. Similarly, compounds **2c,d**, which are bidentate ligand precursors, were obtained in 91% yield after milling of **1a,b** with bromomethylpyridine hydrobromide and sodium bicarbonate for 1.5 h. Double nucleophilic substitution was also performed using 2,6-di(bromomethyl)pyridine as alkylating agent. Milling frequency and time were increased to 30 Hz and 3.5 h, respectively, to finally isolate **2e,f** in 94 and 91% yield.

Notably, the mechanochemical approach enabled the use of smoother conditions and shorter reaction times than those with solution conditions.[9] As a representative example, synthesis of compound **2e** requires 2 days when performed in refluxing dioxane[9a] instead of 3.5 h under solvent-free milling conditions.
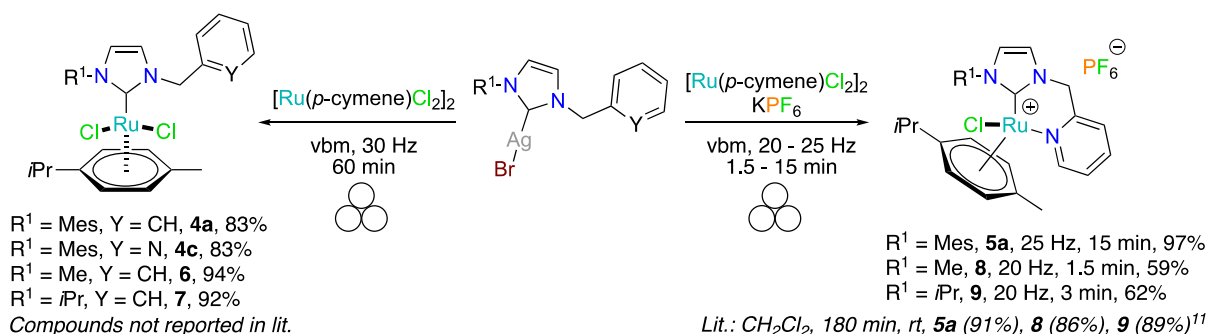
Imidazolium salts **2a−f** were then metalated using silver(I) oxide under solvent-free mechanochemical conditions. Of note, as milling jars are not transparent, there is no need to light protection usually necessary for the synthesis of light-

Scheme 1. Alkylation of *N*-Arylimidazoles and Silver Metalation

Ar = Mes, **2a**, 1 h, 25 Hz, 97%
(Lit.: CH$_2$Cl$_2$, 16 h, 35°C, 100%)[9f]
Ar = 2,6-Dipp, **2b**, 1.5 h, 25 Hz, 93%
(Lit.: CH$_2$Cl$_2$, 16 h, 35°C, 100%)[9f]

Ar = Mes, **2c**, 1.5 h, 25 Hz, 91%
(Lit.: MeOH, 16 h, rt, 86%)[9b]
Ar = 2,6-Dipp, **2d**, 1.75 h, 25 Hz, 91%
(Lit.: MeOH, 16 h, rt, 86%)[9b]

Ar = Mes, **2e**, 3.5 h, 30 Hz, 94%
(Lit.: 1,4-dioxane, 48 h, 100°C, 88%)[9a]
Ar = 2,6-Dipp, **2f**, 3.5 h, 30 Hz, 91%
(Lit.: Na$_2$CO$_3$, MeOH, 16 h, 70°C, 75%)[9e]

Ar = Mes, **3a**, 1.5 h, 90%
(Lit.: CH$_2$Cl$_2$, 16 h, rt, 93%)[9c]
Ar = 2,6-Dipp, **3b**, 1.5 h, 87%
(Lit.: CH$_2$Cl$_2$, 16 h, rt, 96%)[9c]

Ar = Mes, **3c**, 3 h, 91%
(Lit.: CH$_2$Cl$_2$, 16 h, rt, 87%)[9b]
Ar = 2,6-Dipp, **3d**, 3 h, 88%
(Lit.: CH$_2$Cl$_2$, 16 h, rt, 85%)[9b]

Ar = Mes, **3e**, 3 h, 93%
(Lit.: not reported)
Ar = 2,6-Dipp, **3f**, 3 h, 63%
(Lit.: CH$_2$Cl$_2$/MeOH, 16 h, rt, 61%)[9d]

Scheme 2. Mechanosynthesis of Ruthenium Complexes

R^1 = Mes, Y = CH, **4a**, 83%
R^1 = Mes, Y = N, **4c**, 83%
R^1 = Me, Y = CH, **6**, 94%
R^1 = *i*Pr, Y = CH, **7**, 92%
Compounds not reported in lit.

R^1 = Mes, **5a**, 25 Hz, 15 min, 97%
R^1 = Me, **8**, 20 Hz, 1.5 min, 59%
R^1 = *i*Pr, **9**, 20 Hz, 3 min, 62%
*Lit.: CH$_2$Cl$_2$, 180 min, rt, **5a** (91%), **8** (86%), **9** (89%)[11]*

sensitive silver complexes. Contrary to what was observed in the metalation of *N*,*N*-dialkylimidazolium salts,[8e] the reaction mixture was found to be not homogeneous in the milling jar. To solve this issue, addition of water as liquid grinding assistant (0.3 μL/mg of reactants) revealed the paramount conditions.[10] Under these conditions, metalation proceeded in 1.5−3 h, and complexes **3a−f** could be isolated in yields up to 93% (Scheme 1).

Silver complexes **3a** and **3c** were then milled with 0.5 equiv of [Ru(*p*-cymene)Cl$_2$]$_2$ at 30 Hz for 1 h in a stainless-steel jar (Scheme 2). Corresponding complexes **4a** and **4c** were both isolated in 83% yield. No coordination of the pyridine was observed in the case of **4c**. To increase the scope of ruthenium complexes and compare them in ROMP, complexes **6** and **7**, featuring methyl and isopropyl groups in place of the mesityl in the NHC ligand, respectively, were also mechanosynthesized. After 1 h of milling at 30 Hz, complexes **6** and **7** were isolated in 94 and 92% yield, respectively. For the pyridine-containing compounds, addition of a stoichiometric quantity of KPF$_6$ in the milling media enabled the chelation. However, such

reaction was found sensitive to the milling conditions. Reaction of **3c** with [Ru(*p*-cymene)Cl$_2$]$_2$ at 30 Hz for 1 h in the presence of KPF$_6$ yielded a 90:10 mixture of **5a/2c·PF$_6$**, which could not be improved by a prolonged milling. To ensure full conversion and no side product formation, the milling frequency was reduced to 25 Hz, and the material of the jar was changed from stainless steel to PTFE. A softer material such as PTFE will absorb more energy from the impacts of the ball than a harder one. **5a** could be obtained as a pure compound after only 15 min of grinding at 25 Hz. Similarly, complexes **8** and **9**, featuring a methyl and isopropyl group instead of the mesitylene, respectively, could be formed in less than 3 min at 20 Hz. As the transmetalation occurred efficiently, a simple recovery and filtration over Celite of the reaction mixture using 1,3-dioxolane as solvent, a green alternative to dichloromethane, furnished the pure compounds. As a comparison, in solution, 3 h of reaction in dichloromethane were required to obtain **5a**, **8**, and **9**.[11] Notably, the reaction of silver complexes **3b** and **3d**, featuring a sterically hindered 2,6-diisopropylphenyl group, and **3e,f**, bearing

tridentate ligands, with the ruthenium dimer resulted in the formation of the desired complex but with unidentified and inseparable side products.

The obtained ruthenium complexes were then evaluated in the ROMP of NB, using a ratio precatalyst/NB = 1/500 (Table 1). To compare the activity of the different precatalysts,

Table 1. Comparison of Mechanosynthesized Catalysts' Activity in the ROMP of Norbornene[a]

entry	Ru cat	t (min)	yield (%)
1		2	30
2	**4a**	20	96
3		40	99
4	**4c**	2	8
5	**6**	2	3
6	**7**	2	2
7	**5a**	2	2
8	**8**	2	0
9	**9**	2	0

[a]Reaction conditions: norbornene (5.32 mmol), catalyst (0.01 mmol), CH$_2$Cl$_2$ (2.5 mL), N$_2$, and 35 °C.

polymerization reactions were stopped after 2 min of reaction, by quenching with the addition of ethylvinyl ether, to determine the yield of isolated polymer. If complex **4a** gave an interesting 30% yield in polynorbornene, then **4c**, featuring a pyridine attached to the NHC, furnished only 8% yield, probably because of an unproductive coordination/decoordination of the pyridine during the catalytic cycle (Table 1, entries 1 and 4). Replacing the mesityl with a methyl or isopropyl group revealed detrimental as the isolated yield dropped to 3 and 2%, respectively (Table 1, entries 5 and 6). Such behavior is in good agreement with the observations by Noels et al. regarding the ROMP of cyclooctene.[12] Complexes **5a**, **8**, and **9**, featuring a pyridine coordinated to the ruthenium center, were almost inactive in the ROMP of NB, due to a too strong chelation of the ruthenium (Table 1, entries 7−9). Attempts to activate these precatalysts by heating or adding HCl did not allow for any improvement. Thus, complex **4a** was found to be the most active precatalyst for the ROMP of NB. When the reaction time was increased to 20 and 40 min, gratifyingly, yields up to 99% were obtained (Table 1, entries 2 and 3). In order to find an ecofriendly solvent for ROMP, **4a** was then evaluated in 1,3-dioxolane and DMC (dimethylcarbonate) in addition to dichloromethane (Figure 1). Even if the reaction was found to be faster in dichloromethane, the kinetic profiles were remarkable in 1,3-dioxolane and DMC since almost quantitative yields were obtained in 80 min. In particular, ROMP proceeded more rapidly in 1,3-dioxolane than DMC. Of note, ROMP of NB with **4a** was compared to previously reported results using *in situ* generated Noels catalyst.[13] Interestingly, the kinetics were found to be similar, proving that well-defined complex **4a** with an *N*-benzyl,*N*-mesityl NHC ligand possesses an excellent activity in ROMP. See the Supporting Information for details.

In conclusion, mechanochemistry enabled the efficient synthesis of *N*-aryl,*N*-alkyl imidazolium salts and of corresponding heteroleptic NHC-silver(I) complexes. In addition,
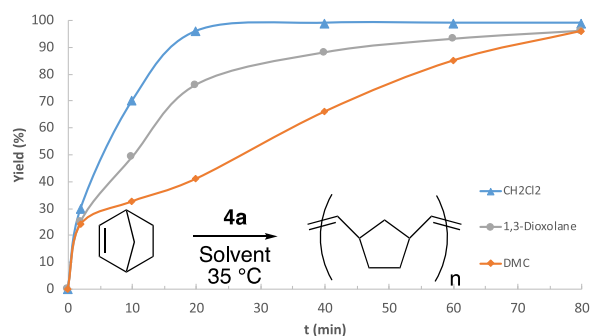
Figure 1. Effect of solvent in the ROMP of norbornene with **4a**. Reaction conditions: norbornene (5.32 mmol), **4a** (0.01 mmol), solvent (2.5 mL), N$_2$, and 35 °C.

mechanotransmetalation allowed generating Noels' like ruthenium coordination complexes in short reaction times, from 1.5 min to 1 h, and in excellent yields. These complexes were evaluated in the ROMP of NB in a series of solvents, and complex **4a** exhibited interesting high kinetic activity, comparable to that of *in situ* generated Noels catalyst. Further study on the tuning of the NHC ligand in such complexes is ongoing in our laboratory.

■ ASSOCIATED CONTENT

ⓈI Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.organomet.0c00013.

> Synthetic procedures, description of compounds, optimization of the ROMP, copies of the ^{1}H and ^{13}C NMR spectra of the compounds (PDF)

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Notes

The authors declare no competing financial interest.

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