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Iodonium-Catalyzed Carbonyl–Olefin Metathesis Reactions

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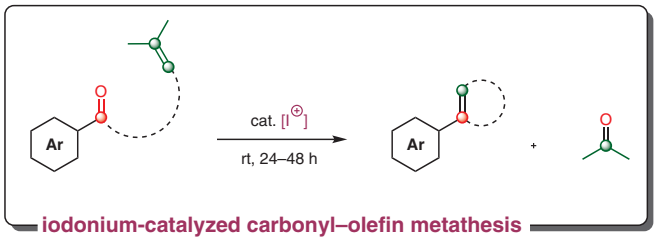
This manuscript is dedicated to the memory of the late Professor Dieter Enders, RWTH Aachen, for his great contributions to organic chemistry and academic mentoring.



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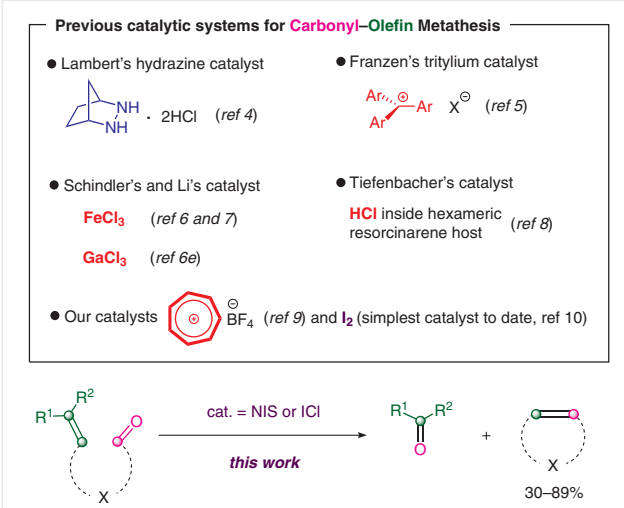
Abstract The carbonyl–olefin metathesis reaction has become increasingly important in organic synthesis due to its versatility in functional group interconversion chemistry. Recent developments in the field have identified a number of transition-metal and organic Lewis acids as effective catalysts for this reaction. Herein, we report the use of simple organic compounds such as *N*-iodosuccinimide or iodine monochloride to catalyze the carbonyl–olefin metathesis process under mild reaction conditions. This work broadens the scope of this chemical transformation to include iodonium sources as simple and practical catalysts.

Key words iodonium, carbonyl–olefin metathesis, metathesis, olefination, catalysis, functional group interconversion

The carbonyl moiety is one of the most ubiquitous functional group in organic chemistry.[1] Olefination of carbonyl compounds has long been an important strategy to generate diverse libraries of synthetically valuable organic substrates or complicated frameworks.[1] It can generally be performed by the Wittig olefination and analogous reactions, however, this reaction associates with product purification and waste generation issues.[1,2] The carbonyl–olefin metathesis (COM) reaction has emerged as an attractive alternative for this type of chemical transformation.[3] Within the last few years, the COM reaction has drawn even more attention due to recent developments to promote the reaction using transition-metal catalysts or organocatalysts. Most notable examples include Lambert's hydrazine[4] and Franzen's tritylium[5] catalysts, followed by Schindler's[6] and Li's[7] iron-catalyzed reactions and Tiefenbacher's supramolecular system.[8]

Last year, our group reported the application of two new catalytic systems, namely tropylium ion[9] and molecular iodine,[10] to facilitate the COM reaction. Most importantly, these catalysts were proven to be effective for all different types of COM reactions, including the intramolecular cyclization, the intermolecular metathesis, as well as the olefin ring-opening metathesis (Scheme 1).[9,10] The catalytic activity of I_2 for the COM reaction is intriguing, as this is inarguably the simplest catalyst known to date for COM reactions. Interestingly, it was revealed in our previous report that the mechanism of how molecular iodine triggers the reaction could be a lot more complicated than the promoter itself.[11] Indeed, I_2 catalyst, or to be more exact pre-catalyst, could generate downstream reactive intermediates in situ to catalyze the COM reaction via (i) radical; (ii) Brønsted acid; (iii) halogen-bonding, or (iv) iodonium pathways (Scheme 2). Therefore, it is of significant interest to gain further insights into the mechanism of this catalytic reaction.



Scheme 1 Recent catalytic developments in COM reaction

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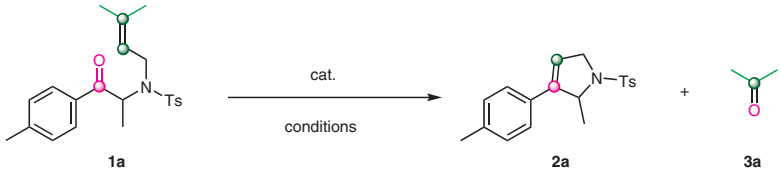
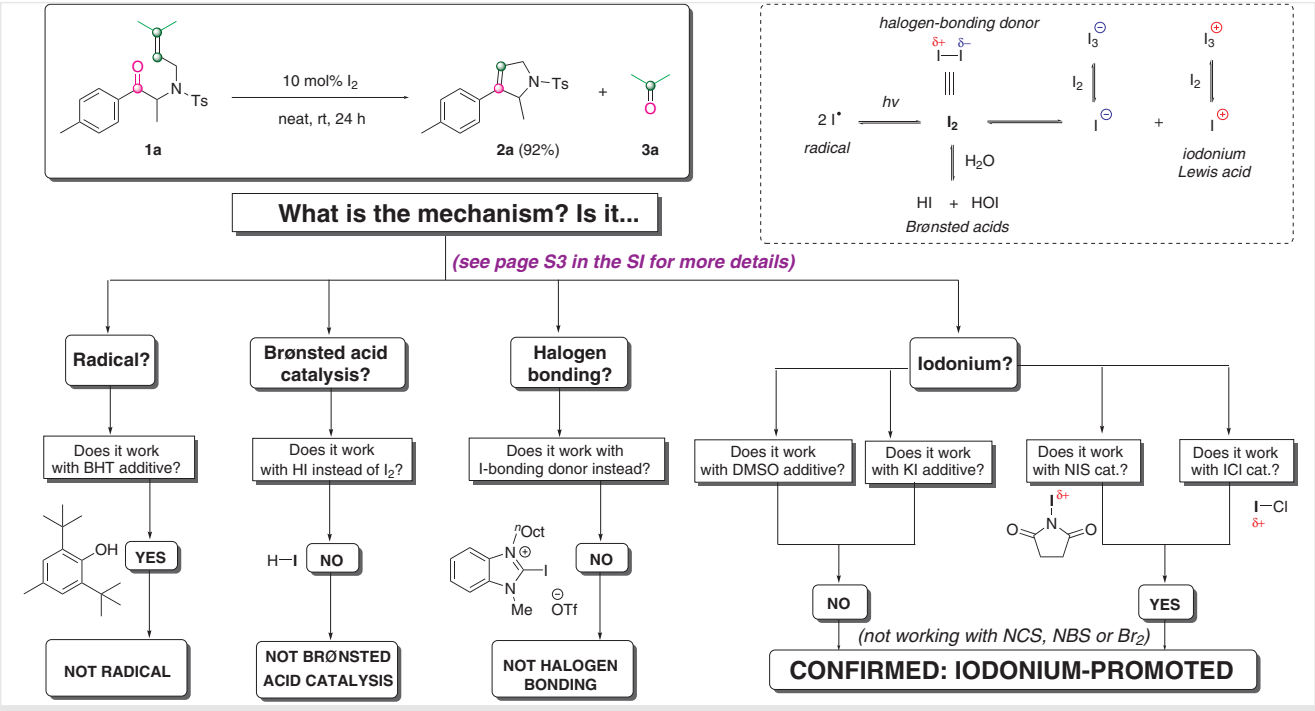
Table 1 Optimization Studies of NIS and ICl as COM Catalysts



Entry[a]	Catalyst (mol%)[b]	Time (h)	Atmosphere[c]	Solvent	Conv. (%)
1	NIS (10)	24	ambient	MeCN	0
2	NIS (10)	24	ambient	toluene	0
3	NIS (10)	24	ambient	THF	0
4	NIS (10)	24	ambient	EtOAc	0
5	NIS (10)	(24) 64	ambient	DCM	(50) 100[d]
6	NIS (10)	24	ambient	DCE	100[d]
7	NIS (5)	(24) 64	ambient	DCE	(40) 100[d]
8	NIS (10)	24	dry N_2	DCE	100[d]
9	ICl (10)	24	ambient	DCE	0
11	ICl (20)	24	ambient	DCE	0
10	ICl (10)	24	dry N_2	DCE	100[d]
11	ICl (5)	24	dry N_2	DCE	100[d]

[a] Reaction conditions: substrate **1a** (0.5 mmol) and catalyst were stirred for indicated time at rt.
[b] NIS was recrystallized, and ICl was added from a stock solution in DCE.
[c] Ambient atmosphere means the reaction was carried out without exclusion of air.
[d] Yields of these reaction were in the range of 75–89%.



Scheme 2 Elucidation of reaction mechanism for the I_2-catalyzed COM reaction

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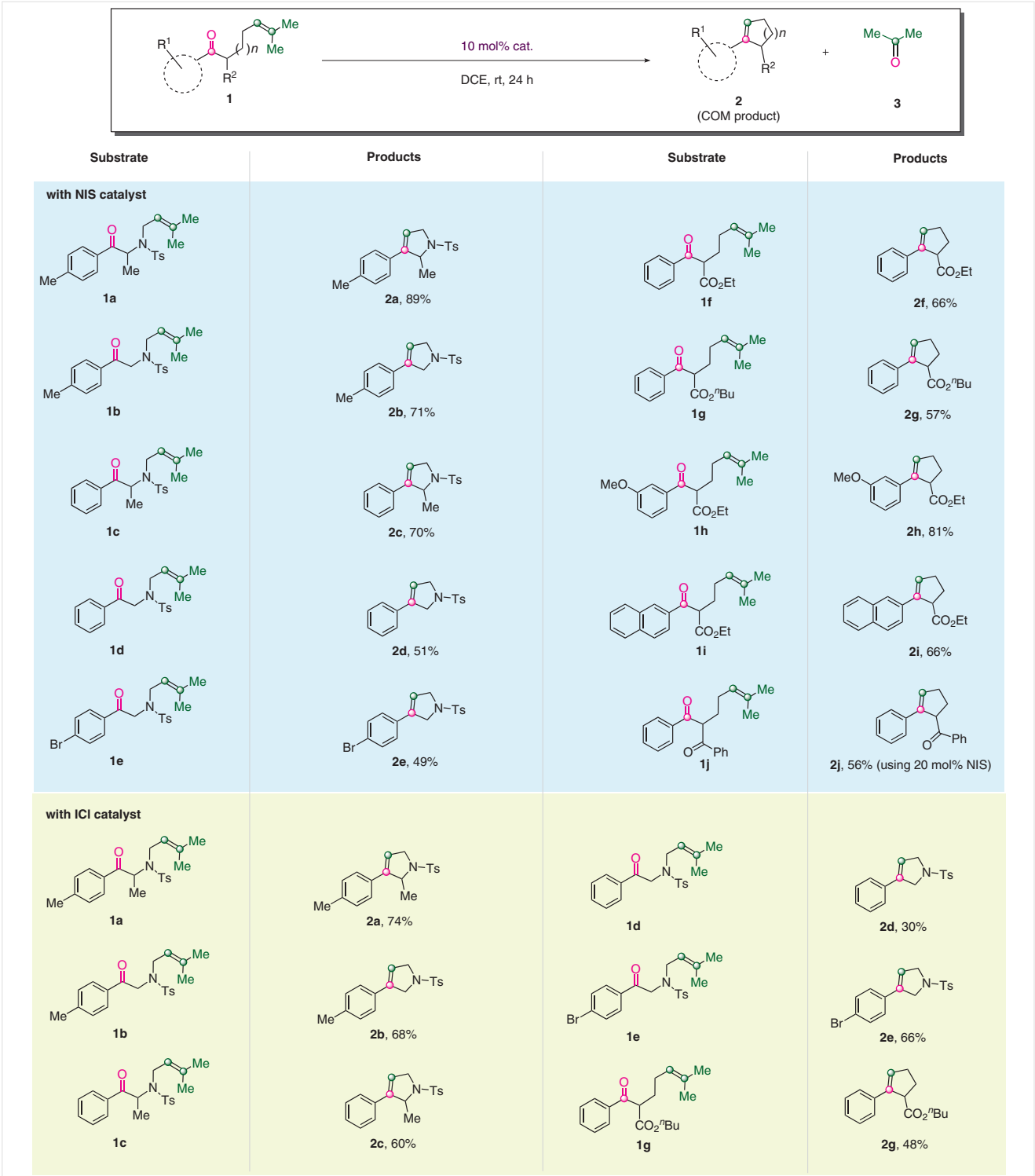
Standard experiments under optimal conditions for I_2-catalyzed intramolecular COM reaction on substrate **1a** using catalytic or stoichiometric amount of HI did not yield any expected product, hinting that Brønsted acid catalysis is unlikely to be the driving force for the reaction (Scheme 2).[12] Similarly, control experiments with catalytic or stoi-



Scheme 3 Substrate scope of intramolecular COM reactions catalyzed by NIS and ICl

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chiometric amount of butylated hydroxytoluene (BHT) as radical scavenger additive (Scheme 2) worked as efficiently as the original catalytic reaction, ruling out the possibility that it follows a free radical pathway.[12] When we exposed substrate **1a** to two different iodine-bonding donors (Scheme 2),[13] no conversions were observed with catalytic amounts of these while the reaction mixtures slowly turned messy over the course of 48–72 hours with stoichiometric amounts.[12] Therefore, halogen-bonding activation is also unlikely to be at play for the COM reaction.

With the iodonium pathway remained to be validated, we performed some further control experiments. The addition of a catalytic amount of DMSO, a solvent that can bind tightly to iodonium ion (I^+), rendered the original I_2 catalyst much less efficient.[12] The addition of potassium iodide in addition to I_2 catalyst, which disfavored the formation of iodonium ion, also suppressed the reaction. Interestingly, two commonly used iodonium sources, namely *N*-iodosuccimide (NIS) and iodine monochloride (ICl), proved to be efficient catalysts for the COM reaction of substrate **1a** as well.[12] On the other hand, chloronium and bromonium sources such as NCS, NBS, and Br_2 did not facilitate the COM reaction,[12] indicating that iodonium is more special and suitable for this type of reaction than the other halonium species. These studies collectively suggest that the I_2-catalyzed COM reaction of substrate **1a** is most likely progressed via the iodonium pathway and, most importantly, other iodonium precursors can also be used to promote this type of reaction.

Intrigued by these results, we subsequently carried out optimization studies for these two newly identified catalysts on the COM reaction of **1a** (Table 1). Both NIS and ICl appeared to work only in chlorinated solvents, and 1,2-dichloroethane (DCE) was the best solvent for the reaction. It required 10 mol% loading of NIS for complete conversion of substrate **1a** in 24 hours at room temperature. While NIS catalyst was working well with or without exclusion of air, ICl catalyst needed an inert atmosphere to function, although the catalyst loading of the latter could be reduced to 5 mol%. However, we decided to use 10 mol% of ICl for consistent results in substrate scope study, as sometime 5 mol% does not give satisfactory conversion.

Having the optimal conditions for both catalysts in hand (Table 1, entries 6 and 11), we went on to use them to catalyze the intramolecular COM reaction for a range of selected substrates (Scheme 3).[14] Most of these substrates were converted into the desired COM products in moderate to high yields by both NIS and ICl, albeit the efficiency was generally lower with ICl. This can be attributed to the instability of ICl under air and moisture during the reaction setup, making NIS a more practical COM catalyst for synthetic application. Nitrogen-bearing substrates **1a–e** seemed to work better than the others (**1f–j**). In the **1a–e** series, substitutions at the α-position to the keto group appeared to assist the COM reaction, as without it (**1b**,**d**,**e**) the efficiency decreased.

Most interestingly, for the non-nitrogen-containing substrates, we did not observe any noticeable regioisomerization in the cyclized products. This was an issue for other catalytic systems, including Schindler's iron[6a,c] and Tiefenbacher supramolecular[8] catalysts as well as our tropylium and molecular iodine catalysts.[9,10] This reduces lengthy and problematic product purification, which clearly is an advantage of using NIS and ICl to promote COM reaction in comparison to previously developed catalysts.

In conclusion, this work validated the iodonium catalytic pathway of molecular iodine promoted carbonyl–olefin metathesis reaction.[15] It also identified NIS and ICl, two commonly used iodonium sources in synthetic laboratories, as efficient catalysts for intramolecular carbonyl–olefin metathesis reactions. These two catalysts work efficiently under mild conditions and offer the advantage of no complication with product regioisomerism.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690297.

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(14) These two catalysts did not seem to promote the intermolecular COM reaction as preliminary reactions gave unsatisfactory outcomes.

(15) **General Procedure A**

A 4 mL vial was charged with NIS (10 mol%) and a stirring bar. Starting material **1** was added to the vial under ambient atmosphere, along with three drops of DCE, added to help with the stirring of reaction mixture. The vial was closed by a cap, and the mixture was stirred for 24 h at room temperature, unless otherwise specified. Upon completion (as determined by TLC analysis), the crude mixture was directly purified by flash column chromatography, to give the metathesis products.

General Procedure B

A 4 mL vial was charged with ICl (10 mol%, as a stock solution in DCE) and a stirring bar. Starting material **1** was added to the vial under nitrogen atmosphere. The vial was kept under nitrogen, and the mixture was stirred for 24 h at room temperature, unless otherwise specified. Upon completion (as determined by TLC analysis), the crude mixture was directly purified by flash column chromatography, to give the metathesis products.

2-Methyl-3-(*p*-tolyl)-1-tosyl-2,5-dihydro-1*H*-pyrrole (2a)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.3 Hz, 2 H), 7.31 (d, *J* = 8.0 Hz, 2 H), 7.27–7.06 (m, 4 H), 5.80 (q, *J* = 2.0 Hz, 1 H), 5.02 (ddddd, *J* = 9.0, 6.2, 4.1, 3.1, 1.7 Hz, 1 H), 4.30 (q, *J* = 2.5 Hz, 2 H), 2.38 (d, *J* = 16.9 Hz, 6 H), 1.50 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.4, 143.2, 138.1, 135.1, 130.1, 129.8, 129.4, 127.3, 126.3, 117.9, 63.0, 54.8, 22.1, 21.5, 21.2 ppm.

3-(*p*-Tolyl)-1-tosyl-2,5-dihydro-1*H*-pyrrole (2b)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.2 Hz, 2H), 7.35–7.26 (m, 7 H), 5.83–5.81 (m, 1 H), 5.03–5.0 (m, 1 H), 4.30–4.28 (m, 2 H), 2.40 (s, 3 H), 1.48 (d, *J* = 6.0 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.5, 143.4, 135.1, 133.0, 129.8, 128.7, 128.2, 127.3, 126.3, 118.8, 62.9, 54.8, 22.1, 21.5 ppm.

Butyl 2-Phenylcyclopent-2-ene-1-carboxylate (2g)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56–7.41 (m, 2 H), 7.41–7.11 (m, 3 H), 6.35 (td, *J* = 2.6, 1.6 Hz, 1 H), 4.13–3.90 (m, 3 H), 2.75 (dddd, *J* = 17.3, 8.9, 4.6, 2.6 Hz, 1 H), 2.68–2.53 (m, 1 H), 2.48–2.14 (m, 1 H), 1.63–1.42 (m, 2 H), 1.37–1.19 (m, 2 H), 0.87 (t, *J* = 7.3 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 175.3, 141.2, 135.5, 130.0, 128.3, 127.2, 125.8, 64.4, 51.3, 32.5, 30.6, 29.3, 19.0, 13.6 ppm. IR (neat): 3055, 2960, 1726, 1457, 1383, 1330 cm^{-1}. HRMS: *m/z* calcd for $[C_{16}H_{20}O_2Na]^+$: 267.1361; found: 267.1356.

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