

Catalytic transfer of carbon atoms enables spirofusion of C–C σ -bonds

Corresponding Author: Dr Hayato Fujimoto

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This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Version 0:

Reviewer comments:

Referee #1

(Remarks to the Author)

Fujimoto, Tobisu and coworkers present on the spiro C-atom transfer utilizing rhodium catalysis and biphenylene derivatives via C–C σ -bond activation. C-atom transfer has emerged as a highly active area of research, with a seminal contribution originating from this laboratory (Science 2023, 379, 484–488). Since then, growing interest has focused on developing new methods and reagents, including approaches based on diazo compounds, hypervalent iodine reagents, and sulfonium-derived species.

In the present work, the authors employ isocyanoiminophosphorane (PINC), a reagent that is generally well studied and even commercially available, yet has so far been largely overlooked for C-atom transfer chemistry. The group has previously combined PINC with Rh catalysis in the context of C-atom transfer (J. Am. Chem. Soc. 2025, 147, 8138–8144). Here, they extend this concept by demonstrating C–C σ -bond activation coupled with C-atom transfer to generate spirocyclic structures, which represent highly appealing targets. Notably, the transformation enables the direct conversion of planar, two-dimensional feedstock molecules into three-dimensional frameworks, a feature that is particularly attractive for materials design.

In my opinion, the overall concept and narrative of the study are very clear and highly original. The work is very elegant, and the proposed elementary steps are well supported by literature precedents and appropriate control experiments. I find the study highly impressive, and the scientific content is certainly suitable for publication in a top-tier journal. However, although the manuscript clearly addresses a broad organic chemistry audience and may also be of interest to the materials science community, I have some reservations regarding its suitability (see below) for the exceptionally broad readership of Nature. In my view, at its current stage the work may be better suited for a leading chemistry-focused journal such as Nature Synthesis or Nature Chemistry.

Given that the transformation is presented as broadly applicable, the reaction conditions appear highly optimized and somewhat specialized. For example, the solvent mixture (nBu₂O/DMF) is not an obvious choice, and including an optimization table in the Supporting Information would help clarify how these conditions were identified. More generally, the reaction conditions seems rather demanding to be generally applied, involving a specific solvent mixture, high catalyst loading, very slow reagent addition of the reagent (1 ml/h) within a glovebox. These requirements only lead to a moderate yield of 53% for 2aa under the best optimized conditions. For the cross-spiro fusion, an additional portion of the catalyst system is required, resulting in a total loading of 20 mol% rhodium and 40 mol% ligand. This further increases significantly the cost of the transformation, particularly with regard to larger-scale applications. In this context, it would be good to know whether the reaction is scalable, for example to the gram scale, which would be necessary for potential applications in materials science.

In addition, the functional group tolerance remains somewhat unclear. It would be valuable to know whether groups such as –CN, –NO₂, –CHO, –C(O)R, alkynes, alkenes, or heterocycles are compatible with the reaction conditions. Demonstrating tolerance toward a broader range of functional groups would help to better assess the generality and practical utility of the transformation. Along these lines, the manuscript would be further strengthened by including a few more structurally complex

spiro systems (for example, involving two sequential C-atom transfer events) to more clearly demonstrate the power of the approach compared with the well-established strategies based on double addition to fluorenone derivatives.

During the course of the reaction, PPh₃ is eliminated. Since PPh₃ is also a strong ligand, it would be useful to clarify whether Ph₃P is indeed formed and isolated as a stoichiometric byproduct. If so, does it slow down the catalysis over time through competitive coordination to the metal center? In this context, it would also be interesting to consider an additional control experiment: If Ph₃P is released under the reaction conditions, treating 6a under the standard conditions in the presence of added Ph₃P might provide useful insight, since 6a and PPh₃ should also form a resting-state phosphazine intermediate. If this is indeed the case, the transformation might also be feasible starting from the corresponding diazo compound, which should be readily accessible independently from the fluorenone precursor.

Referee #2

(Remarks to the Author)

-Summary of the key results:

This manuscript describes the rhodium-catalyzed catalytic transfer of a single carbon atom to biphenylene substrates to transform them into rigid three-dimensional 9,9'-spirobifluorenes. The source of carbon is N-isocyanoiminophosphorane (PINC), a reagent already used by the authors for similar purposes. Interestingly, the reaction can be stopped after the formation of phosphazine 4a, enabling the participation of a second biphenylene partner. The isolation of that intermediate is also a key argument to support the proposed mechanism (in addition to DFT calculations). The availability of the ¹³C labelled reagent also allows the obtention of the corresponding isotopically labelled products.

-Originality and significance: if not novel, please include reference:

This work falls within a currently very active area of research known as "skeletal editing." Specifically, the authors have developed a protocol for inserting a carbon atom into a C–C sigma bond (the bond linking two aromatic rings in biphenylenes), thereby generating a spiro carbon atom (following the formation of four C–C bonds with the transferred carbon atom). This transformation is highly original. Until now, C-atom transfer to obtain spiro carbons has been achieved through the activation of pi bonds, but never via a C–C bond. The most similar example that I can think about corresponds to the previous work by the authors of this paper, who have recently used the subsequent activation of C–Cl and C–H bonds to form quaternary carbon centers. So, from the point of view of originality, I have little to object to. The synthesis described is, in my opinion, very elegant.

Once the quality of this work is acknowledged, I also have to say that I expect the impact of the specific transformation described to be limited. The reaction needs very specific substrates (biphenylenes), which are not commonly available ones, and which require a series of prior synthetic steps to be prepared. Contrary to the authors' statements in the abstract and the introduction, I do not think that they can be considered "simple" feedstocks (as will be the case of olefins, C–H bonds...).

Thus, I believe this reaction might be used in the future to prepare targeted 9,9'-spirobifluorenes, but not as a general strategy to introduce three dimensions in polyarenes already prepared (as somehow implied in Figure 1a).

-Data & methodology: validity of approach, quality of data, quality of presentation

From the methodologic point of view, the work has been competently carried out. The SI is complete, the methods are properly described and the characterizations have been done properly.

-Conclusions:

I agree with the conclusions except for the last sentence, which I think is excessive.

-Suggested improvements:

I think the authors don't stress enough the thermal stability of their PINC reagent and on the fact that it is compatible with metal catalysis. In my opinion those two factors are crucial to warrant its use in the future. This reviewer has not been able to resist making the comparison with the Hansmann diazocompound shown in Figure 1. Scanning differential calorimetry of that reagent indicates that it is almost an explosive; neither is clearly compatible with metal catalysts. However, the less reactive PINC does a similar job under milder conditions and controlled by metals, which means a) higher functional group tolerance, and b) possibility to develop in the future regio-/enantioselective versions of the reactions under study. It is for these reasons that I believe the authors should include in the SI the calorimetric analysis of the PINC and comment on this issue.

A more intensive study of the tolerance of functional groups on the substrates is necessary. Functional groups such as aldehydes, amines, alcohols, nitriles, amides..., are simply not represented in the scope table, which, in my opinion, is too reduced.

-Clarity and context:

The manuscript is written in a clear manner. It is easy to read, the schemes are easy to follow and present the results in a concise and direct manner. The references are adequate.

Version 1:

Reviewer comments:

Referee #1

(Remarks to the Author)

Fujimoto, Tobisu and co-workers have submitted a revised manuscript that addresses my comments in detail, including the optimization of the originally reported procedure. The authors have also expanded the scope of the study by investigating a broader range of functional groups and demonstrating for one substrate two-fold C-atom transfer. Furthermore, they have provided control experiments that clarify the role of PPh_3 in the transformation. All relevant information has been incorporated into the manuscript and the Supporting Information.

The quality of the work has improved substantially compared to the original submission. As noted in my first review, I consider this an intellectually compelling conceptual contribution with high originality in the mechanistic design. The PINC reagent is commercially available and, in contrast to other C-atom sources, exhibits high stability. This was further supported by the additional DSC data provided in the SI. Moreover, its combination with transition-metal catalysis should, in principle, allow tuning of the selectivity and may even enable enantioselective C-atom transfer in the future. The work also appeals to a broader audience: beyond the new methodology, the products themselves are of value for materials applications. Overall, this is a well-conceived and convincingly presented contribution.

I identify two remaining weaknesses. The first, which I share with the second reviewer, concerns the rather specialized biphenylene starting materials: these are neither commercially abundant nor accessible through a short, general synthetic route. The second, which I also raised in my initial review, pertains to the reaction conditions. The requirement for slow addition, a solvent mixture combined with a relatively high Rh/ligand loading renders the protocol rather unattractive for potential scale-up applications. However, I note that the manuscript does not purport to deliver a generally broadly applicable, practical synthetic protocol. The key strength of this work lies in establishing a novel conceptual framework for C-atom transfer via σ -bond (not π -bond) C–C activation, a direction that is both timely and exciting. In this context, I do not consider the limitations outlined above sufficient to preclude publication, and I recommend acceptance.

Referee #2

(Remarks to the Author)

In my view, the authors have done their best to address the reviewers' criticisms. They have optimized the reaction conditions, highlighted the qualities of the reagent they use, and slightly broadened the scope of the reaction regarding functional group tolerance.

As I already indicated in my previous report, this article describes a very original chemical reaction. The insertion of a carbon atom into organic substrates is not a common transformation seen daily. In that sense, I understand the authors' wish to publish this work in a journal like Nature. On the other hand, I wonder about the actual synthetic utility, and frankly, I do not see it clear. I still believe that this reaction will end up being just a curiosity because it requires the use of complex substrates that themselves need several synthetic steps to obtain. The functional group tolerance is neither great. If the "spiro-fusion" shown in Figure 1a were real, I would have no choice but to congratulate the authors, because that reaction would be fabulous. The fact is, however, that the authors need bisphenylenes, and not biphenyl derivatives.

In conclusion, I think this is a very beautiful work, but I also think that its application and synthetic impact will be limited.

made.

In cases where reviewers are anonymous, credit should be given to 'Anonymous Referee' and the source.

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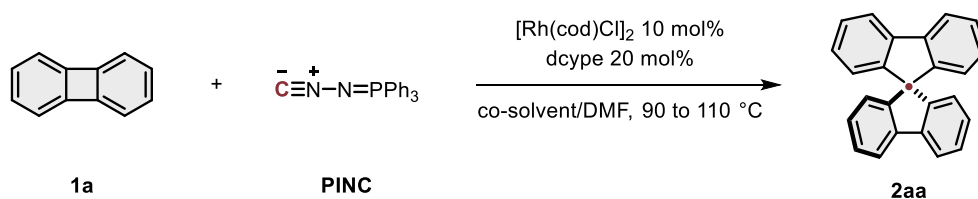
Responses to the comments from reviewer 1:

1. Given that the transformation is presented as broadly applicable, the reaction conditions appear highly optimized and somewhat specialized. For example, the solvent mixture (*n*Bu₂O/DMF) is not an obvious choice, and including an optimization table in the Supporting Information would help clarify how these conditions were identified. More generally, the reaction conditions seems rather demanding to be generally applied, involving a specific solvent mixture, high catalyst loading, very slow reagent addition of the reagent (1ml/h) within a glovebox. These requirements only lead to a moderate yield of 53% for **2aa** under the best optimized conditions. For the cross spiro fusion, an additional portion of the catalyst system is required, resulting in a total loading of 20 mol% rhodium and 40 mol% ligand. This further increases significantly the cost of the transformation, particularly with regard to larger-scale applications. In this context, it would be good to know whether the reaction is scalable, for example to the gram scale, which would be necessary for potential applications in materials science.

We thank the referee for raising these important points regarding the reaction conditions and practical applicability of the method. In response, we conducted additional optimization studies to clarify the rationale for the solvent system, reduce the catalyst loading, simplify the experimental procedure, and demonstrate the scalability of the reaction. These studies substantially improved the practicality of the transformation, as described below.

• Solvent effect

DMF was initially selected because PINC is readily soluble in DMF at room temperature, which enables its controlled addition as a homogeneous solution. Importantly, the reaction can also be performed using DMF as the sole solvent, affording the desired spirobifluorene in 56% yield. Because the second carbene-insertion step requires heating above 100 °C, we examined high-boiling co-solvents and found that the addition of dibutyl ether (*n*Bu₂O) improved the yield to 75%. In contrast, the use of toluene as the co-solvent resulted in only 9% yield. Thus, *n*Bu₂O/DMF solvent system was adopted based on both the solubility of PINC and the improved efficiency of the reaction at elevated temperature. The corresponding optimization data have now been included in the Supporting Information (Table S1).



Entry	co-solvent	Yield of 2aa (%)
1	<i>n</i> Bu ₂ O	72
2	DMF	56
3	toluene	9

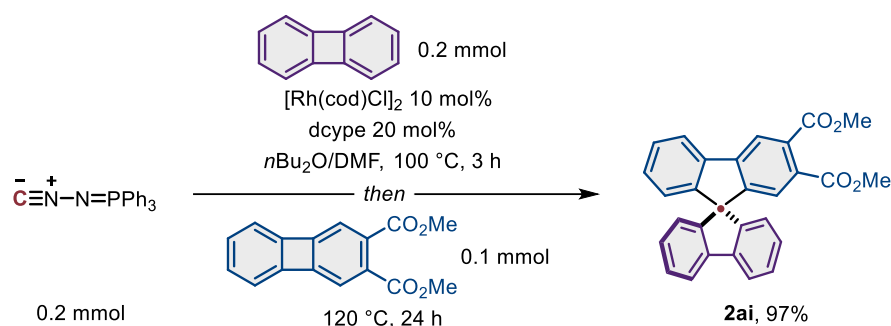
• Catalyst loading and scalability

We next examined whether the catalyst loading could be reduced. By optimizing the PINC addition rate and reaction temperature, the desired product was obtained in 56% yield using only 3 mol% of the Rh catalyst (entry 4), substantially lower than the catalyst loading used in the original protocol. Using these conditions, we further performed the reaction on a 10 mmol scale. Notably, the entire reaction setup, including the controlled addition of the PINC solution, was carried out on the benchtop without the use of a glovebox. The reaction proceeded in 50%

^b Reaction conducted at 110 °C throughout, instead of the standard temperature program (90 to 110 °C).



We also further optimized the cross-spiro-fusion protocol to reduce the catalyst loading and simplify the operation. In the original procedure, the phosphazine intermediate was isolated before addition of the second biphenylene, and a second portion of the Rh catalyst system was required. Because the second biphenylene was used on a 0.10 mmol scale, the two catalyst charges corresponded to a total loading of 20 mol% [Rh(cod)Cl]₂. We have now found that the second biphenylene can be added directly to the reaction mixture without isolation of the phosphazine intermediate or addition of a second portion of the catalyst. Under these one-pot conditions, the desired cross-spiro product was obtained in 97% yield based on the second biphenylene, using a single 10 mol% charge of [Rh(cod)Cl]₂ relative to the second biphenylene. Thus, the revised protocol eliminates intermediate isolation and the second catalyst charge, reducing the total amount of [Rh(cod)Cl]₂ required for the cross-spiro-fusion step by half.



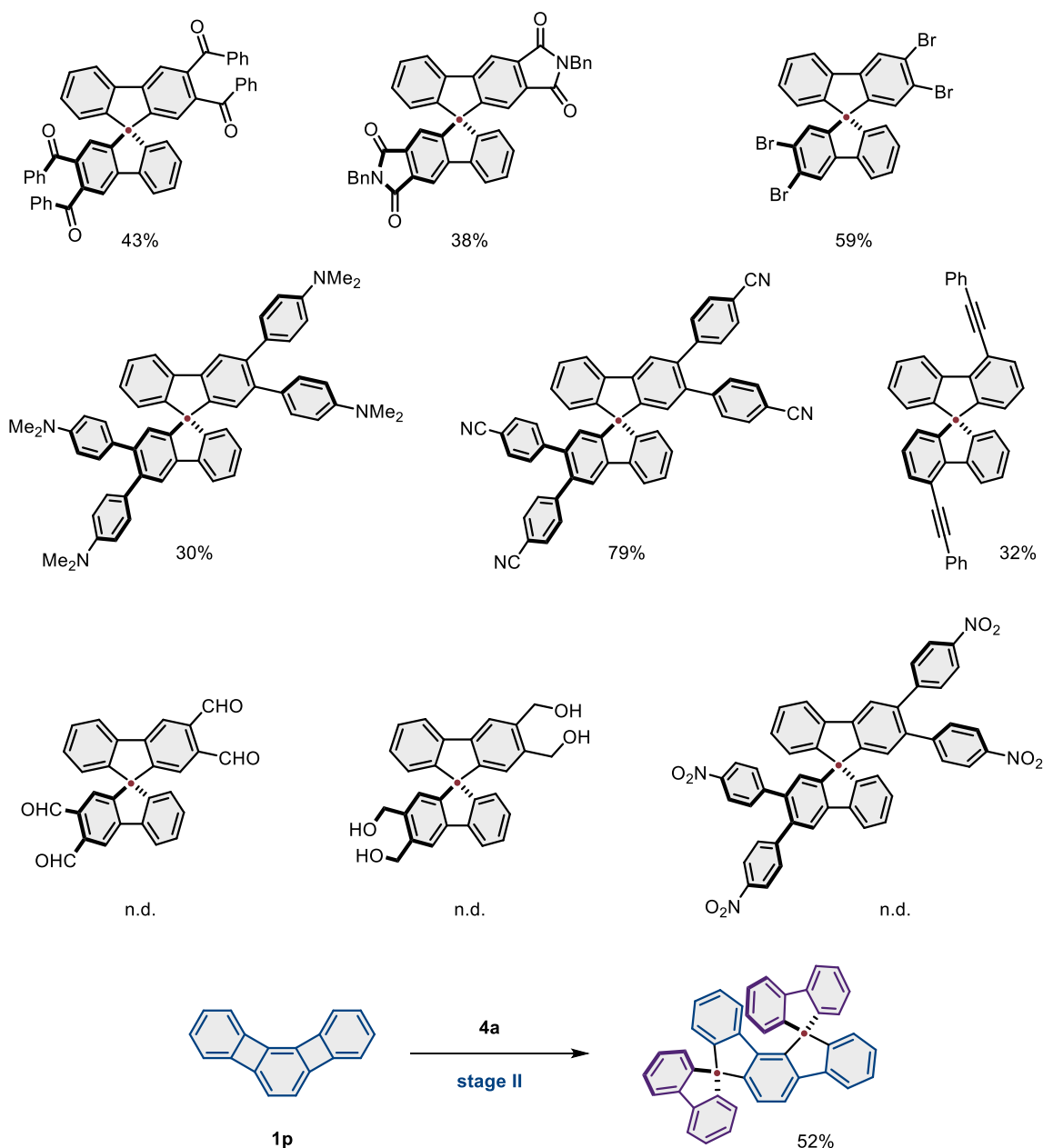
These new results have been incorporated into the revised manuscript and Supporting Information.

- In addition, the functional group tolerance remains somewhat unclear. It would be valuable to know whether groups such as $-CN$, $-NO_2$, $-CHO$, $-C(O)R$, alkynes, alkenes, or heterocycles are compatible with the reaction conditions. Demonstrating tolerance toward a broader range of functional groups would help to better assess the generality and practical utility of the transformation. Along these lines, the manuscript would be further strengthened by including a few more structurally complex spiro systems (for example, involving two sequential C atom transfer events) to more clearly demonstrate the power of the approach compared with the well established strategies based on double addition to fluorenone derivatives.*

Thank you for this valuable suggestion. We substantially expanded the substrate scope to more thoroughly evaluate the functional-group tolerance of the reaction. The revised scope now includes substrates bearing ketone, amide, bromo, amino, cyano, and alkyne functionalities. The compatibility of the bromo substituent is particularly noteworthy, as the resulting brominated spiro product provides a useful handle for further functionalization, thereby enhancing the synthetic utility of the present method. Moreover, the alkynyl-substituted substrate underwent regioselective C–C bond cleavage while retaining the alkyne functionality. We also examined substrates containing aldehyde, alcohol, and nitro groups. Although these substrates did not afford the desired spiro-fusion products under the standard conditions, these results help define the current limitation of the transformation.

We also demonstrate the construction of more structurally complex spiro systems through a two-fold carbon-atom-transfer process. Benzo[3,4]cyclobuta[1,2-*a*]biphenylene, which contains two embedded biphenylene motifs, underwent two consecutive carbon-atom-transfer events to furnish the inner–outer double-spiro-fused product in 52% yield. This result demonstrates that the present strategy can be extended beyond simple spirobifluorenes to the rapid construction of more complex spiro architectures through multiple C–C bond activations and carbon-atom-transfer events in a single operation.

The additional successful examples, as well as these limitation studies, have been incorporated into the revised manuscript and Supporting Information.

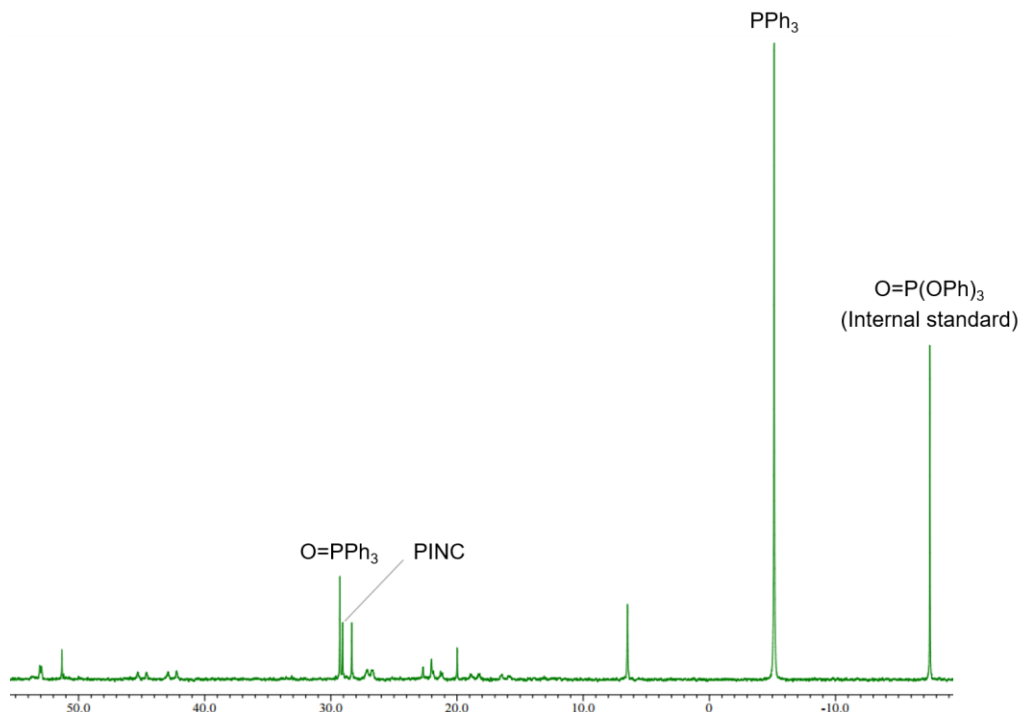


3. During the course of the reaction, PPh_3 is eliminated. Since PPh_3 is also a strong ligand, it would be useful to clarify whether Ph_3P is indeed formed and isolated as a stoichiometric byproduct. If so, does it slow down the catalysis over time through competitive coordination to the metal center? In this context, it would also be interesting to consider an additional control experiment: If Ph_3P is released under the reaction conditions, treating **6a** under the standard conditions in the presence of added Ph_3P might provide useful insight, since **6a** and PPh_3 should also form a resting-state phosphazine intermediate. If this is indeed the case, the transformation might also be feasible starting from the corresponding diazo compound, which should be readily accessible independently from the fluorenone precursor.

Thank you for your insightful comment. We performed additional experiments to clarify the formation and role of PPh_3 during the reaction.

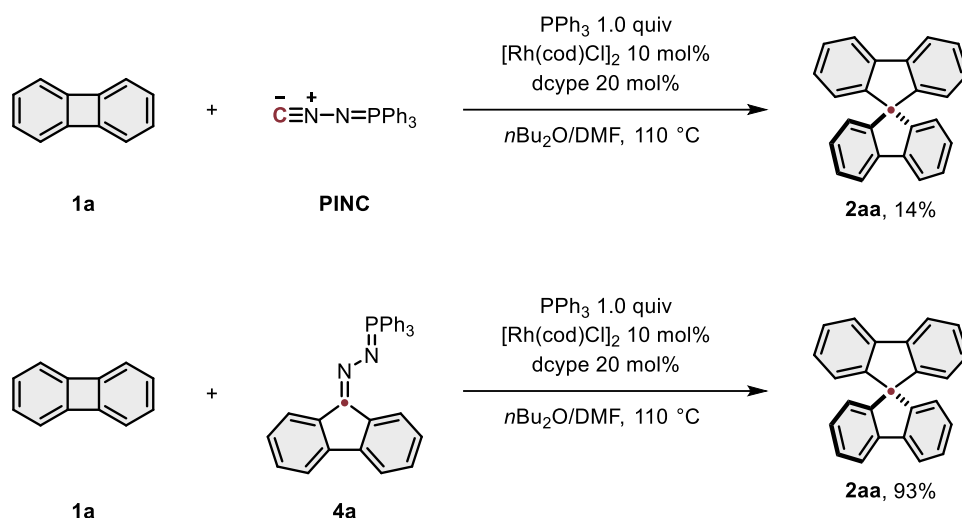
• Formation and inhibitory effect of PPh_3

Quantitative ^{31}P NMR analysis of the crude reaction mixture after completion of the standard reaction revealed PPh_3 as the major phosphorus-containing product (50%), together with $\text{O}=\text{PPh}_3$ (5%) and unreacted PINC (3%). These results confirm that PPh_3 is indeed released during the reaction. The ^{31}P NMR spectrum has now been included in the Supplementary Information (Fig. S2).



We next examined whether free PPh_3 inhibits the Rh-catalyzed reaction. When 1.0 equiv of PPh_3 was added from the beginning of the standard reaction, the yield of spirobifluorene decreased to 14%, indicating that PPh_3 can interfere with the catalytic process when present during the initial stage of the reaction. However, under the standard reaction conditions, PPh_3 is expected to be generated primarily upon dissociation of the phosphazine intermediate at elevated temperature and therefore to be present at only low concentration during the initial catalytic cycle for the formation of the phosphazine intermediate.

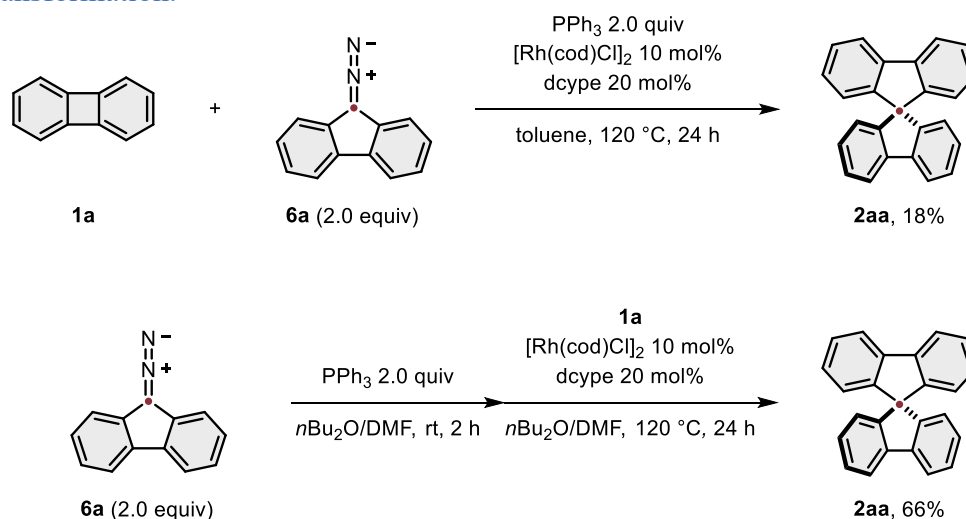
To more closely reproduce the stage at which PPh_3 is actually generated, we therefore examined the second carbon-atom-transfer step independently. Treatment of the isolated phosphazine intermediate with biphenylene in the presence of an additional 1.0 equiv of PPh_3 afforded spirobifluorene in 93% yield, essentially identical to that obtained in the absence of added PPh_3 . Thus, although PPh_3 can inhibit the reaction when present from the outset, its accumulation does not significantly inhibit the second carbon-atom-transfer step under the reaction conditions. These results suggest that competitive coordination of PPh_3 does not substantially compromise catalytic turnover at the stage at which PPh_3 is generated during the actual reaction.



• Reaction from the diazo compound

We also investigated the referee's suggestion that the corresponding diazo compound might serve as an alternative precursor. In the absence of PPh_3 , the diazo compound did not afford the desired spirobifluorene under the standard reaction conditions. In contrast, addition of PPh_3 resulted in formation of the desired product in 18% yield. Furthermore, when the diazo compound and PPh_3 were stirred in the reaction solvent at room temperature for 2 h before addition of the remaining reaction components, the desired spirobifluorene was obtained in 66% NMR yield.

These results are consistent with formation of the phosphazine from the diazo compound and PPh_3 and further support the phosphazine as a productive intermediate in the carbon-atom-transfer process. Importantly, they also establish a complementary synthetic entry to the spiro-fusion reaction from an independently accessible diazo compound. Thus, the phosphazine intermediate can serve as a convergence point between the PINC-based carbon-atom-transfer pathway and a conventional diazo precursor, further expanding the synthetic versatility of the present transformation.



These new results have been incorporated into the revised manuscript and Supporting Information.

Responses to the comments from reviewer 2:

- 1. This work falls within a currently very active area of research known as "skeletal editing." Specifically, the authors have developed a protocol for inserting a carbon atom into a C–C sigma bond (the bond linking two aromatic rings in biphenylenes), thereby generating a spiro carbon atom (following the formation of four C–C bonds with the transferred carbon atom). This transformation is highly original. Until now, C-atom transfer to obtain spiro carbons has been achieved through the activation of pi bonds, but never via a C–C bond. The most similar example that I can think about corresponds to the previous work by the authors of this paper, who have recently used the subsequent activation of C–Cl and C–H bonds to form quaternary carbon centers. So, from the point of view of originality, I have little to object to. The synthesis described is, in my opinion, very elegant. Once the quality of this work is acknowledged, I also have to say that I expect the impact of the specific transformation described to be limited. The reaction needs very specific substrates (biphenylenes), which are not commonly available ones, and which require a series of prior synthetic steps to be prepared. Contrary to the authors' statements in the abstract and the introduction, I do not think that they can be considered "simple" feedstocks (as will be the case of olefins, C–H bonds...). Thus, I believe this reaction might be used in the future to prepare targeted 9,9'-spirobifluorenes, but not as a general strategy to introduce three dimensions in polyarenes already prepared (as somehow implied in Figure 1a).*

We thank the referee for the positive assessment of the originality of this transformation.

We agree with the referee that biphenylenes represent a more specialized class of substrates than ubiquitous feedstocks such as alkenes, and that our original wording could give an overly broad impression of the applicability of the present transformation. We have therefore removed the description of biphenylenes as "simple feedstocks" from the revised manuscript.

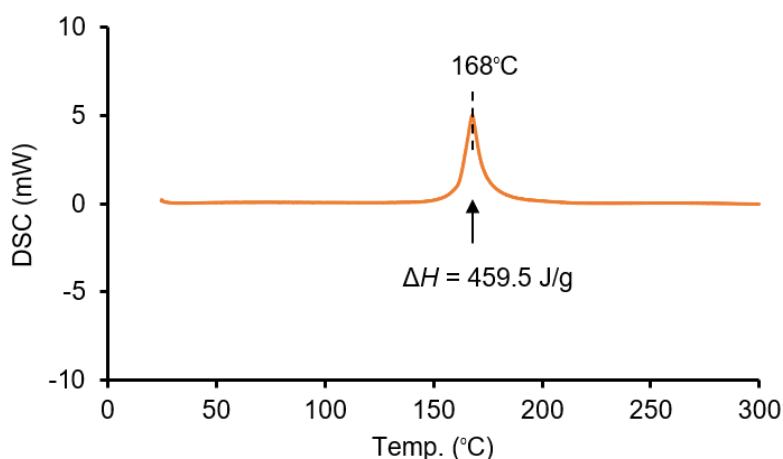
We nevertheless believe that the significance of the present work lies not only in the synthesis of a particular class of spirobifluorenes, but also in the new reaction mode enabled by the combination of carbon-atom transfer and C–C σ -bond activation. Previous carbon-atom-transfer approaches to spiro-fusion have relied predominantly on the intrinsic reactivity of π -bonds toward carbene-type species. In contrast, the present study expands spiro-fusion beyond such π -bond-based reactivity by coupling carbon-atom transfer with transition-metal-mediated C–C σ -bond activation. We believe that this concept provides a first step toward extending carbon-atom-transfer chemistry to the three-dimensionalization of polyarenes.

- 2. I think the authors don't stress enough the thermal stability of their PINC reactive and on the fact that it is compatible with metal catalysis. In my opinion those two factors are crucial to warrant its use in the future. This reviewer has not been able to resist making the comparison with the Hansmann diazocompound shown in Figure 1. Scanning differential calorimetry of that reagent indicates that it is almost an explosive; neither is clearly compatible with metal catalysts. However, the less reactive PINC does a similar job under milder conditions and controlled by metals, which means a) higher functional group tolerance, and b) possibility to develop in the future regio-/enantioselective versions of the reactions under study. It is for these reason that I believe the authors should include in the SI the calorimetric analysis of the PINC and comment on this issue.*

Thank you for this insightful comment. We agree that the thermal properties of PINC and, particularly, its compatibility with transition-metal catalysis are important features that deserve greater emphasis.

• Thermal analysis of PINC

In response to the referee's suggestion, we performed differential scanning calorimetry (DSC) analysis of PINC. At a heating rate of 5 °C/min, PINC exhibited an exothermic event with a peak temperature of 168 °C ($\Delta H = 459.5$ J/g). Notably, this temperature is substantially higher than the temperatures employed in the present Rh-catalyzed spiro-fusion reaction (90–110 °C). The DSC profile and experimental details have now been included in the Supplementary Information (Fig. S3).



• Compatibility with transition-metal catalysis

We also agree with the referee that the compatibility of PINC with transition-metal catalysts is an important characteristic of this carbon-atom-transfer reagent. We believe that this compatibility arises not only from its thermal robustness but also from its molecular structure. In contrast to many diazo-based carbon-atom-transfer reagents, PINC possesses an isocyanide moiety that can coordinate to a metal center while retaining its molecular framework. This coordination ability enables PINC to engage directly with the metal catalysis while retaining its molecular framework, thereby allowing the carbon-atom-transfer process to proceed within the coordination sphere of the metal.

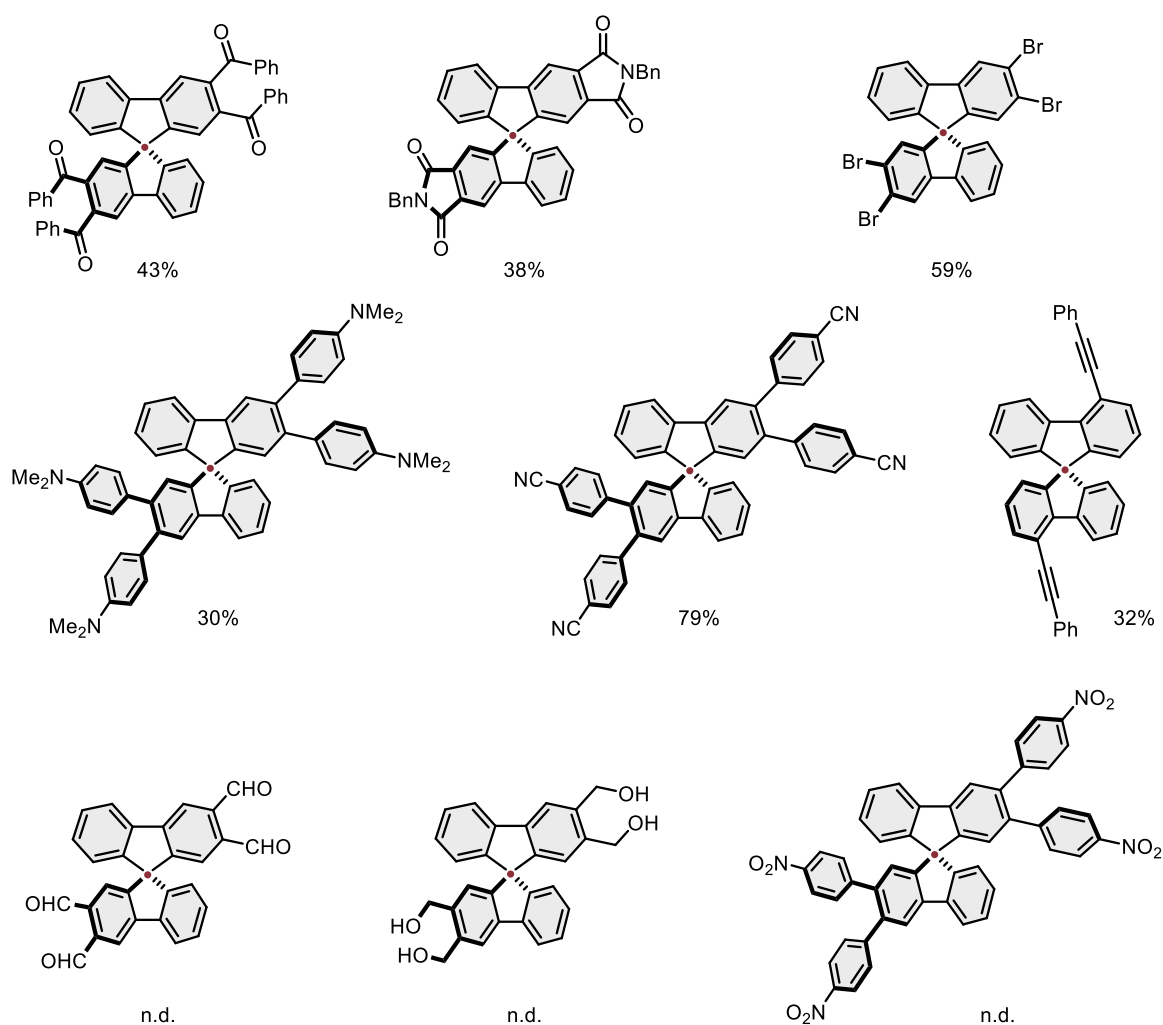
In the present transformation, this feature enables PINC to participate in a Rh-catalyzed sequence involving C–C σ -bond activation and formation of the spiro carbon center. Indeed, several unsymmetrically substituted biphenylenes examined in the present study undergo spiro fusion with high regioselectivity, demonstrating that the carbon-atom-transfer process can be effectively controlled by the transition-metal catalyst. More broadly, the compatibility of PINC with metal catalysis may provide opportunities for the future development of regio- and enantioselective carbon-atom-transfer reactions through catalyst and ligand design.

We have revised the manuscript to emphasize both the thermal robustness of PINC and its distinctive compatibility with transition-metal catalysis.

3. *A more intensive study of the tolerance of functional groups on the substrates is necessary. Functional groups such as aldehydes, amines, alcohols, nitriles, amides..., are simply not represented in the scope table, which, in my opinion, is too reduced. A more intensive study of the tolerance of functional groups on the substrates is necessary. Functional groups such*

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Thank you for this suggestion. We have substantially expanded the substrate scope to more thoroughly evaluate the functional-group tolerance of the reaction. The revised scope now includes substrates bearing ketone, amide, bromo, amino, cyano, and alkyne functionalities. We also examined substrates containing aldehyde, alcohol, and nitro groups. Although these substrates did not afford the desired spiro-fusion products under the standard conditions, these experiments helped define the current limitations of the transformation. The additional scope and limitation studies have been incorporated into the revised manuscript and Supporting Information.



Responses to the comments from reviewer 1:

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The quality of the work has improved substantially compared to the original submission. As noted in my first review, I consider this an intellectually compelling conceptual contribution with high originality in the mechanistic design. The PINC reagent is commercially available and, in contrast to other C-atom sources, exhibits high stability. This was further supported by the additional DSC data provided in the SI. Moreover, its combination with transition-metal catalysis should, in principle, allow tuning of the selectivity and may even enable enantioselective C-atom transfer in the future. The work also appeals to a broader audience: beyond the new methodology, the products themselves are of value for materials applications. Overall, this is a well-conceived and convincingly presented contribution.

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We thank the reviewer for the positive assessment and recommendation for acceptance. We acknowledge the limitations associated with the biphenylene substrates and the current reaction conditions. Accordingly, we have revised the summary paragraph to avoid describing the transformation as a “general” method and to specify the demonstrated scope more clearly. The revised manuscript emphasizes the conceptual advance of carbon-atom insertion into C–C σ -bond without implying broad practical applicability.

Responses to the comments from reviewer 2:

1. *In my view, the authors have done their best to address the reviewers' criticisms. They have optimized the reaction conditions, highlighted the qualities of the reagent they use, and slightly broadened the scope of the reaction regarding functional group tolerance.*

As I already indicated in my previous report, this article describes a very original chemical reaction. The insertion of a carbon atom into organic substrates is not a common transformation seen daily. In that sense, I understand the authors' wish to publish this work in a journal like Nature. On the other hand, I wonder about the actual synthetic utility, and frankly, I do not see it clear. I still believe that this reaction will end up being just a curiosity because it requires the use of complex substrates that themselves need several synthetic steps to obtain. The functional group tolerance is neither great. If the "spiro-fusion" shown in Figure 1a were real, I would have no choice but to congratulate the

authors, because that reaction would be fabulous. The fact is, however, that the authors need bisphenylenes, and not biphenyl derivatives.

In conclusion, I think this is a very beautiful work, but I also think that its application and synthetic impact will be limited.

We thank the reviewer for recognizing the originality of the transformation and our efforts to address the previous comments. We acknowledge that the demonstrated scope depends on biphenylene substrates and that their synthetic accessibility and the functional group tolerance constrain the current applicability of the method.

To communicate these boundaries more clearly, we have removed the description of the method as “general” from the summary paragraph and redesigned Fig. 1. The former panels a–c have been removed. The revised Fig. 1A illustrates the conceptual bond transformation, whereas Fig. 1B explicitly depicts the biphenylene substrates required for the demonstrated σ – σ and σ – π spiro-fusion reactions. These revisions clarify that the demonstrated transformations require biphenylene substrates.