Chemical Science

ROYAL SOCIETY OF CHEMISTRY

EDGE ARTICLE

View Article Online
View Journal

Cite this: DOI: 10.1039/d5sc09520d

All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 5th December 2025
Accepted 8th February 2026

DOI: 10.1039/d5sc09520d

rsc.li/chemical-science

Deoxygenative phosphonation of ketones by titanium

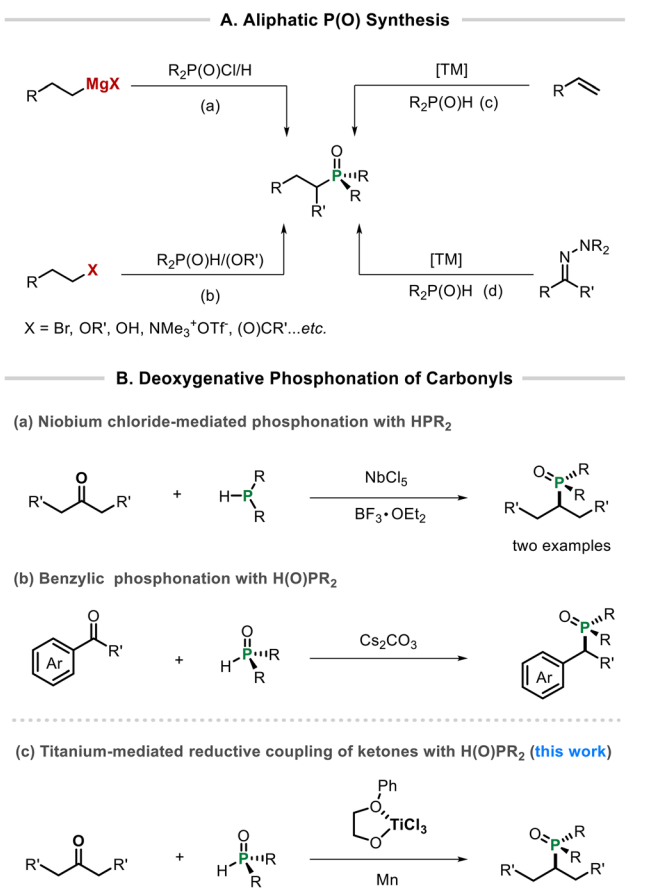
Yuquan Wang,[a] Kai Yin,[b] Xiaobo Pang[a] and Xing-Zhong Shu *[a]

Tertiary phosphine oxides are ubiquitous motifs with essential roles across synthetic chemistry and life sciences, yet C(sp^3)–P coupling remains underdeveloped. Herein, we report an accessible di-oxo-titanium trichloride complex, operating in combination with Mn powder, that enables a deoxygenative C(sp^3)–P coupling of ketones with secondary phosphine oxides. The transformation proceeds under mild conditions and shows good compatibility with carbonyl substrates, including cyclic and acyclic ketones, as well as aliphatic aldehydes. Functionalities such as carboxyl, acetal, alkyne, sulfonate, phenol, and alcohol are well tolerated.

Tertiary phosphine oxides display diverse biological activities and serve as versatile ligands or ligand precursors.[1] While C(sp^2)–P bond formation is well established,[2] strategies for constructing C(sp^3)–P bonds remain underdeveloped. Traditional approaches typically involve substitution reactions of alkyl halides or alkyl metal reagents (Scheme 1A, a and b), such as Michaelis–Arbuzov rearrangements[3] or H-phosphinate additions.[4] Other methods include cross-coupling reactions,[5] hydrophosphination of olefins (Scheme 1A, c),[6] and carbene insertion into P(O)–H bonds (Scheme 1A, d).[7] Despite these advances, further extension of phosphonation strategies to more readily available functional groups would enhance the practical utility of this chemistry.

Ketones are among the most widely available functionalities in organic synthesis, rendering them attractive precursors for accessing aliphatic tertiary phosphine oxides *via* direct phosphonation. In this context, the pioneering work by Suzuki and co-workers disclosed a niobium chloride–mediated deoxygenative phosphonation of aldehydes with P(III) reagents, in which only two ketone examples were demonstrated (Scheme 1B, a).[8] Very recently, the use of bench-stable H(O)PR_2 for phosphonation of benzylic ketones has been realized (Scheme 1B, b).[9] Related progress has also been made in the deoxygenative phosphonation of esters and acids to install H(O)PR_2 at benzylic positions.[10] However, despite these advances, a broadly applicable and mild deoxygenative phosphonation of structurally diverse ketones remains underdeveloped.

Radical-based strategies offer new opportunities to expand the scope of coupling partners. For example, MacMillan and co-workers recently reported two isolated cases of radical phosphonation of NHC-activated primary alcohols with HP(O)Ar_2 to afford alkyl–P(O)Ar_2 products.[11] However, progress in this area remains limited, in sharp contrast to the numerous reports on



Scheme 1 Progress in deoxygenative phosphonation of ketones.

[a]State Key Laboratory of Natural Product Chemistry (SKLAOC), College of Chemistry and Chemical Engineering, Lanzhou University, 222 South Tianshui Road, Lanzhou, 730000, China. E-mail: shuxingzh@lzu.edu.cn

[b]Zhejiang Nanjiao Chemistry Co., Ltd., Shaoxing 312369, China. E-mail: ykgoals@163.com

radical alkylation of P(III) reagents such as $ClPPh_2$, Me_3SnPPh_2, $P(OR)_3$, and $P(SPh)_3$.[12] Moreover, methods enabling the installation of phosphine oxides at stable and readily available functional positions would substantially broaden their practical utility.

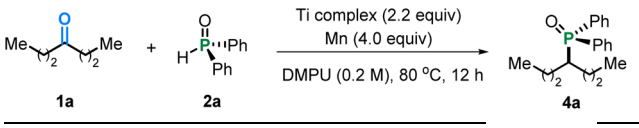
Low-valent titanium complexes play a pivotal role in enabling radical transformations of C–O compounds,[13,14] especially for carbonyl compounds.[15] Since the discovery of the McMurry coupling,[16] a wide range of reductive carbonyl transformations have been realized, including pinacol couplings *via* carbonyl–carbonyl dimerization,[17] umpolung-type carbonyl–cyano couplings to form α-hydroxy ketones,[18] as well as reductive cross-couplings and [3 + 2] cycloadditions with halides,[19] *N*,*N*′-dimethylformamide,[20] and activated alkenes.[21] These advances underscore the exceptional capacity of low-valent titanium species to mediate radical pathways and construct diverse C–C frameworks under mild conditions. However, their application in C–X bond-forming reactions remains largely unexplored.[22]

Motivated by these encouraging results and building upon our recent progress in the deoxygenation functionalization of C–O compounds,[23] we introduce a titanium-mediated deoxygenative phosphonation reaction of ketones for constructing C(sp^3)–P bonds (Scheme 1b). The method facilitates an intermolecular cross-coupling between ketones and diaryl phosphine oxides through a radical pathway, proceeds under mild conditions and shows good functional group compatibility. This transformation will provide a simplified and efficient alternative to the existing methods[24] and expand the scope of radical transformations of carbonyl compounds by titanium.

We initiated our investigation by evaluating the reaction between ketone **1a** and diphenylphosphine oxide **2a**. Optimal efficiency was achieved using titanium complex **3m** (2.2 equiv.), Mn powder (4.0 equiv.), and DMPU (0.2 M), affording the desired product in 80% isolated yields (Table 1, entry 1). Replacing DMPU with DMA led to a modest decrease in yield (entry 3), whereas THF, despite its widespread use in related titanocene systems, resulted in strong inhibition of product formation (entry 2). Lowering the reaction temperature to 60 °C (entry 4) or replacing Mn with Zn (entry 5), a reductant of weaker reducing strength, both resulted in substantial reductions in efficiency. Control experiments verified that both the Ti complex and Mn reductant are essential (entry 6), as omission of either component completely suppressed formation of the target product.

The ligand sphere around titanium exerts a decisive influence on the reaction outcome. Cp_2TiCl_2 (**3a**) predominantly promoted P-centered homocoupling of **2a** and fails to deliver the desired product. In contrast, Cp^*TiCl_3 (**3b**) enabled formation of product **4a** in moderate yield. Other classical titanium complexes, including $TiCl_4$(collidine) (**3c**) and the alkoxide complex $(^iPrO)_4Ti$ (**3e**), are ineffective, and unreacted substrates were recovered. Incorporation of less sterically encumbered di-oxo donors, as in complexes derived from isopropanol (**3h**) and catechol (**3i**), markedly improved coupling efficiency. Conversely, more rigid and sterically congested ligand frameworks, such as BINOL- or Salen-supported Ti complexes (**3d** and **3g**), significantly reduce reactivity. Among all evaluated Ti pre-catalysts, the di-oxo titanium trichloride series incorporating simple 1,2-diol backbones (**3j–3m**) performed most effectively, especially the ethylene glycol-derived complexes (**3k**, **3l**, and **3m**). Within this group, the arylated complex **3m** was identified as the optimal precatalyst for enabling the coupling.

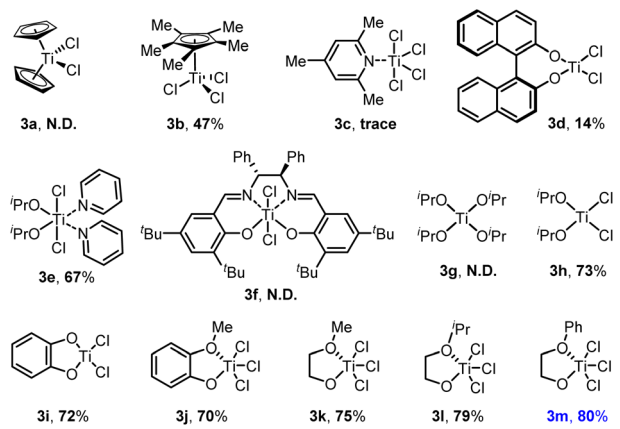
Table 1 Optimization of the reaction conditions[a]



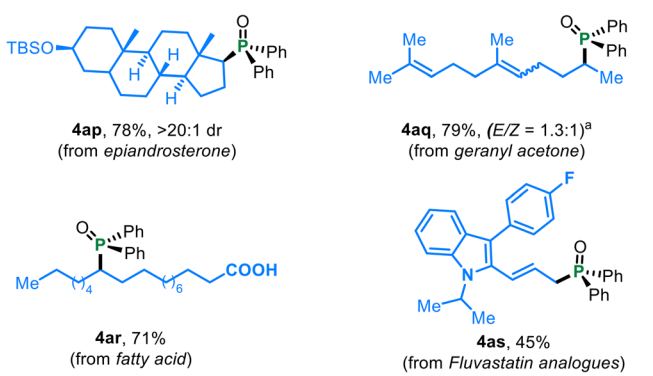
1a 2a 4a

Entry	Change from standard conditions	4a (%)
1	None	81 (80)[b]
2	THF	18%
3	DMA	69%
4	60 °C	71
5	Zn instead of Mn	11
6	Without Ti or Mn	0

Effect of Ti-Complex

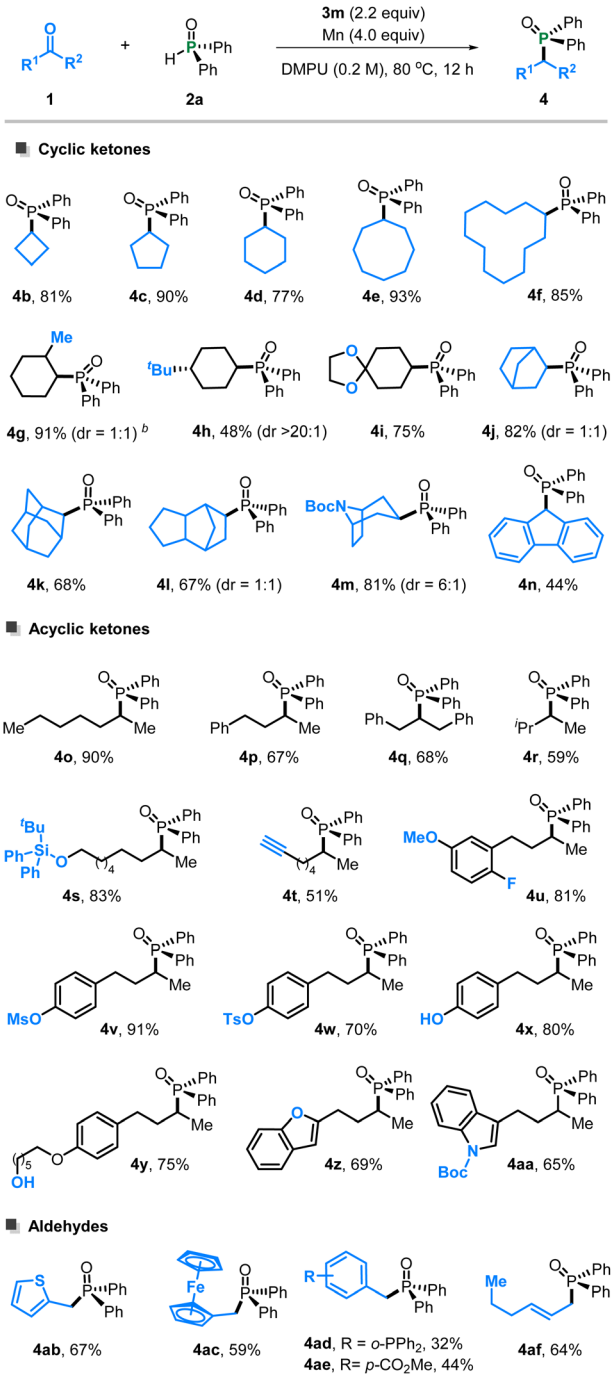


[a] Reaction conditions: **1a** (0.1 mmol) and **2a** (0.15 mmol) were used; the yields were determined by ^1H NMR analysis using CH_2Br_2 as an internal standard. [b] Isolated yield obtained from **1a** (0.2 mmol) and **2a** (0.3 mmol) is given. [c] Bench-top reaction.



Scheme 2 Deoxygenative phosphonation of ketone-containing bioactive molecules. [b]Ketone substrate **1ag** (*E*/*Z* = 1.5 : 1) was used.

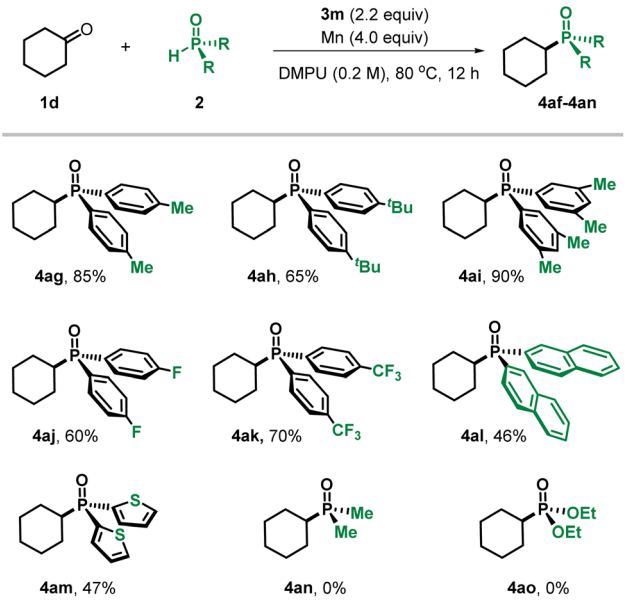
Table 2 The substrate scope of ketones and aldehydes[a]



[a] Ketones/aldehydes **1** (0.2 mmol) and phosphine oxide **2b** (0.3 mmol) were used; isolated yields are given. [b] **1g** (0.3 mmol) and **2b** (0.2 mmol) were used.

With the optimized conditions in hand, we evaluated the substrate scope of ketones with diphenylphosphine oxide **1b** (Scheme 2). The reaction proved effective for cyclic ketones, accommodating ring sizes from 4 to 12 members (**4b–4f**) and delivering the corresponding phosphonated products in good yields. Structurally rigid polycyclic ketones also participated smoothly (**4j–4f**), demonstrating the capacity of this Ti platform to activate conformationally and sterically constrained carbonyl frameworks. Cyclic ketones bearing substituents at different ring positions (**4g–4i**), including those with steric crowding adjacent to the carbonyl site (**4g**), were equally compatible, indicating the steric tolerance of this titanium complex (Table 2).

Table 3 The substrate scope of phosphine oxides[a]



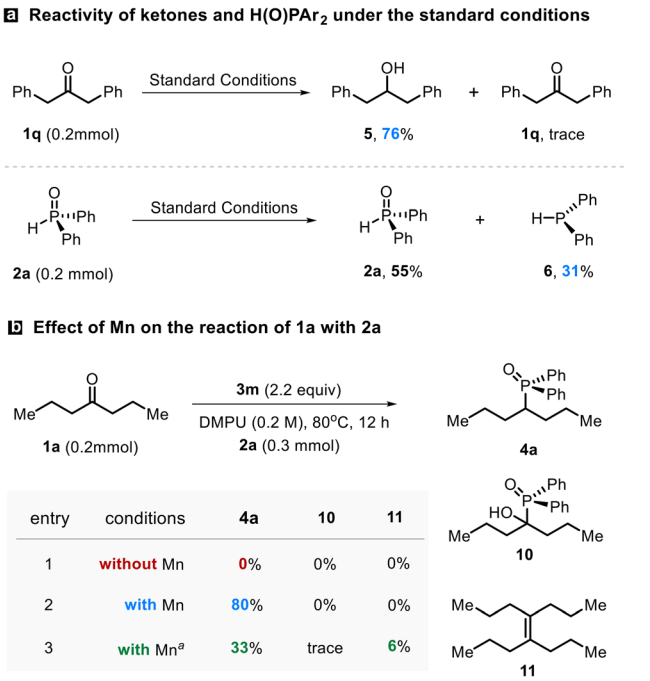
[a] Cyclohexanone **1** (0.2 mmol) and phosphine oxides **2** (0.3 mmol) were used; isolated yields are given.

The method is also effective for acyclic aliphatic ketones featuring varied chain lengths (**4a**, **4o–4p**) or increased steric demand around the carbonyl unit (**4q** and **4r**), furnishing products in 69–90% yields. Functionalities including silyl ethers (**4s**), alkynes (**4r**), ethers, fluorine (**4u**), and sulfonates (**4v** and **4w**) are tolerated. Notably, ketones containing hydroxy-derived motifs (**4v–4y**), especially for the phenols (**4x**) and aliphatic alcohol-based frameworks (**4y**), which are typically ligating or deactivating in classical low-valent Ti systems, remained intact under the present conditions. This highlights the good stability and robustness of the titanium complex used.

This titanium system also enabled efficient deoxygenative phosphonation of aldehydes, demonstrating good tolerance toward diverse functional motifs. Aldehydes containing thiophene, ferrocenecarbonyl (**4ac**), phosphines (**4ad**), esters (**4ae**),[10] and acrylaldehyde units (**4af**) all underwent smooth C–O cleavage and phosphonylation without compromised selectivity, further underscoring the versatility and practical utility of the method in complex settings.

The substrate scope of phosphine oxides was then evaluated using cyclohexanone as the coupling partner (Table 3). Diverse diarylphosphine oxides participated in the transformation, including those decorated with electron-donating substituents (**4ag–4ai**) as well as electron-withdrawing groups (**4aj–4ak**), all undergoing smooth C–P bond formation. Phosphine oxides bearing conjugated naphthyl (**4al**) and heteroaryl (**4am**) variants were tolerated in the current titanium system. In contrast, phosphine oxides in which the aryl groups were replaced by alkyl (**4an**) and alkoxy (**4ao**) moieties did not furnish the desired products.

The methodology further demonstrated competence in the late-stage functionalization of bioactive molecules. Ketone-containing compounds, including epiandrosterone (**4ap**), geranyl acetone (**4aq**), unprotected fatty acid (**4ar**), and fluvastatin analogues (**4as**), underwent deoxygenative phosphonation to furnish the corresponding C–P coupled products in synthetically useful yields.



Scheme 3 Mechanistic investigations. [a]Titanium complex **3m** was pre-activated with Mn powder for 12 h, followed by Mn removal through filtration before the addition of **1a** and **2a** to start the transformation.

To gain mechanistic insight into the transformation, a series of control experiments were executed. Independent exposure of ketone **1q** and phosphine oxide **2a** to the standard manifold led to efficient reduction of **1q**, affording the corresponding alcohol **5** in 76% yield,[25] whereas phosphine oxide **2a** exhibits substantially weaker interaction with the titanium species, with more than half recovered (Scheme 3a). These observations indicate that ketones possess higher reactivity over phosphine oxides toward the active Ti species.

The role of Mn in Ti initiation was then examined. In the absence of Mn, no productive C–P coupling occurred, and both **1a** and **2a** were almost fully restored, consistent with a Mn-enabled Ti(IV) to low-valent Ti reduction even being required to access the catalytically competent state (Scheme 3b, entries 1 *vs.* 2). The filtrate obtained from preactivation of **3m** with Mn dust (see the SI for details) promoted the coupling of **1a** and **2a** to afford **4a** in 33% yield (Scheme 3b, entry 3), with 52% recovery of ketone **1a** and minor formation of McMurry byproduct **11**. These results indicate that *in situ* generated low-valent titanium species are required to initiate the transformation. ^{31}P NMR analysis revealed a signal corresponding to α-hydroxyphosphonates (**10**) at 27.9 ppm,[26] suggesting that it may be an intermediate in the transformation.

The real-time ^{31}P NMR monitoring further validated this proposal. As shown in Fig. 1, product **4a** appeared within 35 minutes, accompanied by a transient and low-intensity resonance for **10** at 27.9 ppm. The reaction reached completion within 2 hours without detection of other P-containing adducts derived from **2a**. In contrast, the deoxygenated phosphine $HPPh_2$ (**6**, −40.8 ppm) only emerged after extended reaction times (6 h) and accumulated gradually, indicating that **6** forms downstream and outside the catalytic C–P bond-forming process.

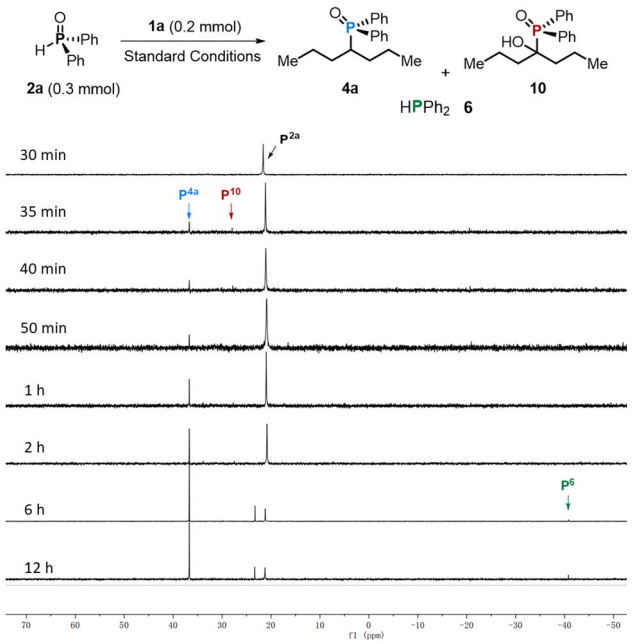
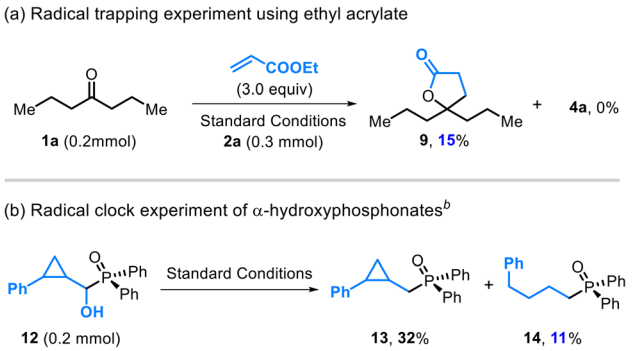
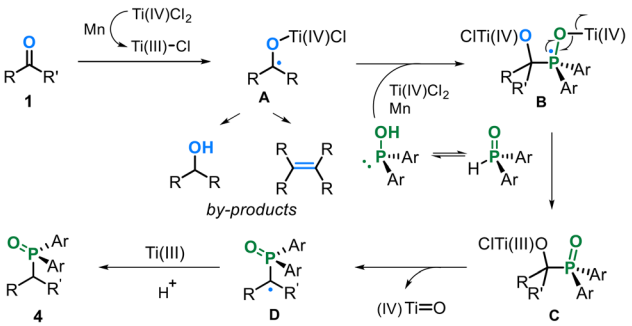


Fig. 1 Real-time ^{31}P NMR monitoring of the coupling of **1a** and **2a**.



Scheme 4 Radical verification studies.



Scheme 5 Proposed mechanism.

The intermediacy of radicals was supported by orthogonal experiments. Addition of Michael acceptors delivered a radical-trapped-esterified product **9** in 15% yield (Scheme 4a),[27] indicating accessible carbon-centered radicals. A radical clock experiment employing cyclopropyl-containing α-hydroxyphosphonates **12** afforded the ring-opened product **14** (Scheme 4b), revealing radical-mediated C–O scission during deoxygenation. The initially formed alkenyl fragment from cyclopropane opening underwent subsequent reduction to **14** under the current Ti/Mn system.

Based on the above results and literature reports,[28] a plausible reaction mechanism is proposed (Scheme 5). The Lewis acidity of the Ti complex enables P(V) to P(III) isomerization,[29] while carbonyl deoxygenation under the Ti(IV)/Mn manifold generates alkyl radical **A**, which is captured by P(III) species to form intermediate **B**.[11,30] Subsequent β-scission restores the P(V) species and Ti(IV) reduction to afford low-valent complex **C**, followed by radical dehydroxylation and protonation to release the deoxygenatively phosphonated product.

Conclusions

In conclusion, we have developed a titanium-mediated deoxygenative C(sp^3)–P coupling of ketones and aldehydes with secondary phosphine oxides, providing a practical route to diverse aliphatic organophosphorus compounds. The reaction proceeds *via* a distinct radical pathway, in which the combined Lewis acidity and single-electron reductive capacity of the titanium complex are essential for C–O bond radical activation and

productive phosphonylation. The protocol operates under mild conditions and tolerates a wide range of functional groups, including carboxyl, phenolic OH, and alcohol groups that typically challenge classical polar phosphonation manifolds. Further deoxygenative functionalization of aldehydes/ketones is ongoing in our laboratory.

Author contributions

X.-Z. S. conceived and supervised the project. X.-Z. S., X. P. and Y. W. designed the experiments. Y. W. performed the experiments and analysed the data. Y. K. assisted with data analysis and reaction design.

Conflicts of interest

The authors declare no competing financial interests.

Data availability

CCDC 2467845 contains the supplementary crystallographic data for this paper.[31]

All experimental data, procedures for data analysis, and pertinent data sets are provided in the supplementary information (SI). Supplementary information is available. See DOI: https://doi.org/10.1039/d5sc09520d.

Acknowledgements

X.-Z. S. and X. P. thank the National Natural Science Foundation of China (22471104, 22271127, and 22401122), Science and Technology Program Projects of Gansu Province (25RCKA023), Science and Technology Major Program of Gansu Province of China (22ZD6FA006 and 23ZDFA015), and High-Level Talent Program of Lanzhou Municipality for their financial support.

Notes and references

1 (*a*) J. Sikorski and E. Logusch, in *Aliphatic Carbon–Phosphorus Compounds as Herbicides*, Marcel Dekker, 1992, pp. 737–806; (*b*) M. Eto, in *Handbook of Organophosphorus Chemistry*, ed. R. Engel, Marcel Dekker, 1992, pp. 807–873; (*c*) T. M. Shaikh, C.-M. Weng and F.-E. Hong, *Coord. Chem. Rev.*, 2012, **256**, 771–803; (*d*) U. Pradere, E. C. Garnier-Amblard, S. J. Coats, F. Amblard and R. F. Schinazi, *Chem. Rev.*, 2014, **114**, 9154–9218; (*e*) A. Gallen, A. Riera, X. Verdaguer and A. Grabulosa, *Catal. Sci. Technol.*, 2019, **9**, 5504–5521; (*f*) M. You, Z. Zhang, C. Chen, Z. Mei, X. Zhang, J. Bai, H. Huang and Q. Xiao, *Green Chem.*, 2025, **27**, 3743–3750; (*g*) C. Chen, Z. Mei, M. You, Z. Zhang, H. Huang and Q. Xiao, *Org. Chem. Front.*, 2025, **12**, 3681–3686.

2 (*a*) T. Hirao, T. Masunaga, Y. Ohshiro and T. Agawa, *Tetrahedron Lett.*, 1980, **21**, 3595–3598; (*b*) D. Gelman, L. Jiang and S. L. Buchwald, *Org. Lett.*, 2003, **5**, 2315–2318; (*c*) L.-B. Han, C. Zhang, H. Yazawa and S. Shimada, *J. Am. Chem. Soc.*, 2004, **126**, 5080–5081; (*d*) A. L. Schwan, *Chem. Soc. Rev.*, 2004, **33**, 218–224; (*e*) Y. Gao, G. Wang, L. Chen, P. Xu, Y. Zhao, Y. Zhou and L.-B. Han, *J. Am. Chem. Soc.*, 2009, **131**, 7956–7957; (*f*) G. Evano, K. Tadiparthi and F. Couty, *Chem. Commun.*, 2011, **47**, 179–181; (*g*) A. J. Bloomfield and S. B. Herzon, *Org. Lett.*, 2012, **14**, 4370–4373; (*h*) C.-G. Feng, M. Ye, K.-J. Xiao, S. Li and J.-Q. Yu, *J. Am. Chem. Soc.*, 2013, **135**, 9322–9325; (*i*) Y.-M. Li, M. Sun, H.-L. Wang, Q.-P. Tian and S.-D. Yang, *Angew. Chem., Int. Ed.*, 2013, **52**, 3972–3976; (*j*) A.-X. Zhou, L.-L. Mao, G.-W. Wang and S.-D. Yang, *Chem. Commun.*, 2014, **50**, 8529–8532; (*k*) W. C. Fu, C. M. So and F. Y. Kwong, *Org. Lett.*, 2015, **17**, 5906–5909; (*l*) J. Yang, J. Xiao, T. Chen, S.-F. Yin and L.-B. Han, *Chem. Commun.*, 2016, **52**, 12233–12236; (*m*) J. Yang, T. Chen and L.-B. Han, *J. Am. Chem. Soc.*, 2015, **137**, 1782–1785; (*n*) J. Yang, J. Xiao, T. Chen and L.-B. Han, *J. Org. Chem.*, 2016, **81**, 3911–3916; (*o*) Y.-N. Ma and S.-D. Yang, *Chem. Rec.*, 2016, **16**, 977–986; (*p*) L. Rout and T. Punniyamurthy, *Coord. Chem. Rev.*, 2021, **431**, 213675; (*q*) X. Zhang, S.-Q. Wang and S.-D. Yang, *Sci. China: Chem.*, 2023, **66**, 2569–2575; (*r*) M. Huang, H. Huang, M. You, X. Zhang, L. Sun, C. Chen, Z. Mei, R. Yang and Q. Xiao, *Green Chem.*, 2024, **26**, 295–299.

3 (*a*) K. D. Berlin and G. B. Butler, *Chem. Rev.*, 1960, **60**, 243–260; (*b*) A. K. Bhattacharya, *Chem. Rev.*, 1981, **81**, 415–430; (*c*) P.-Y. Renard, P. Vayron, E. Leclerc, A. Valleix and C. Mioskowski, *Angew. Chem., Int. Ed.*, 2003, **42**, 2389–2392; (*d*) P.-Y. Renard, P. Vayron and C. Mioskowski, *Org. Lett.*, 2003, **5**, 1661–1664; (*e*) L. Longwitz and T. Werner, *Angew. Chem., Int. Ed.*, 2020, **59**, 2760–2763.

4 (*a*) E. K. Baylis, *Tetrahedron Lett.*, 1995, **36**, 9385–9388; (*b*) J. Kehler, B. Ebert, O. Dahl and P. Krogsgaard-Larsen, *Tetrahedron*, 1999, **55**, 771–784; (*c*) Y. A. Rina and J. A. R. Schmidt, *Organometallics*, 2019, **38**, 4261–4270.

5 (*a*) C.-T. Yang, J. Han, J. Liu, Y. Li, F. Zhang, M. Gu, S. Hu and X. Wang, *RSC Adv.*, 2017, **7**, 24652–24655; (*b*) L. Chen, Y. Zhu, T. Chen, L. Liu, J.-S. Zhang and L.-B. Han, *Org. Biomol. Chem.*, 2018, **16**, 5090–5093; (*c*) T. Chen, Q. Tan, X. Liu, L. Liu, T. Huang and L.-B. Han, *Synthesis*, 2021, **53**, 95–106; (*d*) Q. Li, C.-Q. Zhao, T. Chen and L.-B. Han, *RSC Adv.*, 2022, **12**, 18441–18444; (*e*) C.-K. Li, Z.-K. Tao, A. Shoberu, W. Zhang and J.-P. Zou, *Org. Lett.*, 2022, **24**, 6083–6087; (*f*) R. Wang, J. Wang, Y. Zhang, B. Wang, Y. Xia, F. Xue, W. Jin and C. Liu, *Adv. Synth. Catal.*, 2023, **365**, 900–905; (*g*) S.-Y. Zhao, Y.-Y. Huang, S.-H. Deng, Z.-P. Guan and Z.-B. Dong, *Org. Chem. Front.*, 2024, **11**, 4882–4894; (*h*) J.-L. Tu, Z. Shen and B. Huang, *Tetrahedron*, 2024, **168**, 134352; (*i*) D.-W. Shi, M. Li, R.-J. Yang, X.-Y. Zhao, T. Zhang, J. Huangfu, L. Xu, K. Wang, Y.-X. Ma and B. Yang, *J. Org. Chem.*, 2025, **90**, 5578–5585.

6 (*a*) T. Hirai and L.-B. Han, *Org. Lett.*, 2007, **9**, 53–56; (*b*) B. Yang, H.-Y. Zhang and S.-D. Yang, *Org. Biomol. Chem.*, 2015, **13**, 3561–3565; (*c*) J. Liu, H.-Z. Xiao, Q. Fu and D.-G. Yu, *Chem. Synth.*, 2021, **1**, 9; (*d*) Q. Xu, C. Guo, B. Li, Z. Zhang, Y. Qiu, S. Tian, L. Zheng, L. Gu, W. Yan, D. Wang and J. Zhang, *J. Am. Chem. Soc.*, 2022, **144**, 4321–4326; (*e*) G. Zhang, H. He, X. Chen, S.-F. Ni and R. Zeng, *Org. Lett.*, 2023, **25**, 5356–5360; (*f*) M.-Q. Tang, Z.-J. Yang, A.-J. Han and Z.-T. He, *Angew. Chem., Int. Ed.*, 2025, **64**,

e202413428; (*g*) J.-T. Cheng, X. Yuan, Z. Yang, K. Liu and J. Wang, *Angew. Chem., Int. Ed.*, 2025, **64**, e202519578; (*h*) W.-H. Wang, S.-Y. Zhang, Y.-X. Zhang, Y.-Q. Wang and Q.-W. Zhang, *J. Am. Chem. Soc.*, 2025, **147**, 14797–14805; (*i*) C. Ma, X. Wang, T. Soós, J. Zhang and J. Yang, *Nat. Commun.*, 2025, **16**, 5436; (*j*) R. Lin, Y. Zhang, T. Xiong, H. Huang, P. Xie, Y. Zhang, N. Huang, W. Hu and J. Jiang, *ACS Catal.*, 2025, **15**, 16236–16246; (*k*) M. Gong, C. Lin, X. Gu, N. Huang and J. Jiang, *Org. Lett.*, 2025, **27**, 10594–10599.

7 (*a*) L. Wu, X. Zhang, C.-Q. Chen and A.-K. Zhou, *Org. Biomol. Chem.*, 2012, **10**, 7859–7862; (*b*) Z.-S. Chen, Z.-Z. Zhou, H.-L. Hua, X.-H. Duan, J.-Y. Luo, J. Wang, P.-X. Zhou and Y.-M. Liang, *Tetrahedron*, 2013, **69**, 1065–1068; (*c*) S. Hyde, J. Veliks, B. Liégault, D. Grassi, M. Taillefer and V. Gouverneur, *Angew. Chem., Int. Ed.*, 2016, **55**, 3785–3789; (*d*) R. Shen, C. Dong, J. Yang and L.-B. Han, *Adv. Synth. Catal.*, 2018, **360**, 4252–4258; (*e*) L. Zhang, B. M. DeMuynck, A. N. Paneque, J. E. Rutherford and D. A. Nagib, *Science*, 2022, **377**, 649–654; (*f*) X. Mo, Y. Xie, L. Wei, X. Gu, M. Zhang, X. Zhang and J. Jiang, *Org. Lett.*, 2023, **25**, 2338–2343.

8 K. Suzuki, T. Hashimoto, H. Maeta and T. Matsumoto, *Synlett*, 1992, **1992**, 125–128.

9 F. Liu, J. Dong, R. Cheng, S.-F. Yin, L. Chen, L. Su, R. Qiu, Y. Zhou, L.-B. Han and C.-J. Li, *Sci. Adv.*, 2025, **11**, eads4626.

10 (*a*) M. B. Kurosawa, R. Isshiki, K. Muto and J. Yamaguchi, *J. Am. Chem. Soc.*, 2020, **142**, 7386–7392; (*b*) L. Gan, T. Xu, Q. Tan, M. Cen, L. Wang, J. Zhao, K. Liu, L. Liu, W.-H. Chen, L.-B. Han, J. E. Nycz and T. Chen, *Chem. Sci.*, 2023, **14**, 5519–5526.

11 N. B. Bissonnette, N. Bisballe, A. V. Tran, J. A. Rossi-Ashton and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2024, **146**, 7942–7949.

12 (*a*) D. H. R. Barton, D. Bridon and S. Z. Zard, *Tetrahedron Lett.*, 1986, **27**, 4309–4312; (*b*) D. H. R. Barton and J. Zhu, *J. Am. Chem. Soc.*, 1993, **115**, 2071–2072; (*c*) A. Sato, H. Yorimitsu and K. Oshima, *J. Am. Chem. Soc.*, 2006, **128**, 4240–4241; (*d*) S. E. Vaillard, C. Muck-Lichtenfeld, S. Grimme and A. Studer, *Angew. Chem., Int. Ed.*, 2007, **46**, 6533–6536; (*e*) D. T. Xie, H. L. Chen, D. Wei, B. Y. Wei, Z. H. Li, J. W. Zhang, W. Yu and B. Han, *Angew. Chem., Int. Ed.*, 2022, **61**, e202203398; (*f*) S. K. Pagire, C. Shu, D. Reich, A. Noble and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2023, **145**, 18649–18657; (*g*) L. Chai, J. Wang, J. Yang, J. Yin, Z. Zhang, Y. Cheng, L. Zhu, X. S. Xue and C. Li, *CCS Chem.*, 2024, **6**, 1312–1323; (*h*) J. Yin, X. Lin, L. Chai, C.-Y. Wang, L. Zhu and C. Li, *Chem*, 2023, **9**, 1945–1954.

13 For selected examples of epoxides, see: (*a*) T. V. Rajanbabu and W. A. Nugent, *J. Am. Chem. Soc.*, 1989, **111**, 4525–4527; (*b*) A. Gansäuer, H. Bluhm and M. Pierobon, *J. Am. Chem. Soc.*, 1998, **120**, 12849–12859; (*c*) Y. Zhao and D. J. Weix, *J. Am. Chem. Soc.*, 2015, **137**, 3237–3240; (*d*) C. Yao, T. Dahmen, A. Gansäuer and J. Norton, *Science*, 2019, **364**, 764–767; (*e*) K. Y. Ye, T. McCallum and S. Lin, *J. Am. Chem. Soc.*, 2019, **141**, 9548–9554; (*f*) A. Gansäuer, *Synlett*, 2020, **32**, 447–456; (*g*) L. Li, S. Yang, Z. Xu, S. Li, J. Jiang and Y.-Q. Zhang, *J. Am. Chem. Soc.*, 2024, **146**, 13546–13557; (*h*) L. Zhang, W. Wang, C. Shen and K. Dong, *ACS Catal.*, 2025, **15**, 7578–7587.

14 For selected examples of alcohols, see: (*a*) E. E. van Tamelen and M. A. Schwartz, *J. Am. Chem. Soc.*, 1965, **87**, 3277–3278; (*b*) J. E. McMurry, M. G. Silvestri, M. P. Fleming, T. Hoz and M. W. Grayston, *J. Org. Chem.*, 1978, **43**, 3249–3255; (*c*) H. R. Diéguez, A. López, V. Domingo, J. F. Arteaga, J. A. Dobado, M. M. Herrador, J. F. Quílez del Moral and A. F. Barrero, *J. Am. Chem. Soc.*, 2010, **132**, 254–259; (*d*) T. Suga, S. Shimazu and Y. Ukaji, *Org. Lett.*, 2018, **20**, 5389–5392; (*e*) T. Suga and Y. Ukaji, *Org. Lett.*, 2018, **20**, 7846–7850; (*f*) T. Suga, T. Takahashi and Y. Ukaji, *Adv. Synth. Catal.*, 2020, **362**, 5622–5627; (*g*) K. Sumiyama, N. Toriumi and N. Iwasawa, *Eur. J. Org Chem.*, 2021, 2474–2478; (*h*) L. Yao, J. Bao, Y. Wang and J. Gui, *Org. Lett.*, 2024, **26**, 1243–1248; (*i*) X. Zheng, X.-J. Dai, H.-Q. Yuan, C.-X. Ye, J. Ma and P.-Q. Huang, *Angew. Chem., Int. Ed.*, 2013, **52**, 3578–3582; (*j*) T. Suga, Y. Takahashi, C. Miki and Y. Ukaji, *Angew. Chem., Int. Ed.*, 2022, **61**, e202112533; (*k*) H. Tian, R. Zhang, L. Shi, C. Zhao and X. Wang, *Chin. J. Chem.*, 2023, **41**, 1783–1790.

15 For selected reviews, see:(*a*) B. Rossi, S. Prosperini, N. Pastori, A. Clerici and C. Punta, *Molecules*, 2012, **17**, 14700–14732; (*b*) J. Streuff and A. Gansäuer, *Angew. Chem., Int. Ed.*, 2015, **54**, 14232–14242; (*c*) A. Rosales, I. Rodríguez-García, J. Muñoz-Bascón, E. Roldan-Molina, N. M. Padial, L. P. Morales, M. García-Ocaña and J. E. Oltra, *Eur. J. Org Chem.*, 2015, 4567–4591; (*d*) J. M. Botubol-Ares, M. J. Durán-Peña, J. R. Hanson, R. Hernández-Galán and I. G. Collado, *Synthesis*, 2018, **50**, 2163–2180; (*e*) J. M. Botubol-Ares, M. J. Durán-Peña, J. R. Hanson, R. Hernández-Galán and I. G. Collado, *Synthesis*, 2018, **50**, 2163–2180; (*f*) M. Manßen and L. L. Schafer, *Chem. Soc. Rev.*, 2020, **49**, 6947–6994; (*g*) X. Wu, Y. Chang and S. Lin, *Chem*, 2022, **8**, 1805–1821; (*h*) T. Hilche, S. L. Younas, A. Gansäuer and J. Streuff, *ChemCatChem*, 2022, **14**, e202200530; (*i*) J.-L. Tu and B. Huang, *Org. Biomol. Chem.*, 2024, **22**, 6650–6664.

16 (*a*) J. E. McMurry and M. P. Fleming, *J. Am. Chem. Soc.*, 1974, **96**, 4708–4709; (*b*) A. Fürstner and A. Hupperts, *J. Am. Chem. Soc.*, 1995, **117**, 4468–4475.

17 (*a*) E. J. Corey, R. L. Danheiser and S. Chandrasekaran, *J. Org. Chem.*, 1976, **41**, 260–265; (*b*) A. Gansäuer, *Chem. Commun.*, 1997, 457–458; (*c*) M. S. Dunlap and K. M. Nicholas, *Synth. Commun.*, 1999, **29**, 1097–1106; (*d*) F. Calogero, G. Magagnano, S. Potenti, F. Pasca, A. Fermi, A. Gualandi, P. Ceroni, G. Bergamini and P. G. Cozzi, *Chem. Sci.*, 2022, **13**, 5973–5981.

18 (*a*) Y. Yamamoto, D. Matsumi and K. Itoh, *Chem. Commun.*, 1998, 875–876; (*b*) J. Streuff, M. Feurer, P. Bichovski, G. Frey and U. Gellrich, *Angew. Chem., Int. Ed.*, 2012, **51**, 8661–8664; (*c*) M. Feurer, G. Frey, H.-T. Luu, D. Kratzert and J. Streuff, *Chem. Commun.*, 2014, **50**, 5370–5372; (*d*) M. A. Unkrig-Bau, S. L. Leijendekker and J. Streuff, *ChemCatChem*, 2025, **17**, e202401337.

19 (*a*) R. E. Estévez, J. Justicia, B. Bazdi, N. Fuentes, M. Paradas, D. Choquesillo-Lazarte, J. M. García-Ruiz, R. Robles,

A. Gansäuer, J. M. Cuerva and J. E. Oltra, *Chem.–Eur. J.*, 2009, **15**, 2774–2791; (*b*) J. Justicia, I. Sancho-Sanz, E. Alvarez-Manzaneda, J. E. Oltra and J. M. Cuerva, *Adv. Synth. Catal.*, 2009, **351**, 2295–2300; (*c*) F.-S. Li, Y.-Q. Chen, S.-J. Lin, C.-Z. Shi, X.-Y. Li, Y.-C. Sun, Z.-W. Guo and L. Shi, *Org. Chem. Front.*, 2020, **7**, 3434–3438; (*d*) A. Gualandi, F. Calogero, M. Mazzarini, S. Guazzi, A. Fermi, G. Bergamini and P. G. Cozzi, *ACS Catal.*, 2020, **10**, 3857–3863.

20 Y. Wang and X.-Z. Shu, *Org. Lett.*, 2025, **27**, 6059–6064.

21 (*a*) R. E. Estévez, J. L. Oller-López, R. Robles, C. R. Melgarejo, A. Gansäuer, J. M. Cuerva and J. E. Oltra, *Org. Lett.*, 2006, **8**, 5433–5436; (*b*) J. Streuff, *Chem.–Eur. J.*, 2011, **17**, 5507–5510; (*c*) P. Bichovski, T. M. Haas, D. Kratzert and J. Streuff, *Chem.–Eur. J.*, 2015, **21**, 2339–2342; (*d*) P. Bichovski, T. M. Haas, M. Keller and J. Streuff, *Org. Biomol. Chem.*, 2016, **14**, 5673–5682; (*e*) W. Hao, X. Wu, J. Z. Sun, J. C. Siu, S. N. MacMillan and S. Lin, *J. Am. Chem. Soc.*, 2017, **139**, 12141–12144.

22 (*a*) A. Clerici and O. Porta, *Tetrahedron Lett.*, 1990, **31**, 2069–2072; (*b*) R. Cannella, A. Clerici, N. Pastori, E. Regolini and O. Porta, *Org. Lett.*, 2005, **7**, 645–648; (*c*) A. Clerici, R. Cannella, W. Panzeri, N. Pastori, E. Regolini and O. Porta, *Tetrahedron Lett.*, 2005, **46**, 8351–8354; (*d*) A. Clerici, R. Cannella, N. Pastori, W. Panzeri and O. Porta, *Tetrahedron*, 2006, **62**, 5986–5994; (*e*) R. Cannella, A. Clerici, W. Panzeri, N. Pastori, C. Punta and O. Porta, *J. Am. Chem. Soc.*, 2006, **128**, 5358–5359; (*f*) A. Clerici, A. Ghilardi, N. Pastori, C. Punta and O. Porta, *Org. Lett.*, 2008, **10**, 5063–5066; (*g*) N. Pastori, C. Greco, A. Clerici, C. Punta and O. Porta, *Org. Lett.*, 2010, **12**, 3898–3901; (*h*) B. Rossi, N. Pastori, A. Clerici and C. Punta, *Tetrahedron*, 2012, **68**, 10151–10156.

23 (*a*) X. Pang, P.-F. Su and X.-Z. Shu, *Acc. Chem. Res.*, 2022, **55**, 2491–2509; (*b*) X. Pang and X.-Z. Shu, *Chin. J. Chem.*, 2023, **41**, 1637–1652; (*c*) H. Xie, J. Guo, Y.-Q. Wang, K. Wang, P. Guo, P.-F. Su, X. Wang and X.-Z. Shu, *J. Am. Chem. Soc.*, 2020, **142**, 16787–16794; (*d*) H. Xie, S. Wang, Y. Wang, P. Guo and X.-Z. Shu, *ACS Catal.*, 2022, **12**, 1018–1023; (*e*) P. Guo, K. Wang, W.-J. Jin, H. Xie, L. Qi, X.-Y. Liu and X.-Z. Shu, *J. Am. Chem. Soc.*, 2021, **143**, 513–523; (*f*) W.-Y. Ma, G.-Y. Han, S. Kang, X. Pang, X.-Y. Liu and X.-Z. Shu, *J. Am. Chem. Soc.*, 2021, **143**, 15930–15935; (*g*) H. Xie, S. Wang and X.-Z. Shu, *J. Am. Chem. Soc.*, 2024, **146**, 32269–32275.

24 (*a*) J. Wang, J. Xiao, Z.-L. Tang, D.-H. Lan and L.-B. Han, *J. Org. Chem.*, 2024, **89**, 5109–5117; (*b*) X. Wu, S. Lu, W. Zhong and T. Xu, *Nat. Commun.*, 2025, **16**, 3628; (*c*) X. Wu, A. Alimu, W. Zhong and T. Xu, *Org. Lett.*, 2025, **27**, 6025.

25 Isotope-labeling experiments indicate that the proton incorporated during the reduction originates from trace amounts of water present in the reaction system (see the SI for details).

26 J. Qiao, Z. Liu, R.-N. Ci, Q.-G. Wang, B. Chen, C.-H. Tung and L.-Z. Wu, Quantum Dots Photocatalysis Enabled Direct Activation of Acetone for Radical-Radical Cross-Coupling, *Adv. Funct. Mater.*, 2025, e02878.

27 E. A. Boyd, C. Shin, D. J. Charboneau, J. C. Peters and S. E. Reisman, *Science*, 2024, **385**, 847–853.

28 (*a*) W. G. Bentrude, *Acc. Chem. Res.*, 1982, **15**, 117–125; (*b*) W. G. Bentrude, J. J. L. Fu and P. E. Rogers, *J. Am. Chem. Soc.*, 1973, **95**, 3625–3635.

29 D. Zhao and R. Wang, *Chem. Soc. Rev.*, 2012, **41**, 2095–2108.

30 (*a*) J. A. Rossi-Ashton, A. K. Clarke, W. P. Unsworth and R. J. K. Taylor, *ACS Catal.*, 2020, **10**, 7250–7261; (*b*) R. S. Shaikh, S. J. S. Düsel and B. König, *ACS Catal.*, 2016, **6**, 8410–8414; (*c*) R. S. Shaikh, I. Ghosh and B. König, *Chem.–Eur. J.*, 2017, **23**, 12120–12124; (*d*) Y. Jian, M. Chen, B. Huang, W. Jia, C. Yang and W. Xia, *Org. Lett.*, 2018, **20**, 5370–5374; (*e*) W. Lecroq, P. Bazille, F. Morlet-Savary, M. Breugst, J. Lalevée, A. C. Gaumont and S. Lakhdar, *Org. Lett.*, 2018, **20**, 4164–4167; (*f*) H. Zeng, Q. Dou and C. J. Li, *Org. Lett.*, 2019, **21**, 1301–1305.

31 CCDC 2467845: Experimental Crystal Structure Determination, 2026, DOI: 10.5517/ccdc.csd.cc2ntzxd.