RSC Mechanochemistry

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *RSC Mechanochem.*, 2026, **3**, 218

Received 28th October 2025
Accepted 23rd January 2026

DOI: 10.1039/d5mr00132c

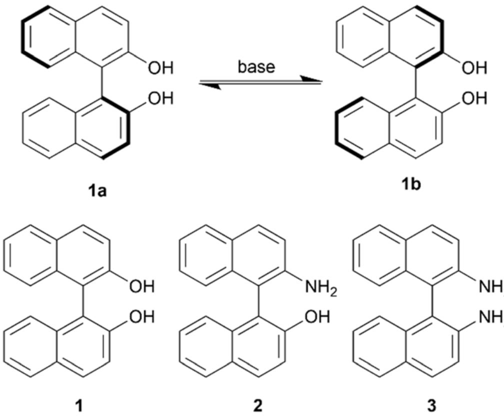
rsc.li/RSCMechanochem

When chirality breaks: mechanochemical degradation of biaryl atropisomers

Leon Poljanić, Tom Leyssens, Laurent Collard and Daniel M. Baier*

We investigated the stereochemical stability of biaryl atropisomers under conditions typically employed in organic mechanosynthesis. Systematic variation of reaction parameters revealed three degradation pathways: racemisation, cyclisation, and oligomerisation. This previously overlooked behaviour critically impacts catalytic performance in asymmetric synthesis, highlighting the need for rigorous stability assessment during mechanochemical reactions.

Atropisomerism, first described over a century ago, is a form of axial chirality resulting from restricted rotation around a single bond.[1,2] In contrast to compounds with stereocenters, which typically racemize *via* bond breaking and formation, atropisomers racemize through bond rotation. Among these, 1,1′-bi-2-naphthol (BINOL) and its derivatives (Scheme 1) are of particular interest due to their high rotational barriers, making them valuable as chiral ligands and catalysts in asymmetric synthesis.[3–5] Asymmetric synthesis is a central pillar of modern organic chemistry, enabling the stereoselective construction of chiral molecules, an achievement recognized by the 2021 Nobel Prize in Chemistry. For such transformations, maintaining the enantiopurity of the chiral catalyst is critical, as any degradation could compromise catalytic performance. Traditionally, asymmetric synthesis relies on solvent-based approaches.[6] However, these methods often involve toxic reagents and generate large amounts of solvent waste. Mechanochemistry, defined as the use of mechanical force to drive chemical transformations, has emerged as a sustainable alternative. Mechanochemical techniques such as ball milling offer several advantages, including reduced solvent use, high efficiency, low energy input, and access to unique reactivities.[7–14] Reactions can proceed faster or with improved selectivity compared to their solution-based counterparts. Recognized by IUPAC as a world-changing technology,[15] mechanochemistry now finds wide application in organic synthesis, including condensations, nucleophilic additions, cascade and Diels–Alder reactions, and various catalytic processes,[16–21] though its effects on chiral catalysts remain poorly understood.[17,19,20] In recent years, it became clear that stereochemical information can be lost under mechanochemical conditions through racemisation or side reactions.[22–24] Recent studies have even reported the opposite process of deracemisation *via* ball milling.[25,26] BINOL and related biaryls are stereochemically stable below 190 °C, yet their behaviour under mechanical stress, remains largely uninvestigated.[27] Therefore, we studied the stereochemical integrity of various biaryl atropisomers under conditions typical for mechanochemical asymmetric synthesis. We systematically explore how stereoinformation is affected by parameters such as milling time, frequency, liquid-assisted grinding (LAG), and the presence of organic and inorganic bases, both solid and liquid. By evaluating these effects, we aim to establish the stability limits of atropisomers under ball milling conditions, of interest for the future development of more effective stereoselective mechanochemical reactions.



Scheme 1 Top: Reaction scheme for the racemisation of (*S*)-BINOL (**1a**) to (*R*)-BINOL (**1b**). Bottom: Substrate scope: 2,2′-dihydroxy-1,1′-binaphthalene (BINOL, **1**), 2-amino-2′-hydroxy-1,1′-binaphthalene (NOBIN, **2**), 2,2′-diamino-1,1′-binaphthalene (BINAM, **3**).

Department of Molecular Chemistry, Materials and Catalysis, Institute of Condensed Matter and Nanosciences, Université Catholique de Louvain, Place Louis Pasteur 1, 1348 Louvain-la-Neuve, Belgium. E-mail: Daniel.Baier@uclouvain.be

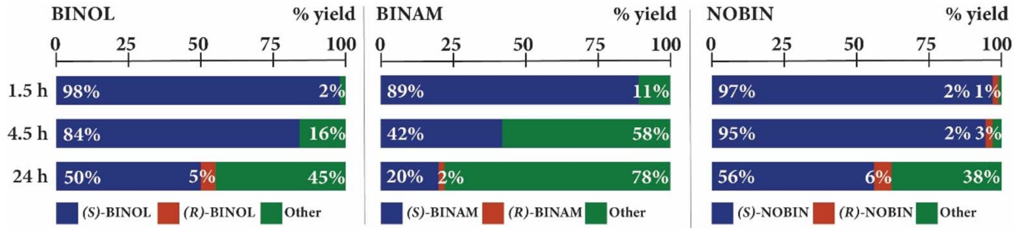


Fig. 1 Degradation of (*S*)-BINOL, (*S*)-BINAM and (*S*)-NOBIN under ball milling conditions: **1a**, **2a** (100 mg, 0.35 mmol) or **3a** (50 mg, 0.18 mmol) were added to a zirconium oxide milling vessel (10 mL) with two zirconium oxide balls (diameter: 10 mm) and milled in an MM400 ball mill at 30 Hz. Percentages were determined using quantitative HPLC. 'Other' refers to species formed *via* cyclisation and oligomerisation.

Ball milling was initially performed using 100 mg of (*S*)-BINOL (**1a**) in a 10 mL ZrO_2 vessel with two 10 mm ZrO_2 balls at a milling frequency of 30 Hz for 90 minutes. For clarity, we note that throughout this work the term "yield" refers to the percentage of recovered starting material. Reproducibility was successfully demonstrated for a representative selection of measurements performed in triplicate with the yield showing a typical standard deviation of 1% to 3%. Quantitative chiral HPLC analysis showed a yield of 98% of **1a**, with 2% attributed to degradation of the starting material. Prolonged milling led to increased degradation, with the yield of **1a** decreasing to 84% after 4.5 h and to 50% after 24 h (Fig. 1, left). After 24 h, 5% of (*R*)-BINOL (**1b**) was detected, indicating partial racemisation as a degradation pathway. To examine substituent effects on the biaryl scaffold, the study was extended to two BINOL derivatives of relevance to asymmetric synthesis: 2-amino-2′-hydroxy-1,1′-binaphthalene (NOBIN, **2**) and 2,2′-diamino-1,1′-binaphthalene (BINAM, **3**). Milling (*S*)-BINAM (**2a**) resulted in substantial degradation, with yields decreasing from 89% after 1.5 h to 42% after 4.5 h and 20% after 24 h (Fig. 1, centre). Racemisation was only observed after 24 h with 2% of (*R*)-BINAM (**2b**) detected. In contrast, (*S*)-NOBIN (**3a**) showed multiple degradation pathways already after 1.5 h, with 2% of (*R*)-NOBIN (**3b**) found and 1% attributed to other degradation pathways (Fig. 1, right). After 24 h, both degradation pathways intensified, yielding 56% of **3a** and 6% of **3b**, making NOBIN the most stable derivative within the studied series.

After establishing the stability of BINOL and its derivatives under neat milling conditions, we examined the effect of bases commonly employed in organic mechanosynthesis. Pyrrolidine and 1,8-diazabicyclo(5.4.0)undec-7-ene (DBU) were selected as representative organic bases. Milling of **1a** for 1.5 h gave comparable yields in the presence of pyrrolidine (92%) and DBU (90%) (Fig. 2, entries 1 and 9). Prolonged milling led to increased degradation in both cases, but at different rates. With pyrrolidine, yields decreased to 89% after 4.5 h and 65% and 24 h, with 20% of **1b** observed after 24 h. This indicates that extended milling primarily intensifies non-racemisation degradation pathways, whereas racemisation proceeds at a comparatively constant rate. As the ball mill temperature remains below the 190 °C threshold for thermally induced racemisation, the observed racemisation is likely driven by mechanical forces. Milling with DBU resulted in more pronounced degradation, with yields of 78% and 22% after 4.5 h and 24 h, respectively (Fig. 2, entries 2, 6, 10 and 14). Notably, racemisation did not increase with milling time in the presence of DBU, with 3% of **1b** observed at both after 4.5 h and 24 h. Increasing the amount of base decreased the yield of **1a** to 75%

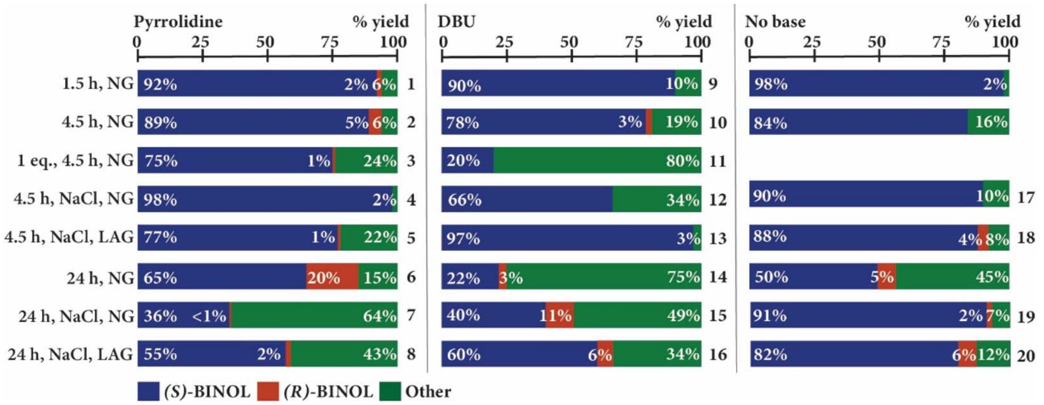


Fig. 2 Degradation of (*S*)-BINOL under ball milling conditions: **1a** (100 mg, 0.35 mmol) and base were added to a zirconium oxide milling vessel (10 mL) with two zirconium oxide balls (diameter: 10 mm) and milled in an MM400 ball mill at 30 Hz. Percentages were determined using quantitative HPLC. 0.1 eq. of base are used unless otherwise specified next to the corresponding bar. Toluene was used as the LAG additive (η = 0.1 mL mg^{-1}). Abbreviations: NG = neat grinding, LAG = liquid-assisted grinding, DBU = 1,8-diazabicyclo(5.4.0)undec-7-ene. 'Other' refers to species formed *via* cyclisation and oligomerisation.

(pyrrolidine) and 20% (DBU), suggesting increased loss of starting material under these conditions (Fig. 2, entries 3 and 11). Additionally, the extent of racemisation as a degradation mechanism decreased (from 6% to 1% for pyrrolidine, and from 3% to 0% for DBU), suggesting that racemisation is a minor degradation pathway at higher liquid base loadings. Another important parameter in mechanochemistry is the presence of an additive. To study this, we used NaCl, which is commonly used to alter the ball-to-powder ratio and improve energy transfer.[28] With pyrrolidine, shorter milling times showed almost no degradation (Fig. 2, entry 4), whereas prolonged milling led to significant degradation with a yield of **1a** of 36% with almost no racemisation as a degradation process (0.49% of **1b** observed) (Fig. 2, entry 7). This indicates that the additive initially mitigates the impact of mechanical forces, though this effect decreases over time, even leading to yields lower than without the additive present (Fig. 2, entries 6 and 7). With DBU, degradation was found already after 4.5 h, with yields of 66% after 4.5 h and 40% after 24 h, and racemisation observed after 24 h as 11% of **1b** was detected (Fig. 2, entries 12 and 15), emphasizing the different base behaviour under identical mechanochemical conditions. In the case of DBU, additive presence successfully mitigated some of the degradation (Fig. 2, entries 14 and 15). Next, we investigated LAG, in which a small amount of liquid is added to alter reactivity.[29,30] In the case of pyrrolidine, using toluene as LAG additive under otherwise identical conditions gave a **1a** yield of 77% after 4.5 h, which is significantly larger degradation compared to neat grinding (NG) (Fig. 2, entries 4 and 5). Milling for 24 h produced 57% of **1a**, higher than for NG, with 2% of **1b** found (Fig. 1, entries 7 and 8). These findings indicate that, with pyrrolidine, toluene promotes mixing and may lower the barrier for degradation by facilitating molecular mobility. In contrast, when DBU was used, toluene markedly suppressed degradation, with 97% yield of **1a** after 4.5 h and 60% after 24 h (Fig. 2, entries 13 and 16). This contrasting behaviour suggests that the effect of liquid-assisted grinding (LAG) is sensitive to the nature of the base, with degradation likely occurring in a mobile phase formed by the liquid additive and base, leading to system-specific pathways beyond the scope of the present study. Base-free conditions were tested to evaluate the influence of NaCl on BINOL degradation (Fig. 2, entries 17 and 19). Across all reaction times yields remain around 90%, demonstrating that the initial transformation and early side reactions are inherent to the milling process at low temperature. However, racemisation increased with time and was more pronounced under LAG than NG (Fig. 2, entries 18 and 20).

To investigate the influence of the physical state of the base, both liquid and solid bases were examined, as it is known that these can have an influence on mechanochemical reactions.[31] As solid bases, potassium carbonate (K_2CO_3) and caesium carbonate (Cs_2CO_3) were chosen. Employing 1 eq. of K_2CO_3 resulted in 69% of **1a** with 3% of **1b**, while Cs_2CO_3 resulted in 88% of **1a** with 3% of **1b** (Fig. 3, entries 1 and 7). Prolonging the milling to 24 h led to substantial degradation with both bases, with yields decreasing to 7% and 33% for K_2CO_3 and Cs_2CO_3, respectively, while racemisation remained comparable to that observed at shorter milling times (Fig. 3, entries 13 and 19). These results outline that racemisation may be the initial degradation pathway, with further mechanical energy driving other degradation pathways. In the presence of K_2CO_3, addition of toluene reduced degradation, with 86% of **1a** after 4.5 h and 67% after 24 h, but had the opposite effect with Cs_2CO_3, giving 79% of **1a** after 4.5 h and 24% after 24 h (Fig. 3, entries 2, 8, 14, 20). These contrasting trends further emphasize that the impact of LAG cannot be generalised and depends on the nature of the base. Addition of NaCl also led to different outcomes. For K_2CO_3, degradation was reduced, with 82% of **1a** after 4.5 h and 52% after 24 h. This was further improved by toluene addition as the yield decreased from 80% after 4.5 h to 72% after 24 h, with a modest increase in **1b** (from 5% under NG to 8% under LAG) (Fig. 3, entries 3, 4, 15, 16). On the contrary, addition of NaCl increased degradation in the presence of Cs_2CO_3 for both milling times (67% of **1a** for 4.5 h and 11% for 24 h), which was partially mitigated with toluene addition (Fig. 3, entries 9, 10, 21 and 22). Moreover, extended LAG in this case favoured racemisation with 20% of **1b** detected. This suggests that racemisation as a degradation process may proceed more efficiently in a liquid phase, potentially due to increased molecular mobility. Increasing the base loading to 25 eq. significantly suppressed degradation for both carbonates. With K_2CO_3, 93% of **1a** was found for NG and 97% for LAG, decreasing to 74% and 77% after 24 h, respectively, with racemisation more pronounced under LAG conditions (Fig. 3, entries 5, 6, 17 and 18). A similar trend was observed for Cs_2CO_3, with yields of 92% (NG) and 85% (LAG) after 4.5 h, and 87% (NG) and 74% (LAG)

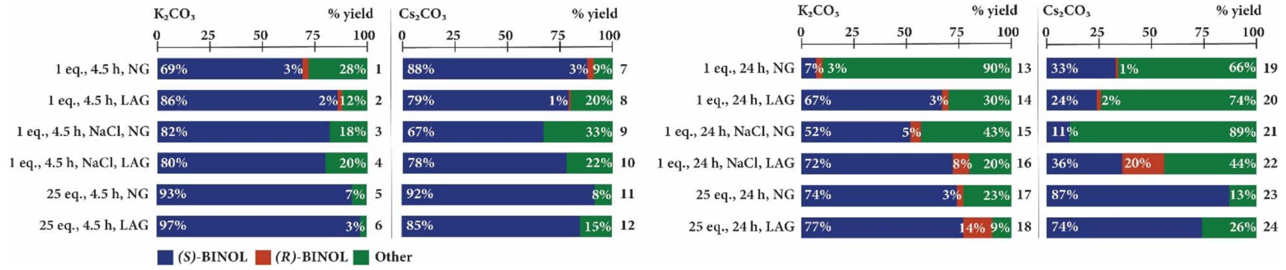
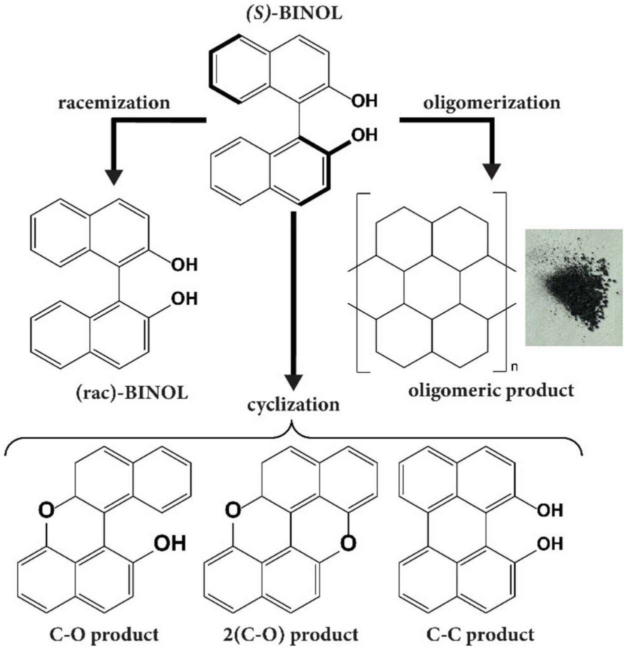


Fig. 3 Degradation of (*S*)-BINOL under ball milling conditions: **1a** (100 mg, 0.35 mmol) and base were added to a zirconium oxide milling vessel (10 mL) with two zirconium oxide balls (diameter: 10 mm) and milled in an MM400 ball mill at 30 Hz. Percentages were determined using calibration curves obtained by HPLC. Toluene was used as the LAG additive ($\eta = 0.1$ mL mg^{-1}). Abbreviations: NG = neat grinding, LAG = liquid-assisted grinding. 'Other' refers to species formed *via* cyclisation and oligomerisation.

after 24 h (Fig. 3, entries 11, 12, 23 and 24). The differences in reaction outcome between K_2CO_3 and Cs_2CO_3 can be explained by cation effects, as the larger, lower charge-density Cs^+ cation interacts differently than K^+ according to HSAB principles.[32] We hypothesize, that under basic conditions, prolonged milling could maintain BINOL in its phenolate form, which is significantly more prone to aerobic oxidation than the neutral diol. While we did not observe or quantify oxygen-driven ligand oxidation directly, phenolates and 2-naphthols are known to engage in aerobic oxidative pathways under certain conditions (often *via* phenoxyl radicals or metal-mediated O_2 activation), which can lead to coupling and oligomer formation. We therefore suspect oxygen-promoted side reactions as plausible contributor during extended milling, especially in the presence of adventitious O_2 and CO_2.[33–36]

To further understand the degradation of **1a** under mechanochemical conditions, we turned to mass spectrometry (MS) and nuclear magnetic resonance (NMR) spectroscopy. After milling, the mixture was washed with water and dilute HCl, neutralised, extracted with ethyl acetate, and concentrated under reduced pressure. During extraction, a striking colour change was observed in the crude mixture, progressing from dark green to black with increased milling time. Upon extraction, a black, insoluble material adhered to the separating funnel. Due to insolubility, it was not possible to analyse this material, but it was possible to isolate it and report it, as seen in Scheme 2. The soluble fraction from the organic phase, isolated after evaporation, was also examined. ^{1}H-NMR spectra of the reaction mixture showed new peaks at around 7.70, 8.10 and 9.20 ppm (see Fig. S171, SI). Simulated spectra suggested the formation of cyclisation side products; however, due to structural similarities, unambiguous identification was not possible. To resolve this, TOF-MS with APCI$^+$ ionisation was employed, revealing that the new peaks originated from BINOL cyclisation accompanied by significant material degradation during milling. Several potential side products were consistent with intramolecular cyclisation *via* C–C or C–O bond formation, both previously reported under oxidative or thermal conditions.[5,13] Evidence for intramolecular C–C bond formation, analogous to the Scholl reaction was found, in line with prior reports under mechanochemical conditions.[11,37,38] These reactions typically yield highly conjugated, insoluble π-stacked materials. In the case of BINOL derivatives, this aggregation could be a major degradation pathway, especially under prolonged milling. The colour change and insolubility are consistent with the formation of extended π-stacked materials, a hypothesis further supported by MS results showing higher molecular weights indicative of potential oligomeric products (see Fig. S175, SI). This tendency is particularly pronounced in smaller biaryl scaffolds like BINOL, where oligomerisation may outcompete discrete intramolecular cyclisations.[38] The presence of this material, combined with the observed racemisation and cyclisation indicate multiple degradation pathways resulting in the loss of stereoinformation. Additionally, the effect of milling frequency was investigated (see Table S4 in SI). Degradation still occurred at lower frequencies, though to a lesser extent as frequency decreased. However, no racemisation was observed, indicating that higher frequencies are required to initiate this process. Using PTFE as the milling vessel did not significantly change the outcome of reaction, as witnessed by relatively low yields (ranging from 11% to 90%), occurrence of racemisation (up to 3%) and changes of colour of the mixture (indicating oligomerisation). These findings suggest that degradation happens *via* several pathways regardless of the nature of the milling vessel. It is important to distinguish between the two processes influencing stereochemical outcomes: oxidative degradation reduces catalytic activity but does not alter product enantiopurity, whereas racemisation leaves catalytic activity intact but decreases enantiopurity by an amount corresponding to twice the extent of racemisation.



Scheme 2 Possible mechanochemical degradation pathways of (*S*)-BINOL under ball milling conditions. The oligomeric product is shown schematically for visualization purposes only.

Based on these results, we next selected a limited set of representative milling conditions and applied them to BINAM and NOBIN (Fig. 4). Using 0.1 eq. pyrrolidine under LAG conditions for 24 h, BINAM afforded a 45% yield of **2a** with minimal racemisation (0.59%), whereas NOBIN gave a higher yield of **3a** (73%) but significantly greater racemisation (12%). Comparing these results with BINOL, which gave a 57% yield with 2% racemisation, shows that the relative significance of different degradation pathways varies between derivatives. In the absence of base, both derivatives show significant degradation, with BINAM yielding only 11% of **2a** with almost no racemisation (0.28%), while NOBIN yielded 36% of **3a**, with 9% racemisation. BINOL, under the same conditions, showed least degradation of the three (yield of 81% and racemisation of 6%) making it the most stereochemically stable derivative for this condition. When 25 eq. of K_2CO_3 was used under NG conditions for 24 h, BINAM gave a yield of **2a** of 73% with no racemisation, while NOBIN gave a yield of **3a** of 83% and 2% racemisation.

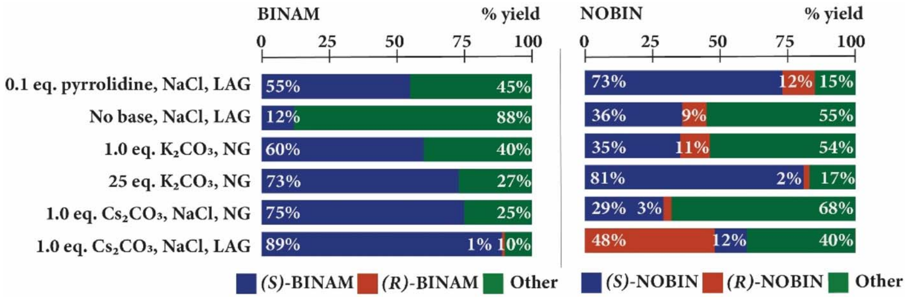


Fig. 4 Left: Degradation of (S)-BINAM, Right: Degradation of (S)-NOBIN under ball milling conditions: **2a** (100 mg, 0.35 mmol) or **3a** (50 mg, 0.18 mmol) and base were added to a zirconium oxide milling vessel (10 mL) with two zirconium oxide balls (diameter: 10 mm) and milled in an MM400 ball mill at 30 Hz. Due to the lack of **3a**, the final experiment with NOBIN used **3b** as starting material. Percentages were determined using calibration curves obtained by HPLC. Toluene was used as the LAG additive ($\eta = 0.1$ mL mg^{-1}). Abbreviations: NG = neat grinding, LAG = liquid-assisted grinding. 'Other' refers to species formed *via* cyclisation and oligomerisation.

Comparing these results with BINOL (77% yield and 3% racemisation) show that for these conditions degradation goes to a similar extent regardless of the derivative. Using 1 eq. of K_2CO_3 yield 60% of BINAM with negligible racemisation (0.25%), while NOBIN gave 35% yield with 11% racemisation. Out of the three, BINOL seems to be the most susceptible to degradation, shown by only 7% yield and 3% racemisation, adding to the substrate-dependent degradation pathway hypothesis. Both NG and LAG with Cs_2CO_3 for BINAM resulted in high yields (75% and 89%, respectively) with virtually no racemisation (0.19% and 1.04%, respectively). In contrast, NOBIN was more susceptible to degradation: NG yielded 29% of **3a** with 3% racemisation, while LAG decreased yield to 48% and increased racemisation to 12%. Under these conditions, BINOL and NOBIN show similar behaviour, as NG with BINOL gave 11% yield with no racemisation, while LAG increased yield to 36% with 20% racemisation. To investigate the yield loss, MS spectra were recorded for selected post-reaction samples of BINAM and NOBIN. The results indicated that cyclisation is a major degradation pathway in both cases: BINAM predominantly formed C–N and C–N/C–N side products, whereas NOBIN yielded C–C, C–O, and mixed C–O/C–N products (see Fig. S177 and S179, SI). Moreover, full MS spectra of the analysed samples show higher molecular weights indicative of potential oligomeric products. This behaviour mirrors that observed for BINOL, suggesting that intramolecular cyclisation leading to highly conjugated side products is a general degradation pathway for this class of compounds under mechanochemical conditions. While mechanochemistry offers powerful advantages, our findings show that it can also trigger degradation pathways. These pathways cause irreversible material loss, degradation, and racemisation: outcomes that are detrimental to the efficiency of asymmetric synthesis. Controlling mechanochemical conditions to prevent degradation is therefore essential for preserving stereoinformation and yield, ensuring the success of asymmetric synthesis.

Conclusions

In summary, we show that atropisomeric biaryls undergo multiple degradation pathways under ball milling, including racemisation, cyclisation, and oligomerisation, with the relative contributions strongly dependent on reaction conditions. These findings highlight that mechanochemical protocols for asymmetric synthesis must account for base, time, and solvent effects to avoid loss of stereochemistry. Notably, oxidation lowers catalytic activity without affecting product enantiopurity, whereas racemisation leaves activity unchanged but directly diminishes enantiopurity. More broadly, this work provides a basis for preserving the stability of chiral biaryl scaffolds, paving the way toward robust, base-tolerant strategies in mechanochemical asymmetric synthesis.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information is available. See DOI: https://doi.org/10.1039/d5mr00132c.

Acknowledgements

This research has been performed as a part of the PhD work of Leon Poljanic, affiliated with Université Catholique de Louvain, funded by the FRIA doctoral grant from the Fund for Scientific Research (F. R. S.-FNRS) and supported by the F. R. S.-FNRS grant PDR T.0185.25.

Notes and references

1 G. H. Christie and J. Kenner, *J. Chem. Soc. Trans.*, 1922, **121**, 614.
2 S. R. LaPlante, L. D. Fader, K. R. Fandrick, D. R. Fandrick, O. Hucke, R. Kemper, S. P. F. Miller and P. J. Edwards, *J. Med. Chem.*, 2011, **54**, 7005.
3 J. M. Brunel, *Chem. Rev.*, 2005, **105**, 857.
4 Y. Chen, S. Yekta and A. K. Yudin, *Chem. Rev.*, 2003, **103**, 3155.
5 J. Zhang, K. Wang and C. Zhu, *JACS Au*, 2024, **4**, 502.

6 Y.-B. Wang and B. Tan, *Acc. Chem. Res.*, 2018, **51**, 534.

7 K. Kubota, Y. Pang, A. Miura and H. Ito, *Science*, 2019, **366**, 1500.

8 A. C. Jones, M. T. J. Williams, J. C. Morrill and D. L. Browne, *ACS Catal.*, 2022, **12**, 13681.

9 A. C. Jones, J. A. Leitch, S. E. Raby-Buck and D. L. Browne, *Nat. Synth.*, 2022, **1**, 763.

10 F. Cuccu, L. De Luca, F. Delogu, E. Colacino, N. Solin, R. Mocci and A. Porcheddu, *ChemSusChem*, 2022, **15**, e202200362.

11 W. Pickhardt, S. Grätz and L. Borchardt, *Chem.–Eur. J.*, 2020, **26**, 12903.

12 S. L. James, C. J. Adams, C. Bolm, D. Braga, P. Collier, T. Friščić, F. Grepioni, K. D. M. Harris, G. Hyett, W. Jones, A. Krebs, J. Mack, L. Maini, A. G. Orpen, I. P. Parkin, W. C. Shearouse, J. W. Steed and D. C. Waddell, *Chem. Soc. Rev.*, 2012, **41**, 413.

13 J.-L. Do and T. Friščić, *Synlett*, 2017, **28**, 2066.

14 T. Friščić, C. Mottillo and H. M. Titi, *Angew. Chem., Int. Ed.*, 2020, **59**, 1018.

15 F. Gomollón-Bel, *Chem. Int.*, 2019, **41**, 12.

16 G.-W. Wang, *Chem. Soc. Rev.*, 2013, **42**, 7668.

17 T. Rantanen, I. Schiffers and C. Bolm, *Org. Process Res. Dev.*, 2007, **11**, 592.

18 Y. S. Zholdassov, L. Yuan, S. R. Garcia, R. W. Kwok, A. Boscoboinik, D. J. Valles, M. Marianski, A. Martini, R. W. Carpick and A. B. Braunschweig, *Science*, 2023, **380**, 1053.

19 P. Ying, T. Ying, H. Chen, K. Xiang, W. Su, H. Xie and J. Yu, *Org. Chem. Front.*, 2024, **11**, 127.

20 J. G. Hernández and C. Bolm, *J. Org. Chem.*, 2017, **8**, 4007.

21 M. T. J. Williams, L. C. Morrill and D. L. Browne, *ChemSusChem*, 2022, **15**, e202102157.

22 C. Lopes, L. Casali, F. Emmerling, T. Leyssens, V. Dupray, C. Brandel and Y. Cartigny, *RSC Mechanochem.*, 2025, **2**, 83.

23 R. P. Kaiser, E. F. Krake, L. Backer, J. Urlaub, W. Baumann, N. Handler, H. Buschmann, T. Beweries, U. Holzgrabe and C. Bolm, *Chem. Commun.*, 2021, **57**, 11956.

24 C. Quaranta, I. d'Anciães Almeida Silva, S. Moos, E. Bartalucci, L. Hendrickx, B. M. D. Fahl, C. Pasqualini, F. Puccetti, M. Zobel, C. Bolm and T. Wiegand, *Angew. Chem., Int. Ed.*, 2024, e202410801.

25 J. Gieling, G. Wéry, C. Lopes, J. De Meester, C. Brandel, Y. Cartigny, T. Leyssens and D. M. Baier, *Chem.–Eur. J.*, 2025, **31**, e202404120.

26 C. Lopes, Y. Cartigny, C. Brandel, V. Dupray, C. Body, O. Shemchuk and T. Leyssens, *Chem.–Eur. J.*, 2023, **29**, e202300585.

27 D. C. Patel, R. M. Woods, Z. S. Breitbach, A. Berthod and D. W. Armstrong, *Tetrahedron Asymmetry*, 2017, **28**, 1557.

28 S. Grätz, D. Beyer, V. Tkachova, S. Hellmann, R. Berger, X. Feng and L. Borchardt, *Chem. Commun.*, 2018, **54**, 5307.

29 P. Ying, J. Yu and W. Su, *Adv. Synth. Catal.*, 2021, **363**, 1246.

30 T. Friščić, L. S. Childs, S. A. A. Rizvi and W. Jones, *CrystEngComm*, 2009, **11**, 418.

31 K. Yoo, S. Fabig, S. Grätz and L. Borchardt, *Faraday Discuss.*, 2023, **241**, 206.

32 K. L. Denlinger, L. Ortiz-Trankina, P. Carr, K. Benson, D. C. Waddell and J. Mack, *Beilstein J. Org. Chem.*, 2018, **14**, 688.

33 D.-H. Lee, j. B. Son, S. Jung, J. Song and S. W. Ham, *Tetrahedron Lett.*, 2005, **46**, 7721.

34 N. d'Allesandro, G. Bianchi, X. Fang, F. Jin, H.-P. Schuchmann and C. von Sonntag, *J. Chem. Soc., Perkin Trans.*, 2000, **2**, 1862.

35 Q.-X. Guo, Z.-J. Wu, Z.-B. Luo, Q.-Z. Liu, J.-L. Ye, S.-W. Luo, L.-F. Cun and l.-Z. Gong, *J. Am. Chem. Soc.*, 2007, **149**, 13927.

36 N. B. Barhate and C.-T. Chen, *Org. Lett.*, 2002, **4**, 2529.

37 B. T. King, J. Kroulik, C. R. Robertson, P. Rempala, C. L. Hilton, J. D. Korinek and L. M. Gortari, *J. Org. Chem.*, 2007, **72**, 2279.

38 D. M. Baier, S. Grätz, B. F. Jahromi, S. Hellmann, K. Bergheim, W. Pickhardt, R. Schmid and L. Borchardt, *RSC Adv.*, 2021, **11**, 38026.