Investigating the Reactivity of Nitrous Oxide with Lithiated Hydrazines: Application to the Synthesis of Diarylethanes from Diarylmethylhydrazines

Journal:	*New Journal of Chemistry*
Manuscript ID	NJ-ART-11-2024-004837.R1
Article Type:	Paper
Date Submitted by the Author:	27-Nov-2024
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ARTICLE

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Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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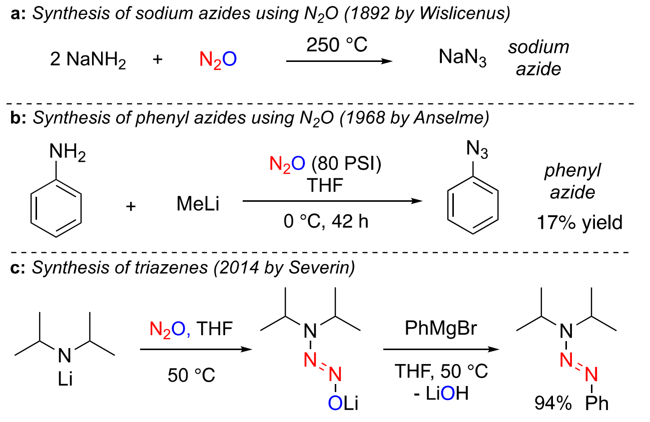
In this study, we investigate the reactivity of nitrous oxide (N_2O) with lithiated diarylmethylhydrazines, leading to the formation of diarylethanes via dinitrogen extrusion. The reaction proceeds through the formation of a lithium oxytetrazene adduct generated by the interaction of the lithium salt of diarylmethylhydrazines with nitrous oxide. Upon heating at 60 °C, this adduct efficiently converts into diarylethane in good yields. Experimental data (IR, UV) and density functional theory (DFT) calculations support the formation of the lithium oxytetrazene intermediate, which subsequently eliminates lithium hydroxide and nitrogen gas, yielding diarylethane. This method demonstrates broad substrate tolerance, accommodating substituted hydrazines with both electron-donating and electron-withdrawing groups, as well as cyclic and unsymmetrical hydrazines.

Introduction

Nitrous oxide (N_2O), commonly known as "laughing gas," initially gained attention through Humphry Davy's psychotropic experiments in 1799[1], leading to its widespread use in the Victorian era as a recreational drug. Its practical utility was further demonstrated in 1844 during an exhibition by Dr. Gardner Colton, where a volunteer experienced significantly reduced pain under the influence of N_2O.[1a] This pivotal moment began its use as an anesthetic, revolutionizing dental practices by mitigating pain during procedures. Beyond its medical applications, N_2O is also a significant environmental concern, classified as a potent greenhouse gas contributing to ozone layer depletion. The primary sources of N_2O emissions include agricultural activities, transportation, and industrial processes.[2] Current strategies to curb these emissions involve reducing nitrogen-based fertilizers in agriculture and adopting more sustainable industrial practices to lessen environmental impact.[3]

In contrast, the chemical utilization of nitrous oxide has been somewhat limited.[1c] Chemically, N_2O is distinguished by its low reactivity, despite substantial thermodynamic instability ($\Delta_fG°_{298}$ = +24.6 kcal/mol).[1b] Hence, the decomposition of N_2O into N_2 and O_2 requires harsh reaction conditions. Specifically, Metal zeolites have succeeded in efficiently splitting N_2O, but only at elevated temperatures.[2] In the 21st century, metal-based activation of N_2O was utilized to oxidize the hydrocarbons, but, the platinum group metals were more efficient.[1c, 4] Recently Cornella and coworkers reported splitting N_2O by the low-valent bismuth redox platform.[5] The same group also reported the synthesis of phenols or alcohols by catalytic activation of N_2O using Ni-catalysts.[6] Regarding a non-metal-based approach for N_2O transformation, nucleophilic carbenes have proven successful.[7] Thus, Severin and coworkers developed the reactions of N_2O with *N*-heterocyclic carbenes (NHC), isolating NHC-N_2O adducts and further transforming them into the corresponding cyclic urea's by O-transfer.[8] Contrastingly, the reactivity of N_2O with other organic nucleophiles (C, N, P) was just found in some scattered reports.[1c] A few reports of metallocarbon nucleophiles were documented, including the reaction of nitrous oxide to form useful products such as diazomethane, alkyl/aryl alcohols, etc.[1c, 9] An early report showed sodium triphenylmethide reacts with N_2O to form diazotate, convertible to the carbinol with ethanol.[10] Carbolithium compounds also reacted with N_2O; n-BuLi produced diazene and Li_2O, while methyllithium yielded diazomethane in the presence of ethanol.[9a, 11]

Though most Grignard reagents don't react with N_2O, some aliphatic types can form diazene derivatives. In recent years, these strong lithiated nucleophiles have been utilized to synthesize



Scheme 1. Reaction of nitrous oxide with *N*-nucleophiles.

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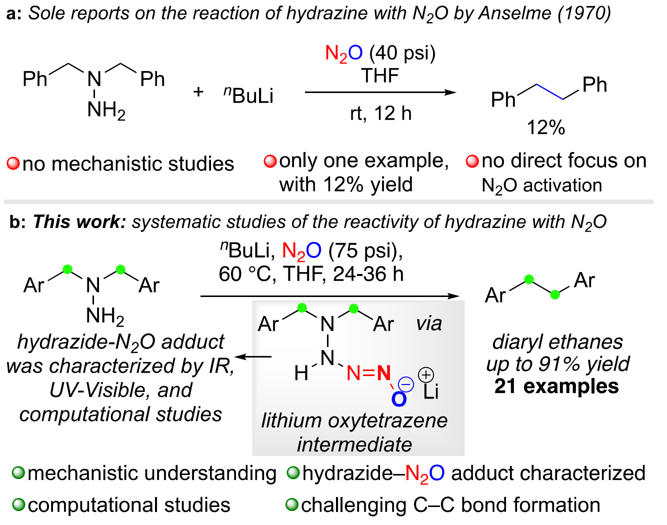
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

benzotriazin-4(3H)-one[12], and triazolopyridines[13] using N_2O as a diazo transfer agent. Early this year, a breakthrough report on the nonmetal-based N_2O activation was reported by Hansmann and coworkers.[14] In their work, they reported the synthesis of isolable diazophosphorous ylide: a stable reagent for carbon-atom transfer, by splitting N_2O.

Although recent advances have been in the reactivity of N_2O with *C*-nucleophiles, reports involving *N*-nucleophiles remain limited. A thorough literature survey revealed that the first documented reaction of an *N*-nucleophile with N_2O was reported in 1892 by Wislicenus, who prepared sodium azide from sodium amide and nitrous oxide at elevated temperatures (Scheme 1a).[1c, 15] This method was later adopted by industry for large-scale sodium azide synthesis. In 1968, Anselme and colleagues developed a method to synthesize phenyl azide by reacting the aniline salt with N_2O (Scheme 1b).[16] However, the yields were relatively low, demonstrating the challenges of using N_2O as a synthon for organic transformations. Almost after six decades, in 2014, Severin and co-workers harnessed N_2O to synthesize triazenes (Scheme 1c),[17] by treating lithium diisopropylamide (LDA) with N_2O to form an LDA-N_2O adduct, which, upon reaction with phenyl magnesium bromide produced the triazene.

A literature survey of the reactivity of *N*-nucleophiles with N_2O further indicated that only metalated amines (i.e. aliphatic or aromatic amides) have served as *N*-nucleophiles to react with N_2O. We hypothesized that hydrazines, a class of *N*-nucleophiles, could react with N_2O to split it and further transform it into a little-known functional group. A concealed report was found in 1970; Koga and colleagues described the reaction of hydrazine anion with tosyl azide, oxygen, and N_2O. This study showed that dibenzylhydrazine anion could react with N_2O at ambient conditions to produce diphenylethane, albeit in poor yield (Scheme 2a).[18] This report excited us as it supported our hypothesis.



Scheme 2. Reactivity of metalated hydrazines with N_2O.

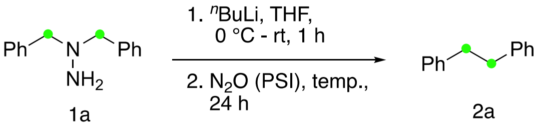
To tackle the abovementioned challenges, our research sought to study the reactivity of N_2O with hydrazines and transform them to achieve C–C bond formation (Scheme 2b). To provide a better understanding of the reaction pathway, our focus will be to characterize the hydrazide–N_2O intermediate and to establish the energetics of the reaction pathway computationally. We also seek to establish the scope of the C–C coupling to diarylethanes enabled by the thermolysis of the hydrazide-N_2O.

Results and Discussion

We commenced our N_2O studies with 1,1-dibenzyl hydrazine as a model substrate. First, 1,1-dibenzyl hydrazine was treated with *n*-butyl lithium (^{n}BuLi) in a high-pressure reactor tube to generate a lithiated salt *in situ*. N_2O gas was then introduced at 25 psi into the high-pressure reactor at ambient temperature for 24 hours. The reaction was then quenched with cold water, resulting in a 20% yield of the deletion product, diphenylethane **2a** (Table 1, entry 1). In subsequent experiments, we increased the N_2O pressure to 75 psi while keeping the other conditions constant (room temperature and 24-hour reaction time). This modification led to a notable improvement in the yield of the deletion product **2a**, reaching 41% (entry 2).

Further optimization involved heating the reaction mixture to 60 °C under the same pressure (75 psi) for 24 hr. This modification in the reaction conditions facilitated the complete conversion of the hydrazine, yielding 91% diphenylethane **2a** (entry 3). To further assess the influence of temperature and pressure on the reaction, we reduced the N_2O pressure to 25 psi while maintaining the temperature at 60 °C. This resulted in a significant drop in the product yield (entry 4), underscoring the critical roles of elevated temperature and increased pressure in this transformation. Considering the highly basic reaction conditions, we explored replacing ^{n}BuLi with sodium hydride (NaH) under identical temperature and pressure conditions (entry 5). Consequently, we obtained no diphenylethane, while recovering dibenzylhydrazine from the reaction mixture.

Table 1. Optimization of the reaction conditions. [a]

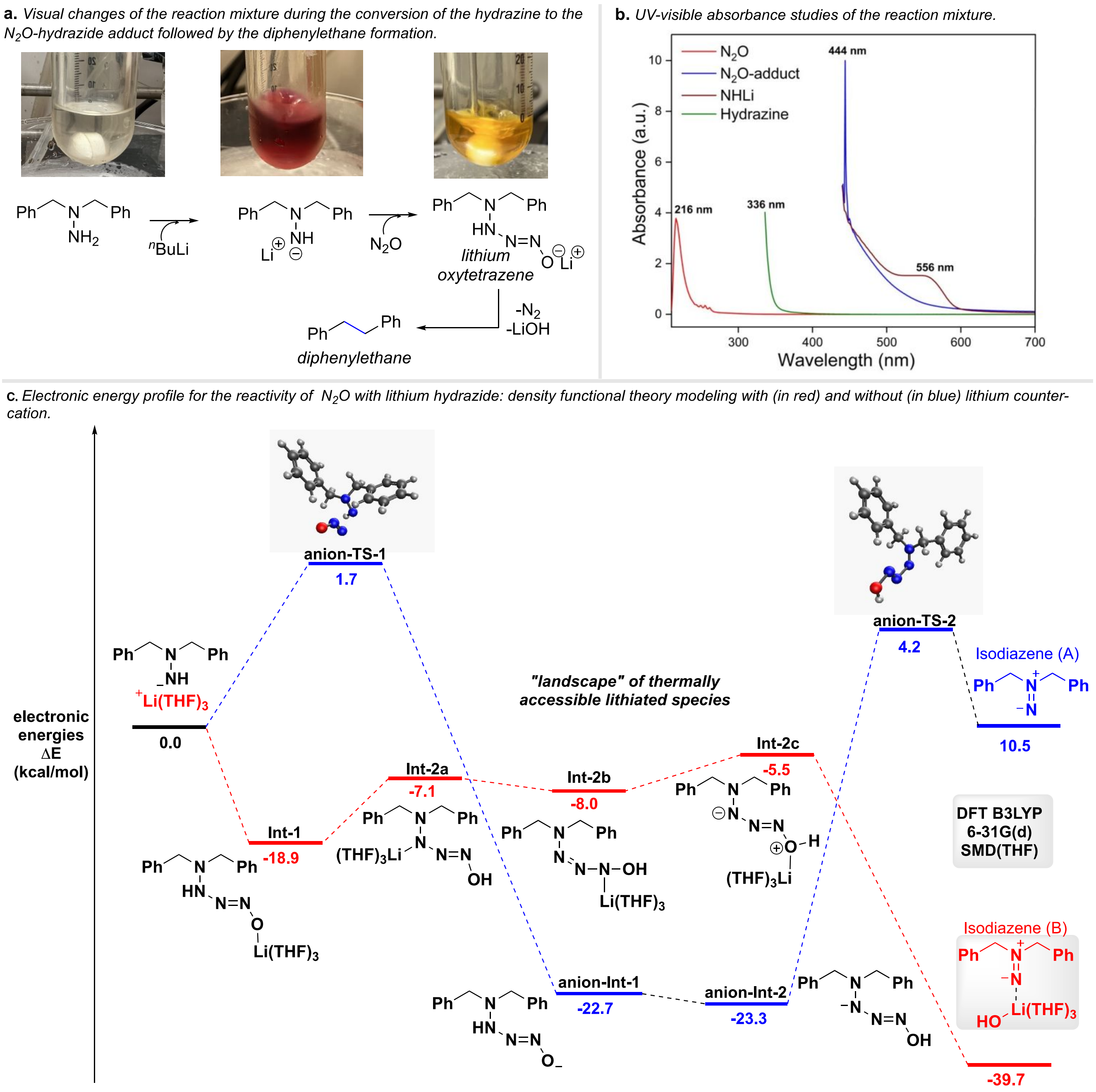


Entry	Temperature	N_2O	Yield[b]
1.	rt	25 psi	20%
2.	rt	75 psi	41%
3.	**60 ℃**	**75 psi**	**91%**
4.	60 ℃	25 psi	38%
5[c].	60 ℃	75 psi	NR
6.	60 ℃	-	NR

[a] reaction conditions: 1a (0.5 mmol), nBuLi (0.55 mmol), THF (0.1 M).[b]yield was determined by ^1H NMR using 1,3,5-trimethoxybenzene as an internal standard. [c] NaH was used as a base.

To delineate the essential role of N_2O in this reaction, a control experiment was performed, and the reaction was conducted at 60 °C without N_2O (entry 6). As expected, the reaction did not proceed towards a productive pathway, with the starting material 1,1-dibenzylhydrazine being recovered. These observations strongly suggest that the high pressure of N_2O not only assists in capturing the hydrazide anion to form a stable N_2O adduct but also that the increased temperature promotes the thermodynamically and entropically favorable extrusion of dinitrogen and lithium hydroxide, a critical step in the efficient production of diphenylethane. These results provide the optimized reaction conditions for this transformation.

After optimizing the reaction conditions, we sought to understand and elucidate the reaction pathway for this transformation. We hypothesized the reaction proceeds via a lithium oxytetrazene-type intermediate, which further fragments into the desired product diarylethane, dinitrogen gas, and lithium hydroxide (LiOH). During the experiment, we observed a significant color change at each step of the sequence (Figure 1a), and these color changes guided us to perform several studies to capture and characterize the nitrous oxide–hydrazides adduct, putatively lithium oxytetrazene. First, we attempted to detect the N_2O adduct by electrospray ionization mass spectrometry (ESI-MS), but no fragment mass peaks from the expected N_2O-hydrazide adduct could be assigned. Presumably, the injection process, or its ionization, caused its decomposition. We then turned our studies to IR spectroscopy. N_2O gas in tetrahydrofuran (THF) showed a characteristic stretching absorption at 2222 cm^{-1}. The parent dibenzylhydrazine exhibited IR peaks at 1400-1610 cm^{-1} (C=C), 2820-3050 cm^{-1} (C–H), and around 3300 cm^{-1} (N–H). Reacting dibenzylhydrazine with ^{n}BuLi in THF transformed it into lithium hydrazide, confirmed by new IR peaks at 1452 cm^{-1} and 1379 cm^{-1}, and a diminished N–H peak. Introducing N_2O into this mixture caused the N–H stretching frequency to vanish, replaced by a new peak at 1419 cm^{-1} (see section F in SI for additional details), suggesting the presence of an N=N functional group[19] and the formation of a nitrous oxide adduct (lithium oxytetrazene). We also analyzed each step of



a. *Visual changes of the reaction mixture during the conversion of the hydrazine to the N_2O-hydrazide adduct followed by the diphenylethane formation.*

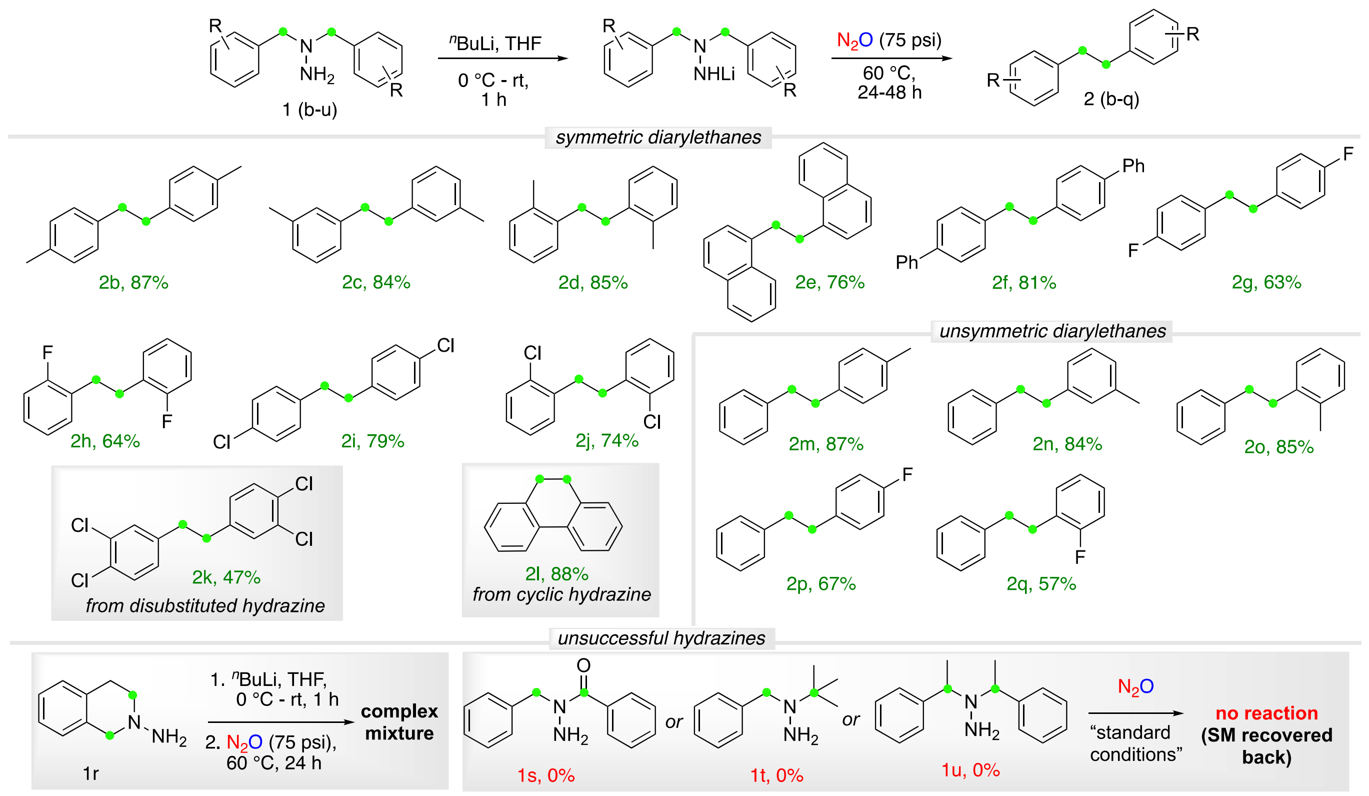
b. *UV-visible absorbance studies of the reaction mixture.*

c. *Electronic energy profile for the reactivity of N_2O with lithium hydrazide: density functional theory modeling with (in red) and without (in blue) lithium counter-cation.*

Figure 1. Mechanistic studies for the reactivity of N_2O with dibenzylhydrazide. (**a**) monitoring the progress of the reaction and incorporation of N_2O via visual changes. (**b**) monitoring the progress of the reaction by using the UV-visible spectroscopic technique. (**c**) Understanding the reaction pathway of this transformation. Due to the high concentrations (0.1 M) of the solutions, the 336 nm and 444 nm absorptions were off-scale.

the reaction via UV-visible spectroscopy. In THF, N_2O absorbs at 216 nm, while the starting hydrazine shows a strong absorbance at around 336 nm without any bands in the 400-600 nm range. The lithium hydrazide (deep red color, Figure 1a) absorbs at 556 nm. The introduction of N_2O into the reaction mixture of the lithium hydrazide produced an orange solution (Figure 1a) with an absorbance of 444 nm and a disappearance of the absorbance at 556 nm (Figure 1b). Quantum mechanical calculations estimate a HOMO-LUMO gap size corresponding to absorptions around 141 nm for pure N_2O, 487 nm for lithium hydrazide, and 428 nm for the lithium oxytetrazene intermediate. This model is qualitatively accurate and further supports the suggested intermediates of this reaction.

To further support our experimental conclusions, we developed a model of this stepwise process using density functional theory (DFT).[20] Lithium amides frequently form large multi-nuclear oligomers in solution, which can be computationally expensive to treat using quantum mechanical models. Despite this, key interactions and structures within our putative mechanism can be described using DFT. Computations were done using the B3LYP exchange-correlation functional at the 6-31G(d) level of theory. This level was chosen for its relatively high accuracy and low computational cost. Initial structures and potential energy surface (PES) scans were performed in the gas phase, while solvation effects were considered using SMD(THF) single-point calculations at the same level of theory.[21] Transition states were confirmed by Hessian analysis and characterized by a single, physically relevant imaginary vibrational frequency. Likewise, intermediates were characterized by zero imaginary vibrational frequencies with a gradient also equal to zero. We considered the role of ion-pairing on geometries and energetics using a single lithium coordinated to three explicit THF molecules (Figure 1c – red pathway). This revealed a landscape of thermally accessible mono-lithiated species, all of which were low in energy relative to the starting materials. Chemical intuition draws our attention to two of these structures, Int-1 and Int-2c, as particularly important to our putative mechanism. Visualization of the frontier molecular orbitals of Int-1 showed a HOMO localized mostly to the N-N system as two out-of-phase p-orbitals and a highly delocalized LUMO concentrated on the explicit solvation shell (see section G in SI) This implies that charge transfer excitation is likely, contributing to the vibrant colors observed. A series of 1D and 2D electronic energy scans were conducted to search for transition states connecting the lithiated starting materials and products to Int-1 and Int-2c respectively, but these efforts were ultimately fruitless (see section **H** from SI for details). Because these species exist as oligomers, there is likely no unique position for lithiation in solution, so we next opted to study the isolated anions (Figure 1c–blue pathway). This pathway begins with the association of N_2O and the hydrazine anion, forming N-H oxytetrazene anion-Int-1 in a thermodynamically favorable process. This species shows considerable bending of the nitrous oxide moiety and a transoid configuration. This is followed by a proton transfer from *N-* to *O-*, which may be an intermolecular process since the transoid configuration of the oxytetrazene disfavors an intramolecular cyclic transition state. Loss of the first N_2 molecule and hydroxyl group (likely in the form of LiOH) is a thermodynamically uphill process; however, this step is still kinetically viable, especially at elevated temperatures. After the rate-limiting step where N_2 and LiOH are lost, all subsequent steps from the isodiazene are deemed to be fast and irreversible, as concluded by Levin and Gutierrez.[22] Qualitatively, we can look at the potential energy surface as "bowl-shaped" with



Scheme 3. Substrate scope for the reactivity of hydrazines with N_2O to achieve diarylethanes[a]. [a]reaction conditions: 1 (0.5 mmol), nBuLi (0.55 mmol), THF solvent (0.1 M). All experiments were stirred for 24-48 hours, and yields were the isolated yields. SM= starting material.

the escape from the adduct bowl leading to either the isodiazene (which will rapidly decompose to the diaryl alkane) or recovery of the starting material if energy is insufficient. This explains why several substrates failed to extrude the hydrazide functionality and re-afforded starting material with no by-product. Our model is further supported by the intense color change observed in the solution upon purging with N_2O before pyrolysis (Figure 1a), which corresponds to the bottom of this bowl-shaped PES.

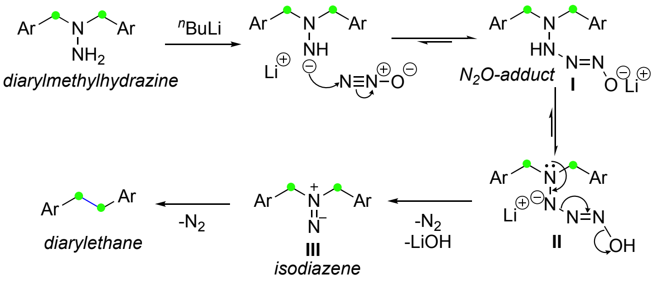
After characterizing the reaction intermediate (lithium oxytetrazene) and understanding the plausible reaction pathway, we broadened the substrate scope of hydrazines to highlight its adaptability and practical utility. We focused on the impact of introducing electron-donating groups on the phenyl rings of dibenzyl hydrazines at various positions, including *para-, meta-,* and *ortho*-substitutions (Scheme 3). Our reaction system largely tolerated these modifications. For example, when a moderately electron-donating methyl ($-CH_3$) group was introduced at each position (**2b**-**2d**) on the phenyl ring, we obtained excellent yields of the corresponding diarylethanes. Incorporating a phenyl ring in the *para* position of the dibenzylhydrazine **2f** was also tolerated well. Similarly, the dinaphthyl-substituted hydrazine produced 1,2-binaphthylethane **2e** in good yield.

Conversely, incorporating an electron-withdrawing group into the hydrazine resulted in a modest reduction in the yield of the corresponding diarylethane as illustrated with the fluoro, and chloro groups (-F, -Cl), providing moderate yields of the respective diarylethanes (**2g-2j**). We also tested the disubstituted hydrazine containing a moderately electron-withdrawing 3,4-dichloro group on the phenyl ring, which resulted in a slightly lower yield of the desired diarylethene (**2k**). From the cyclic hydrazine, an excellent yield of 9,10-dihydrophenanthrene (**2g**) was obtained using our standard conditions.

Experiments with unsymmetrical diarylethanes, where a substitution was made at the *para-, meta-,* and *ortho*-position on one of the phenyl rings, consistently resulted in the exclusive formation of unsymmetrical diarylalkanes. In terms of electron-donating groups, the inclusion of a methyl ($-CH_3$) group at the para- (**2m**), meta- (**2n**), and ortho-positions (**2o**) on one of the phenyl rings yielded excellent results. Additionally, the introduction of an electron-withdrawing fluoro (-F) group at the para- (**2p**) and ortho-positions (**2q**) proved effective, albeit in somewhat diminished yield. This series of experiments demonstrates the robustness and flexibility of our optimized reaction conditions in accommodating a variety of chemical modifications, thereby enhancing the versatility and applicability of this methodology in synthesis. The absence of cross-over products with examples (**2m-2q**) indicates that C–C bond formation proceeds through a concerted process or one that avoids freely diffusing subvalent carbon intermediates. This selectivity[23] feature is consistent with the downstream generation of the corresponding 1,1-diaryl isodiazene, which may undergo a concerted C–C bond formation as described by Levin and coworkers.[24] Overall, our substrate scope demonstrates the applicability and robustness of our methodology.

We also identified certain hydrazines incompatible with our method, as listed in Scheme 3. For instance, experiments with a hydrazine derivative of tetrahydroisoquinoline (**1r**) led to substantial decomposition. We then investigated amido hydrazine (**1s**), which was recovered after the reaction. The unreactivity of the amido hydrazine could be explained by the decreased nucleophilicity of the resulting lithium salt towards N_2O. We also investigated the reaction of a mixed benzylic and aliphatic acyclic hydrazine, tert-butyl benzyl hydrazine (**1t**), and a sterically hindered hydrazine, α,α′-dimethyldibenzyl hydrazine (**1u**). Both hydrazine substrates were unreactive and recovered after the reaction under the standard conditions. This series of experiments highlights the need for strong N-nucleophiles to react with N_2O and the requirement of relatively weak benzylic.[7]

Following the successful experimental and computational analysis of potential intermediate adducts formed between nitrous oxide and hydrazine, we have elucidated a viable reaction pathway for this transformation, characterized by a detailed mechanism (Scheme 4). The process begins with the reaction of the diarylmethylhydrazine with *n*-butyl lithium to form the diarylmethylhydrazide anion. This potent *N*-nucleophile then attacks the terminal nitrogen of the nitrous oxide, leading to the formation of a lithium oxytetrazene intermediate (intermediate-I). This step can be reversible, especially under low N_2O pressure and high temperatures. At normal atmospheric pressures, the reaction efficiency notably declines, thus supporting the possibility of reversibility in this step. Progressing from intermediate-I, the reaction pathway continues to intermediate. In this next stage, the negative charge becomes more effectively stabilized on the nitrogen atom within the oxytetrazene structure. This sequence of reactions leads to the elimination of lithium hydroxide (LiOH) and the release of a molecule of dinitrogen (N_2), thereby forming an isodiazene intermediate (III). This intermediate is particularly reactive and rapidly decomposes to form the diaryl species by releasing a second dinitrogen molecule. Since the crossover product was never observed with unsymmetrical dibenzylic substrates, this indicates the operation either of a concerted C-C bond formation or stepwise radical cage effect, which confines the radicals in proximity.[23] Ultimately, this reaction mechanism effectively transforms the initial diarylmethylhydrazine into the respective diarylethane. This transformation involves the extrusion of nitrogen atoms with the establishment of a new carbon-carbon bond, facilitated by the splitting of nitrous oxide. We have shown that when this synthon is joined with an appropriate reaction partner, N_2O can function as an energy currency to drive, in this instance, the formation of carbon-carbon bonds.



Scheme 4. Plausible reaction pathway for the formation of diarylethanes from bis-diarylmethylhydrazines reacting with N_2O.

Conclusions

In conclusion, we have successfully developed a novel approach that utilizes nitrous oxide to form carbon-carbon bonds by extruding dinitrogen from diarylhydrazines. The proposed mechanism, involving the formation of a key lithium oxytetrazene intermediate, is strongly supported by experimental evidence and quantum chemical calculations. This work not only enhances our understanding of nitrous oxide's reactivity with nucleophiles but also introduces a new application for this widely available feedstock in chemical synthesis. Additionally, our method contributes to developing environmentally friendly processes for converting greenhouse gases into valuable chemical products. The method demonstrates broad compatibility with various hydrazines, including those with different electronic substitutions and cyclic structures, consistently delivering high yields of diarylethanes.

Author Contributions

SPS developed this work and completed the writing of this manuscript with the help of Dr. IS and Dr. KMN. SPS, DH and UC expanded the scope of this methodology. SPS performed all the experimental mechanistic studies. DH performed all the computational mechanistic studies with the help of Dr. IS and Dr. KMN. Dr. KMN guided DH in solving the problems he faced during the computational studies.

Conflicts of interest

There are no conflicts to declare.

Acknowledgments

This work was supported by the NSF CHE-1753187, and a Collaborative Research Faculty Fellowship (CRFF) Grant from the Dodge Family College of Arts and Sciences, the University of Oklahoma. We thank Dr. Novruz Akhmedov and Dr Steven Foster of the Research Support Services, University of Oklahoma, for assistance with NMR and mass spectra, respectively. We also thank Dr. Bayram Saparov and Ms. Kanika Parashar for their help with the UV-visible spectral studies. Helpful discussions with Prof. Yihan Shao regarding the DFT calculations are also greatly appreciated. We also thank the OU Supercomputing Center for Education & Research (OSCER) at the University of Oklahoma where all computations were performed for this work.

References

1. a) M. A. Gillman, Mini-review: a brief history of nitrous oxide (N2O) use in neuropsychiatry, *Curr. Drug Res. Rev.*, 2019, **11**, 12-20; b) K. A. Dubkov, G. I. Panov and V. N. Parmon, Nitrous oxide as a selective oxidant for ketonization of C= C double bonds in organic compounds, *Russ. Chem. Rev.*, 2017, **86**, 510; c) K. Severin, Synthetic chemistry with nitrous oxide, *Chem. Soc. Rev.*, 2015, **44**, 6375-6386.
2. A. V. Leont'ev, A. Ol'ga, M. V. Proskurnina and N. S. Zefirov, Modern chemistry of nitrous oxide, *Russ. Chem. Rev.*, 2001, **70**, 91-104.
3. X. Wu, J. Du, Y. Gao, H. Wang, C. Zhang, R. Zhang, H. He, G. Lu and Z. Wu, Progress and challenges in nitrous oxide decomposition and valorization, *Chem. Soc. Rev.*, 2024, **53**, 8379-8423.
4. a) T. L. Stuchinskaya and I. V. Kozhevnikov, Novel efficient catalysts based on Ru or Pd oxide for selective liquid-phase oxidation of alcohols with nitrous oxide, *Catal. Commun.*, 2003, **4**, 609-614; b) A. G. Tskhovrebov, E. Solari, R. Scopelliti and K. Severin, Activation of Nitrous Oxide by Dinuclear Ruthenium Complexes, *Organometallics*, 2012, **31**, 7235-7240.
5. Y. Pang, M. Leutzsch, N. Nöthling and J. Cornella, Catalytic Activation of N2O at a Low-Valent Bismuth Redox Platform, *J. Am. Chem. Soc.*, 2020, **142**, 19473-19479.
6. a) S. Ni, F. L. Vaillant, A. Mateos-Calbet, R. Martin and J. Cornella, Ni-catalyzed oxygen transfer from N2O onto sp3-hybridized carbons, *J. Am. Chem. Soc.*, 2022, **144**, 18223-18228; b) F. Le Vaillant, A. Mateos Calbet, S. González-Pelayo, E. J. Reijerse, S. Ni, J. Busch and J. Cornella, Catalytic synthesis of phenols with nitrous oxide, *Nature*, 2022, **604**, 677-683.
7. A. Genoux and K. Severin, Nitrous oxide as diazo transfer reagent, *Chem. Sci.*, 2024, **15**, 13605-13617.
8. a) A. G. Tskhovrebov, E. Solari, M. D. Wodrich, R. Scopelliti and K. Severin, Covalent Capture of Nitrous Oxide by N-Heterocyclic Carbenes, *Angew. Chem. Int. Ed.*, 2011, **1**, 232-234; b) A. G. Tskhovrebov, B. Vuichoud, E. Solari, R. Scopelliti and K. Severin, Adducts of nitrous oxide and N-heterocyclic carbenes: syntheses, structures, and reactivity, *J. Am. Chem. Soc.*, 2013, **135**, 9486-9492; c) A. G. Tskhovrebov, L. C. Naested, E. Solari, R. Scopelliti and K. Severin, Synthesis of azoimidazolium dyes with nitrous oxide, *Angew. Chem.*, 2015, **127**, 1305-1308; d) L. Y. Eymann, R. Scopelliti, F. T. Fadaei, G. Cecot, E. Solari and K. Severin, Fixation of nitrous oxide by mesoionic and carbanionic N-heterocyclic carbenes, *Chem. Commun.*, 2017, **53**, 4331-4334; e) L. Y. Eymann, P. Varava, A. M. Shved, B. F. Curchod, Y. Liu, O. M. Planes, A. Sienkiewicz, R. Scopelliti, F. Fadaei Tirani and K. Severin, Synthesis of organic super-electron-donors by reaction of nitrous oxide with N-heterocyclic olefins, *J. Am. Chem. Soc.*, 2019, **141**, 17112-17116.
9. a) F. M. Beringer, J. A. Farr Jr and S. Sands, The Reactions of Nitrous Oxide with Organolithium Compounds1, *J. Am. Chem. Soc.*, 1953, **75**, 3984-3987; b) E. Müller and W. Rundel, Untersuchungen an Diazomethanen, VIII. Eine Neue Synthese von Diazomethan und von Isodiazomethan, *Chem. Ber.*, 1957, **90**, 1302-1306; c) M. L. Hays and T. P. Hanusa, A reinvestigation of the reaction of arylcalcium iodides with nitrous oxide, *Tetrahedron Lett*, 1995, **36**, 2435-2436; d) M. Kurosawa, T. Nankawa, T. Matsuda, K. Kubo, M. Kurihara and H. Nishihara, Synthesis of azo-bridged ferrocene oligomers and a polymer and electrochemical and optical analysis of internuclear electronic interactions in their mixed-valence states, *Inorg. Chem.*, 1999, **38**, 5113-5123.
10. D. SCHLOSSER, Organosodium and Organopotassium Compounds, *Liebigs Ann. Chem.*, 1929, **473**, 1.
11. R. Meier and W. Frank, Über die Reaktion von Phenyllithium mit Stickoxydul (II. Mitteil. Über Reaktionen metallorganischer Verbindungen mit Stickoxydul), *Chem. Ber.*, 1956, **89**, 2747-2750.
12. Z. Lai, C. Wang, J. Li and S. Cui, Redox cyclization of amides and sulfonamides with nitrous oxide for direct synthesis of heterocycles, *Org. Lett.*, 2020, **22**, 2017-2021.

13. I. R. Landman, F. Fadaei-Tirani and K. Severin, Nitrous oxide as a diazo transfer reagent: the synthesis of triazolopyridines, *Chem. Commun.*, 2021, **57**, 11537-11540.

14. T. Koike, J.-K. Yu and M. M. Hansmann, Ph_3PCN_2: A stable reagent for carbon-atom transfer, *Science*, 2024, **385**, 305-311.

15. F. Bergmann, *Ueber die Einwirkung von Chlor auf m-Amido-p-Kresol*, Buchdr. F. Sömmering, 1892.

16. a) R. Meier, Reaktionen metallorganischer Verbindungen mit Stickoxydul, *Chem. Ber.*, 1953, **86**, 1483-1492; b) G. Koga and J.-P. Anselme, The formation of azides by the reaction of amine anions with nitrous oxide, *Chem. Commun.*, 1968, 446-447.

17. G. Kiefer, T. Riedel, P. J. Dyson, R. Scopelliti and K. Severin, Synthesis of triazenes with nitrous oxide, *Angew. Chem. Int. Ed.*, 2015, **54**, 302-305.

18. G. Koga and J. P. Anselme, N-Nitrenes. IX. Reaction of 1, 1-dibenzylhydrazine anions with tosyl azide, oxygen, and nitrous oxide, *J. Org. Chem.*, 1970, **35**, 960-964.

19. F. Zimmermann, T. Lippert, C. Beyer, J. Stebani, O. Nuyken and A. Wokaun, N= N vibrational frequencies and fragmentation patterns of substituted 1-aryl-3, 3-dialkyl-triazenes: comparison with other high-nitrogen compounds, *Appl. Spectrosc.*, 1993, **47**, 986-993.

20. Y. Shao, Z. Gan, E. Epifanovsky, A. T. Gilbert, M. Wormit, J. Kussmann, A. W. Lange, A. Behn, J. Deng and X. Feng, Advances in molecular quantum chemistry contained in the Q-Chem 4 program package, *Mol. Phys.*, 2015, **113**, 184-215.

21. A. V. Marenich, C. J. Cramer and D. G. Truhlar, Universal solvation model based on solute electron density and on a continuum model of the solvent defined by the bulk dielectric constant and atomic surface tensions, *J. Phys. Chem.B*, 2009, **113**, 6378-6396.

22. J. Masson-Makdissi, R. F. Lalisse, M. Yuan, B. D. Dherange, O. Gutierrez and M. D. Levin, Evidence for Dearomatizing Spirocyclization and Dynamic Effects in the Quasi-stereospecific Nitrogen Deletion of Tetrahydroisoquinolines, *J. Am. Chem. Soc.*, 2024, **146**, 17719-17727.

23. a) J. T. Barry, D. J. Berg and D. R. Tyler, Radical Cage Effects: The Prediction of Radical Cage Pair Recombination Efficiencies Using Microviscosity Across a Range of Solvent Types, *J. Am. Chem. Soc.*, 2017, **139**, 14399-14405; b) A. B. Oelkers and D. R. Tyler, Radical cage effects: A method for measuring recombination efficiencies of secondary geminate radical cage pairs using pump–probe transient absorption methods, *Photochem. Photobiol. Sci.*, 2008, **7**, 1386-1390.

24. S. H. Kennedy, B. D. Dherange, K. J. Berger and M. D. Levin, Skeletal editing through direct nitrogen deletion of secondary amines, *Nature*, 2021, **593**, 223-227.

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Data Availability Statement

To Whom It May Concern:

The data supporting this article have been included as part of the Supplementary Information.

Sincerely,

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