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# A Reinvestigation of the Reaction of Arylcalcium Iodides with Nitrous Oxide

Melanie L. Hays and Timothy P. Hanusa*

Department of Chemistry, Vanderbilt University, Nashville, TN, USA 37235

***Abstract:*** The previously reported reaction of phenylcalcium iodide with $N_2O$ in ether to form products with aryl–N bonds has been reexamined with various solvents and methylated aryliodides. The yield of azobenzene is maximized using DME as the solvent, and the insertion reactions may involve diorganocalcium ($Ar_2Ca$) intermediates.

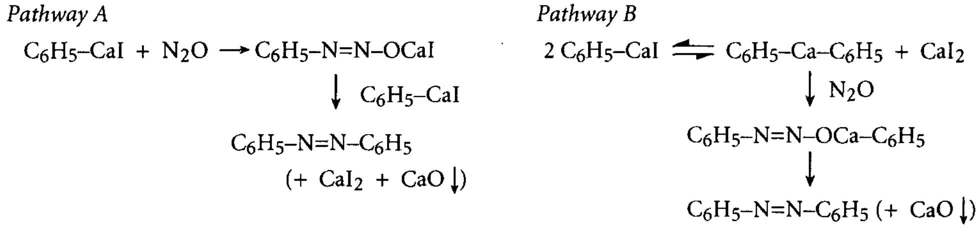
Nitrous oxide has been used as a convenient oxygen transfer reagent in transition metal organometallic chemistry,[1] but essentially no use has been made of $N_2O$ in organic synthesis. It is too inert to react with Grignard reagents, although Meier and Rappold identified several products from the reaction of $N_2O$ with the Grignard analogue phenylcalcium iodide.[2] Among the isolated compounds were azobenzene (15%), benzidene, *N*-phenylbenzidene and biphenyl (20%), the latter probably the result of Wurtz coupling. In light of the variety of species generated in this novel C–N bond-forming reaction, we sought to determine whether the conditions could be modified to favor the production of specific aryl-nitrogen compounds.

Arylcalcium iodides were generated from iodobenzene or methylated iodobenzenes and elemental calcium in several ethereal solvents at reflux, and allowed to react with $N_2O$ at room temperature.[3] As previously reported, phenylcalcium iodide in diethyl ether generated a range of products with $N_2O$. Biphenyl was the most abundant (58% of total), whereas azobenzene, although present, was in less than 2% yield. These amounts differ from those found by Meier and Rappold, but ether cleavage reactions are known to complicate the reactions of phenylcalcium iodide in diethyl ether.[4]

The products and their distributions changed when the solvent was varied and methylated iodobenzenes were used. Phenylcalcium iodide failed to form when methyl-*t*-butyl ether was used as a solvent. The higher boiling point of dimethoxyethane relative to diethyl ether was expected to increase the rate of formation of the organocalcium reagents and perhaps decrease competition from aryl coupling reactions. The reaction of $C_6H_5I$, Ca and $N_2O$ in DME did produce azobenzene in substantial amounts (61% yield); its ratio to biphenyl was 1.7:1. Yields from reactions of phenylcalcium iodide in pure DME could, however, be erratic; for no readily identifiable reason, certain reactions generated an insoluble material and insertion products were not formed. The addition of 5% THF to the DME led to more reproducible insertion reactions, while minimizing the impact from THF degradation (see below). In DME, 4-iodotoluene generates the corresponding methylated azobenzene in 33% yield, with an azobenzene/biaryl ratio of 12.7:1, whereas the only identified product from 1-iodo-3,5-dimethylbenzene in DME is the Wurtz-coupled biaryl.

Although often used in other organoalkaline-earth syntheses,[4,5] THF proved to be less than an optimum solvent with these systems. Competition from the reaction of $(C_6H_5)CaI$ with THF to open its ring and generate the aryl ether $C_6H_5{-}O{-}(CH_2)_3CH_3$ limited the formation of other products to less than 20% of the theoretical maximum. Azobenzene was formed in 6% yield from phenylcalcium iodide in THF; biphenyl and benzidene together formed only 10% of the product mixture. Formation of the organocalcium reagent is slow using 2-iodotoluene, and large amounts of the aryl ether byproduct are generated; the ratio of the biaryl product to the substituted azobenzene is 9:1. Unlike its behavior in DME, 1-iodo-3,5-dimethylbenzene in THF produced the corresponding azobenzene in 7% yield, with no evidence for other insertion products or the biaryls; 4-iodotoluene produced the same result. With the sterically bulky 1-iodo-2,3,5,6-tetramethyl- and 1-iodo-2,3,4,5,6-pentamethylbenzenes, there is no visible formation of the ArCaI reagents in THF.

The process by which C–N bonds are formed in these reactions is not well understood. For azobenzene, a diazotate formed directly from phenylcalcium iodide and $N_2O$ could be a key intermediate in the mechanism; subsequent attack by another PhCaI molecule would generate the second aryl–N bond (pathway A).[2] Given the propensity for alkyl and arylcalcium halides to undergo disproportionation by Schlenk equilibria (i.e., $2\,RCaX \rightleftharpoons R_2Ca + CaX_2$),[6] however, a reasonable alternate (or concurrent) route could involve the diorganocalcium species $(C_6H_5)_2Ca$; insertion of $N_2O$ into a Ca–Ph bond, followed by intramolecular phenyl migration, would also yield azobenzene (pathway B).



To test the feasibility of the latter mechanism, a solution of diphenylcalcium was prepared in THF and treated with $N_2O$.[7] Product analysis by GC/MS indicated that azobenzene (10.2% isolated yield) was the major product of the reaction; other products matched those from the reaction conducted with iodobenzene. These results suggest that iodide need not be present for the insertion reactions to occur, and that intramolecular rearrangements may be involved even when iodobenzenes are used.

In summary, we have found that the amount and distribution of the products from arylcalcium iodides and nitrous oxide vary significantly with the solvent and type of substitution on the aryl ring. Azobenzenes are the favored products in DME, and are produced in useful amounts from iodobenzene and 4-iodotoluene. Diphenylcalcium itself can undergo insertion with nitrous oxide; thus diarylcalcium compounds may be convenient reagents for further investigations of $N_2O$ insertion reactions.

## REFERENCES and NOTES

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2. Meier, R.; Rappold, K. *Angew. Chem.* **1953**, *65*, 560-561.
3. In a typical reaction, calcium shot (99%) (3.82 g) and iodobenzene (3 mL) in diethyl ether (30 mL) were gently refluxed for 45 min under nitrogen; this was followed by vigorous stirring for 18 h at room temperature. The solution turned red as the organocalcium reagent formed. A stream of $N_2O$ (99.99%) was passed through the deep red solution for 15 min, after which the reaction was allowed to stir under $N_2O$ for 24 h. The solution was then decanted from the remaining calcium, which was washed with ether. The combined ethereal fractions were dried over $MgSO_4$, and the ether removed, leaving a mixture of products. GC/MS analysis was used to obtain the product distribution. No significant difference in product yield was observed from the use of calcium shot, granules or dendritic calcium (99.99%) as long as the surface of the calcium had not been passivated. $N_2O$ itself can passivate the calcium and should be bubbled through the reaction solution *after* the formation of the organocalcium halide.
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7. Diphenylmercury (2.44 g, 6.88 mmol) and granular calcium (1.20 g, 30.0 mmol) were mixed in THF (75 mL) and the reaction allowed to stir for 36 h. The resulting solution of diphenylcalcium was allowed to react *in situ* with $N_2O$. $Ph_2Hg$ itself is inert to $N_2O$ (Hays, M. L.; Hanusa, T. P., unpublished results), so that the subsequently formed insertion products do not arise from unreacted $Ph_2Hg$.

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