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Half-Arsed Papers

PPG: Personal Protective Groups as a Defence Against Laboratory Carcinogens

Cucumber Bandersnatch,[A] *Günther Schlonk*[B*]

A. *The Invective Collective, University of Little Whinging*

B. *School of Inorganometallics, University of West Failure*

Oft has it been said that organic chemists die twenty years younger than everyone else.[1] While statistical evidence for this assertion remains patchy, blame has already been apportioned to the fug of reagent vapours and solvent fumes that permeate even the airiest labs. Methyl iodide, hexane, hydrochloric acid, dichloromethane, benzene, the list goes on. Most of our reliable reagents and solvents are in fact deceitful double-agents, slipping past our biological defences like Tom Cruise through a hall of lasers, only marginally smaller.[2] Once inside, these pernicious bastards take to our DNA like 12-year-olds to a library book. In the case of these chemicals, however, the damage is more severe than a few scrawled phalli. Some dissenting voices have made themselves heard about the carcinogenic clamour, such as Desmond Pondandt from the University of Bitchfield, UK. Professor Pondandt has posited that chemist-mortality is actually a result of the chronic stress, insomnia and alcohol dependency ubiquitous to this field.[3] While this theory has undeniable merit, it does not diminish the significance of working in an atmosphere more toxic than a nightclub on Venus. Given that Günther's 116th birthday is approaching, it seems appropriate that we devote some time to the question of preventing the corrosive effects of lab fumes on health. Methyl iodide was chosen as a model contaminant, as it is volatile, carcinogenic and acutely toxic. Like many common reagents, the toxicity derives from the ease with which it alkylates the nucleophilic residues present in proteins and DNA. When the analogous problem of unwanted reactivity presents itself in organic synthesis, the solution is typically to use protecting groups (PG's) to shield the susceptible portions of a molecule (figure 1). This led us to ponder: if it works on a molecule, why not a person? Are we not made of molecules, after all?

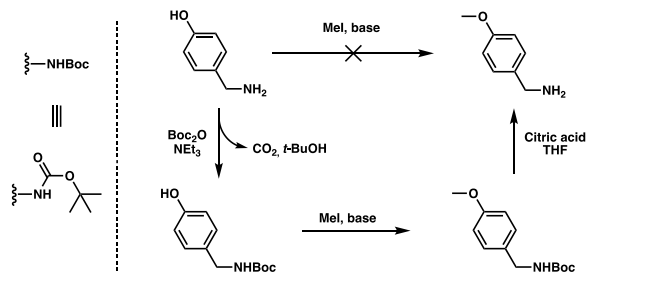

Figure 1: An example of a protecting-group (Boc) and its application

For that extra level of protection, PPE needs to go one step further than coats and glasses. We propose that by applying protecting groups to the proteins lining the sinuses and lungs of a post-grad, the subject could be sheltered from rapacious alkylating agents like MeI. In such an endeavour, choice of protecting group is essential. For ease of application, a volatile reagent should be used to introduce the protecting group. This excludes the Nosyl and Fmoc groups, as introducing solids into the lungs may create more problems than it solves. The introduction of the protecting group should not liberate any deleterious side products, such as HCl. Thus, TMS and Cbz are out, alongside a host of others. Finally, mild conditions must be available to remove the PG, when the day's work is concluded. Table 1 shows a breakdown of some common N-protecting groups as differentiated by our criteria.

Protecting Group Structure	Volatility	Side Products	Deprotection
Ns	X	HCl	Skunk Nasal-Spray
Fmoc	X	HCl	Piperidine Mouthwash
Cbz	✓	HCl	H_2, Pd snuff
Bz	✓	HBr	H_2, 20 bar
Boc	✓	CO_2, *t*-BuOH	Snorting Sherbet
Ts	X	X	$LiAlH_4$ Swab

Table 1: Bio-compatibility of common N-protecting groups

Of the surveyed PG's, half were insufficiently volatile for easy application to the respiratory tissue. Of the remaining three, benzyl groups are too hard to remove, and generate HBr during their application. Cbz groups may be removed with an H_2 inhaler and a box of palladium snuff, but HCl is formed concomitantly with CBz amines. This left the Boc PG as the only viable candidate. While a solid at room temperature, Boc_2O exhibits sufficient vapour pressure to fully coat a human lung with 10 minutes of constant inhalation.[4] The biproducts of Boc protection are CO_2 and *t*-butanol, neither of which are particularly toxic, in the scheme of things. Finally, we hypothesised that snorting a line of sherbet would constitute a mild method of deprotection. Lab rat prices are at an all-time high this year, so we have chosen to test this methodology *in Shih Tzu*.

Experimental Section

Procedure for Boc-protection of respiratory tissue: Boc_2O (5 g) was placed in a spoon and gently heated with a cigarette lighter. The test subject (a 3-year old Shih Tzu[5]) inhaled the liberated vapours for a 10-minute period. Test subjects (either Boc-protected or control) were dressed in lab-coat and glasses, then exposed to an atmosphere of methyl iodide (500 ppm) for a period of 14 hours (to represent a typical postgrad working day).

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goodenough.immaterial.science@gmail.com
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Procedure for deprotection: Sherbet (10 g, 10% citric acid w/wt.) was macerated with aid of a credit card, formed into lines, and administered nasally to the subjects.

Results and Conclusions

Ten dogs were treated with Boc_2O, and the same number constituted the control group. While the protection procedure was executed smoothly, upon exposure to the MeI atmosphere, all test subjects expired. This makes analysing the efficacy of our treatment troublesome, but one finding we can claim with certainty is that our regimen is just as good as the control. From this foundation, we hope to optimise the Boc-protection of respiratory tissue, and carry our lab-trials forward to testing in the C57BL/6 strain of post-grads.

Notes and references

1 Old mate Garry, 2018, *Down the pub.* **11:30 pm.**
2 B. Willis, J. Statham, S. Stallone, 2019, *J. Toxanomalies,* **3**, 17.
3 J. King, D. Pipe, D. Pondandt, 2020 *J. Self Med. Chem.* **32**, 809.
4 K. Hippocrates, 412 BC, *Chem. Med. Comm. Med. Chem.* **56**, 347.
5 Shih Tzu were sourced from *Labradomics Ltd.*

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