The Journal of Immaterial Science

Miscommunication

Received 5th September 2021
Accepted: 8th September 2021
DOIOU: C5

Applications of Cursed Chemistry in the Total Synthesis of Impracticatechol

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Abstract: Burnie Urethra's group have set themselves a Herculean task: the total synthesis of Impracticatechol (1). The highly complicated structure features a dozen stereocenters and a raft of functional groups including a pentavalent carbon. This malevolent moiety constitutes a significant challenge to the synthetic chemist, as until now, no methodology has been reported pertaining to their preparation. Herein, we describe an easy and promiscuous protocol for generating pentavalent carbon centers via a one-pot curse-transfer cyclisation reaction, inspired by r/cursed_chemistry.

Specific: We may or may not have destroyed a few flasks during the research process.

Following the amazing discovery of Impracticatechol[1] (figure 1) by Urethra *et al*, we found the challenge of total synthesis to be very relatable to us and our nightmares, so we decided to take part in the research process. The first step of the total synthesis has been explored already, leaving the remaining 41 reactions incomplete.

Considering the horrid nature of this structure, we consulted r/cursed_chemistry, a highly reliable source of unconventional reactions and compounds disregarded by chemists of sound mind.

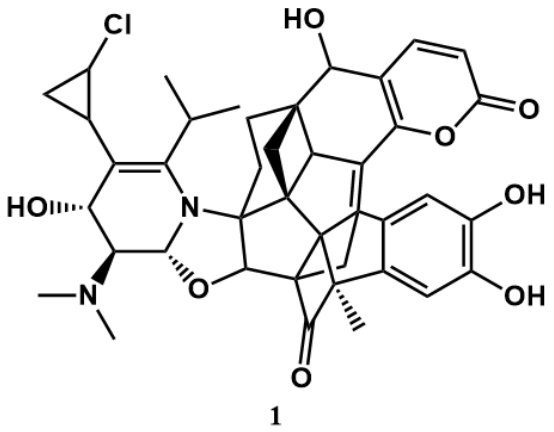


Figure 1: This abomination called Impracticatechol

Pentavalent carbons (also known as Texas carbons) have been thoroughly explored by this community, as have highly nitrogenated structures and many other marvellous examples (figure 2).

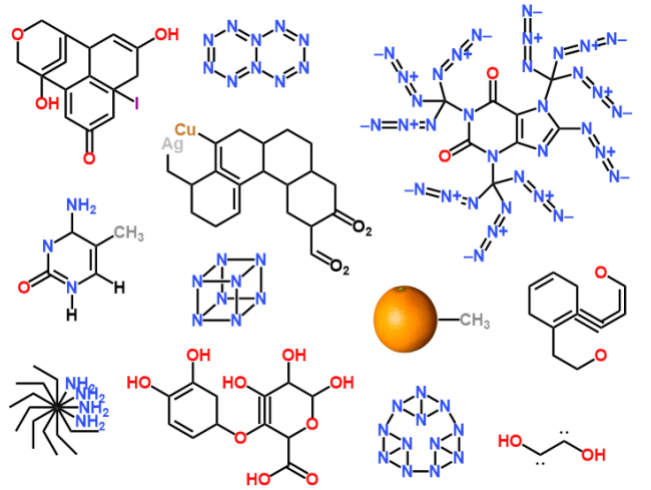


Figure 2: Some structures reported by the Reddit group

Our research suggested that a heptaazacubane (**2**) could act as a sufficiently cursed reactive intermediate which should theoretically be able to perform an intramolecular curse-transfer to generate a pentavalent carbon.

Proposal and optimisation of the reaction conditions

In order to make the heptaazacubane intermediate, we proposed to use the trinitromethyl group as a CN_3 fragment that can be installed via nucleophilic substitution to an alkyl halide (figure 3). The four other nitrogen atoms could be added by a combination of liquid air (80:20 N_2/O_2) and hydrazine. We hope that using two nitrogen sources and the cooling effect of liquid air would stabilise the heptaazacubane intermediate.

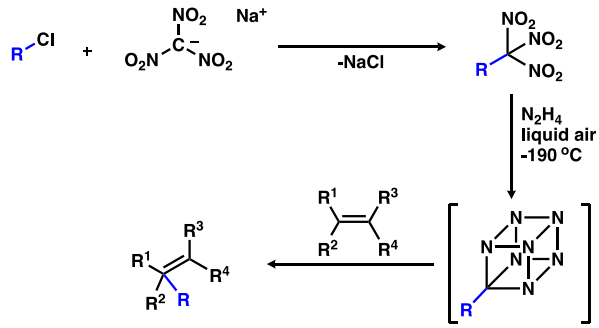
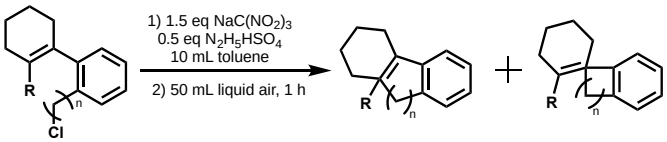


Figure 3: Proposed mechanism for generating pentavalent carbons

As such, we have attempted the synthesis of the benzyl derivative **(2)** by combining benzyl chloride, hydrazine sulphate and trinitromethyl-sodium in a flask, the experiment being performed in the parking lot of our building for safety reasons (scheme 1). By slowly adding liquid air, nothing really happened. After five minutes, the flask detonated, and, by asking lab staff to rate the explosion from 1 to 10, we guess the yield of heptaazacubane was roughly 69%.



Scheme 1: Standard conditions for curse-transfer cyclisation

With evidence for a heptaazacubane intermediate in hand, we tested the intramolecular curse-transfer cyclisation of alkene-chlorides **3–11** (figure 3), and on intermediate **13** from the Impracticatechol synthesis.

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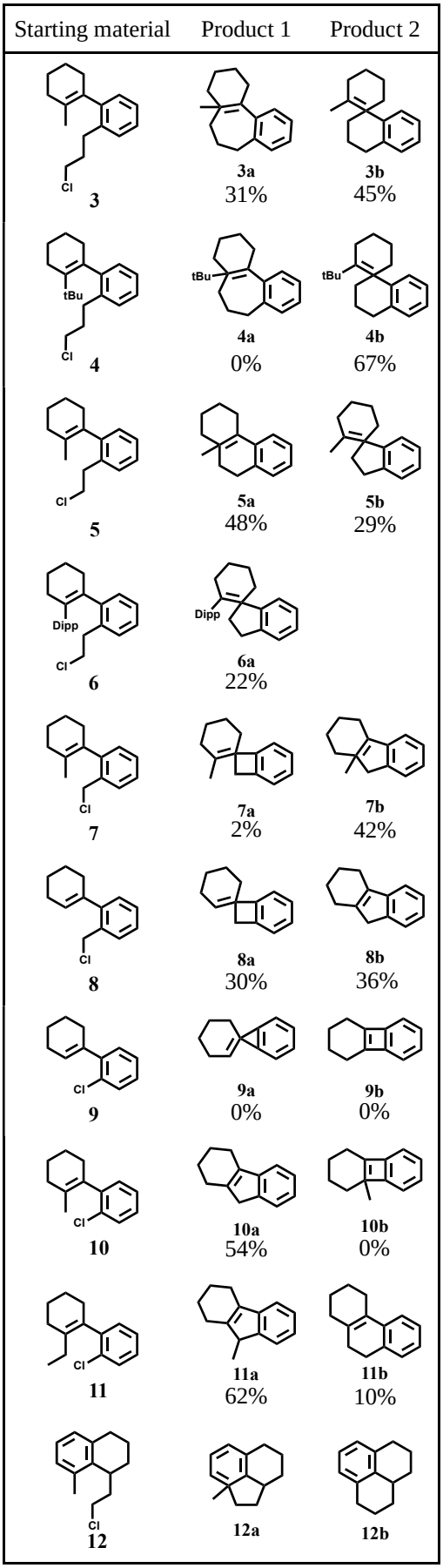

Figure 3: Scope of the curse-transfer reaction

Results and discussion

As shown in figure 3, the reaction can work on both end of the double bond, unless the position is sterically hindered. In the case of small rings, the presence of an alkyl group gives the possibility of alkyl hydrogen abstraction which becomes favoured over the pentavalent product. Without it, the reaction doesn't work for very small rings, as shown by the low yield of **9**.

While conducting this research, we have dealt with a number of accidents including detonation, losing a reagent sample and possibly killing a stray cat. One useful piece of information we have discovered is that we now know 1-(2-chloroethyl)-8-methyl-1,2,3,4-tetrahydronaphthalene **(12)** is not very toxic to humans.

Seeing the great success of our previous reactions, we attempted the cyclisation of precursor **13** by using our standard conditions.

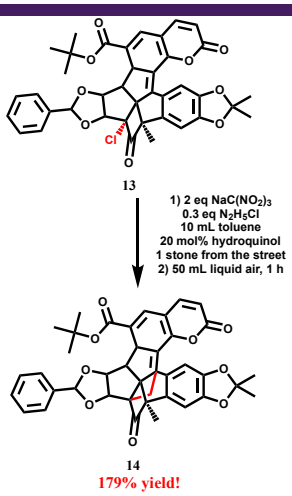

Figure 4: Synthesis of an Impracticatechol precursor

We obtained **14** with a yield of roughly 5%, but the product exhibited hydrolysis and hydrazine-ketone condensation. In order to optimize the conditions, we switched to the less acidic hydrazine HCl in a smaller amount, while also adding more trinitromethane salt. We added 20 mol% of hydroquinol as a mild reductive agent in order to compensate for the missing hydrazine, and a stone we found on the road because we read that some people use clay to catalyse reactions so it might work for us too.[2] We were pleasantly surprised to find that the yield of **14** after extraction is 179%, but the other lab team in our building criticised it (they are probably just jealous).

Experimental procedures

The solvents and glassware were provided by our laboratory, the hydrazine salts and hydroquinol were purchased from Ligma-Eldritch, and the chloro-alkenes and trinitromethane salt were obtained from old mate Garry from around the back of the pub. We do not know where **13** came from, but we confirmed its structure by ^{1}H-NMR analysis and a taste test. All of the experiments were performed in our parking lot, hiding behind an improvised plexiglass shield at a 5-meter distance from the flasks.

The first experiment: A 500 mL three-neck flask is filled with 0.02 mol (2.3 mL) of benzyl chloride, 0.04 mol of trinitromethyl sodium (6.92 g), 0.02 mol of hydrazine bisulfate (2.6 g) and 10 mL of benzene. We add a stir bar, an addition funnel and then cover the flask in aluminium foil to prevent photochemical decomposition. The addition funnel is filled with 50 mL of liquid air which is then added dropwise under strong stirring, starting a chronometer and phone camera at this point. After 5 minutes 36 seconds, the flask detonates. The video is present in the supplementary material.

General procedure for the cyclization reaction: 0.02 mol of the chosen reagent is added in a three-neck flask together with 0.03 mol of trinitromethyl sodium (5.19 g), 0.02 mol of hydrazine bisulphate (1.3 g) and 10 mL of toluene. 50 mL of liquid air is slowly added under

strong stirring and left for one hour. We let the mixture return to room temperature and then we separate the components by column chromatography with hexane/ethyl acetate (5:1). Some of the products were mixtures and were differentiated via ^{1}H-NMR.

Improved synthesis for Impracticatechol: 0.02 mol of **13**, 0.04 mol of trinitromethyl sodium (6.92 g), 6 mmol of hydrazine hydrochloride (0.41 g), 4 mmol of hydroquinol (0.44 g), 10 mL of toluene and one rock (autoclaved for 3h) are added to a three-neck flask. The rest of the procedure is identical with the one above.

Conclusions

We have created an abomination and we do not regret it. We developed a procedure for the creation of pentavalent carbon centers with the help of substituted heptaazacubanes made by *in situ* assembly. Jonathan ate the manuscript of the supplementary data so it is now unavailable.

About the Authors

Frederick Washing and Ben Dover have recently graduated and are currently trying to find a job. Jonathan Mhama randomly came into the building so now he is part of the lab staff.

Author Contributions

Frederick Washing made all of the illustrations and planned the synthesis procedures with Ben Dover. All of the experiments and purification procedures were performed by Ben Dover. Jonathan Mhama helped with obtaining the compounds and left empty milk cartons in the fridge.

Conflicts of Interest

We apologise for violating the chemistry laws.

Notes and references

1 M. Mould, H. Ether, B. Urethra, *A Partial Total Syntheis of Impracticatechol,* 2021, *J. Immat. Sci,* **1**, 6.

2 A.M.Elfadly, I.F. Zeid, F.Z. Yehia, M.M. Abouelela, A.M. Rabie, *Production of aromatic hydrocarbons from catalytic pyrolysis of lignin over acid-activated bentonite clay, Fuel Processing Technology Vol. 163, 2017*