Multicomponent Reactions – 'Kinderleicht'

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Supporting information

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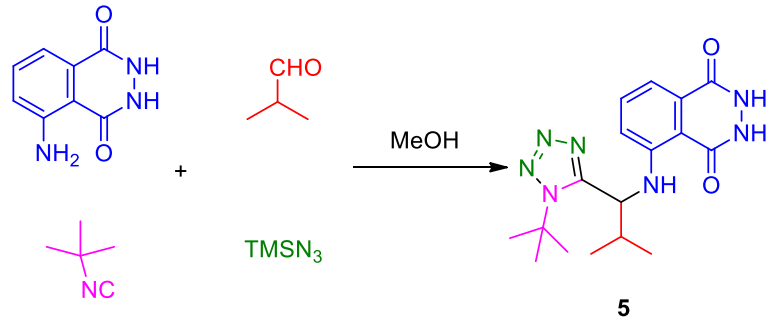
Experimental procedures-guidelines

Synthesis of 5-((1-(1-(tert-butyl)-1*H*-tetrazol-5-yl)-2-methylpropyl)amino)-2,3-dihydrophthalazine-1,4-dione (5)



5

What you need	Remarks/tips
Microwave vial (10 ml) Microwave oven Stirring bar Syringes, pipettes	Product obtained as gray solid

- Luminol (cas: 521-31-3; M_r = 177.16 g/mol)
- Isobutyraldehyde (cas: 78-84-2; M_r = 72.11 g/mol; d = 0.79 g/cm^3; bp: 63 ^{o}C)
- tert-Butyl isocyanide (cas: 7188-38-7; M_r = 83.13 g/mol; d = 0.735 g/cm^3; bp: 91 ^{o}C)
- Trimethylsilyl azide (cas: 4648-54-8; M_r = 115.211 g/mol; d = 0.876 g/cm^3; bp: 92-95 ^{o}C)

The TLC (DCM-MeOH 4:1) monitors the completion of the reaction. There was not any unreacted luminol detected, only traces of the isocyanide. In the picture below the adduct **5** is depicted in TLC in two different wavelengths with a characteristic absorption after its purification.

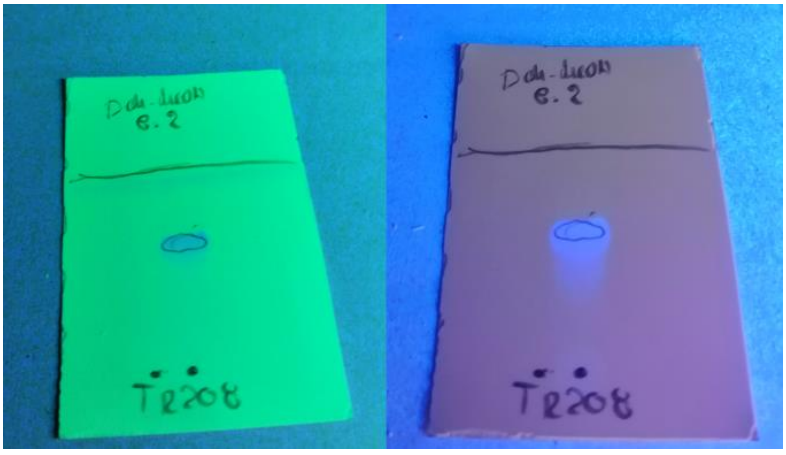
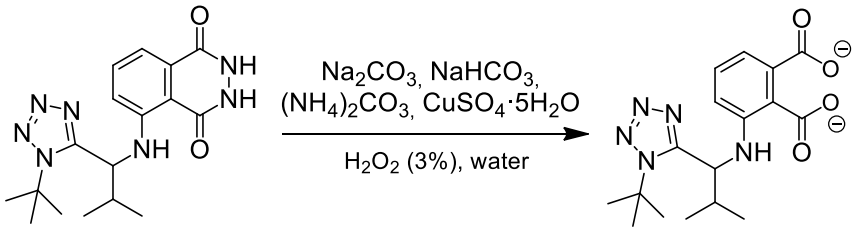


Figure S1. (A) Picture in left; 254 nm wavelength, (B) Picture in right; 366 nm wavelength

Chemiluminescence of the tetrazole derivative 5



What you need	Remarks/tips
Luminol-tetrazole derivative **5**	Obtained by previous experiment
Syringes, pipettes	Fresh solutions give better and long-lasting results
Stirring bar	Deionized water
Funnel	Mixing of the solutions has to be slow
Erlenmeyer flasks and vials	
Stirring plate or shaker	

- compound **5** (M_r = 357.19 g/mol)
- Na_2CO_3 (cas: 497-19-8, M_r = 105.99 g/mol)
- $NaHCO_3$ (cas: 144-55-8, M_r = 84.01 g/mol),
- $(NH_4)_2CO_3$ (cas: 506-87-6, M_r = 96.09 g/mol)
- $CuSO_4 \cdot 5H_2O$ (cas: 7758-98-7, M_r = 249.69 g/mol)
- H_2O_2 {cas: 7722-84-1, M_r = 34.01 g/mol, d = 1.11 g/cm^3 (30% w/w solution)}

It is worth mentioning that the sodium bicarbonate in solution acts to buffer the carbonic acid (H_2CO_3) being produced, keeping the solution basic. Ammonium carbonate enhances both the duration of chemiluminescence and it could be useful in other variations of the experiment that slight pressure is needed (ammonia gas), i.e. fountains or spiral glass tubing.[1,2]

[1] Shakhashiri, Bassam, *Chemical Demonstrations*, Vol. 1, U. Wisconsin Press, **1983**, p. 156
[2] Summerlin, L, Ealy, J, *Chemical Demonstrations*, American Chemical Society, **1985**, p. 138.

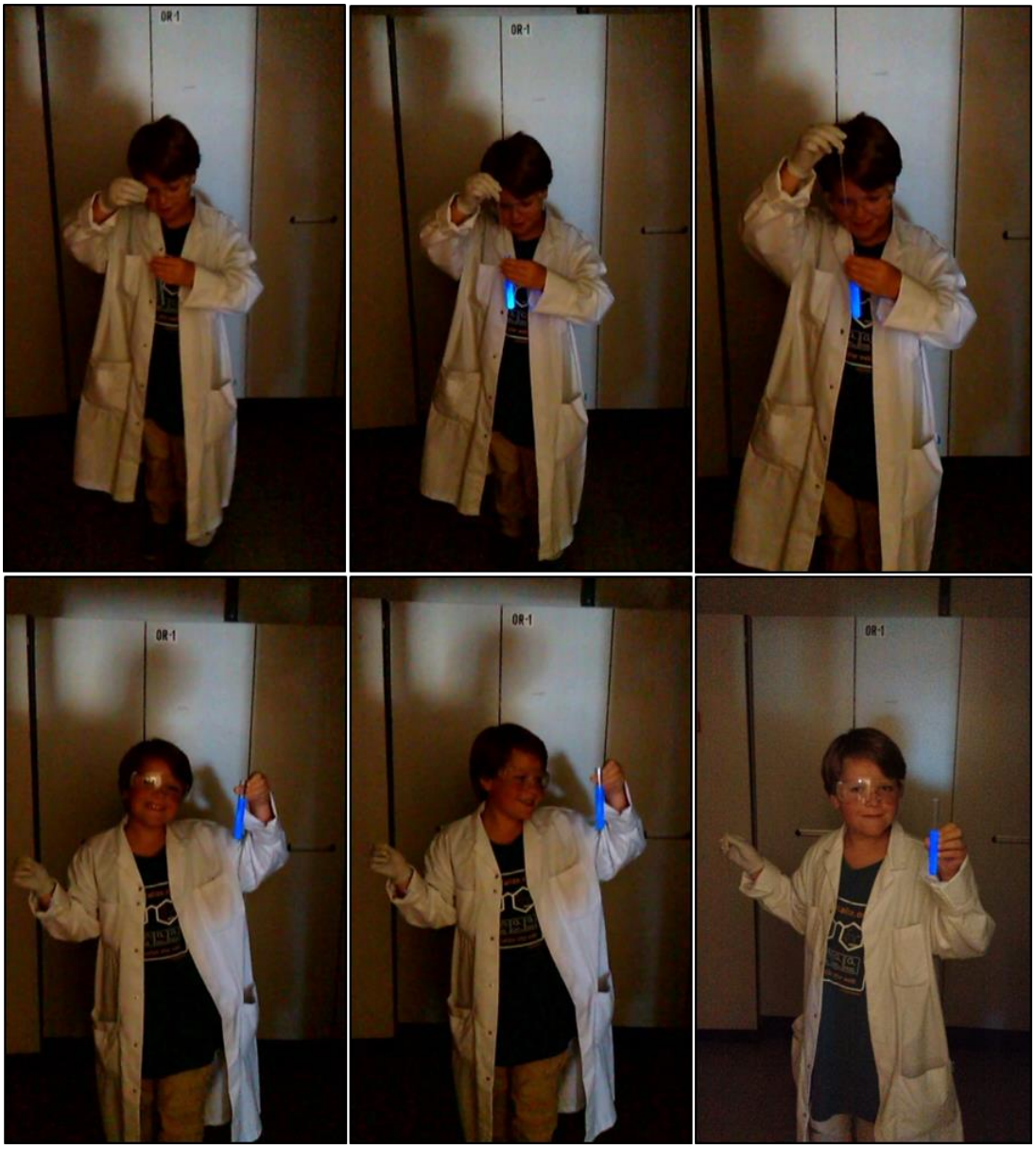


Figure S2. Curiosity, observation and explanation stimulate the interest of this student for science (photos and videos were produced by authors).

Hazards identification

Classification of the substance or mixture

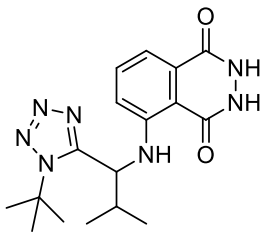
Name	CAS	Classification (REGULATION EC)	Hazard statements	Prevention
Isobutyraldehyde for synthesis	78-84-2	No 1272/2008	Flammable liquid, Category 2, H225 (*Highly flammable liquid and vapour*)	• Keep away from heat/sparks/open flames/hot surfaces. - No smoking • Keep container tightly closed storage • Store in a well-ventilated place • Keep cool
Trimethylsilyl azide for synthesis	4648-54-8	No 1272/2008	Flammable liquid, Category 2, H225 (*Highly flammable liquid and vapour*) Acute toxicity, Category 3, Inhalation, H331 Acute toxicity, Category 3, Dermal, H311 Acute toxicity, Category 3, Oral, H301 (*Toxic if swallowed, in contact with skin or if inhaled*)	• Keep away from heat/sparks/open flames/hot surfaces - No smoking • Wear protective gloves/ protective clothing • If on skin: Wash with plenty of soap and water • If exposed or if you feel unwell: Immediately call a poison center or doctor/physician. • Store in a well-ventilated place Keep cool
5-Amino-2,3-dihydrophthalazine-1,4-dione for synthesis (luminol)	521-31-3	No 1907/2006	This item is not a hazardous substance and does not contain hazardous ingredients, substances with European Community workplace exposure limits or substances of very high concern (SVHC) above their respective disclosure limits	
tert-Butyl isocyanide	7188-38-7	No 1272/2008	Flammable liquids (Category 2), H225 (Highly flammable liquid and vapour) Acute toxicity, Inhalation (Category 2), H330 (Toxic if swallowed, in contact with skin or if inhaled)	• Keep away from heat, hot surfaces, sparks, open flames and • Other ignition sources. No smoking. • If inhaled: Remove person to fresh air and keep comfortable for breathing. • Immediately call a poison center/doctor

NMR interpretation and structure elucidation

The following interpretation of the spectra of ^{1}H NMR and ^{13}C NMR of the 5-((1-(1-(tert-butyl)-1*H*-tetrazol-5-yl)-2-methylpropyl)amino)-2,3-dihydrophthalazine-1,4-dione (**5**) could be used as a tool for further studies on NMR structure elucidation. By that way, the student can learn how we approach and "solve" a proposed structure from a reaction.

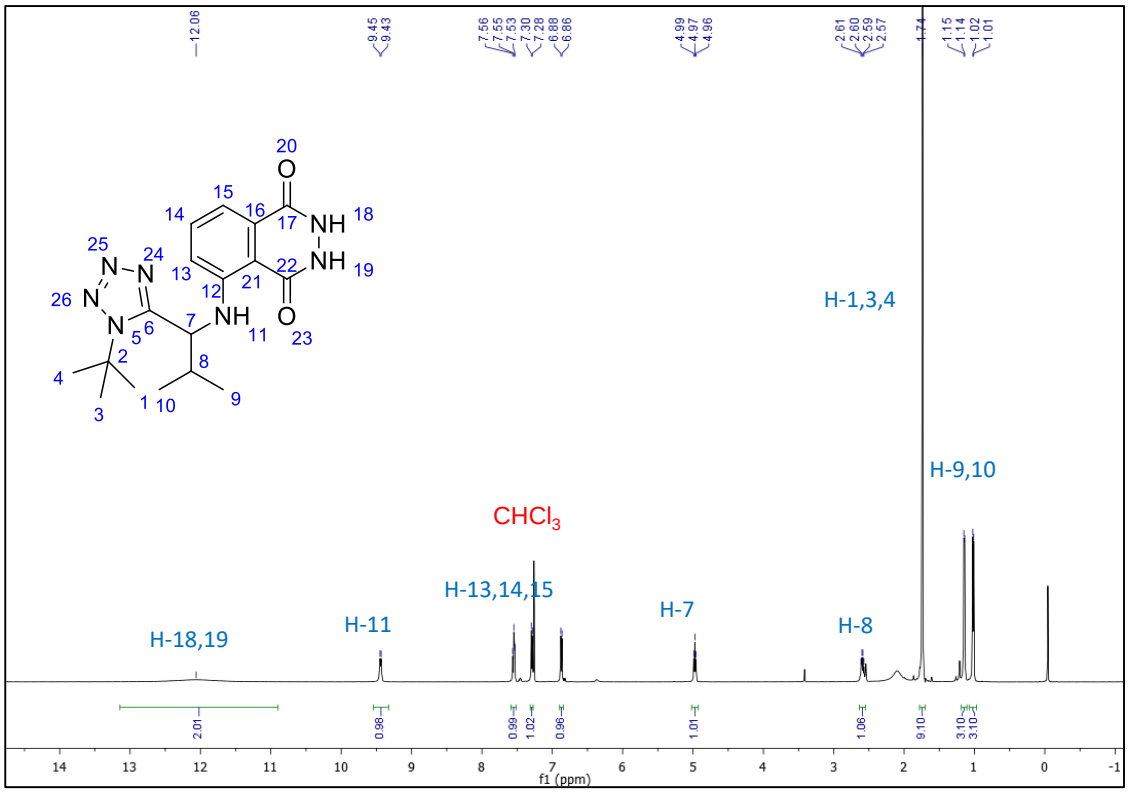
Thus, the two NH groups from the luminol moiety resonate at 12.06 δ as a broaded singlet. The other N-H (H-11) appears at 9.44 δ as a double due to the adjacent C-H (H-7). Regarding the phenyl group, the H-14 appears as triplet at 7.55 δ, the H-15 and H-13 as doublets at 7.29 δ and 6.87 δ, respectively with their carbon signals at 110-112 δ. The H-7 resonates at 4.97 δ as triplet and its carbon at 52.3 δ, whereas the H-8 appears as octuplet at 2.61-2.57 δ due to the two methyl groups (H-9,10) and H-7. The C-8 appears at 33.8 δ. The tert-butyl group resonates as a singlet at 1.74 δ with the carbons at 29.6 δ and the two methyl groups, H-10 and H-9, at 1.15 and 1.02 as doublets, with their carbon signals at 19.2 and 17.7 δ, respectively.

Specifically:

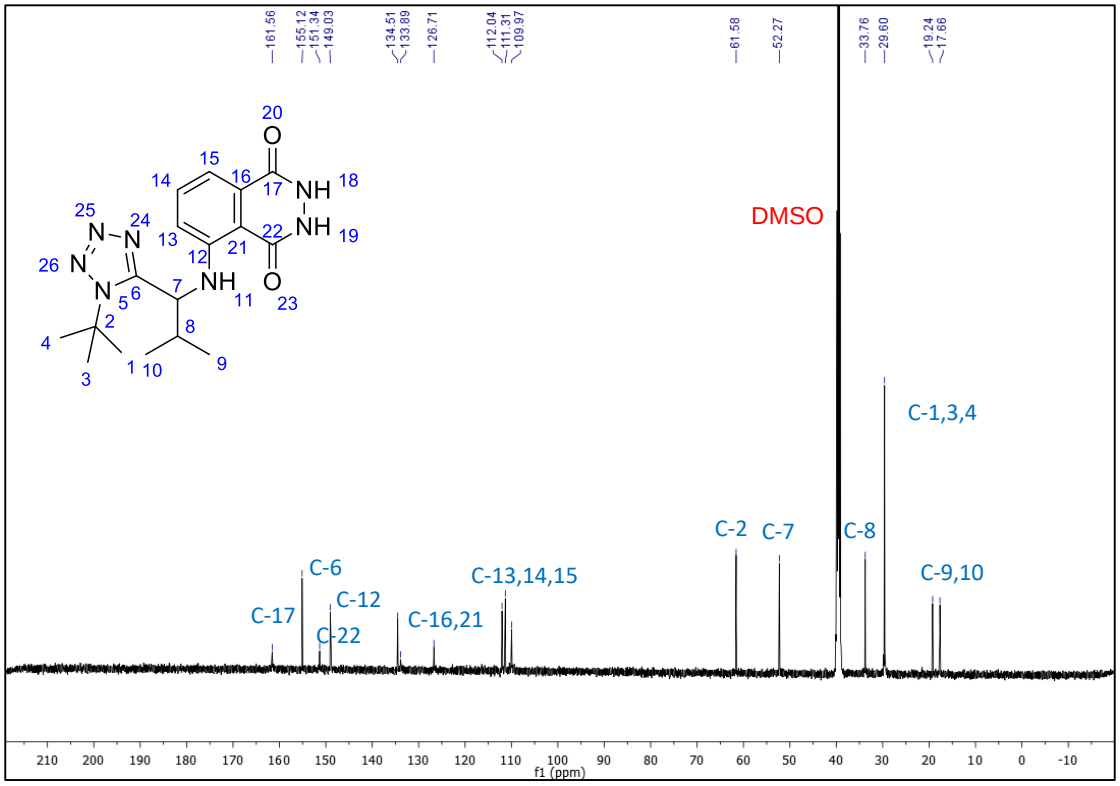


Gray solid; 62% yield; ^{1}H NMR (500 MHz, $CDCl_3$, DMSO) δ 12.06 (s, 2H), 9.44 (d, *J* = 8.1 Hz, 1H), 7.55 (t, *J* = 8.1 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 4.97 (t, *J* = 7.9 Hz, 1H), 2.61 – 2.57 (m, 1H), 1.74 (s, 9H), 1.15 (d, *J* = 6.7 Hz, 3H), 1.02 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (126 MHz, DMSO) δ 161.6, 155.1, 151.3, 149.0, 134.5, 133.9, 126.7, 112.0, 111.3, 110.0, 61.6, 52.3, 33.8, 29.6, 19.2, 17.7.

^{1}H NMR ($CDCl_3$, DMSO)



^{13}C NMR (DMSO)



Interactive diagrams

This is an example of how Rees *et al* interactive diagrams were employed to facilitate our students' inquiry. The table depicts two students' initial questions and answers indicating what changes they could attempt regarding components reacting with Luminol (Step III and IV) and predictions or conclusions they made regarding light intensity (Step IV) and mechanism (Step IV). Student initial reactions are recorded in step 1 in which they reported what they observed. Following their observations students were asked to ask the first question that came to mind. The second step involved posing questions that made their initial hypothesis testable and thus falsifiable. Step three involved identifying how a change in an independent variable can affect a dependent variable and finally the last step involves drawing conclusions in which students affirmed, altered, reformulated or disproved their initial core science concepts.

Students	Step I	Step II	Step III	Step IV
	1. What did I observe? 2. What am I wondering?	1. What could I measure or observe about the event? 2. What could I change or vary that may affect what I can observe?	1. What will I change? 2. What I will not change?	What is my prediction and why?
Nikolaos Tripolitsiotis	1. Bright light 2. How is this happening?	1. Intensity of light 2. One of the components	1. Change one of the components 2. Luminol	Maybe one component will interfere with luminol and the color intensity decreases
Konstantinos Gatzonas	1. Blue light 2. How long the light emission lasts?	1. Time of emission of the blue light 2. Reactants adding order	1. The order of adding the reactants 2. Luminol	No change in color because the Ugi reaction has a defined mechanism and the color is based on the luminol component