Supporting Information: Teaching Old Presumptive Tests New Digital Tricks with Computer Vision for Forensic Applications

Nathalie Bugeja, Cameron Oliver, Nicole McGrath, Jake McGuire, Chunhui Yan, Felicity Carlysle-Davies, and Marc Reid

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In addition to the experimental details provided herein, an additional zipped folder of machine-readable data is provided. See Section 7 for details.

1. General Considerations

All reagents were obtained from commercial suppliers and used without further purification, unless otherwise stated. Mandelin and Dille-Koppanyi reagents were prepared in-house, as described in Section 4.1 and 4.2 (below). Commercial Zimmermann reagent (Part A: aqueous potassium hydroxide; Part B: 1,3-dinitrobenzene in MeOH) was purchased from www.safetest4.co.uk. Drug standards were provided by the Centre for Forensic Science at the University of Strathclyde, within the remit of the controlled drugs license. These standards included all amphetamine, benzodiazepine, and barbiturate drug derivatives mentioned in the manuscript.

2. Equipment

All items listed below were required for the apparatus set-up used for video recording all spot tests reported in this study:

Lightbox (GODOX LST40 LED Mini Photography Studio Tent 40 cm^3)
https://www.amazon.co.uk/GODOX-Photography-Power%E3%80%8115000-19000-Lumen%E3%80%815800K%C2%B1200K-Temperature/dp/B081DFNM71/ref=sr_1_3?dchild=1&keywords=godox%2Blight%2Bbox&qid=1627425438&s=electronics&sr=1-3&th=1

Webcam (Microsoft Q2F-00015 LifeCam Studio Webcam)
https://www.amazon.co.uk/gp/product/B009IUJMH0/ref=ppx_yo_dt_b_asin_image_o02_s01?i.e.,=UTF8&psc=1

Light Meter (V·Resourcing Handheld Illuminance Meter)
https://www.amazon.co.uk/gp/product/B07NRWCSB6/ref=ppx_yo_dt_b_asin_title_o00_s00?ie=UTF8&psc=1

Hotplate Stirrer (Scilogex Circular Top Ceramic Hotplate Stirrer)
https://www.scilogex.com/scilogex-sci280-pro-circular-top-led-digital-hotplate-stirrers.html

Mass Balance (VWR Analytical balance LA124i)
https://www.pocdscientific.com.au/equipment/balances/VWRI611-2261

2.1 Apparatus Set up

The apparatus was set up as shown (**Figure S1**). The lighting was controlled to create even, diffuse illumination around the vial. The stirrer hotplate was set to 300 revolutions per minute (RPM) to ensure uniform mixing of the drug and reagent within the vial in each experiment.
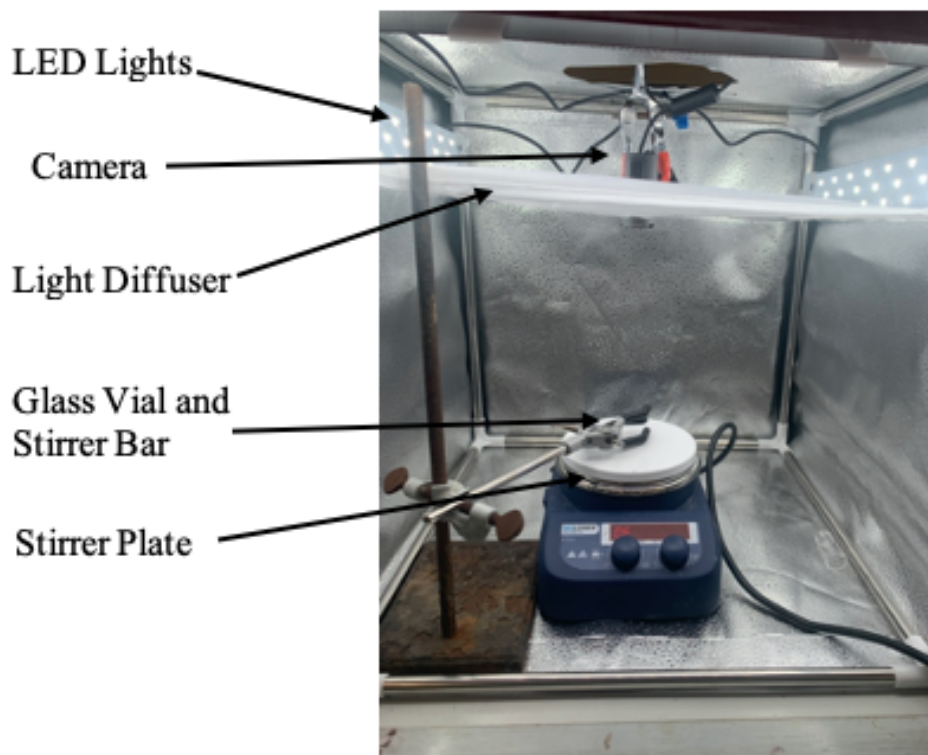
Figure S1: Top – Labelled apparatus set up for video-recording of forensic spot tests. Bottom – close-up of the vial positioning.

2.2 Light Sources

Using the above-detailed light box, with 3 strips of white light LEDs and a light diffuser fabric strip created conditions helping to minimise glare on the reaction vials, and minimise the impact of external light sources (natural, time-dependent laboratory light and synthetic light from fluorescent lighting). Using a digital light meter, the LED lights were adjusted during every experiment conducted to reach a light reading of as near to 2667 lux as possible.

2.3 Camera Settings

A Microsoft USB webcam was connected to a laptop and used to record the spot tests. The camera was positioned directly above the vial and captured a birds-eye view of the reaction (Figure S1). A resolution of 1080p at 30 frames per second was used to record the videos.

3. General Procedure for Presumptive ('Spot') Test Video Recording

3.1 Preparation of Reagents

3.1.1 Mandelin Reagent

The Mandelin reagent was prepared by dissolving ammonium meta-vanadate (1 g, 8.62 mmol) in water (1.5 mL), making the solution up to 100 mL in a volumetric flask with concentrated sulfuric acid.

3.1.2 Dille-Koppanyi Reagent

The Dille-Koppanyi reagent was also made up of two solutions:

A: Cobalt(II) acetate tetrahydrate (0.1 g, 0.56 mmol) and glacial acetic acid (0.2 mL) made up to 100 mL of methanol.

B: Isopropylamine (5 mL) made up to 100 mL with methanol.

3.1.3 Modified Dille-Koppanyi Reagent

As per the Dille-Koppanyi reagent but replacing iso-propylamine for n-propylamine.

3.1.4 Zimmermann Reagent

Commercial Zimmermann reagent (Part A: aqueous potassium hydroxide; Part B: 1,3-dinitrobenzene in MeOH) was purchased from www.safetest4.co.uk.
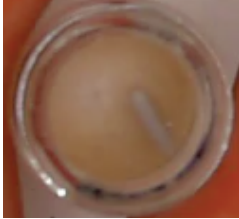
3.2 Running and recording spot test reactions

For each spot test, 2 mg of the selected drug was weighed into a 4-dram (approx. 15 mL) vial, along with a magnetic stirrer bar and placed on the stirrer plate which was set to 300RPM every time. A light reading of 2667 lux (on average) was taken using a digital light meter before the video recording was started.
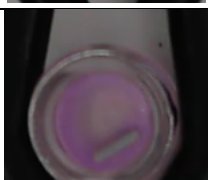
For both the Dille-Koppanyi and the Zimmerman reagents, 250 μL of solution A and 250 μL of solution B were added into the vial via pipette, in that order. In these cases, addition of solution B was used to initiate the colour change for positive spot tests. This initiation event was also used to set time-zero for the kinetic analyses of ΔE versus time (and related) profiles.

After approx. 5 minutes, the video recordings were stopped and the colours of the resultant solutions were compared to the RAL K7 colour chart, each being assigned an RAL code. Each video was then used as input for Kineticolor software analysis to generate output graphs of ΔE versus time. Spot tests were carried out in triplicate.

3.2.1 Images of colour changes from Zimmermann Benzodiazepine spot tests

Drug	Zimmermann result (5 mins)	RAL (5 mins)
Diazepam		3007
Nitrazepam		1021
Flurazepam		8016
Ketazolam		3012
Flunitrazepam		3007
Chlordiazepoxide		9010

3.2.2 Images of colour changes from Dille-Koppanyi Barbiturate spot tests

Drug	Dille-Koppanyi result (5 mins)	RAL (5 mins)
Barbitone		4008
Butobarbitone		4008
Cyclobarbitone		4013
Hexabarbitone		4003
Pentobarbitone		4006
Sec-butobarbitone		4008
Sodium barbitone		4006

3.3 Preparation of Cut Drug Samples to Simulate Street Samples

As with the entire study, all drug samples exposed to the various spot tests had a total mass of 2 mg. For the 1:1 drug:impurity samples prepared for the study in **Figure 6**, 5-10 mg each of the drug and the selected impurity were weighed out separately before being combined and cut (mixed) together thorough with a metal spatula for approximately 15 mins uninterrupted.

From this cut mixture, 2 mg quantities were weighed out and used as the 'street' samples. These samples were then tested, recorded, and analysed as described in section 3.2 (above) and 4 (below).

3.3.1 Additional discussion on <mark>Figure 7</mark>

The effect the cutting agents on pure substances during spot tests of was investigating through the preparation of 'street samples', consisting of a ratio of 1:1 (w/w) of pure substance to cutting agent. A commonly used cutting agent in street samples is caffeine. This adulterant is used due to its low-cost and pharmacological enhancing effect. Therefore, four spot tests with Mandelin reagent were performed: a negative control, consisting of Mandelin reagent only, two positive controls of pure Caffeine and Methamphetamine, and 1:1 (w/w) sample of Methamphetamine to Caffeine.

Figure S2: Images of spot test at start (left) and end (right) of the reaction of Methamphetamine with Mandelin reagent.

Figure S3: Images of spot test at start (left) and end (right) of the reaction of Caffeine with Mandelin reagent.

Figure S4: Images of spot test at start (left) and end (right) of the reaction of 1:1 w/w Methamphetamine: Caffeine with Mandelin reagent.

The ΔE profiles indicate a prolonged change in colour in the reaction with Methamphetamine when compared to the other profiles.

The resultant colour changes for methamphetamine cut with glucose are shown in the figures below.

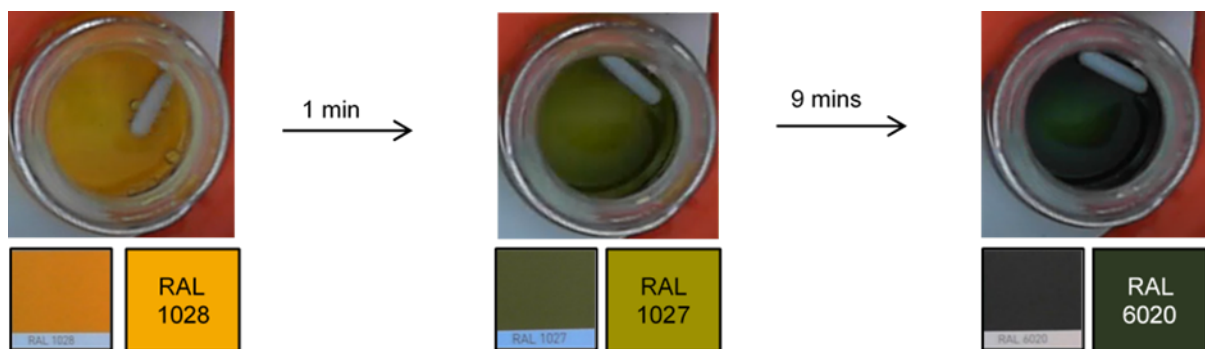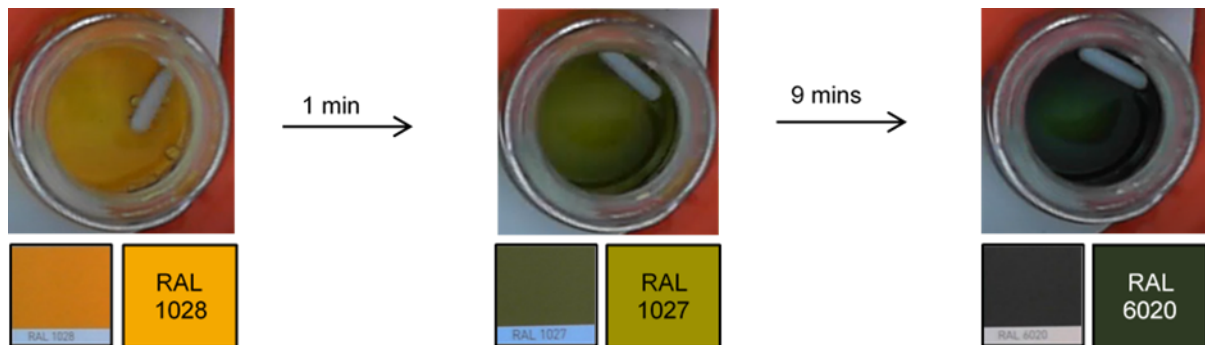**Figure S5**: Images of spot test at start (left) and end (right) of the reaction of Methamphetamine with Mandelin reagent.

Figure S6: Images of spot test at start (left) and end (right) of the reaction of Glucose with Mandelin reagent.
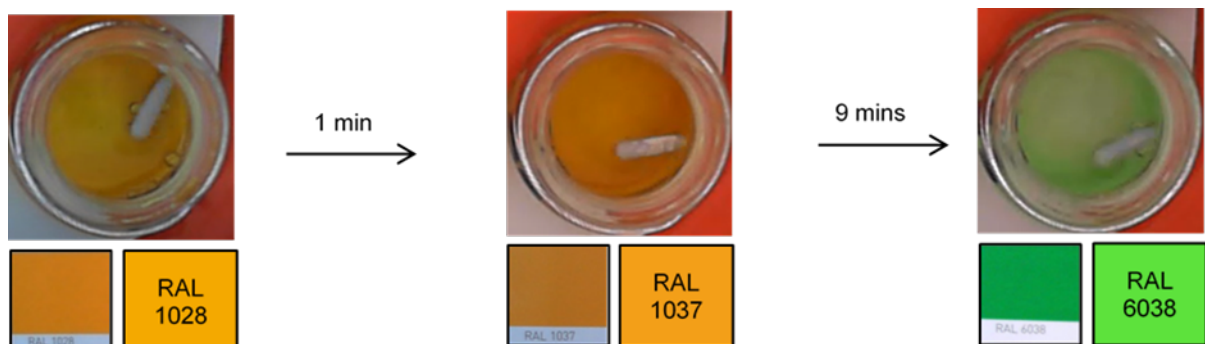
Figure S7: Images of spot test at start (left) and end (right) of the reaction of 1:1 (w/w) Methamphetamine: Glucose with Mandelin reagent.

4. Kineticolor Analysis

Video analysis was performed using the developmental video analysis software, *Kineticolor*. Earlier applications of this software have been reported in the literature.[1,2] All video data in this report were analyzed using the March 2022 version of the Kineticolor software. A licensed version of the software is available on request from the University of Strathclyde, via the corresponding author and the Innovation and Industry Engagement team (quoting technology reference Tech 2141).

All videos were analyzed by breaking videos into their constituent frames, and each frame being analyzed, at the pixel level, in turn. A user-selected region of interest was analyzed, averaging all pixel values in the selected range. All background data outside the selected region was ignored in the analysis. Data were analyzed according to a user-selected number of frames to be skipped. Output machine-readable data related to all figures in the manuscript are listed in Section 7 and available as a separate zipped folder as part of the supporting information.

The analyzed frames were curated in plots of various color or mixing components versus time to enable semi-quantitative and comparative kinetic analysis between different video analysis datasets.

Extracted color data were provided from across a common subset of color models, namely: RGB, HSV, CIE-L*a*b*, and CIE-XYZ. For the purposes of this report, analysis primarily focused on plots of ΔE versus time. ΔE is the color-independent measure of contrast, measured as the Euclidean distance between two colors in the CIE_L*a*b* color space.

5. Colour Analysis Survey

A survey was performed to assess the subjectivity of similar coloured spot tests (Figure 4, manuscript). This was done by the anonymous participation of 43 participants. To avoid bias, participants were invited, by email, and provided with minimal context of the colours they were assessing. Participants were told that the survey contributed to an MSc project. All questions were open-ended and not leading. Questions included requests to describe a single colour of a spot test, with additional questions then used to ask participants to specifically compare the colours between pairs of spot tests. All images presented to participants were cropped with the white tile still visible, enabling participants to see the contrast between the background and the coloured solution. Survey data were written and collected using a Google Form and stored in an output CSV spreadsheet file, readable in Microsoft Excel. This spreadsheet is provided in the supporting information zipped folder.

6. Computational Chemistry

6.1 Geometry Optimizations

Density functional theory (DFT)[3] was employed to calculate the gas-phase electronic structures and energies for structures shown in **Table 7** of the manuscript. All structures were optimized with the hybrid meta-GGA exchange correlation functional M06-2X.[4] The M06-2X density functional was used in conjunction with the Def2TZVP basis set[5] for all atoms except cobalt. For cobalt, the LANL2DZ basis set and effective core potential (ECP) were employed.[6] Harmonic vibrational frequencies were calculated at the same level of theory to characterize respective minima (no imaginary frequencies). All calculations were run at the default temperature of 298.15 K. All calculations using the M06-2X functional have been performed using Gaussian 09 quantum chemistry program package.[7] All functionals, basis sets, and effective core potentials were sourced from the Basis Set Exchange (https://www.basissetexchange.org/).[8] All coordinates provided are listed in Cartesian format, with charge and multiplicity of each system given at the top of the coordinate list (I.e. 0 1 = neutral singlet; 1 1 = 1+ charged singlet). Further computational details specific to certain parts of the manuscript are described below in the relevant sections. All rendered 3D images were produced using CYLview (version 2).[9] Machine-readable .log and .xyz output files are provided in the zipped folder supplied as part of the supporting information.

Input keywords for Gaussian calculations were expressed in the .com files as follows.

For barbitonate (deprotonated barbitone):
```
m062/Def2TZVP opt freq Int(UltraFineGrid)
```

For all cobalt-containing calculations:
```
um062x/gen pseudo=read opt freq Int(UltraFineGrid) scf=(maxcycles=128, xqc)
```

6.2 Steric Maps

From optimized geometries of unsaturated cobalt(II) complexes of the form $[Co(barbitone)(NR_3)_2]^+$, an xyz file was created, adding an additional hydrogen atom (serving as a 'ghost' atom). The added hydrogen was made to bond to the cobalt centre of the optimized complex geometry, and placed at a distance of 2.00 Å from the cobalt atom. The hydrogen atom was positioned perpendicular to $NR_3 - NR_3 -$ barbitone plane.

The saved xyz file was then used as input for the SambVca 2.1 web-based software used to calculated steric maps for each of the two unsaturated cobalt complexes considered in **Figure 12** of the manuscript.

The cobalt atom was selected as that bound to the centre of the buried volume sphere.

The z-axis was defined using the 'ghost' Co–H bond added in the making of the xyz file.

The xz-plane was defined using the three N-atoms bound to the Co centre from each of the three ancillary ligands present.

The 'ghost' H-atom bound to the Co centre was selected to be deleted prior to any buried volume/steric map calculation.

Bond radii were scaled by 1.17. A default sphere radius of 3.5 Å was selected.

A distance of 2.00 Å was selected for the distance of the Co atom from the centre of the sphere. This was done so as to treat the Co centre similarly to how a P-atom would be treated in steric map calculations for phosphines more typically applied in SambVca.

A default mesh spacing of 0.10 was selected for numerical integration.

Hydrogen atoms were not included in the buried volume and steric map calculations.

Outputs from the steric map calculations are provided in HTML and PDF formats in the zipped folder of additional supporting information.

6.3 Binding Energy Calculations

Deconstructed binding energy calculations required three separate calculations per complex-barbitone pair: the complex-barbitone complex, the unsaturated complex fragment, and the free barbitone substrate fragment. **NOTE** – following DFT optimization of relevant fragments and complexes in each complex-barbitone pair, only the electronic energies (not enthalpies or free energies) were required for the follow-up Boys-Bernardi counterpoise analysis, described in detail in the references provided.

The key calculation was to produce the counterpoise corrected electronic energy for the complex-barbitone complex. This was performed in Gaussian09 using the keyword *counterpoise=2* in a separate calculation *after* the complex of the formula $[Co(NR_3)_2(barbitone)_2]$ had already been formally optimized.

To allow for the counterpoise calculation, the $[Co(NR_3)_2(barbitone)_2]$ complex was split into two *atom groups* using *GaussView* visualization software. These groups are colour-coded in black and blue in **Table 7**, reprinted below:
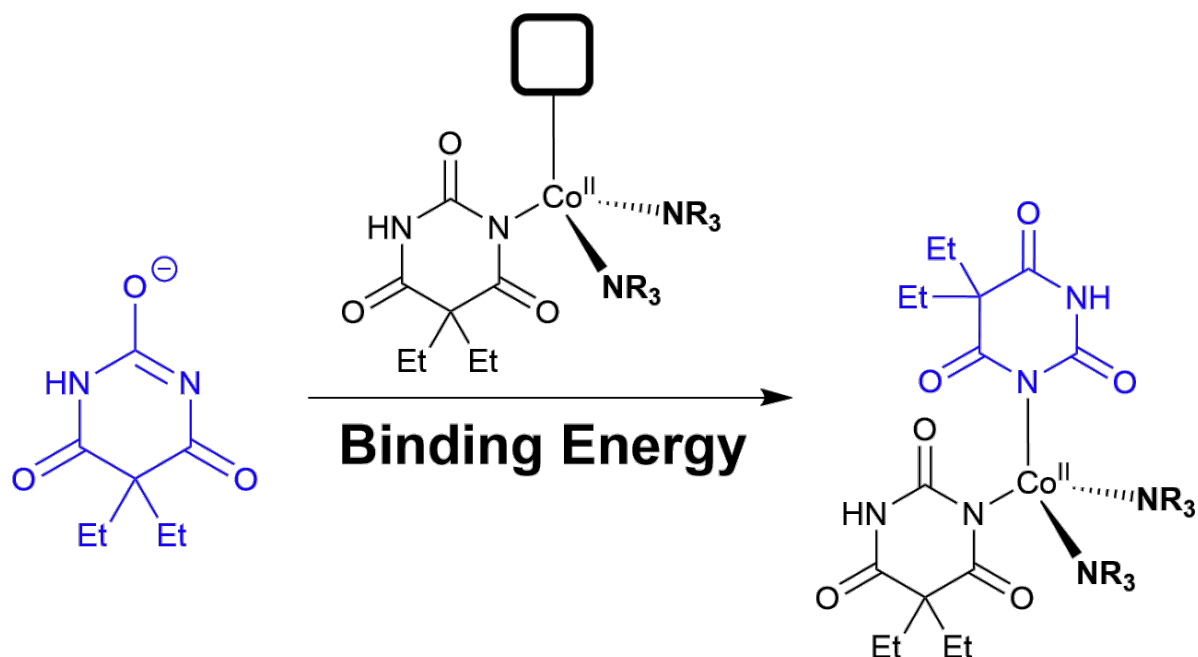
Equation S1 (below) represents the key electronic energy values calculated and reported in **Table 7**.

$$E_{bind} = \underbrace{\left[E_{AB}^{\alpha\beta}(AB) - E_{AB}^{\alpha\beta}(A) - E_{AB}^{\alpha\beta}(B)\right]}_{E_{int}} + \underbrace{[E_{AB}^{\alpha}(A) - E_{A}^{\alpha}(A)] + \left[E_{AB}^{\beta}(B) - E_{B}^{\beta}(B)\right]}_{E_{dist}}$$

key: $$Energy_{geometry}^{basis\ set}(fragment)$$

All energy values, for both [Co(i-PrNH$_2$)$_2$(barbitone)$_2$] and [Co(n-PrNH$_2$)$_2$(barbitone)$_2$], are available in the zipped folder of machine-readable supporting information. The ouput .log files from Gaussian09 are also available in the same zipped folder.

6.4 Output Coordinates for Geometry Optimizations

n-Pr_FULL-COMPLEX
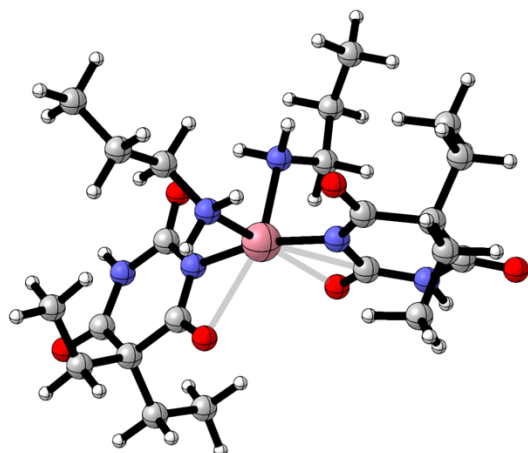
Sum of Electronic and Zero-point Energies = -1786.930314 Hartree
Sum of Electronic and Thermal Energies = -1786.889114 Hartree
Sum of Electronic and Thermal Enthalpies = -1786.888170 Hartree
Sum of Electronic and Thermal Free Energies = -1787.008069 Hartree

Dipole Moment = 3.6275 Debye

```
0 2
H              -4.64407      1.19570     -1.91184
C              -3.88607     -1.51669     -0.04234
C              -4.50868     -1.58320      1.36614
H              -5.53637     -1.93009      1.25061
H              -3.95320     -2.33587      1.92672
C              -3.91582     -2.90689     -0.70491
H              -3.38655     -3.58985     -0.03949
H              -4.96036     -3.21735     -0.75696
C              -3.28312     -2.92325     -2.09077
H              -3.32797     -3.92343     -2.52049
H              -3.80546     -2.24843     -2.77251
H              -2.23271     -2.62586     -2.05041
C              -4.48045     -0.24857      2.10103
H              -5.04125      0.51697      1.56013
H              -4.92173     -0.34247      3.09280
H              -3.45485      0.11013      2.22767
C              -2.75508      0.90698     -1.17901
C              -4.72399     -0.56804     -0.88120
C              -2.43942     -1.08038      0.09743
O              -5.89334     -0.76697     -1.10537
O              -1.65422     -1.76334      0.75414
O              -2.36014      1.96056     -1.64761
N              -4.08946      0.54856     -1.36786
Co             -0.04434      0.02783     -0.01732
H               3.07172     -2.28987     -2.13416
C               4.25251     -0.81528      0.69966
C               4.77352     -1.69712      1.84835
H               5.78398     -2.01361      1.58619
H               4.83162     -1.06296      2.73353
C               5.20048      0.38229      0.47796
H               5.27034      0.91091      1.42921
```

H	6.18479	-0.02121	0.23650
C	4.73077	1.33150	-0.61793
H	5.42735	2.16115	-0.73580
H	4.65747	0.82422	-1.58344
H	3.75113	1.75410	-0.37927
C	3.89059	-2.90800	2.12087
H	3.83633	-3.56390	1.24925
H	4.28758	-3.49527	2.94816
H	2.87518	-2.60586	2.38563
C	1.89717	-1.17667	-0.87128
C	4.26413	-1.64688	-0.57810
C	2.88374	-0.25431	1.09017
O	5.26126	-2.18011	-0.99120
O	2.76658	0.40456	2.10975
O	0.85761	-1.25056	-1.54357
N	1.83016	-0.48061	0.27401
N	3.07247	-1.75646	-1.27498
C	1.04012	1.69752	-2.40100
H	0.35905	1.03405	-2.93443
H	1.11871	2.44622	-0.48750
H	-0.40761	2.35586	-1.12313
N	0.49164	1.87906	-1.04910
H	-0.89136	0.03402	2.33510
H	0.56659	0.78795	2.30900
C	-1.03615	2.05763	1.99123
H	-0.38040	2.82033	1.56457
N	-0.35435	0.76211	1.86658
H	1.99427	1.16901	-2.30906
H	-1.93283	2.02779	1.36736
C	1.23878	2.99339	-3.17665
H	1.54999	2.73909	-4.19272
H	0.27467	3.50271	-3.26232
C	2.27181	3.91839	-2.54451
H	3.23385	3.41112	-2.43930
H	2.42902	4.80962	-3.15155
H	1.96119	4.25694	-1.55396
C	-1.39894	2.42610	3.42157
H	-2.03442	1.63913	3.83947
H	-0.48946	2.45071	4.02798
C	-2.11876	3.76603	3.49498
H	-3.04033	3.74493	2.91056
H	-2.37854	4.02008	4.52190
H	-1.49248	4.56789	3.10005
N	-1.97340	0.05640	-0.46800

i-Pr_FULL-COMPLEX

Sum of Electronic and Zero-point Energies = -1786.939406 Hartree
Sum of Electronic and Thermal Energies = -1786.898345 Hartree
Sum of Electronic and Thermal Enthalpies = -1786.897400 Hartree
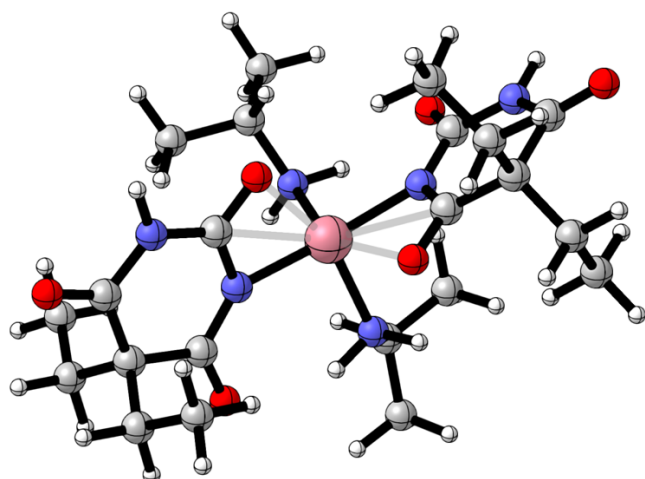Sum of Electronic and Thermal Free Energies = -1787.015507 Hartree

Dipole Moment = 3.4092 Debye

0 2

H	-4.94747	1.29424	-1.17036
C	-3.61406	-1.66021	-0.21030
C	-4.12032	-2.33199	1.07812
H	-5.06058	-2.82928	0.83684
H	-3.38972	-3.09370	1.35238
C	-3.42135	-2.71629	-1.31950
H	-2.73761	-3.46920	-0.92549
H	-4.39171	-3.18674	-1.48531
C	-2.87659	-2.13735	-2.61933
H	-2.76444	-2.92130	-3.36773
H	-3.55128	-1.38396	-3.03206
H	-1.89697	-1.67719	-2.47047
C	-4.32081	-1.35181	2.22657
H	-5.05835	-0.58751	1.97264
H	-4.67240	-1.86711	3.11980
H	-3.38458	-0.84854	2.48142
C	-2.98495	1.14845	-0.61003
C	-4.66489	-0.67110	-0.68245
C	-2.26679	-1.01935	0.06177
O	-5.80338	-0.99992	-0.91161
O	-1.33129	-1.70521	0.47725
O	-2.78898	2.33603	-0.80618
N	-4.25722	0.63074	-0.84539
Co	-0.06704	0.37541	0.12112
H	2.72696	-1.47933	-2.75140
C	4.15928	-1.00410	0.29982
C	4.45629	-2.28326	1.10849
H	5.39730	-2.69199	0.73751
H	4.60166	-1.97369	2.14392
C	5.32992	-0.01145	0.43114
H	5.46554	0.18152	1.49585
H	6.22433	-0.51118	0.05688

C	5.09730	1.29473	-0.31749
H	5.95171	1.96135	-0.20481
H	4.95507	1.12119	-1.38711
H	4.21612	1.81605	0.06351
C	3.35001	-3.32671	1.01671
H	3.21460	-3.67469	-0.00961
H	3.59145	-4.19614	1.62716
H	2.39573	-2.92903	1.36951
C	1.75460	-0.59126	-1.17914
C	4.04525	-1.40529	-1.16559
C	2.90752	-0.34864	0.88644
O	4.95521	-1.90997	-1.77051
O	2.89568	-0.01030	2.05835
O	0.67482	-0.41955	-1.76690
N	1.83205	-0.15575	0.08802
N	2.82949	-1.18090	-1.79057
C	0.40305	2.73322	-1.93954
H	-0.07642	1.91891	-2.48701
C	-0.19404	4.05879	-2.39237
H	0.26588	4.88835	-1.84830
H	-0.02129	4.21633	-3.45815
H	-1.26907	4.07508	-2.21033
C	1.90037	2.68594	-2.19055
H	2.39641	3.51502	-1.67661
H	2.33980	1.75715	-1.82980
H	2.11369	2.77799	-3.25533
H	0.77433	3.04260	0.05462
H	-0.81268	2.79631	-0.30827
N	0.13729	2.48159	-0.50468
H	-0.83930	-0.12065	2.50241
H	0.77690	0.16312	2.43320
C	-0.31694	1.84495	2.82998
H	0.39373	2.52473	2.35220
C	-1.73098	2.34773	2.59890
H	-2.45202	1.65672	3.04544
H	-1.86913	3.32141	3.06896
H	-1.96401	2.43779	1.53876
C	0.01857	1.75526	4.31234
H	1.03615	1.38991	4.45827
H	-0.06827	2.73260	4.78823
H	-0.67079	1.07172	4.81470
N	-0.13711	0.53735	2.16759
N	-2.03423	0.29481	-0.15686

n-Pr_UNSATURATED

Sum of Electronic and Zero-point Energies = -1140.152142 Hartree
Sum of Electronic and Thermal Energies = -1140.125170 Hartree
Sum of Electronic and Thermal Enthalpies = -1140.124226 Hartree
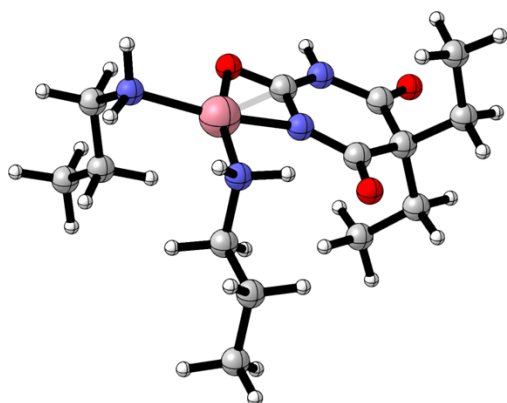Sum of Electronic and Thermal Free Energies = -1140.212626 Hartree

Dipole Moment = 9.6933 Debye

1 2

Co	-1.24993	-0.52711	-0.93932
H	2.00358	-3.00048	0.46142
C	2.89955	0.30757	0.26033
C	3.16070	1.04547	1.59189
H	4.16369	0.77090	1.91977
H	3.15790	2.11253	1.36792
C	3.96905	0.69679	-0.78239
H	3.91942	1.77981	-0.89786
H	4.94039	0.44591	-0.35524
C	3.78382	0.00690	-2.12717
H	4.55908	0.31806	-2.82542
H	3.84924	-1.07951	-2.03328
H	2.82015	0.25903	-2.57626
C	2.13965	0.72411	2.67518
H	2.14158	-0.33914	2.92637
H	2.36604	1.27241	3.58820
H	1.12902	1.00509	2.36705
C	0.74490	-1.51446	-0.16360
C	3.03429	-1.18962	0.52791
C	1.53626	0.74528	-0.26181
O	4.04116	-1.68898	0.93317
O	1.29166	1.90252	-0.52841
O	-0.28766	-2.21265	-0.38158
N	0.57376	-0.21277	-0.41852
N	1.91177	-2.00718	0.28475
C	-3.42219	-2.17861	-0.17802
H	-2.69793	-2.99086	-0.12173
H	-3.01731	-1.92118	-2.18873
H	-3.78187	-0.65372	-1.51978
N	-3.04990	-1.34057	-1.35331
H	-0.73580	1.78305	-1.56250
H	-2.29222	1.62275	-2.05247
C	-2.05922	2.08768	-0.05592
H	-3.04141	1.70818	0.23592
N	-1.64550	1.38937	-1.30302

```
H            -4.41468      -2.60979     -0.31969
H            -1.34408       1.80047      0.71907
C            -3.37759      -1.34702      1.09172
H            -2.36960      -0.92373      1.22342
H            -4.06744      -0.50223      1.00042
C            -3.72720      -2.17547      2.32108
H            -3.03020      -3.00546      2.43951
H            -3.68867      -1.56929      3.22403
H            -4.73331      -2.58700      2.23585
C            -2.08228       3.59824     -0.20667
H            -1.08621       3.93018     -0.51106
H            -2.77454       3.87105     -1.00866
C            -2.48976       4.28355      1.09097
H            -1.79156       4.04414      1.89415
H            -2.49940       5.36514      0.97032
H            -3.48771       3.97407      1.40531
```

baritonate
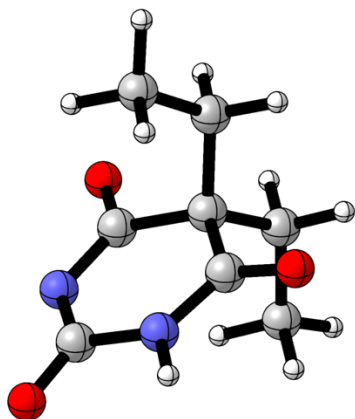

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Sum of Electronic and Zero-point Energies = -646.582122 Hartree
Sum of Electronic and Thermal Energies = -646.569551 Hartree
Sum of Electronic and Thermal Enthalpies = -646.568607 Hartree
Sum of Electronic and Thermal Free Energies = -646.621437 Hartree

Dipole Moment = 5.8063 Debye

-1 1
H             0.74974       3.20677     -0.00264
C             1.12280      -0.11997     -0.00014
C             0.69036      -0.89504      1.25529
H            -0.39359      -1.02581      1.21287
H             1.16447      -1.87589      1.19732
C             0.69063      -0.89696     -1.25447
H             1.16474      -1.87771     -1.19491
H            -0.39332      -1.02767     -1.21209
C             1.08743      -0.20556     -2.55343
H             0.77944      -0.79474     -3.41917
H             0.61792       0.77758     -2.63435
H             2.16940      -0.06903     -2.60155
C             1.08689      -0.20167      2.55328
H             0.61735       0.78158      2.63262
H             0.77873      -0.78955      3.41985
H             2.16883      -0.06505      2.60141
C             2.62886       2.32587     -0.00171
```

C	0.39674	1.20930	-0.00123
C	2.67068	-0.01038	-0.00003
O	-0.82226	1.29080	-0.00148
O	3.26547	-1.08597	0.00073
O	3.11316	3.44795	-0.00238
N	3.30637	1.17306	-0.00078
N	1.19202	2.29919	-0.00193

i-Pr_UNSATURATED

Sum of Electronic and Zero-point Energies = -1140.165613 Hartree
Sum of Electronic and Thermal Energies = -1140.139692 Hartree
Sum of Electronic and Thermal Enthalpies = -1140.138747 Hartree
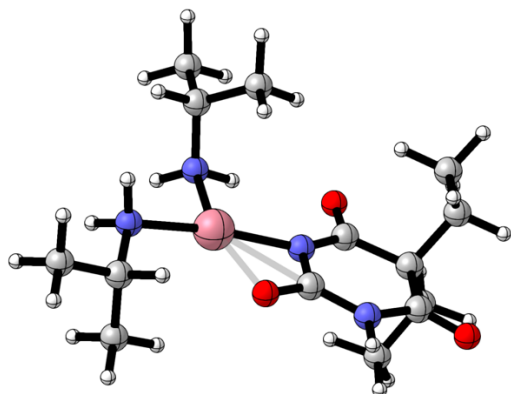Sum of Electronic and Thermal Free Energies = -1140.222414 Hartree
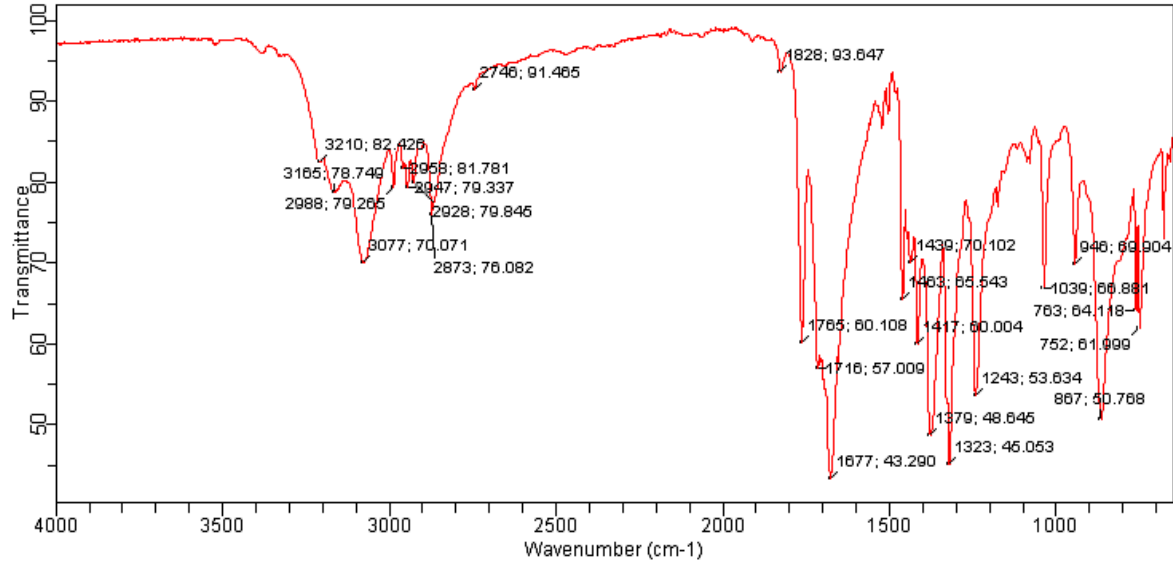
Dipole Moment = 9.9649 Debye

1 2

Co	1.39795	-0.05150	-0.15202
H	-1.71935	-2.69041	-1.56239
C	-2.98856	-0.07012	0.25437
C	-3.83081	0.96518	-0.52205
H	-4.83347	0.55035	-0.62891
H	-3.89705	1.85375	0.10626
C	-3.65070	-0.38251	1.61367
H	-3.74168	0.56418	2.14696
H	-4.65525	-0.75086	1.40367
C	-2.87629	-1.39387	2.44812
H	-3.38646	-1.57993	3.39180
H	-2.78643	-2.35331	1.93327
H	-1.87304	-1.03156	2.68496
C	-3.25244	1.31566	-1.88652
H	-3.21344	0.44289	-2.54215
H	-3.86726	2.06544	-2.38177
H	-2.24303	1.72620	-1.79923
C	-0.56776	-1.23281	-0.70562
C	-2.97385	-1.35883	-0.56412
C	-1.61512	0.53517	0.52036
O	-3.96743	-1.95799	-0.85006
O	-1.47932	1.56751	1.14394
O	0.56881	-1.63591	-1.08865
N	-0.52059	-0.11992	0.03344
N	-1.72679	-1.84582	-1.00314
C	3.61455	-1.83550	-0.07398

```
H          2.99580      -2.49516      -0.68420
C          5.08152      -2.18617      -0.24402
H          5.70904      -1.53475       0.36923
H          5.26256      -3.21430       0.06719
H          5.39463      -2.09145      -1.28439
C          3.15951      -1.92304       1.37390
H          3.68931      -1.19534       1.99442
H          2.08019      -1.75876       1.48030
H          3.36331      -2.91371       1.77746
H          3.98677       0.19156      -0.12998
H          3.52275      -0.40760      -1.56570
N          3.32699      -0.45065      -0.56691
H          0.71812       1.79777       1.28214
H          2.30748       1.63771       1.64361
C          1.93681       2.79454      -0.03433
H          2.97682       2.68654      -0.35399
C          1.02021       2.68778      -1.24379
H         -0.02422       2.69534      -0.92433
H          1.18116       3.52674      -1.91911
H          1.20086       1.77413      -1.82478
C          1.76095       4.11348       0.69839
H          2.40413       4.16885       1.57755
H          2.01083       4.94845       0.04481
H          0.72308       4.22859       1.01882
N          1.64675       1.64305       0.87016
```
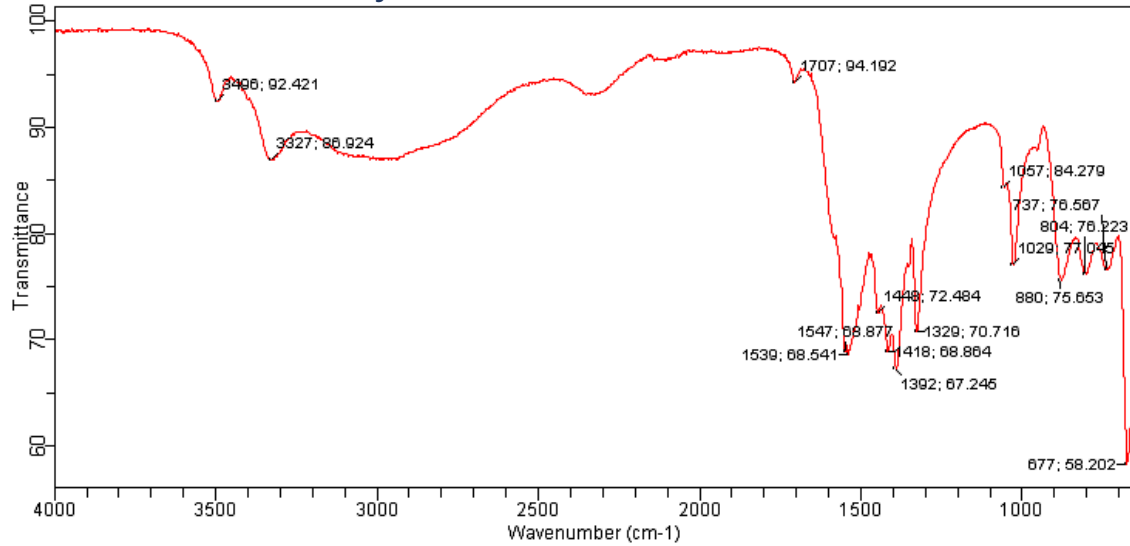
6.5 Attempted crystallization of Dille-Kopannyi test products

Carrying out above-described Dille-Koppanyi tests with barbitone resulted in several samples that, when left to evaporate to dryness at room temperature, produced purple crystals. All attempted to analyse these crystals by X-ray diffraction provided results of a quality too poor to publish. Nonetheless, the isolated crystals (suspected Dille-Koppanyi products of the formula [Co(barb)$_2$(RNH$_2$)$_2$] were analysed by ATR-FT-IR using an Agilent 5500 series FTIR spectrometer, fitted with a diamond-ATR sampling module (https://www.agilent.com/en/product/molecular-spectroscopy/ftir-spectroscopy/ftir-compact-portable-systems/5500-series-compact-ftir).
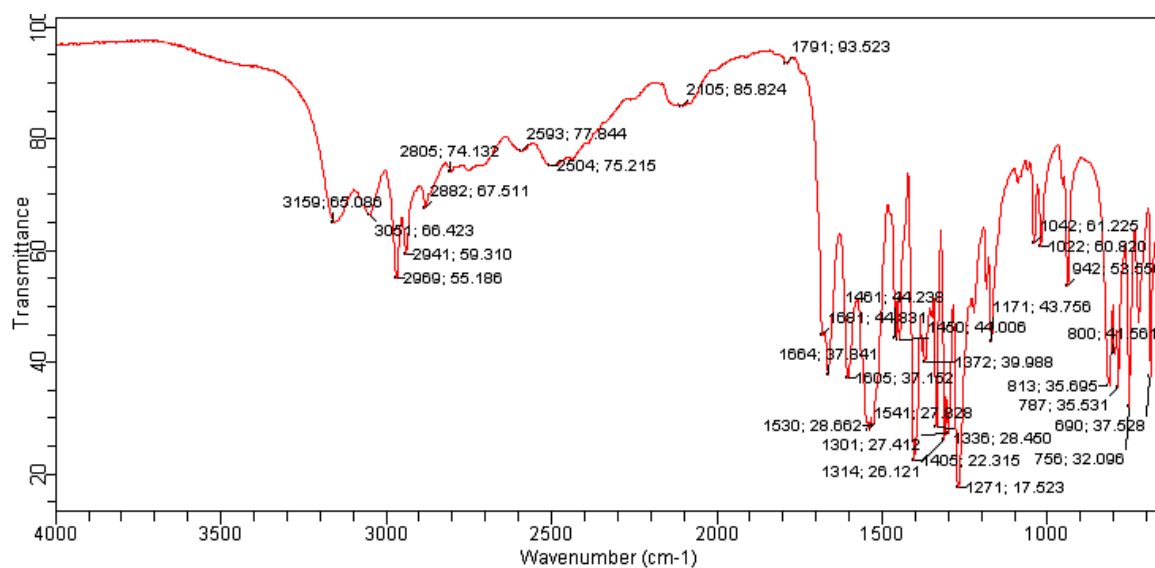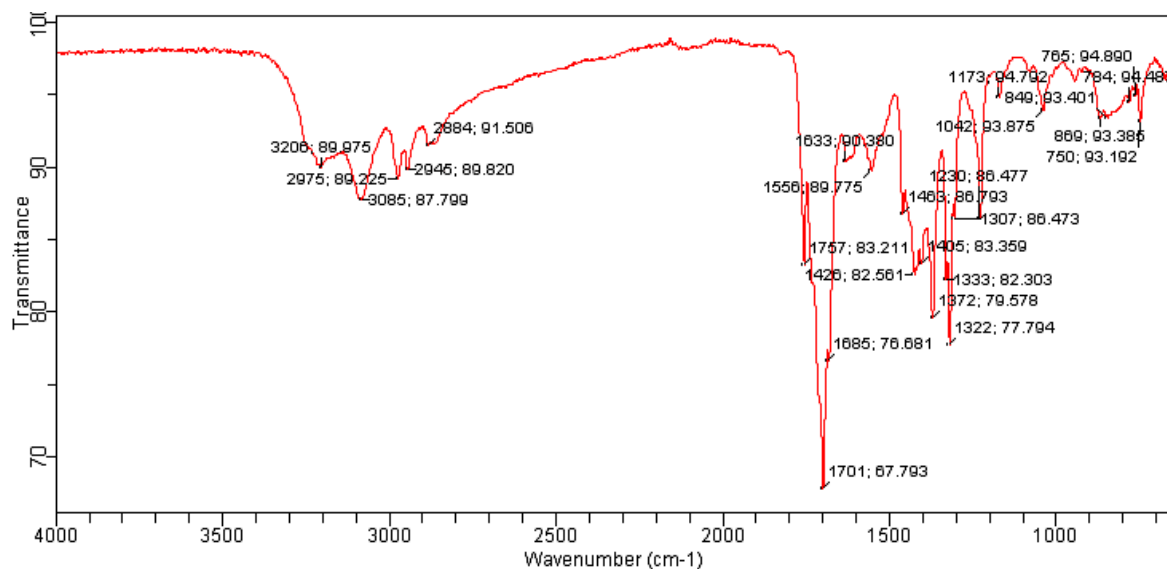
6.5.1 Barbitone

6.5.2 Cobalt acetate tetrahydrate

6.5.3 Suspected [Co(barb)₂(i-PrNH₂)₂] from original Dille-Koppanyi test for barbitone

6.5.4 Suspected [Co(barb)₂(n-PrNH₂)₂] from original Dille-Koppanyi test for barbitone

All four PDF printouts of these FTIR spectra are available in the zipped folder of supporting information under the **Figure 11** parent folder. See Section 7 for more details.

7. Notes on Available Machine-readable Data

Excel files, Python scripts, and PDF outputs for all data discussed in the manuscript in available in an accompanying zipped folder, as part of this supporting information package:

Folder	Subfolder	Contents
Figure 4	N/A	Figure 4.xlsx
Figure 5	N/A	Figure 5.xlsx
Figure 6_Table 2	N/A	Figure 6.xlsx Table 2.xlsx
Figure 7_Table 3	N/A	Figure 7_Table 3.xlsx
Figure 8	N/A	Figure 8.xlsx
Figure 9_Table 5	N/A	Figure 9_amphetamine data.xlsx Figure 9_benzodiazepine data.xlsx
Figure 9_Table 5	Table 5_RMSE code and input csv files	amphetamine.csv flurazepam.csv mdma.csv methamphetamine.csv nitrazepam.csv RMSE.py unknown_A.csv unknown_B.csv
Figure 10	N/A	Figure 10.xlsx
Figure 11	N/A	Figure 11.xlsx
Figure 11	FT-IR	barbitone_2022-03-08T12-16-11.pdf barbitone and dille-koppanyi reagent crystals_2022-03-08T12-45-25.pdf barbitone and modified dille-koppanyi reagent crystals_2022-03-08T12-54-51.pdf cobalt(II) acetate tetrahydrate_2022-03-08T12-28-24.pdf
Figure 12	Geometry Optimizations and Thermal Calcs	i-Pr_UNSATURATED.log n-Pr_UNSATURATED.log
Figure 12	Steric Map inputs and outputs	i-Pr_UNSATURATED.xyz n-Pr_UNSATURATED.xyz SambVca-Result_i-Pr_UNSATURATED.pdf SambVca-Result_n-Pr_UNSATURATED.pdf
Table 7	N/A	Table 7.xlsx
Table 8	N/A	Barbitonate.log Table 8.xlsx i-Pr_COUNTERPOISE.log i-Pr_FULL_opt-freq.log n-Pr_COUNTERPOISE.log n-Pr_FULL_opt-freq.log
Video Kinetics demo	Amphetamine Methamphetamine	*Images and folders in a hierarchy optimized for direct use of Video Kinetics.ipynb in the top of this subfolder.*

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