Lab Notes from an Unintentional BZ Experience
by Dr. James A. Moore

Introduction by Keith H.
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The following pages are from a lab notebook detailing the synthesis of the dissociative dysphoriant BZ (3-Quinuclidinyl benzilate). It includes notes from an accidental ingestion of the substance by chemist Dr. James Moore in 1962. The introduction was written by a student of Dr. Moore's.

I knew Dr. James Moore at the University of Delaware while I was a student there in the late 1970s and early 1980s. I don't recall how I learned of his connection to the CIA. It wasn't something he seemed particularly proud of nor did he seem to regret it. It was just a part of his past that he did not mind talking about it when asked. I suspect most people who knew him never heard about it.

Dr. Moore was the classic chemist. I remember him in the lab swirling a flask in one hand and drinking water from a Pyrex lab beaker in the other—not considering for a minute the risk he was taking. He was kind and witty, with a droll wit that I loved. During one of our conversations in his office discussing his CIA days, he pulled a notebook off the shelf and showed me the experiments scanned below. I was fascinated and asked if I could photocopy them. Any young chemists reading this could learn a great deal from the way he kept a lab journal. I've never seen Albert Hofmann's lab notebook, but I wonder if he recorded any of his fantastic discoveries in the lab with details like this? I suspect he did as any good scientist would.

Searching the web for information about James Moore and this CIA connection yields a broad range of results. In some, he's portrayed as a sinister CIA operative posing as a chemist at the U of Delaware. Others describe him as a professor being paid by the government to make some random compounds (as happens all the time). As a grad student I remember being paid $100 per compound for unique chemical entities I made as intermediates in a long synthesis that my advisor (not Dr. Moore) collected from my lab work and sent to the NIH. I don't know the truth about Dr. Moore of course, but having known him for a few years, albeit decades after this era, I suspect the account in Chapter 7 of John Marks' The Search for the "Manchurian Candidate": The CIA and Mind Control1 is a reasonable approximation. He was admittedly a short-order cook for the CIA, and definitely knew what he was synthesizing, but I don't believe for a minute there was ever any evil intent.

The experiments below, from Dr. Moore's 1962 lab books, describe his synthesis of 3-quinuclidinyl benzilate (BZ) for the CIA that he accidentally ingested during synthesis and the resulting five days of disorientation and use of an antidote (that he told me was recommended by his CIA contact) to bring himself back. Of particular note are the observations of the experience he recorded and the changes in his handwriting during the experiment. Chemists in the audience will appreciate that he recrystallized the Tacrine he took as an antidote from benzene (!) before taking it. The other is simply a classic synthesis of DMT.

— Keith H.

1 : Marks J. *The Search for the "Manchurian Candidate": The CIA and Mind Control*. (Chapter 7). McGraw-Hill. 1980. Online version accessed Oct 11, 2011 at http://www.druglibrary.org/schaffer/lsd/marks7.htm.

1962 Experience Report Transcript
by Dr. James A. Moore

After handling the compound for about 2 days pharmacological reactions became apparent: Stumbling gait, inability to concentrate or converse effectively, dilated pupils, pink fingernails & blotchy pink hands with fingers dark pink and swollen—very little tactile sense. Tendency toward tremors; sudden deep breathing. Very weak legs. Dry skin—no sweating; distortion of distance and time.

The above symptoms were still almost full-blown on Wed 28 Nov, about 48 hours after onset (first noticed Mon. 26 Nov.

Thurs. 29 Nov: Legs better, tremors fewer. Skin still pink. Eyes still very dilated & painful.

Fri. Symptoms about the same - hands less swollen - pupils still dilated—At 7:00 PM and 12:00 midnight took 100 mg. 5-amino-1,2,3,4 tetrahydroacridine (from K. Koniacial [spelling??]—recx / benzene—mp. 182-183

Sat Dec 4—pupils normal size—better motor control although legs still weak & tired.

22 Nov. 1962: Indole-3-glyoxalyl chloride & diethylamide:

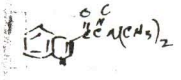
In a 5-l. Morck flask with stirrer (glass blade), dropping funnel & thermometer was placed a soln of 110 g. indole (E.K.C.) in 1.5 l. anhydrous ether. Cooled to ~4° in ice & added dropwise over ~40 min. soln of 125 g. oxalyl chloride in 300 ml ether.

This is 110/117 = 0.94 moles indole
125/127 = 0.98 moles oxalyl.

Soln became yellow after 1st few drops were added, then orange, then colorless crystals began to separate, giving bright yellow suspension. Mildly exothermic -- kept at 4-6° throughout addition. Then stirred another 40 min allowing temp to rise to 20°.

Then cooled in salt-ice bath (same pot) & added 200 g (4.4 moles) of anhydrous dimethylamine in 500 ml ether. (A somewhat smaller excess of dimethylamine would have been used if it had not been a matter of 100 g. ampoules). After about 2/3 of the amine had been added the white mixture was so thick it couldn't be stirred. Added additional 800 ml ether & then rest of amine & stirred about ½ hr.

Then filtered & washed well with ether & water (several times -- slurried up). White solid air dried: pale pink -- 179 g. (dried 90°)

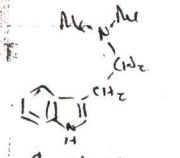


MW. 216.

0.83 moles = 88% based on ~~indole~~.

179/216

N,N-Dimethyltryptamine: In a 12 l. pot with Hg-sealed stirrer, condenser & addg dropping funnel was placed 5 l. dioxane (M.C.B. pract) & 227 g. LiAlH4. This is 5.9 moles LAH. Added soln of the 179 g of indole in about 1.2 l. dioxane -- small amt insoluble solid -- $Me_2\overset{+}{N}H_2\ Cl^-$? Smell of Me_2NH on addition to hydride.



$C_{12}H_{16}N_2$
MW 188

The hydride soln was first heated to ~60° before beginning addition. Heat shut off, but warmed up during addition to ~~about~~ fairly steady reflux. Addition required 1 hr. Then continued stirring &

reflux -- variac (lower element) 80 volts. Reaction mixture was grey suspension. Began reflux at 6:00 PM 23 Nov. Stopped reflux & began to cool 3:00 PM 25 Nov -- total reflux with stirring -- 45 hrs.

.83
1.25
1.04 moles LiAlH4 consumed-theory

5.9
1.
4.9 moles to kill!

requires 10 moles EtOAc - 890 cc!

After cooling, 900 ml. ethyl acetate was added very slowly with stirring - allowed to stay around 50° by adjusting rate of addition .. about 1 cc/min. This treatment was intermittent during 5 days -- ~150 ml/day, then stop & allow to cool.

After ~800 ml of EtOAc had been added there was no further perceptible temp. rise on further addition.

Began to add 150 ml ≅ 50 ml H_2O.

Then began addition of dioxane-water - 3:2. Mild evolution of H_2 -- not all hydride gone at this point. After ~10 cc, the sticky foam began to build up, so discontinued addn of H_2O & added another 100 ml of ethyl acetate -- foaming less serious -- no appreciable rise in temp. Also added 50 ml acetone -- seemed to increase foaming?

Hope to tell that the acetone or ethyl acetate didn't alkylate the indole!

The difficulty here is the ring of solid that was gradually thrown up by the stirrer on the walls above the liquid level. This ring of solid contained visible bits of hydride. Practically impossible to scrape this off, however. Also would not want to add enough dioxane to bring liquid level up -- would require at least a liter.

Increased the stirrer speed & added addnl 200 ml dioxane this permitted contact with the ring of solid. Resumed addn of aq-dioxane -- went quite smoothly. Some heat evolved on adding H_2O. Eventually added about 400 ml water.

Stood overnight, then filtered. About 7 l. filtrate -- evap. in vac. The voluminous inorganic ppt was washed thoroughly with 1 l. dioxane -- mixed up to thin paste & filtered. Washed cake again with MeOH. Combined filtrates & orig soln.

Cont. from p. 71 :

The combined organic layers from the LiAlH4 reduction were concentrated *in vac*, then toluene was added & distilled off to give 500 ml of solution - dark amber-red - slightly fluorescent - should be dry. Toluene soln filtered to remove trace of alumina & conc. to about 350 ml volume.

A small aliquot of the toluene soln was extracted with aq. tartaric acid -- some color & solute went into neutral water. The aq. tartaric acid extract was washed once with ether & then basified & extracted with ether -- ether dried & evap. to nice clear oil but this could not be crystallized. Also very faint Ehrlich test -- much stronger Ehrlich color with original toluene soln.

Tried twice to get a xsln hydrochloride -- direct from toluene soln & also from extracted base -- used ethanolic HCl -- remained taffy both times.

A more promising possibility is the precipitation of the base from the toluene soln by adding ethanolic tartaric acid. This gives a white solid, after addn of ether, which is semi-crystalline.

10 Dec -- Xsls finally began to grow from the oil that had been obtained by acid extraction & basification. Xslized very slowly, but almost completely solid.

15 Dec: Entire batch extracted with tartaric acid -- three sep funnels -- #2 & #3 contained 100 ml ether each. Extracted with 150 g tartaric acid in 1 l. H_2O - divided into 6 portions of ~ 150 ml each. Passed under the two ethers. Then combined acid extracts basified with KOH & reextracted base with ether (1 l.). Ether solns washed with 4 × 20 ml H_2O (some color removed) & evap to thin syrup. Could not get crystallization sustained -- the base was too soluble.

16 Dec. Evap further *in vac* with hot H_2O & then mantle -- there was quite a bit of water, dioxane & probably ethanol still present, since all of these water-soluble solvents would carry through extraction.

Continued on p. 76

'60-'61

24 Nov. 1962: 3-Quinuclidinyl benzilate:

3 Quinuclidinol -- Recd. from Willmaster Chem. Co. -- pale tan pink xstls -- 50 g. was recx / acetone -- small amt. amorphous insol. & some pink color removed with charcoal -- obtained 44 g. of colorless xstls in 2 crops -- mp. uncor. 222-224° extensive subl.

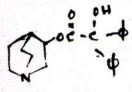
Prepn of benzilate ester (cf. US. 2,843,593 -- Chem Abstr. 53 1385 (1959).)

Toluene was dried by distillation & to ~100 cc of hot toluene in a 500 ml 3 neck flask with Teflon stirrer blade was added 2.4 g (.104 gatoms) Na -- whipped up to very coarse sand & cooled to room temp. 0.17 moles

Then added soln of ~~38~~ 40 g. methyl benzilate (Willmaster -- mp. 74-75°) in 150 ml toluene. [This is larger ester : Na ratio than used in reference]. Added at room temp. during about 1 hr. N_2 evolution fairly brisk at first. After all Na was gone the soln was light yellow with turbidity but no insoluble in evidence.

Added 12.7 g. 3-quinuclidinol (0.1 mole) Soln heated to reflux -- became amber, then red-brown. Tested condensate with H_2CrO_4 -- finally showed no more MeOH present after 45 min reflux -- about 1/2 of the toluene had been removed to reach this stage (in larger run must replenish the toluene as refluxing toluene - MeOH is removed).

The toluene soln was cooled in salt ice -- very viscous. Diluted with ether -- tended to pitch out solid -- would have been better to have had more toluene. Cold soln extracted with ~1 N. HCl -- very messy operation -- thick emulsion at first -- finally with more ether was possible to separate -- extracted 3x -- kept as cold as practical in ice bath.



$C_{21}H_{23}O_3N$

~~MW 329.4~~

MW 337.

The aq. HCl soln (~300 ml -- pale yellow) was then basified with ~20% KOH (at 0°). Heavy oil -- extracted with $CHCl_3$ -- some solid already with the $CHCl_3$ in sep. funnel. Extracted with 200 & 2 x 100 ml $CHCl_3$ -- pink, turbid soln -- washed with water -- required a large amt of $MgSO_4$ to get (almost) clear soln -- Evap & added acetone at vol. of ~80 ml -- crystallized to solid mush -- washed thoroughly with several large volumes of acetone -- white powder -- mp (uncorr) 166-168°, wt. 13.1 g. -- 1st crop -- 40%.

25 Nov: 3-Quinuclidinyl benzilate:

Larger run -- simplified work up:

4.6 g (0.2 g-atoms) sodium was thrown into 400 ml hot toluene (dried by distillation). Cooled -- rather coarse sand -- stirrer not fast enough.

Then added soln of 106 g (0.4 mole + 10% xs) of methyl benzilate dissolved in 100 ml toluene. Stirred -- H_2 evolved -- developed a dark pink color which could be discharged by adding more benzilate soln. Cooled at first, then warmed to ~45° at end to hasten disappearance of Na. Pink color disappeared after all Na gone.

Now assuming yield is actually pretty good, we will add 51 g. of 3-quinuclidinol & this should leave just a little benzilate unreacted. Should then be able to wash with H_2O, remove toluene & xs ligr ester directly from acetone.

To the above soln of ester + sodium was added 51 g (0.4 moles) of the crude 3-quinuclidinol (Mill master -- unrexx). Color deepened - heated to reflux -- Refluxed 20 min & then removed sample -- strong base on test. Removed about 150 ml toluene & added fresh. Kept on removing distillate & checking samples with dichromate - HNO_3 soln. Color change (methanol) became progressively weaker. During the reflux the soln would periodically "boil up" & flood condenser & then subside. Some solid forming at?

After removing another 150 ml toluene test for base was very slow & just about the point that more fresh toluene would have been needed, xs this began from boiling soln! Immediately stopped stirring & heating - total time at reflux 70 minutes.

The greasy xs oil in mass was transferred to Erlenmeyer using some acetone to rinse -- the solid dissolved in acetone, and is evidently the Na alcoholate of the hydroxy ester product. There should be present .4 moles of ester -- half of it in

form of Na alcoholate. The NaOR was neutralized by adding of 11 ml. of glacial acetic acid + some acetone. All solid dissolved -- murky turbid amber solution. Added a little (2 cc) ether -- where this hit it gave curdy xstln pptate. Then added few ml H_2O -- debating whether to wash when xstls suddenly appeared in main bulk of soln. Chilled to complete xstln & collected -- still rather sticky.

Recx / MeOH - H_2O -- this is designed more as wash to remove NaOAc, etc. than true xstln -- xstlized / oil - pure white 27g. large second crop taken on dilution -- this is not a good recx medium. The second crop was collected -- some toluene + dark color present. Slurried up in cold acetone & refiltered -- tended to get brown on surface in air. Air dried & combined with 1st Combined 1st & 2 crops 50 g. M.p.: extensive darkening above 110-120° - began to melt at 161°, clear 164° (uncorr).

Clearly needs to be recx.

Further crystals began to grow out of orig. M.L. (toluene - acetone).

After handling the compound for about 2 days, pharmacological reactions became apparent: Stumbling gait, inability to concentrate or converse effectively, dilated pupils, pink fingernails & blotchy pink hands with fingers dark pink & swollen -- very little tactile sense. Tendency toward tremors; sudden deep breathing. Very weak legs. Dry skin -- no sweating; distortion of distance & time.

The above symptoms were still ~~in~~ almost full-blown on Wed 28 Nov, about 48 hrs after onset (first noticed Mon, 26 Nov.

Thurs. 29 Nov: Legs better, tremors fewer. Skin still pink. Eyes still very dilated & painful.

Fri - Symptoms about the same - hands less swollen - pupils still dilated -- At 10:00 PM & 12:00 midnight took 100 mg. 5-amino-1,2,3,4 tetrahydroacridine (from K. Kornacich -- recx / benzene - m.p. 182-183°.

Sat Dec 1 -- pupils normal size -- better motor control although legs still very weak & tired.

Margin notes:

.112 cap
Theor 170
1st crop
27 g

220
170
50

50 / 337 = .148 moles

.148 / .4 = 37%.

16 Dec '62.

N,N-Dimethyltryptamine cont. from p. 72.

The thick oil after the removal of solvents was seeded with Regis N,N-dimethyltryptamine -- crystallization sustained nicely -- diluted with a little hexane -- set semi solid. Slush filtered after ~ 20 minutes -- washed with ether-hexane (chilled to -10°) -- white cubes -- very nice -- mp. 66-67° (uncor.) 41 g. first crop.

ML & washes evap. on steam bath to syrup -- more hexane than during crystallization of 1st crop -- evidently impurities more soluble in hexane than the desired base, so that in 2nd crop, base had to be taken from oil, rather than solution as in the 2nd crop. The conc. ML + wash gave nice second crop: stored overnight at -5°. Filtered & washed -- 33 g -- under very slightly off-white. mp. 66-67° (uncor.)

41
33
13
87

Evap again to very thick syrup for 3d crop -- washed as above -- slightly yellower in bulk than 2nd crop -- 13 g, mp. 65.5-66° -- combined with 1st 2.

Took 4th crop -- 6.2 g, mp. 64.5-66° -- " " " 93.

.83 moles amide Reduced

.83 x 188

Theoretical = 156 g.

ML: very dark & viscous. Diluted with ether & added ethanolic tartaric acid -- heavy taffy separated. Washed as well as possible with ether & then dissolved in water. Boneblacked with large amt carbon, then basified. The orange aq. soln, extracted with ether & evap dried (Na_2SO_4) ether soln to syrup -- xstlized & washed -- snow white, but less than 1 g. All crops pooled.

88
6.2
.8
95.0

Total wt: 95 g. = 61 % yield. on reduction.

59 g of this pool sent to Stevenson. 36 g of the pool was ground thoroughly in mortar and blended with 20 g. of tartaric acid. The resulting powder was not hygroscopic, but did dissolve readily in water. This 56 g of "dry tartrate" sent to Stevenson as II-76b. This contains 65 % amine by weight. This is 30 % more than one equiv. of acid for BH^+ hydrogen tartrate. Sent to Stevenson as II-76 A.