Novel Condensation of D-LA into D-LSD via PyPOB

by Casey William "Freeblood" Hardison

Although the following piece is technically oriented, we feel that it will be of intellectual interest for those with an understanding of chemistry. Author Casey Hardison is a long-time friend to staff members of The Entheogen Review. *His article "An Amateur Qualitative Study of 48 2C-T-7 Subjective Bioassays" appeared in the* MAPS Bulletin *10(2): 11. He is currently serving a 20-year term imprisoned in the United Kingdom, one of the harshest punishments delivered in the U.K.: seven years outside the 1978 "Operation Julie" sentence of Richard Kemp, and six years outside the guidelines set by the 1996 Joseph Hurley case. We encourage* ER *readers to correspond with Casey via the address below.*

A recent publication by Dr. David E. Nichols (Nichols et al. 2002) on the isomeric lysergamides of demethlazetidine catalyzed a revolution in the realm of clandestine LSD synthesis. I do not know if Dr. Nichols is to be credited with the first use of PyBOP for lysergamide condensation, as theoretical discussions on the use of a variety of peptide-coupling reagents have been occurring on The Hive (www.the-hive.ws) and Rhodium (www.rhodium.ws/chemistry/et2lsd.txt) web sites since 2001.

In early 2004, I engaged Dr. Nichols in a theoretical discussion as to his expected limits on scale-ability and it was clear that he did not know, as he is limited to NIDA quantities of the lysergic acid, i.e. > 250 mg.

After studying Dr. Nichols' papers and the Internet, and doing further book research on peptide synthesis (Coste et al. 1990), I conducted a series of experiments to determine the limits and parameters of the reaction, i.e., the best solvent, the best tertiary scavenger amine, the best sequence of introducing the reagents, and the most effective reaction time.

I worked with several solvents, but I found CH_2Cl_2 to be most suitable, as it evaporates easily and keeps the reaction temperature low.

I worked with several tertiary amines, but *N,N*-diethylmethylamine added slowly after the dry lysergic acid gave the most effective results and work-up.

I varied the reaction time between 30 to 120 minutes; however, I am of the opinion that the reaction completes in less than one hour. All reactions were conducted under a 15w red light, in an Argon atmosphere, and with dried Sigma-Aldrich solvents and reagents.

EXPERIMENTAL

2.80 grams of lysergic acid was added to 100 ml of magnetically stirring CH_2Cl_2. To this was added 1.81 grams *N,N*-diethlmethylamine and the solution was allowed to stir for five minutes. Then 5.70 grams of PyPOB was added and the solution was allowed to stir for an additional five minutes. Then 0.84 grams of diethylamine was added and the reaction was allowed to stir at RT for 60 minutes.

The reaction mixture was quenched with 100 ml of 7.5M concentrated NH_4OH, the layers were separated and the aqueous phase was then thrice extracted with 30 ml CH_2Cl_2, the organic layers were combined and rotary evaporated at 35°C under high vacuum.

The residue was dissolved in 40 ml of cold saturated $NaHCO_3$ and extracted thrice with 20 ml EtOAc, the organic layers were combined and washed with deionized H_2O, brine, and then dried over $MgSO_4$, filtered and rotary evaporated at 40°C under high vacuum to a constant weight. Yield 3.13 grams before chromatography, 93%.

Another run of 5.12 grams lysergic acid with the same amines, equivalents, and times, yielded 5.55 grams after chromatography, 90%.

THE WORK ENDS

It is unfortunate that as I was perfecting this reaction, I was under police surveillance, brought to the attention of the London DEA by an informant in the United States. Donations accepted and desired (checks, money orders, books, letters, love, etc.); correspondence can be sent to:

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