TITLE: Synthesis of 1-phenyl-3,5-diaryl-4-bromopyrazoles, 1-phenyl-3-t-butyl-5-aryl-4-bromopyrazoles, and 1-phenyl-3-t-butyl-5-aryl-4-bromoisoxazoles.

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Introduction:

Previous studies conducted have shown the C_4 of different hetrocyclic compounds to be sensitive to subsitent effects on aryl groups [1]. We seek to investiage if the same transmission effects discovered in those heterocyclic systems will occur in 1-phenyl-3-aryl/t-butyl-5-diaryl-4-bromopyrazoles (**Br-Pz**) and 1-phenyl-3-t-butyl-5-aryl-4-bromoisoxazoles using ^{13}C NMR spectroscopy. The addition of a bulky bromine atom to the C_4 position of the aromatic systems causes the aryl groups on the C_3 and C_5 to twist in 3,5-diarylsoxazole [1]. We seek to determine if the same torsional strain is present when a non-aromatic bulky group is on C_3 position.

Methods:

1-Phenyl-3-aryl/t-butyl-5-arylpyrazole (**Pz**) derivatives will be synthesized from their corresponding 1-Phenyl-3-aryl/t-butyl-5-arylpyrazolines by DDQ (2,3-Dichloro-5,6-dicyano-1,4-benzoquinone) oxidation in toluene. Meanwhile, 1-phenyl-3-t-butyl-5-aryl-isoxazoles will be synthesized from dibromide derivatives that are synthesized from the corresponding chalcones in a Br_2/acetic acid solution with heat. Following, **Pz**s and 1-phenyl-3-t-butyl-5-aryl-isoxazoles will be brominated at the C_4 position by a reaction with NBS in acetic acid to yield **Br-Pz**s and 1-phenyl-3-t-butyl-5-aryl-4-bromoisoxazoles. Compounds will be purified and characterized by standard methods. ^1H NMR spectra and ^{13}C NMR spectra will be collected in $CDCl_3$ and DMSO-d_6 respectively using standard NMR parameters. Molecular modeling (MM) studies were conducted using the Spartan '14 MMFF force field.

Results:

MM results predicted 1-Phenyl-3-aryl-5-arylpyrazole to have a torsion angles of 3^o and 54^o for the C_3 and C_5 aryls respectively. Bromination of the compound yielded torsion angles of 30^o and 60^o for the same aryl groups. 1-Phenyl-3-aryl/t-butyl-5-arylpyrazole was predicted to have a C_3 of 59^o and a C_5 of 53^o while the brominated compound had a C_3 of 61^o and a C_5 of 59^o. Results however showed that torsional angles of the 1-phenyl-3-t-butyl-5-arylisoxazole and 1-phenyl-3-t-butyl-5-aryl-4-bromoisoxazole essentially did not change.

Discussion:

We have yet to successfully synthesize the 4-bromo compounds. If our bromination method fails, we will have to discover a new method to make the 4-bromo compounds.

References:

1. Yu, J., Edjah, B., Argueta-Gonzalez, H., Ross, S., Gaulden, P., Shanderson, R, Dave, J., & Baumstark, A. L. (2015). 13C NMR Spectroscopy of Heterocycles: 3,5-Diaryl-4-bromoisoxazoles. Heterocyclic Communications, 21(5). 279-283. doi: 10.1515/hc-2015-0111