ROLE REVERSAL IN THE CYCLOCONDENSATION OF CYCLOPENTADIENE WITH HETERODIENOPHILES DERIVED FROM ARYL AMINES AND ALDEHYDES: SYNTHESIS OF NOVEL TETRAHYDROQUINOLINES

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> Summary: Immonium ions derived from aryl amines and aldehydes function not as heterodienophiles but rather as heterodienes in the presence of cyclopentadiene giving rise to novel tetrahydroquinolines.

We have reported² on a previous occasion that simple immonium salts generated in situ from primary alkyl amines and formaldehyde undergo facile cyclocondensation with cyclopentadiene giving rise to azanorbornenes in excellent yield (cf. Equation 1).³ For example addition of neat cyclopentadiene (2.0 equiv) to a

$$C_6H_5CH_2NH_2HX \xrightarrow{HCHO} [C_6H_5CH_2NH=CH_2X] \xrightarrow{H_2O} (1)$$

2.5 M aqueous solution of benzylamine hydrochloride (1.0 equiv) and 37% aqueous formaldehyde solution (1.4 equiv) gave rise after 3 h at ambient temperature to a near quantitative yield of N-benzyl-2-aza-5-norbornene. In sharp contrast, use of aniline in the reaction depicted in Equation 1 does not give rise to any of the corresponding N-phenyl-2-azanorbornene (1), but instead leads to the formation of the novel tetrahydroquinoline based pentacyclic products 2 and 3. Addition of a 1.4 M solution of aniline in acetonitrile containing 1.0 equiv of trifluoroacetic acid to a cooled (0°C) heterogeneous mixture of cyclopentadiene (5.0 equiv) in 37% aqueous formaldehyde (5.0 equiv) solution gave rise after 1 h at ambient temperature to a 98% yield of two crystalline compounds 2 and 3 in a ratio of 3.7:1 which were readily separable by silica gel chromatography.⁴ The structure of 2, mp 95-96°C, was unambiguously established by single-crystal x-ray analysis.⁵



Use of 4-aminobenzoic acid and 4-nitroaniline in the above reaction gave rise to pentacyclic compounds 4 and 5 in 84% and 94% yields respectively. Somewhat



surprising was the fact that exposure of the bis-TFA salt of 4aminophenethylamine in acetonitrile to excess cyclopentadiene and 2.0 equivalents of 37% aqueous formaldehyde solution gave rise after 45 min to pentacyclic amine 6 which was isolated in 89% yield as its TFA salt. The absence of any aza norbornene products (cf. 7-9) suggests that, under the exceedingly mild reaction conditions, the retro aza Diels-Alder process is extremely facile.⁶



Use of a preformed Schiff base in the above reaction leads to the formation of

amine	time, h	product	yield% ^b
	3		85
COOH NH2	2		82
CI NH2	2		90
	3	H = H = H = H = H = H = H = H = H = H =	98

<u>Table I.</u> Reaction of in situ generated Schiff bases with cyclopentadiene under acid catalysis.^a

^aAll reactions were conducted at ambient temperature by addition of 1.0 equiv of benzaldehyde to a mixture of arylamine as its TFA salt and cyclopentadiene in acetonitrile. ^bIsolated yield.

tetrahydroquinoline derivatives in excellent yield.⁷ For example, addition of trifluoroacetic acid (0.9 equiv) to a 0.8 M solution of the Schiff base derived from benzaldehyde and aniline in acetonitrile containing excess cyclopentadiene afforded upon standing for 2 h a 71% yield of the tetrahydroquinoline derivative **10**, mp 120.5-121.5°C, whose structure was unambiguously established by single crys-



tal x-ray analysis.⁸ Similar results can be obtained by admixture of aryl amines and benzaldehyde in the presence of cyclopentadiene and trifluoroacetic acid (see Table I).⁹

<u>References</u>

- 1. Predoctoral Fellowship from La Universidad de Los Andes, Venezuela.
- 2. Larsen, S.D.; Grieco, P.A. J. Am. Chem. Soc., 1985, 107, 1768.
- 3. For a review on heterodienophiles see: Weinreb, S.M.; Staib, R.R. <u>Tetrahedron. 1982, 38</u>, 3087.
- 4. All new compounds have been fully characterized including CH analysis.
- 5. Compound 2 crystallizes in the monoclinic space group P21/n with a = 8.757 (3) Å, b = 18.016(8) Å, c = 9.005(4) Å, beta = 111.95(2)° and gamma = 89.97(0)° at -155°C; C_{Calc} = 1.252 gm/cm³ for Z = 4. A total of 1833 reflections were measured of which 1225 were determined to be observable, F₀ > 2.33 σ (F₀). All atoms were located and refined to final residuals of R_F = 0.0523 and R_{WF} = 0.0512.
- 6. Grieco, P.A.; Parker, D.T.; Fobare, W.F.; Ruckle, R. J. Am. Chem. Soc., 1987, 109, 5859.
- Aromatic amines, aldehydes, and alkenes in the presence of concentrated sulfuric acid-glacial acetic acid give rise, in modest yield, to tetrahydroquinolines [Hesse, K.-D. Liebigs Ann. Chem., 1970, 741, 117].
- Compound 10 crystallizes in the centrosymmetric space group P1bar with a = 10.225(3) Å, b = 8.487(2) Å, c = 10.392(3) Å, alpha = 68.15(2)°, beta = 123.79(1)°, and gamma = 118.66 (2)° at -155°C; C_{Calc} = 1.262 gm/cm³ for Z = 2. A total of 2319 reflections were measured of which 1526 were observable F₀ > 2.33 σ (F₀). All atoms were located and refined [RF = 0.0286, RWF = 0.0358].
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