SCHIZOID REACTIVITY OF N-BENZYLIDEME ANILINE TOWARD CLAY-CATALYZED CYCLOADDITIONS

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Abstract : The K10/Fe^{III} montmorillonite catalyzes cycloadditions of N-benzylidene aniline with vinyl ethers. Both [2,2] and [2,4] cycloadducts form. Tetrahydroquinolines and azetidines can thus be obtained.

An entrenched stereotype has four membered rings formed by photochemical $[2_{\pi}+2_{\pi}]$ and six membered rings by thermal $[4_{\pi}+2_{\pi}]$ cycloadditions¹. We report here an apparent exception to this orbital symmetry rule. We came across this abnormality in our on-going study of catalysis of cycloadditions such as the Diels-Alder by inorganic solids². In order to further explore this access through such cycloadditions to nitrogen heterocycles³ we looked at imines for their broad reactivity.

N-benzylidene aniline $\underline{1}$ bears no active hydrogen and cannot tautomerize to the enamine. We opted to cycloadd $\underline{1}$ to electron-rich Z vinyl ethers, under catalysis by the K10 acidic montmorillonite (Süd Chemie) doped with Fe^{III 5-7}. The results are shown in the Scheme and Table 1.

Scheme



The dienophiles were 2,3-dihydrofuran, 2a, 3,4-dihydro-2H-pyran, 2b, and ethylvinyl ether, 2c. Product 2c reacts by [2,4] inverse electron demand Diels-Alder. But 2a and 2b give a conjunction of [2+2] and [2+4] cycloadducts. Products 3 and 4 are identified in the usual way⁸. No tetrahydroisoquinoline nor Michael addition products⁹ form.

The clay catalyst is influential not only in accelerating the reactions - by a factor of 10 with less reactive dienophiles - but also in affecting product distribution. FeCl₃ alone catalyzes the reactions, but the $\frac{3}{4}$ ratio is near unity. Other Lewis acids

entry, solvent	T(°C)	hrs $r(\underline{3}/\underline{4})$		% <u>3</u> b	% <u>4</u>	% <u>1</u>
(substrate <u>2b</u>)						
1 ^c dichloromethane	22	6	1.0	47	47	6
2 diethyl ether	22	6	7.3	51	7	35
3 " "	35	6	7.4	67	9	24
4 ^d " "	35	18	4.8	72	17	11
5 <u>n</u> -pentane	22	6	1.9	15	8	61
6 dichloromethane	22	6	1.8	28	15	57
7 " "	40	6	2.3	35	15	34
8 acetonitrile	83	12	1.4	50	36	14
9 ^e diethyl ether	35	4	12.8	86	7	7
10 ^f " "	35	24				100
(substrate <u>2a</u>)						
11 " "	22	2	11.6	81	7	12
12 [°] " "	22	2	1.3	56	42	2
(substrate <u>2</u>						
13 " "	22	2		95		5

promote formation of $\underline{3a}$ but their use lacks generality: the yield of $\underline{3b}$ is modest¹⁰. Table 1. Results of reactions of $\underline{1}$ with vinyl ethers yielding $\underline{3}$ and $\underline{4}^a$.

a) reactions run with 2.5 mmole of reactants and 0.3-0.4g catalyst in 20mL of dry solvent; $\frac{2}{100}$ is added to $\frac{1}{100}$ well mixed with catalyst predried at 150°C. b) percentages were determined by 200 MHz pmr. c) 10% mole equivalents FeCl₃; no K10. d) 10% mole equivalents 4-tert-butylphenol. e) 1.5 mole equivalents of Fe^{III}in K10/Fe^{III}. f) dienophiles include cyclohexene, maleic anhydride, and propargyl alcohol.

Both cycloaddition modes are regiospecific and stereospecific, leading exclusively to products $\underline{3}$ and $\underline{4}^8$. The coupling constants show the three substituents in the six-membered rings $\underline{3}\underline{a}\underline{-}\underline{c}$ to be <u>cis</u>, <u>cis</u> as befits a Diels-Alder cycloaddition. Likewise, the phenyl and R' substituents in $\underline{4}$ are <u>cis</u>, from the large magnitude of ${}^3J_{3,4}$. Comparable couplings have been found for cyclobutane derivatives¹¹. Stereospecific formation of $\underline{4}$ cannot occur by a concerted process, this would violate the Woodward-Hoffmann rules. If it results from a stepwise pathway, through a diradical or a zwitterionic intermediate, it is then rather remarkable that a single stereoisomer is obtained. The observed product $\underline{4}$ corresponds to diastereofacial specificity, the <u>si</u> face of $\underline{2}$ (at the future C-3) coming to overlap with the re face of <u>1</u> (at the future C-4).

Despite the regio- and stereospecificity in the formation of $\frac{4}{2}$, we believe it to arise from a zwitterionic pathway. A strong indication is provided by solvent effects¹²: the $\frac{3}{4}$ ratio falls with an increase in the dielectric constant of the solvent; it is 7.4 in the low dielectric diethyl ether and only 1.4 in the high dielectric acetonitrile.

Both the [2,4] and [2,2]cycloaddition modes require an electron-rich olefin as partner to <u>1</u>, and normal olefins do not react (Table 1, entry 10). Protonation of the imine

nitrogen by strongly acidic (H₀ ca. -7) clay makes the diene even more electron-deficient in the [2,4]. As previously observed, radical cations catalyze the $[2,4]^{12}$ and use of 4-tert-butylphenol as a source raises markedly the $\frac{3}{4}$ ratio (Table 1, entry 9).

Finally, the diastereofacial specificity in the formation of $\frac{4}{2}$ can be reconciled with a zwitterionic (or a diradical) pathway. Assuming an unprotonated imine, the (<u>re,re</u>) zwitterion would be destabilized by stereoelectronic (or anomeric) effects when a bond forms between the imine nitrogen and the oxygen-bearing carbon of the vinyl ether.

To sum up, results presented here show a most interesting interplay of orbital- and of charge-control¹³.

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a) P. Laszlo and P.J. Stang, <u>Organic Spectroscopy</u>, Harper and Row,
New York, 1971;
b) <u>3a</u>: (pmr, CDC1<sub>3</sub>)&: 5.31(d,1H,C-4),4.73(d,1H,C-2),3.9-3.7(bs,1H,NH)
2.9-2.73(m,1H,C-3),1.49(m,1H,C-5'),1.18(m,1H,C-5),3.6-3.8(m,2H,C-6,C-6')
J(Hz): J<sub>2,3</sub>=2.56, J<sub>3,4</sub>=7.49; (cmr,CDC1<sub>3</sub>)&: 76.1(C-4), 57.6(C-2),45.9(C-3).
<u>3b</u>: (pmr,CDC1<sub>9</sub>)&: 5.31(d,1H,C-4),4.67(d,1H,C-2),3.85(bs,1H,NH),2.3-2.0(m,1H,C-3),
J(Hz): J<sub>2,3</sub>=2.44,J<sub>3,4</sub>=5.62; (cmr,CDC1<sub>3</sub>)&:73.0(C-4),59.5(C-2),39.2(C-3);
(ms) 265 M+(100), 233 C<sub>17</sub>H<sub>15</sub>N(12), 219 C<sub>16</sub>H<sub>13</sub>N(16), 205 C<sub>15</sub>H<sub>11</sub>N(81), 193 C<sub>14</sub>H<sub>11</sub>N(40),
181 C<sub>13</sub>H<sub>11</sub>N(12), 129(49).
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\underline{3c}: (pmr,CDCl<sub>3</sub>) \delta: 4.52(dd,1H,C-4),4.81(dd,1H,C-2),3.93(bs,1H,NH),2.40
      (ddd,1H,C-3), J(Hz): J<sub>3,4</sub>=8.47,J<sub>3</sub>',4=5.69,J<sub>3,3</sub>'=-11.64,J<sub>2,3</sub>=11.54,J<sub>2,3</sub>'=2.62,
      (cmr,CDC1<sub>3</sub>) \delta:74,1(C-4),56.0(C-2),37.2(C-3).
      4a: (pmr,CDC1<sub>2</sub>)δ: 3.79(d,1H,C-2),2.39(dddd,1H,C-3),4.53(d,1H,C-4),
      2.0(dddd,1H,C-5),1.7(dddd,1H,C-5'),3.96(ddd,1H,C-6),3.76(ddd,1H,C-6');
      J(Hz): J_{3,4}=10.98, J_{2,3}=5.05, J_{3,5}=8.0, J_{3,5}=2.02, J_{5,5}=-8.23,
      J_{5,6}^{=8.41}, J_{5,6}^{=6.29}, J_{6,6}^{=-8.66}
      (cmr,CDCl<sub>3</sub>) &: 58.0 (C-2), 43.6 (C-3, 76.3 (C-4), 2 Ar C-R, 6 Ar C-H's;
      (ms): 251 M+.
      <u>4</u><u>b</u>: (pmr,CDC1<sub>3</sub>)δ: 4.76(d,1H,C-4),4.44(d,1H,C-2),2.1(m,1H,C-3),
      J(Hz): J<sub>2,3</sub>=2.44, J<sub>3,4</sub>=10.98; (cmr,CDC1<sub>3</sub>) 74.8(C-4),55.2(C-2),39.2(C-3),
      8 Ar C's; (ms) 265M+(91), 219 C<sub>16</sub>H<sub>13</sub>N(100), 205 C<sub>15</sub>H<sub>11</sub>N(91),
      181 C<sub>13</sub>H<sub>11</sub>N(100), 148 C<sub>11</sub>H<sub>14</sub>N(87), 84 C<sub>5</sub>H<sub>8</sub>O(87).
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