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Lewis acid-catalyzed reactions of *N*-allylanilines with diazo compounds involving aza-Claisen rearrangement

Alexander G. Badamshin,[a,b] Leonid V. Spirikhin,[a] Rinat F. Salikov,[c] Vladimir A. Dokichev[a,b] and Yury V. Tomilov*[c]

[a] *Ufa Institute of Chemistry, Russian Academy of Sciences, 450054 Ufa, Russian Federation. Fax: +7 347 235 6066; e-mail: dokichev@anrb.ru*
[b] *Ufa State Aviation Technical University, 450000 Ufa, Russian Federation*
[c] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 499 135 6390; e-mail: tom@ioc.ac.ru*

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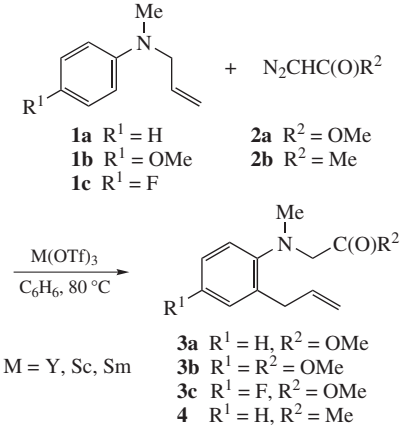
N-Allyl-*N*-methylanilines react with methyl diazoacetate or diazoacetone in the presence of Y, Sc or Sm triflates to give the corresponding methyl *N*-(2-allylaryl)-*N*-methylglycinates or 2-allyl-*N*-methyl-*N*-(2-oxopropyl)aniline. The formation of these compounds involves the aza-Claisen rearrangement.

Catalytic reactions of diazo compounds with unsaturated compounds are widely used in the synthesis of practically important polyfunctional products.[1–5] The direction of occurring reactions (cyclopropanation, 1,3-dipolar cycloaddition, insertion) is considerably affected both by the structure of the olefins and diazo compounds and by the catalyst nature. For example, diazomethane reacts with allylamines in the presence of $(PhCN)_2PdCl_2$ to afford cyclopropanes,[2] whereas the reaction of ethyl diazoacetate with allylamines in the presence of Fe, Co, Ni, Rh or Ru based catalysts occurs as a [2,3]-sigmatropic rearrangement of the resulting *N*-ylides to homoallylic derivatives, *viz*., esters of unsaturated *N*,*N*-dialkylamino acids.[3,6–8] It was recently found that rare-earth metal triflates have an activating effect on 1,3-dipolar cycloaddition of diazo esters to electron-deficient dipolarophiles to give the corresponding 1- or 2-pyrazolines.[9]

In this work we studied the catalytic reaction of *N*-allyl-*N*-methylanilines **1a–c** with methyl diazoacetate **2a** or diazoacetone **2b** in the presence of Lewis acids, namely, yttrium, samarium and scandium triflates.† In fact, *N*-allylaniline **1a** reacts with diazo compounds **2a** or **2b** in the presence of $Y(OTf)_3$ to produce methyl *N*-(2-allylphenyl)-*N*-methylglycinate **3a** or 2-allyl-*N*-methyl-*N*-(2-oxopropyl)aniline **4** in 66 and 56% yields, respectively (Scheme 1). This process is also favoured by other Lewis acids such as $Sc(OTf)_3$ and $Sm(OTf)_3$, but the yield of rearranged product **3a** is somewhat lower: 45 and 38%, respectively, with nearly complete conversion of the starting substrates **1a** and **2a**.

N-Allylaniline derivatives **1b**,**c** react with methyl diazoacetate in a similar way and, if 20 mol% $Y(OTf)_3$ is used, give the corresponding 2-allylanilines **3b** and **3c** in 63 and 50% yields, respectively (see Scheme 1).†



Scheme 1

The structures of the compounds obtained were confirmed by ^1H and ^{13}C NMR spectra using 2D correlation techniques. The HMBC spectrum proved to be most informative for determination

† ^1H and ^{13}C NMR spectra were recorded on a Bruker AVANCE II 300 spectrometer (300 and 75 MHz, respectively) in $CDCl_3$ containing 0.05% Me_4Si as the internal standard. Assignments of ^1H and ^{13}C signals were made with the aid of 1D DEPT-135 and 2D COSY, NOESY, HSQC and HMBC spectra. *N*-Allyl-*N*-methylaniline was obtained using a reported procedure.[14]

General procedure for the synthesis of compounds **3a–c** *and* **4**. A solution of methyl diazoacetate or diazoacetone (0.7 mmol) in benzene (2 ml) was slowly added to a stirred solution of *N*-allylaniline **1a–c** (0.7 mmol) and 0.14 mmol of the catalyst (Y, Sc or Sm triflates) in benzene (2 ml) at 80 °C. The reaction mixture was refluxed for 2–3 h, then dichloromethane (5 ml) was added and the mixture was filtered through a small pad of silica gel. After removal of solvents *in vacuo* 2-allylanilines **3a–c** and **4** were isolated by column chromatography on SiO_2 (hexane–AcOEt, 50:1).

Methyl N-*(2-allylphenyl)*-N-*methylglycinate* **3a**: yield 66%, yellow oil. IR ($CHCl_3$, ν/cm^{-1}): 2977, 2893, 1753, 1637, 1598, 1492, 1435, 1200, 1122, 1019, 997, 915. ^1H NMR, δ: 2.83 (s, 3H, NMe), 3.49 (br. d, 2H, CH_2, ^3J 6.43 Hz), 3.67 (s, 2H, NCH_2), 3.70 (s, 3H, OMe), 5.05–5.08 and 5.09–5.10 (both m, 2×1H, $=CH_2$), 5.95–6.04 (m, 1H, =CH), 7.01–7.05 (m, 1H, Ar), 7.14–7.22 (m, 3H, Ar). ^{13}C NMR, δ: 35.2 (CH_2), 42.1 (NMe), 58.5 (NCH_2), 51.5 (OMe), 115.9 ($=CH_2$), 121.1, 123.7, 126.85, 130.51, (4CH, Ar), 134.6 (C^2), 137.9 (=CH), 150.8 (C^1), 171.1 (COO). Found (%): C, 71.10; H, 7.76, N, 6.43. Calc. for $C_{13}H_{17}NO_2$ (%): C, 71.21; H, 7.81, N, 6.39.

Methyl N-*(2-allyl-4-methoxyphenyl)*-N-*methylglycinate* **3b**: yield 63%, yellow oil. IR ($CHCl_3$, ν/cm^{-1}): 2999, 2971, 2837, 1753, 1500, 1200. ^1H NMR, δ: 2.79 (s, 3H, NMe), 3.49 (br. d, 2H, CH_2, ^3J 6.5 Hz), 3.65 (s, 2H, NCH_2), 3.69 (s, 3H, OMe), 3.76 (s, 3H, OMe), 5.06 (t, 1H, from $=CH_2$, ^3J 1.5 Hz), 5.08–5.13 (m, 1H, from $=CH_2$), 5.88–6.08 (m, 1H, =CH), 6.72 (dd, 1H, H^5, ^3J 8.5 Hz, ^4J 3.0 Hz), 6.75 (d, 1H, H^3, ^4J 3.0 Hz), 7.14 (d, 1H, H^6, ^3J 8.5 Hz). ^{13}C NMR, δ: 35.2 (CH_2), 42.9 (NMe), 51.6 (CO_2Me), 55.5 (OMe), 58.7 (NCH_2), 111.9 (C^5), 115.7 (C^3), 116.0 ($=CH_2$), 122.8 (C^6), 137.0 (C^2), 137.7 (=CH), 144.0 (C^1), 156.3 (C^4), 171.5 (COO). MS, *m*/*z* (%): 249 (34) $[M]^+$, 190 (100) $[M-CO_2Me]^+$, 174 (31). HRMS, *m*/*z*: 250.1433 (calc. for $C_{14}H_{19}NO_3$, *m*/*z*: 250.1438 $[M+H]^+$).

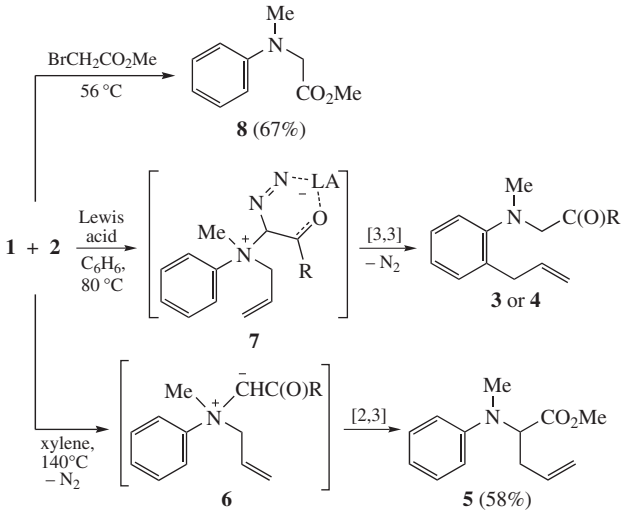
of the position of the allyl substituent. In fact, methylene protons of the allyl substituent in compound **3a** displayed cross-peaks not only with the signals of the vinyl C atoms but also with two quaternary and one methine C atoms of the benzene ring.

Note that in the absence of a diazo compound, no migration of the allyl group in compound **1a** occurs in the presence of $Y(OTf)_3$ at 80 °C, even upon longer heating (6 h). Indeed, unlike the Claisen rearrangement of vinyl and aryl allyl ethers, rearrangement of their nitrogen analogues requires much more drastic conditions, namely, heating to 230–270 °C or use of Lewis acids (mainly $BF_3{\cdot}OEt_2$) at 120–170 °C.[10–12]

In order to estimate the effect of temperature on the reaction of methyl diazoacetate with allylaniline **1a**, we performed their thermolysis in xylene under reflux in the absence of any initiators. Like in case of catalysts based on transition metals,[3,6–8] methyl 2-(*N*-methyl-*N*-phenylamino)pent-4-enoate **5**‡ – a product of [2,3]-sigmatropic rearrangement of *N*-ylide **6** (R = OMe) generated upon thermal carbene decomposition of the diazo compound (Scheme 2) – proved to be the main reaction product.

Thus, the reaction of methyl diazoacetate with allylaniline in the presence of Y, Sc and Sm triflates differs from their reaction proceeding at elevated temperature (140 °C) or in the presence of catalysts based on transition metal compounds, which is undoubtedly due to differences in the nature of the intermediates. In the latter two cases, the process occurs as a [2,3]-sigmatropic rearrangement of *N*-ylides **6** that are formed due to attack of the amino group by the carbene, whereas the same reaction in the presence of rare earth metal triflates occurs as an aromatic aza-Claisen rearrangement of ionic intermediate **7**. In other words, elimination of a nitrogen molecule from the diazo compound in the presence of different initiators probably occurs at different stages of the process.

To estimate whether it is possible to perform the aza-Claisen rearrangement in a series of quaternized aniline salts by analogy with intermediate **7**, we studied the reaction of *N*-allylaniline **1a** with methyl bromoacetate in acetone under reflux conditions.



Scheme 2

However, even under these rather mild conditions, the resulting quaternary salt was unstable and underwent deallylation to give compound **8**.§ In general, this process is known for some *N*-allylanilines. In particular, it proceeds rather efficiently in the presence of palladium and TsOH.[13]

In conclusion, we have found that decomposition of diazo compounds in the presence of *N*-allylanilines and rare-earth metal triflates occurs through a [3,3]-sigmatropic rearrangement of the intermediate ylide with migration of the allyl substituent to an *ortho* position of the aromatic ring, whereas thermal decomposition, similarly to decomposition with transition metal complexes, occurs through a [2,3]-sigmatropic rearrangement with migration of the allyl moiety to the ylide centre.

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Methyl N-*(2-allyl-4-fluorophenyl)*-N-*methylglycinate* **3c**: yield 50%, yellow oil. IR ($CHCl_3$, ν/cm^{-1}): 2979, 2955, 2850, 2803, 1753, 1496, 1204. ^{1}H NMR, δ: 2.80 (s, 3H, NMe), 3.48 (br. d, 2H, CH_2, ^3J 6.5 Hz), 3.67 (s, 2H, NCH_2), 3.69 (s, 3H, OMe), 5.07 (dd, 1H, from $=CH_2$, ^3J 9.6 Hz, ^4J 1.5 Hz), 5.12 (br. d, 1H, from $=CH_2$, ^4J 1.5 Hz), 5.95 (ddt, 1H, =CH, ^3J 16.9, 10.5 and 6.5 Hz), 6.80–6.89 (m, 1H, H^5), 6.89 (dd, 1H, H^3, ^3J 8.7 and 2.7 Hz), 7.15 (dd, 1H, H^6, ^3J 8.7 Hz, ^4J 5.3 Hz). ^{13}C NMR, δ: 35.1 (CH_2), 42.6 (NMe), 51.7 (OMe), 58.3 (NCH_2), 113.3 (d, C^3, $^2J_{C,F}$ 22.0 Hz), 116.5 ($=CH_2$), 116.7 (d, C^5, $^2J_{C,F}$ 22.2 Hz), 123.1 (d, C^6, $^3J_{C,F}$ 8.5 Hz), 137.0 (=CH), 137.6 (d, C^2, $^3J_{C,F}$ 7.3 Hz), 146.6 (C^1), 159.6 (d, C^4, $^1J_{C,F}$ 242.4 Hz), 171.3 (COO). ^{19}F NMR, δ: –119.2 (dd, $J_{H,F}$ 12.2 and 8.7 Hz). MS, *m/z* (%): 237 (19) [M]$^+$, 178 (100) [M – CO_2Me]$^+$, 162 (28). HRMS, *m/z*: 238.1244 (calc. for $C_{13}H_{16}FNO_2$, *m/z*: 238.1238 [M+H]$^+$).

2-Allyl-N-*methyl*-N-*(2-oxopropyl)aniline* **4**: yield 56%, yellow oil. ^{1}H NMR, δ: 2.08 (s, 3H, Me), 2.64 (s, 3H, NMe), 3.44 (d, 2H, CH_2, ^3J 6.2 Hz), 3.62 (s, 2H, NCH_2), 4.95–5.08 (m, 2H, $=CH_2$), 5.87–6.01 (m, 1H, =CH), 6.93–7.06 (m, 1H, Ar), 7.07–7.27 (m, 3H, Ar). ^{13}C NMR, δ: 27.3 (Me), 34.9 (CH_2), 43.1 (NMe), 67.3 (NCH_2), 115.9 ($=CH_2$), 120.6, 123.9, 127.6, 130.6 (CH, Ar), 134.5 (C^2), 137.7 (=CH), 151.1 (C^1), 207.4 (C=O). Found (%): C, 76.70; H, 8.48, N, 6.80. Calc. for $C_{13}H_{17}NO$ (%): C, 76.81; H, 8.43, N, 6.89.

‡ *Methyl 2-(*N-*methyl*-N-*phenylamino)pent-4-enoate* **5**. A solution of compounds **1a** (4 mmol, 0.59 g) and **2a** (8 mmol, 0.80 g) in xylene (4 ml) was refluxed for 2 h, then the solvent was removed *in vacuo* and the residue was separated by chromatography on SiO_2 to yield product **5** (58%), whose spectral data are completely consistent with described earlier.[15]

§ *Methyl* N-*methyl*-N-*phenylglycinate* **8**. A solution of **1a** (6 mmol, 0.88 g) and methyl bromoacetate (8 mmol, 1.55 g) in acetone (10 ml) was refluxed for 24 h. The reaction mixture was cooled, the solvent was removed *in vacuo* and the residue was separated by column chromatography on SiO_2 to yield compound **8** (67%) as a yellow oil. Spectral data of **8** are completely consistent with reported previously.[16]

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