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A CONVENIENT REDUCTION OF N-(2-SUBSTITUTED-1-CYANOETHENYL) ACETAMIDES WITH NaTeH

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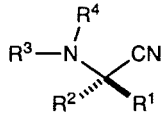
ABSTRACT: N-(1-cyano-2-substituted phenylethyl) acetamides (**4a-h**) were synthesized by reduction of corresponding titled compounds **3a-h** with NaTeH. The procedure was general and convenient for preparation of benzyl substituted acyclic Reissert compounds without using phenylacetaldehydes as starting materials.

α-Aminonitrile (**1**), in which many organic reactions can be happened selectively on either or both of amino and cyano functional groups, is a versatile starting material in the synthesis of heterocyclic compounds. Its N-acyl derivatives (**2**, acyclic Reissert compounds) were often used for the preparation of pyrroles,



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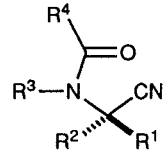

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oxazoles, imidozolinones, and imidazolethiols. N-(1-cyano-2-substituted phenylethyl) acetamide (**4**) also was chosen as a starting material for our research purposes.

Usually, **2** was prepared by N-acylation of corresponding α-aminonirtile (**1**), which was easily obtained by classic Strecker synthesis[7] or modified Strecker synthesis[8,9]. However, all theses methods were limited to prepared **4a-h** because the most of substituted phenylacetaldehydes are not commercial available and not convenient for preparation in the most laboratories. For these reasons, a practical procedure have been developed from our laboratory for the preparation of N-(1-cyano-2-phenylethenyl) acetamide (**3**). Reduction of double bond in **3** should give corresponding **4** by chemical reducing agents and already give some of **4** with very high optical purity by hydrogenation over chiral catalysts[11,12].

Unfortunately, a few of reported successful reagents for selective reduction of conjugated double bonds, such as NaBH4-isopropanol[13], Mg-MeOH[14], Zn-NiCl-$MeOCH_2CH_2OH$-ultra sound[15] were all failed to give product **4**. It is obvious that the double bond in compound **3** is not really belong to traditional α,β-unsaturated nitrile or traditional aromatic conjugated double bond.

The investigation of literature shows that NaTeH, as a versatile reducing reagent, was characterized by convenient preparation and mild reaction condition. It was successfully used for the reduction of double bonds in several kinds of α,β-unsaturated conjugated systems, but without α,β-unsaturated nitriles. Herein we

$$\underset{\mathbf{3}}{PhCH{=}C(CN)NHCOCH_3} \xrightarrow[RT/5h/65\text{-}85\%]{NaTeH/EtOH/N_2} \underset{\mathbf{4}}{PHCH_2CH_2(CN)NHCOCH_3}$$

3,4	Ar	yield(%)	3,4	Ar	yield(%)
a.	C_6H_5	75	**e.**	*p*-$MeOC_6H_4$	65
b.	*o*-ClC_6H_4	79	**f.**	3,4-$(MeO)_2C_6H_3$	78
c.	*p*-ClC_6H_4	73	**g.**	3,4-$CH_2CH_2C_6H_3$	85
d.	*o*-$MeOC_6H_4$	68	**h.**	*p*-$Me_2NC_6H_4$	72

would like to report a mild approach to reduce the double bond selectively in compound **3** to yield **4** in moderate yields with NaTeH. It is worth to note that this procedure offered a general approach for preparation of benzyl substituted acyclic Reissert compounds without using any phenylacetaldehydes.

Using the regular reducing procedure, a mixture of N-(1-cyano-2-phenylethyl) acetamide (**3a**) and NaTeH in EtOH was stirred for 5 h at room temperature to give **4a** smoothly in 75% yield.**3**b-h also offered corresponding saturated products **4**b-h in 65-85%. Other groups, such as chloro, cyano, ether, amine and amide all did not effected by NaTeH under the reaction condition.

EXPERIMENTAL SECTION

All melting points were uncorrected and measured with a Yanaco MP-500 apparatus. IR spectra were recorded on a nicolet FT-IR 5DX spectrometer with KBr pellets. NMR spectra were recorded on a JEOL JNM-PMX 60SI spectromter at room temperature in CD3Cl with TMS as an internal reference. MS was recorded on a VG ZAB-HS spectrometer with 70 ev and elemental analyses were performed on a Perkin-Elmer 240-C instrument.

Synthesis of N-(1-cyano-2-phenylethyl) acetamide (4a), A typical procedure: To a stirred solution of NaTeH prepared from power Te (1.28 g, 10 mmol), $NaBH_4$ (0.9 g, 23.8 mmol) in EtOH (20 mL) under nitrogen, was added a solution of mixture of N-(1-cyano-2-phenylethenyl) acetamide (**3a**, 0.74 g, 4.0 mmol) in EtOH (30 mL) at room temperature. After 5 h, the reaction was quenched by addition of water (30 mL). The mixture was stirred in air for another 1 h and Te was precipitated out as black powder. After the mixture was filtered, the filter was extracted with EtOAc (3 x 20 mL). Combined organic layers were dried over $MgSO_4$ and the solvent was removed to yield the crude product, which were purified by chromatography (silica gel, EtOAc-Petroleum ether 60-90°) to give 0.56 g of (75%) pure product **4a** as crystals. It had m.p. 94-95 °C; IR: ν 3289, 2240, 1658, 1540, 750, 702 cm^{-1}; ^1H NMR: δ 1.98 (s, 3H, CHCO), 3.00 (d, J = 8.0 Hz, 1H, CH), 6.45 (b, 1H, NH), 7.0-7.8 (m, 5H, ArH) ppm; MS(m/z): 188 (M^+, 5.1), 128 (M^+-59, 51.7), 91 (M^+-97, 100). Anal. Cald. for $C_{11}H_{12}N_2O$: C, 70.17, H,6.24, N, 14.89. Found: C, 70.24, H, 6.43, N, 14.95. The compounds 4b-4h were prepared by the same procedure as the above and were characterized by IR, ^1H NMR and MS as following.

N-[1-cyano-2-(2-chlorophenyl)ethyl] acetamide (4b) m.p. 112-113 °C; IR: ν 3329,2246,1680,1532,802 cm^{-1}; ^1H NMR: δ 2.00 (s, 3H, CHCO), 3.20 (d, J = 8.0 Hz, 1H, CH), 6.40 (b, 1H, NH), 6.80-8.00 (m, 5H, ArH) ppm; MS(m/z): 222 (M^+, 6.3), 163 (M^+-59, 35.9), 125 (M^+-97, 85.6). Anal. Cald. for $C_{11}H_{11}ClN_2O$: C, 59.33, H, 4.98, N, 12.58. Found: C, 59.30, H, 4.69, N, 12.43.

N-[1-cyano-2-(4-chlorophenyl)ethyl] acetamide (4c) m.p. 151-152 °C; IR: ν 3281, 3063, 2244,1644, 1541, 822 cm^{-1}; ^1H NMR: δ 1.93 (s, 3H, CHCO), 3.00 (d, J = 8.0 Hz, 1H, CH), 5.00 (q, J = 8.0 Hz, 1H, CH), 6.60 (b, 1H, NH), 7.00-7.50 (m, 5H, ArH) ppm; MS(m/z): 222 (M^+, 3.8), 163 (M^+-59, 58.5), 125 (M^+-97, 100). Anal. Cald. for $C_{11}H_{11}ClN_2O$: C, 59.33, H, 4.98, N, 12.58. Found: C, 59.28, H, 4.80, N, 12.36.

N-[1-cyano-2-(2-methoxyphenyl)ethyl] acetamide (4d) m.p. 119-120 °C; IR: ν 3422, 3036, 2238, 1654, 1537, 754 cm^{-1}; ^1H NMR: δ 1.98 (s, 3H, CH_3CO), 3.20 (d, J = 8.0 Hz, 2H, CH_2), 3.90 (s, 3H, CH_3O), 5.10 (q, J = 8.0 Hz, 1H, CH), 6.72-7.53 (m, 5H, ArH) ppm; MS(m/z): 218 (M^+, 4.3), 159 (M^+-59, 48.8), 121(M^+-97, 89.3). Anal. Cald. for $C_{12}H_{14}N_2O_2$: C, 66.08, H, 6.47, N, 12.89. Found: C, 66.05, H, 6.35, N, 12.72.

N-[1-cyano-2-(4-methoxyphenyl)ethyl] acetamide (4e) m.p. 110-112 °C; IR: ν 3321, 2245, 1664, 1544, 826 cm^{-1}; ^1H NMR: δ 1.98 (s, 3H, CH_3CO), 2.95 (d, J = 8.0 Hz, 2H, CH_2), 3.70 (s, 3H, CH_3O), 5.00 (q, J = 8.0 Hz, 1H, CH), 6.50-7.10 (m, 5H, ArH) ppm; MS(m/z): 218 (M^+, 1.0), 159 (M^+-59, 26.9), 121(M^+-97, 100). Anal. Cald. for $C_{12}H_{14}N_2O_2$: C, 66.08, H, 6.47, N, 12.89. Found: C, 66.01, H, 6.19, N, 12.67.

N-[1-cyano-2-(3,4-dimethoxyphenyl)ethyl] acetamide (4f) m.p. 128-130 °C; IR: ν 3255, 2213, 1655, 1516 cm^{-1}; ^1H NMR: δ 1.98 (s, 3H, CH_3CO), 3.00 (d, J = 8.0 Hz, 2H, CH_2), 3.84 (s, 6H, 2 x OCH_3), 5.00 (q, J = 8.0 Hz, 1H, CH), 6.70-7.10 (m, 5H, ArH) ppm; MS(m/z): 248 (M^+, 5.4), 189 (M^+-59, 22.9), 151(M^+-97, 100). Anal. Cald. for $C_{13}H_{16}N_2O_3$: C, 62.93, H, 6.50, N, 11.29. Found: C, 62.66, H, 6.48, N, 11.23.

N-[1-cyano-2-(3,4-methylenedioxyphenyl)ethyl] acetamide (4g) m.p. 121-122 °C; IR: ν 3258, 2221, 1663, 1627 cm^{-1}; ^1H NMR: δ 1.95 (s,

3H, CH_3CO), 2.95 (d, J = 8.0 Hz, 2H, CH_2), 5.20 (q, J = 8.0 Hz, 1H, CH), 6.00 (s, 2H, OCH_2O), 6.15 (b, 1H, NH), 6.70-7.0 (m, 3H, ArH) ppm; MS(m/z): 232 (M^+, 5.3), 173 (M^+-59, 41.2), 135 (M^+-97, 100). Anal. Cald. for $C_{12}H_{12}N_2O_3$: C, 62.10, H, 5.21, N, 12.07. Found: C, 61.95, H, 5.07, N, 12.08.

N-[1-cyano-2-(4-N,N-dimethylphenyl)ethyl] acetamide (4h) m.p. 120-122 °C; IR: ν 3246, 2246, 1655 cm^{-1}; ^1H NMR: δ 1.98 (s, 3H, CH_3CO), 3.00 (d, J = 8.0 Hz, 2H, CH_2), 3.98 (s, 6H, 2 x CH_3N), 5.10 (q, J = 8 Hz, 1H, CH), 5.85 (b, 1H, NH), 6.51-7.30 (m, 4H, ArH) ppm; MS(m/z): 231 (M^+, 5.0), 172 (M^+-59, 32.3), 134 (M^+-97, 100). Anal. Cald. for $C_{13}H_{17}N_3O$: C, 67.55, H, 7.41, N, 18.18. Found: C, 67.41, H, 7.38, N, 18.24.

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