SHORT PAPER

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Facile synthesis of 2,3-dihydro-2-aryl-4(1H)-quinazolinones promoted by SmI_2†

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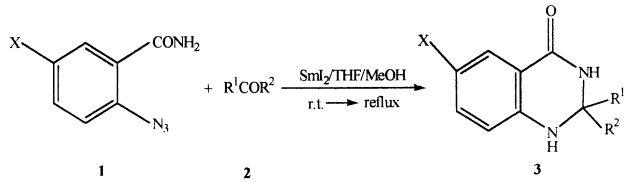
2,3-Dihydro-2-aryl-4(1H)-quinazolinones were prepared in good yields *via* reductive cyclisation of *o*-azidobeneamides with aldehydes and ketones promoted by SmI_2 under mild and neutral conditions.

Keywords: samarium diiodide, reductive cyclisation, *o*-azidobeneamides

2,3-Dihydro-2-aryl-4(1H)-quinazolinones derivatives are very important and useful nitrogen compounds. Some of them are herbicides and plant growth regulators.[1,2] They also are used as diuretics and antitumors.[3,4] A general procedure for the preparation of 2,3-dihydro-2-aryl-4(1H)-quinazolinones consists in condensing the appropriate *o*-aminobenzamide with aldehydes and ketones using *p*-toluenesulfonic acid as catalyst under vigorous reaction conditions.[5,6]

The chemistry of samarium diiodide (SmI_2) is of current interest in organic synthesis. SmI_2 has been developed as a mild, neutral and versatile single electron transfer reductant.[7–11] It is well known that azides compounds can be easily reduced by SmI_2 to the corresponding amines.[12] However, a little attention has been paid to the intermediate derived from an azide group by SmI_2 treatment. We have previously reported reductive coupling of azide compounds with nitriles.[13] Herein we wish to report a facile synthesis of 2,3-dihydro-2-aryl-4(1H)-quinazolinones in one pot *via* reductive cyclization of *o*-azidobenzamides with aldehydes and ketones promoted by SmI_2 under mild and neutral conditions (Scheme 1).

The results are summarised in Table 1. After *o*-azidobenzamide **1** was treated with 2 equiv. of SmI_2 in anhydrous THF at room temperature under a nitrogen atmosphere, the deep blue colour of the mixture changed into yellow immediately. The corresponding aldehydes or ketones **2** were introduced and the desired products **3** were formed. From Table 1, it can be found that aldehydes and aliphatic ketones can react with compounds **1** to afford the desired products **3** in satisfactory yields. However, for aromatic ketones only 2-aminobenezamides were obtained and products **3** were not detected even for a long time under reflux conditions. It was also found that 2 equiv. of SmI_2 were enough to accomplish the reaction, but 6 equiv. of SmI_2 were consumed for the reaction of nitro compounds under similar conditions.[14] Moreover, the reduction of azide compounds was completed quickly, while that of nitro compounds complete within 4 hours. If *o*-aminobenezamides derived from compounds **1** were treated with aldehydes and ketones **2** under the same conditions, product **3** could not be detected.



Scheme 1

Table 1 Reductive cyclisation of *o*-azidebeneamides with aldehydes and ketones promoted by SmI_2 [a]

Entry	X	R^1	R^2	Time/h	Yield/%[b]
a	H	C_6H_5	H	2	89
b	H	4-$CH_3OC_6H_4$	H	2	87
c	H	4-$(CH_3)_3CC_6H_4$	H	3	84
d	H	3-BrC_6H_4	H	2	85
e	H	3,4-$OCH_2OC_6H_3$	H	3	80
f	H	$(CH_2)_3CH_3$	H	2	77
g	Cl	C_6H_5	H	2	88
h	Cl	2-furyl	H	2	87
i	Cl	3-thienyl	H	2	87
j	Cl	$CH_2CH_2CH_3$	CH_3	4	69
k	Cl	-$(CH_2)_5$-		4	70
l	Cl	4-ClC_6H_4	CH_3	20	0
m	Cl	C_6H_5	C_6H_5	20	0

[a] *o*-Azidobeneamides 1 mmol, aldehydes or ketones 1.2 mmol, SmI_2 2 mmol were used.
[b] Isolated yields based on *o*-azidobeneamides.

Although the detailed mechanism of the above reaction has not been clarified, the formation of products **3** may be described by the possible mechanism presented in Scheme 2.[13,17]

In summary, the intermolecular reductive cyclisation reaction of azide compounds with aldehydes and ketones was studied and a facile synthesis of 2,3-dihydro-2-aryl-4(1H)-quinazolinones was provided.

Experimental

Tetrahydrofuran (THF) was distilled from sodium/benzophenone immediately prior to use. All reactions were carried on under a dry nitrogen atmosphere. Melting points were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were determined on a Bruker AC-400 instrument with DMSO-d_6 used as the solvent. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Microanalysis was carried out on a Carlo-Erba 1106 instrument.

General procedure: A solution of azide compound 1 (1 mmol) in anhydrous THF (3 ml) and MeOH (2 ml) was added to SmI_2 (2 mmol) at room temperature under a dry nitrogen atmosphere. The deep blue colour of the mixture changed into yellow immediately. Then aldehydes or ketones **2** (1.2 mmol) was introduced. After being stirred for a given time (see Table 1) in refluxing conditions, the solvent was removed under reduced pressure. The residue was treated with dilute HCl (0.01 M, 20 ml) and extracted with ethyl acetate (3×20 ml). The organic layer was washed with saturated. aq. $Na_2S_2O_3$ (15 ml) and brine (15 ml) respectively and dried over anhydrous $MgSO_4$. After ethyl acetate was removed under reduced pressure, the desired product was obtained by recrystallisation from anhydrous ethanol.

3a: M.p. 221–222°C (Lit.[15], 220–222°C); ^{1}H NMR (DMSO-d_6) δ : 5.78 (1H, br s, NH), 6.77 (1H, d, J = 8 Hz, CH), 7.15–7.64 (9H, m, ArH), 8.32 (1H, br s, NH); ^{13}C NMR (DMSO-d_6) δ : 163.65, 147.93, 147.71, 136.36, 128.51, 128.38, 128.12, 127.41, 126.93, 120.76, 117.17, 115.02, 114.46, 66.62.

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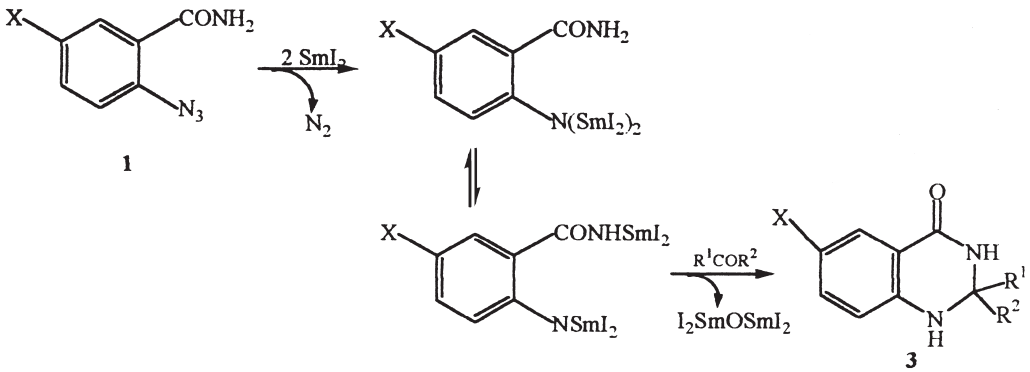
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



Scheme 2

3b: M.p. 180–182°C; ^{1}H NMR (DMSO-d_6) δ : 2.29 (3H, s, CH_3), 5.70 (1H, br s, NH), 6.73 (1H, d, *J* = 8 Hz, CH), 7.19–7.59 (8H, m, ArH), 8.22 (1H, br s, NH); ^{13}C NMR (DMSO-d_6) δ : 163.76, 159.50, 148.09, 133.58, 133.29, 128.27, 128.03, 127.41, 121.57, 117.12, 115.07, 114.49, 113.70, 66.34, 55.24; Anal. calcd for $C_{15}H_{14}N_2O_2$: C 70.85, H 5.55, N 11.02; found C 70.09, H 5.41, N 10.75.

3c: M.p. 219–220°C; ^{1}H NMR (DMSO-d_6) δ : 1.27 (9H, s, 3×CH_3), 5.71 (1H, br s, NH), 6.72 (1H, d, *J* = 8 Hz, CH), 7.23–7.61 (8H, m, ArH), 8.22 (1H, br s, NH); ^{13}C NMR (DMSO-d_6) δ : 163.72, 151.09, 148.04, 138.64, 133.33, 128.91, 127.43, 126.76, 125.16, 120.34, 117.12, 115.03, 114.43, 66.53, 34.41, 31.19; Anal. calcd for $C_{18}H_{20}N_2O$: C 77.11, H 7.19, N 9.99; found C 77.56, H 7.45, N 10.18.

3d: M.p. 231–232°C; ^{1}H NMR (DMSO-d_6) δ : 5.94 (1H, br s, NH), 6.78 (1H, d, *J* = 8 Hz, CH), 7.27–7.70 (8H, m, ArH), 8.53 (1H, br s, NH); ^{13}C NMR (DMSO-d_6) δ : 163.40, 147.77, 147.37, 144.36, 133.65, 133.45, 130.13, 127.48, 123.35, 121.63, 117.60, 115.02, 114.66, 65.24; Anal. calcd for $C_{14}H_{11}BrN_2O$: C 55.47, H 3.66, N 9.24; found C 55.54, H 4.03, N 9.11.

3e: M.p. 199–201°C (Lit.[16], 200–202°C); ^{1}H NMR (DMSO-d_6) δ : 5.67 (1H, br s, NH), 6.01 (2H, s, CH_2), 6.73 (1H, d, *J* = 8 Hz, CH), 7.03–7.60 (9H, m, ArH), 8.22 (1H, br s, NH); ^{13}C NMR (DMSO-d_6) δ : 163.66, 147.91, 147.37, 147.29, 135.64, 133.37, 127.41, 120.50, 117.22, 115.03, 114.50, 107.93, 107.25, 101.19, 66.34.

3f: M.p. 144–145°C; ^{1}H NMR (DMSO-d_6) δ : 0.88 (3H, t, J = 7 Hz, CH_3), 1.30–1.62 (6H, m, 3×CH_2), 6.57 (1H, br s, NH), 6.72 (1H, d, J = 8 Hz, CH), 7.22–7.57 (4H, m, ArH), 7.88 (1H, br s, NH); ^{13}C NMR (DMSO-d_6) δ : 163.97, 148.58, 133.09, 127.41, 116.91, 115.07, 114.43, 64.48, 34.81, 25.49, 22.15, 14.02; Anal. calcd for $C_{12}H_{16}N_2O$: C 70.56, H 7.90, N 13.71; found C 70.13, H 7.67, N 13.59.

3g: M.p. 248–249°C; ^{1}H NMR (DMSO-d_6) δ : 5.79 (1H, br s, NH), 6.77 (1H, d, *J* = 8.8 Hz, CH), 7.21–7.55 (8H, m, ArH), 8.53 (1H, br s, NH); ^{13}C NMR (DMSO-d_6) δ : 162.34, 146.46, 141.31, 132.99, 128.56, 128.40, 128.27, 127.77, 126.63, 126.27, 120.54, 116.38, 115.84, 66.06; Anal. calcd for $C_{14}H_{11}ClN_2O$: C 64.99, H 4.26, N 10.83; found C 65.12, H 4.09, N 9.98.

3h: M.p. 202°C; ^{1}H NMR (DMSO-d_6) δ : 5.79 (1H, br s, NH), 6.27–6.42 (2H, m, ArH), 6.74 (1H, d, *J* = 8.6 Hz, CH), 7.21–7.63 (4H, m, ArH), 8.58 (1H, br s, NH); ^{13}C NMR (DMSO-d_6) δ : 162.04, 154.05, 145.81, 142.80, 132.92, 126.23, 120.80, 116.42, 115.96, 110.23, 107.18, 59.95; Anal. calcd for $C_{12}H_9ClN_2O_2$: C 57.95, H 3.62, N 11.27; found C 57.48, H 3.77, N 11.35.

3i: M.p. 216–218°C; ^{1}H NMR (DMSO-d_6) δ : 5.82 (1H, br s, NH), 6.72 (1H, d, *J* = 8.6 Hz, CH), 7.13–7.54 (6H, m, ArH), 8.51 (1H, br s, NH); ^{13}C NMR (DMSO-d_6) δ : 162.24, 146.36, 143.21, 132.93, 126.82, 126.30, 126.16, 123.17, 120.72, 116.43, 116.08, 62.35; Anal. calcd for $C_{12}H_9ClN_2OS$: C 54.44, H 3.40, N 10.59; found C 54.27, H 3.72, N 11.10.

3j: M.p. 231–233°C; ^{1}H NMR (DMSO-d_6) δ : 1.08 (3H, t, *J* = 9 Hz, CH_3), 1.52 (3H, s, CH_3), 2.26–2.50 (4H, m, CH_2CH_2), 7.03 (1H, br s, NH), 7.46–7.76 (3H, m, ArH), 8.05 (1H, br s, NH); ^{13}C NMR (DMSO-d_6) δ : 161.32, 140.58, 135.08, 132.10, 129.21, 125.33, 122.35, 65.36, 35.12, 22.37, 15.95, 15.60; Anal. calcd for $C_{12}H_{15}ClN_2O$: C 56.58, H 5.89, N 11.00; found C 56.33, H 5.76, N 11.17.

3k: M.p. 241°C; ^{1}H NMR (DMSO-d_6) δ : 1.55–1.64 (10H, m, 5×CH_2), 6.85 (1H, br s, NH), 7.19–7.52 (3H, m, ArH), 8.10 (1H, br s, NH); ^{13}C NMR (DMSO-d_6) δ : 161.98, 145.42, 132.81, 126.11, 120.06, 116.51, 115.48, 67.96, 37.03, 24.46, 20.76; Anal. calcd for $C_{13}H_{15}ClN_2O$: C 58.54, H 5.63, N 10.51; found C 58.62, H 5.70, N 9.95.

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