Allylation of *N*-Benzoylhydrazones (= *N*′-Alkylidene-Substituted Benzohydrazides) by Treatment with Allyl Bromide in the Presence of Zinc in Aqueous Ammonium Chloride Solution[1]

by **Biswanath Das***, **Digambar Balaji Shinde**, **Boddu Shashi Kanth**, and **Jayprakash Narayan Kumar**

Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad 500007, India
(phone: +91-40-7193434; fax: +91-40-7160512; e-mail: biswanathdas@yahoo.com)

N-Benzoylhydrazones (= *N*′-alkylidene-substituted benzohydrazides) **1** are allylated efficiently by reaction with allyl bromide (**2**) in the presence of Zn in aqueous NH_4Cl solution. The products **3** are formed in excellent yields (85–94%) within 35–50 min (*Scheme*, *Table*).

Introduction. – Allylation of imines and related compounds is a valuable organic transformation as it generates a C–C bond and produces homoallylic amine derivatives of synthetic and biological importance [1]. Significant advances in the *Barbier*-type imine allylation have recently been developed [1][2]. However, the methods of allylation of *N*-acylhydrazones (= *N*′-alkylidene-substituted hydrazides) are limited [3], and more importantly, the application of allyl bromide ($CH_2=CHCH_2Br$) has received only scant attention for this transformation [3f]. Moreover, the use of Zn in the *Barbier*-type imine allylation has not been explored much [4]. Here, we report a simple and convenient method for the allylation of *N*-benzoylhydrazones (= *N*′-alkylidene-substituted benzohydrazides) **1** under mild reaction conditions.

Results and Discussion. – In continuation of our work [5] on the development of useful synthetic methodologies, we have discovered that *N*-benzoylhydrazones **1** can undergo allylation efficiently with $CH_2=CHCH_2Br$ (**2**) in the presence of Zn in aqueous NH_4Cl at 0° (*Scheme*). Various *N*-benzoylhydrazones **1** derived from different aldehydes were subjected to the above conversions. The reactions were complete

Scheme

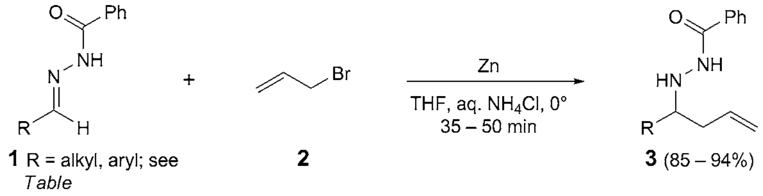

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Table. *Allylation of* N-*Benzoylhydrazones* **1** *with* $CH_2{=}CHCH_2Br$ (**2**)[a])

Entry	R	Product	Time [min]	Yield [%][b])	Ref.
a	Ph	**3a**	40	89	[3b,c]
b	4-F–C_6H_4	**3b**	40	88	
c	4-Cl–C_6H_4	**3c**	35	84	[3h,i]
d	4-Br–C_6H_4	**3d**	42	91	[3i]
e	4-MeO–C_6H_4	**3e**	45	87	[3h,f]
f	4-^{i}Pr–C_6H_4	**3f**	40	85	
g	3,4-$(MeO)_2C_6H_3$	**3g**	50	93	[3d]
h	3,4,5-$(MeO)_3C_6H_2$	**3h**	45	87	
i	3-NO_2–C_6H_4	**3i**	35	89	
j	4-CN–C_6H_4	**3j**	40	91	[3a]
k	furan-2-yl	**3k**	45	86	[3c,f]
l	thiophen-2-yl	**3l**	50	93	[3g]
m	^{i}Pr	**3m**	35	85	[3h,i]
n	$Me(CH_2)_4$	**3n**	40	90	[3b,d]

[a]) Reaction conditions: *N*-benzoylhydrazone **1** (1 mmol), allyl bromide (**2**; 2.2 mmol), Zn (5 mmol), THF (3 ml), and aq. NH_4Cl soln. (3 ml); reaction at 0°. [b]) Yield of pure isolated compound after column chromatography.

within 35–50 min, and the allylated products **3** were formed in excellent yields (85–94%; *Table*).

For the hydrazone preparation, aromatic, heteroaromatic, and aliphatic aldehydes were used. The aromatic aldehydes contained both electron-donating and electron-withdrawing groups. Earlier in some syntheses of **3**, the *N*-benzoylhydrazones derived from aromatic aldehydes containg an electron-donating group were the only ones used [3e][3h]. Longer reaction times and unsatisfactory yields are also the drawbacks associated with various previous methods. For example, the *N*-benzoylhydrazone **1k** derived from furan-2-carboxaldehyde afforded the allylated product **3k** with our method in 45 min with a yield of 86% (*Table*, *Entry k*), while an earlier method [3c] using allyltributylstannane and $SnCl_4$ required more than 20 h to furnish the same product **3k** from **1k** with a yield of 56%. Another drawback of the previous methods was the utilization of costly reagents and catalysts such as $Sc(OTf)_3$ [3a], while our method requires the highly available and less costly metal Zn and an aqueous NH_4Cl solution. Organic reactions in aqueous media have been highly encouraged in recent years due to eco-economic benefits. In our method, an aqueous medium was successfully utilized for the preparation of *N*-(but-3-en-1-yl)hydrazide derivatives. The structures of the products were established from their spectral (IR, ^{1}H- and ^{13}C-NMR, and MS) and anal. data.

Conclusion. – We developed an efficient, cost-effective, and high-yielding method for the allylation of *N*-benzoylhydrazones. The mild reaction conditions, rapid conversions, simple experimental procedure, and the aqueous reaction medium are the notable advantages of the method.

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Experimental Part

Reaction of N-*Benzoylhydrazones with Allyl Bromide: General Procedure.* To a soln. of an *N*-benzoylhydrazone **1** (1 mmol, 266 mg) in THF (3 ml), activated Zn powder (5 mmol, 327 mg) and $CH_2{=}CHCH_2Br$ (**2**; 2.2 mmol, 0.2 ml) were added at 0°, and the mixture was stirred for 2–5 min. Then, sat. NH_4Cl soln. (3 ml) was added dropwise at 0°, and the soln. was stirred for 20–30 min at r.t. The mixture was extracted with AcOEt (2 × 10 ml), the org. layer dried (anh. Na_2SO_4) and concentrated, and the residue subjected to column chromatography (SiO_2, hexane/AcOEt): pure allylated product **3**.

N′*-[1-(4-Fluorophenyl)but-3-en-1-yl]benzohydrazide* (**3b**): IR: 3306, 1638, 1517, 1465, 1217. ^{1}H-NMR: 7.81 (br. *s*, 1 H); 7.60 (*d*, *J* = 8.0, 2 H); 7.49–7.25 (*m*, 6 H); 7.04–6.92 (*m*, 2 H); 5.73 (*m*, 1 H); 5.18–5.02 (*m*, 2 H); 4.11 (*t*, *J* = 7.0, 1 H); 2.31–2.34 (*m*, 2 H). ^{13}C-NMR: 167.1; 162.2 (*d*, *J* = 280); 137.2; 132.8; 131.7; 129.2; 128.5; 127.0; 118.1; 115.1 (*d*, *J* = 10.0); 63.0; 40.2. ESI-MS: 285 ($[M + H]^+$). Anal. calc. for $C_{17}H_{17}FN_2O$: C 71.38, H 5.99, N 9.86; found: C 71.41, H 6.03, N 9.91.

N′*-[1-(4-Isopropylphenyl)but-3-en-1-yl]benzohydrazide* (**3f**): IR: 3285, 1641, 1517, 1461, 1308. ^{1}H-NMR: 7.77 (br. *s*, 1 H); 7.61 (*d*, *J* = 8.0, 2 H); 7.51–7.24 (*m*, 6 H); 7.19 (*d*, *J* = 8.0, 2 H); 5.82 (*m*, 1 H); 5.23–5.08 (*m*, 2 H); 4.12 (*t*, *J* = 7.0, 1 H); 2.90 (*m*, 1 H); 2.56–2.43 (*m*, 2 H); 1.22 (*d*, *J* = 7.0, 6 H). ^{13}C-NMR: 167.1; 148.2; 139.0; 134.9; 132.0; 128.8; 128.0; 127.1; 127.0; 117.9; 63.3; 40.1; 33.8; 23.7. ESI-MS: 309 ($[M + H]^+$). Anal. calc. for $C_{20}H_{24}FN_2O$: C 77.92, H 7.79, N 9.09; found: C 72.96, H 7.82, N 9.12.

N′*-[1-(3,4,5-Trimethoxyphenyl)but-3-en-1-yl]benzohydrazide* (**3h**): IR: 3292, 1641, 1591, 1505, 145. ^{1}H-NMR: 7.71–7.59 (*m*, 3 H); 7.49–7.31 (*m*, 4 H); 6.59 (*s*, 2 H); 5.81 (*m*, 1 H); 5.26–5.09 (*m*, 2 H); 4.02 (*t*, *J* = 7.0, 1 H); 3.80 (*s*, 9 H); 2.48–2.40 (*m*, 2 H). ^{13}C-NMR: 168.1; 152.9; 137.0; 135.2; 134.0; 131.8; 130.2; 128.7; 127.2; 117.9; 105.0; 64.9; 60.5; 55.8; 38.9. ESI-MS: 357 ($[M + H]^+$). Anal. calc. for $C_{17}H_{17}N_3O_3$: C 67.42, H 6.74, N 7.87; found: C 67.47, H 6.79, N 7.81.

N′*-[1-(3-Nitrophenyl)but-3-en-1-yl]benzohydrazide* (**3i**): IR: 3295, 1644, 1607, 1527, 1458. ^{1}H-NMR: 7.72–7.60 (*m*, 3 H); 7.58–7.35 (*m*, 4 H); 7.18 (*t*, *J* = 7.0, 1 H); 6.79–6.54 (*m*, 3 H), 5.92 (*m*, 1 H); 5.21–5.10 (*m*, 2 H); 4.08 (*t*, *J* = 7.0, 1 H); 2.52–2.47 (*m*, 2 H). ^{13}C-NMR: 167.3; 148.2; 135.5; 135.0; 132.2; 129.7; 129.0; 127.3; 118.2; 117.1; 116.8; 112.1; 112.0; 64.1; 40.5. ESI-MS: 312 ($[M + H]^+$). Anal. calc. for $C_{17}H_{17}N_3O_3$: C 65.60, H 5.47, N 13.51; found: C 65.64, H 5.50, N 13.55.

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