



Aerobic photooxidation of benzylamide under visible light irradiation with a combination of 48% aq HBr and Ca(OH)₂

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ABSTRACT

Benzylamides were found to be oxidized to their corresponding diacylamines in the presence of molecular oxygen, catalytic 48% aq HBr, and Ca(OH)₂ under visible light irradiation of a fluorescent lamp.

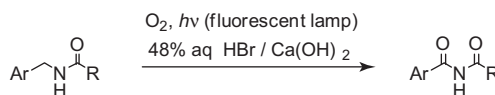
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Diacylamines have not only been used as the starting materials for preparation of N-containing heterocycles,¹ but also have been focused on from the viewpoint of biological activity.² Generally, the preparation of diacylamines involves acylation of amides with anhydrides,³ acyl chlorides,^{2,4} or ketene,⁵ and with α,α,α -trichloromethyl carbonyl compounds⁶ and enol esters;⁷ however, these methods suffer from some problems, such as low yield or high environmental impact of the solvents used or waste produced. With these perspectives, we have studied the oxidation with molecular oxygen, and recently, we found that benzylamides are oxidized to the corresponding diacylamines successfully under external irradiation with 500 W Xenon lamp in the presence of a catalytic amount of iodine.⁸ Although this method is of interest in keeping with the notion of green chemistry due to non-use of heavy metals, waste reduction, use of molecular oxygen, inexpensive acquisition of reagents, and environmentally low-impact solvent, the use of 500 W Xenon lamp is expensive and has harmful effect on the human body, so there is room for improvement. This is the driving force of our further study on this oxidation with a new catalyst, and we have found that a catalytic amount of 48% aq HBr and Ca(OH)₂ enables us to carry out the aerobic photooxidation of a benzylamide to the corresponding diacylamine under visible light irradiation from a general-purpose fluorescent lamp (Scheme 1).⁹ The effective use of VIS is one of the most important research themes which now forwards the development of new energy conversion and energy-using technology, and our new oxidation method is interesting since not much is reported about application of photooxidation with visible light from a general-purpose fluorescent lamp to fine chemistry. Herein we report our data on the scope and limitations of this aerobic photooxidation of benzylamides to the diacylamines under visible light irradiation.

Table 1 shows the results of study of reaction conditions for aerobic oxidation of *N*-benzylacetamide (**1**) under external irradiation with a fluorescent lamp.¹⁰ Among the solvents and catalysts exam-

ined, ethyl acetate in combination with 48% aq HBr and Ca(OH)₂ provides *N*-acetylbenzamide (**2**) most efficiently (entry 35). Without base, benzoic acid was obtained as the main product (entry 13). The fact that **2** was not obtained or was obtained only in low yield without either visible light irradiation or molecular oxygen shows the necessity of both these parameters for this reaction (entries 37 and 38). Interestingly, the obtained yield of **2** without stirring as a reaction condition was almost as same as that under stirring conditions (entry 39). We also noted that this reaction proceeded even under air (entry 40).

Table 2 shows the scope and limitation of this oxidation under the reaction conditions mentioned above. It is noted that this reaction was complete in shorter reaction time compared with our previous reaction which required the special 500 W Xenon lamp.⁸ *N*-Benzylacetamide (**1**), *N*-(4-methylbenzyl)acetamide (**5**), *N*-(4-chlorobenzyl)acetamide (**7**), and *N*-benzyl-3-methylbutylamide (**13**) which possess a moderate electron-donating or electron-withdrawing group at aromatic nucleus, produce the corresponding diacylamines (**2**, **6**, **8**, and **14**) in good yields (entries 1, 3, 4 and 7); however, *N*-(4-methoxybenzyl)acetamide (**3**) is intact under this condition (entry 2). *N*-(2-Methylbenzyl)acetamide (**9**) gives *N*-acetyl-2-methylbenzamide (**10**) only in moderate yield due to steric hindrance of methyl group at *ortho* position (entry 5). *N*-(1-Naphthyl)acetamide (**11**) and *N*-benzylbenzamide (**15**) give the corresponding products, respectively, (**12** and **16**) in 39% and 95% yields when using Mg(OH)₂ instead of Ca(OH)₂ (entries 6 and 8). Interestingly, *N*-benzoylbenzamide (**16**) was obtained in excellent yield (95%), which was obtained in modest yield (55%) in our previous reaction.⁸ *N*-Benzyl-*N*-methylacetamide (**17**) and 2-acetyl-3,4-dihydro-1-isoquinoline (**19**), which are tertiary amides, are also

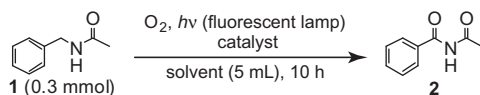


Scheme 1.

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Table 1
Study of reaction conditions for aerobic photooxidation of amide



Entry	Catalyst (equiv)	Solvent	Yield ^a (%)
1	I ₂ (0.2)	EtOAc	11
2	MgI ₂ (0.2)	EtOAc	0
3	Br ₂ (0.2)	EtOAc	54
4	CBR ₄ (0.2)	EtOAc	48
5	LiBr (0.2)	EtOAc	70
6	NaBr (0.2)	EtOAc	0
7	KBr (0.2)	EtOAc	0
8	MgBr ₂ ·Et ₂ O (0.2)	EtOAc	59
9	CaBr ₂ (0.2)	EtOAc	72
10	SrBr ₂ (0.2)	EtOAc	56
11	AlBr ₃ (0.2)	EtOAc	38
12	SmBr ₃ (0.2)	EtOAc	42
13	48% aq HBr (0.2)	EtOAc	39 ^b
14	48% aq HBr (0.2), LiOH (0.2)	EtOAc	83
15	48% aq HBr (0.2), NaOH (0.2)	EtOAc	57
16	48% aq HBr (0.2), KOH (0.2)	EtOAc	46
17	48% aq HBr (0.2), Mg(OH) ₂ (0.1)	EtOAc	81
18	48% aq HBr (0.2), Ca(OH) ₂ (0.1)	EtOAc	86
19	48% aq HBr (0.2), Ba(OH) ₂ (0.1)	EtOAc	55
20	48% aq HBr (0.2), Co(OH) ₂ (0.1)	EtOAc	21
21	48% aq HBr (0.2), Na ₂ CO ₃ (0.1)	EtOAc	11
22	48% aq HBr (0.2), K ₂ CO ₃ (0.1)	EtOAc	10
23	48% aq HBr (0.2), CaCO ₃ (0.1)	EtOAc	64
24	48% aq HBr (0.2), Ca(OH) ₂ (0.1)	Hexane	0
25	48% aq HBr (0.2), Ca(OH) ₂ (0.1)	CH ₂ Cl ₂	0
26	48% aq HBr (0.2), Ca(OH) ₂ (0.1)	<i>i</i> -Pr ₂ O	0
27	48% aq HBr (0.2), Ca(OH) ₂ (0.1)	THF	2
28	48% aq HBr (0.2), Ca(OH) ₂ (0.1)	Acetone	0
29	48% aq HBr (0.2), Ca(OH) ₂ (0.1)	MeCN	57
30	48% aq HBr (0.2), Ca(OH) ₂ (0.1)	MeOH	0
31	48% aq HBr (0.2), Ca(OH) ₂ (0.1)	H ₂ O	0
32	48% aq HBr (0.2), Ca(OH) ₂ (0.2)	EtOAc	73
33	48% aq HBr (0.2), Ca(OH) ₂ (0.05)	EtOAc	74
34	48% aq HBr (0.3), Ca(OH) ₂ (0.15)	EtOAc	68
35	48% aq HBr (0.05), Ca(OH) ₂ (0.025)	EtOAc	95
36	48% aq HBr (0.01), Ca(OH) ₂ (0.005)	EtOAc	0
37	48% aq HBr (0.05), Ca(OH) ₂ (0.025)	EtOAc	0 ^c
38	48% aq HBr (0.05), Ca(OH) ₂ (0.025)	EtOAc	11 ^d
39	48% aq HBr (0.05), Ca(OH) ₂ (0.025)	EtOAc	96 ^e
40	48% aq HBr (0.05), Ca(OH) ₂ (0.025)	EtOAc	66 ^f

^a ¹HNMR yields.

^b Benzoic acid (51%) was obtained.

^c The reaction was carried out in the dark.

^d The reaction was carried out under Ar.

^e The reaction was carried out without stirring.

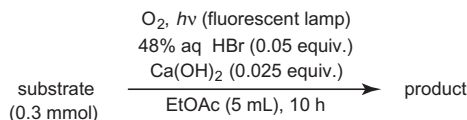
^f The reaction was carried out under air.

oxidized, and the corresponding diacylamines (**18** and **20**) are formed in 71% and 39% yields, respectively.

Scheme 2 shows a plausible path of this oxidation. It takes into account the necessity of continuous irradiation, a catalytic amount of 48% aq HBr, Ca(OH)₂, and molecular oxygen for this reaction. Amide initially reacts with bromine radical, generated from hydrogen bromide by irradiation with fluorescent lamp in the presence of molecular oxygen, to give benzyl radical species **22**. The resulting radical species **22** traps molecular oxygen to afford peroxy radical **23**, which is subsequently transferred to hydroperoxide **24** by abstraction of hydrogen radical from **21** or hydrogen bromide. Diacylamine is formed through dehydration from **24**.¹¹

In conclusion, we report a novel and practical method for preparation of diacylamines by aerobic photooxidation of amides in the presence of the catalytic amount of 48% aq HBr and Ca(OH)₂ under visible light irradiation. This oxidation is a facile and convenient method from the viewpoint of synthetic organic chemistry, and is of relevance from green chemistry perspectives because of using

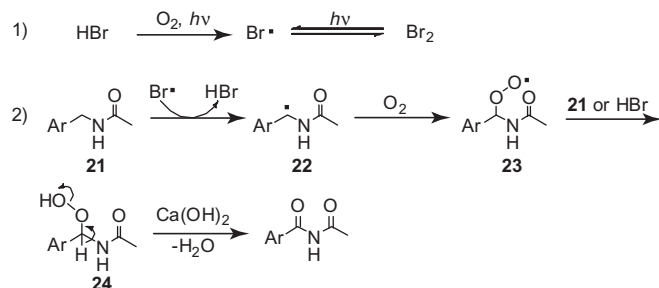
Table 2
Aerobic photooxidation of benzylamides



Entry	Substrate	Product	Yield ^a (%)
1	1	2	88
2	3	4	0
3	5	6	62
4	7	8	76
5	9	10	54
6	11	12	39 ^b
7	13	14	81
8	15	16	95 ^b
9	17	18	71
10	19	20	39

^a All yields were for pure, isolated products.

^b Mg(OH)₂ was used instead of Ca(OH)₂.



Scheme 2. Plausible path of the aerobic photooxidation of amide.

molecular oxygen and visible light irradiation from general-purpose fluorescent lamp. Further studies directed toward additional applications are in progress in our laboratory.

References and notes

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10. A typical procedure (entry 35) follows: A dry EtOAc solution (5 mL) of the *N*-benzylacetamide (**1**, 0.3 mmol), 48% aq HBr (0.015 mmol), and Ca(OH)₂ (0.0075 mmol) in a pyrex test tube equipped with an O₂ balloon, was irradiated for 10 h with four 22 W fluorescent lamps, which were set up at a distance of 65 mm. The reaction mixture was concentrated under reduced pressure, and the pure product was obtained by preparative TLC.
11. We think that Ca(OH)₂ works as base, not as a progenitor of CaBr₂, since CaBr₂ was not detected in optimal condition and was poor catalyst than combination of 48% aq HBr and Ca(OH)₂ (Table 1. Entries 9 and 18).