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Photocatalytic intramolecular carboazidation of *N*-arylacrylamides into 3-(azidomethyl)indolin-2-ones

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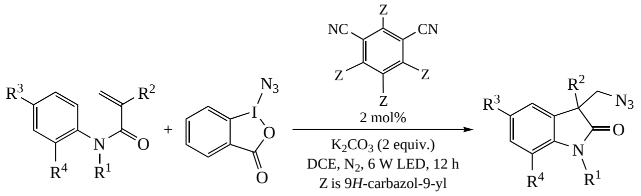
Intramolecular carboazidation of *N*-arylacrylamides with 1-azido-1λ^3-benzo[*d*][1,2]iodaoxol-3(1*H*)-one (the N$_3$-Togni reagent) affording 3-(azidomethyl)indolin-2-ones proceeds at room temperature under visible light irradiation with 2,4,5,6-tetra(carbazol-9-yl)-1,3-dicyanobenzene assistance. The latter provides the formation of azido radicals from the N$_3$-Togni reagent. The investigated substrate scope involves 12 examples.



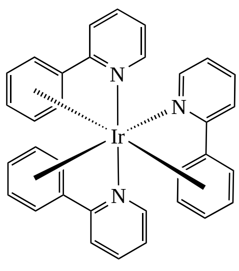
Keywords: carboazidation, arylacrylamides, indolin-2-ones, radical cyclization, N$_3$-Togni reagent, photocatalysis.

Compounds with oxindole skeleton are met among natural products, drug molecules and functional materials,[1–3] and show antitumor, antibacterial and anticancer activities. Generally, such compounds can be prepared through the Mannich, Henry or Michael reactions and cycloaddition transformations.[4] However, in those cases strong acids or strong alkalis were usually required while some syntheses involved multi-step procedures.

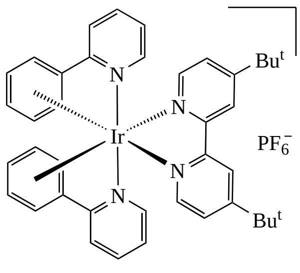
On the other hand, organic azides represent very important class of compounds. They are used in the fields of energetic materials, supramolecular materials and medicinal chemistry.[5,6] The azido group can be introduced into organic molecules by means of nucleophilic addition, nucleophilic substitution,[6] transition metal-catalyzed C–H azidation reaction[7] and other methods. Meantime, the search for other methods for the azide preparation is not undesired. In recent years, the radical azidation has attracted extensive interest. Zard systematically summarized diverse radical azidation reactions.[8] Nevado reported on the azidoarylation of activated alkenes mediated by radicals using azidobenziodoxolone (ABX) as the N$_3$ source.[9] Liu described the azidation reaction of heterocycles using the PhI(OAc)$_2$/TMSN$_3$ system.[10]

Obviously, the combination of the oxindole skeleton and the azido group in one molecule seems of great significance. In recent years, some attempts in this field were documented. Azido radicals were generated from TMSN$_3$ or NaN$_3$ in the presence of oxidants such as PhI(OCOCF$_3$)$_2$[1] or K$_2$S$_2$O$_8$[11] as well as metal catalysts like AgNO$_3$[12,13] and Mn(OAc)$_3$.[14] The addition of N$_3^{\cdot}$ radical at the double bond of *N*-arylacrylamides was followed by intramolecular cyclization to finally produce the corresponding oxindole derivatives. In order to overcome the drawbacks of the above system, which requires the use of a large amount of catalyst or oxidant and high temperature conditions, Wu and coworkers[15] recently reported a visible-light-promoted radical azidation reaction at room temperature. Although the reaction conditions were mild, MnCl$_2$ was used as a principal additive to achieve satisfactory yields. To further develop a simple and effective method to access azido oxindoles, herein we report on a visible-light-promoted carboazidation of arylacrylamides using N$_3$-Togni reagent in the absence of extra oxidants.

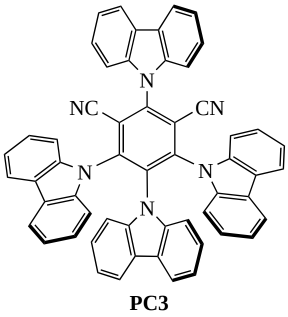
Initially, *N*-methyl-*N*-phenylmethacrylamide **1a** and N$_3$-Togni reagent (1-azido-1λ^3-benzo[*d*][1,2]iodaoxol-3(1*H*)-one) **2** were selected as the model substrates to screen the reaction conditions (Scheme 1, Table 1). Several photocatalysts (PCs) such as **PC1**–**PC4** were evaluated (see Table 1, entries 1–4). Good 74% yield of **3a** was achieved by employing **PC3** as the photocatalyst, K$_2$CO$_3$ as the base in dichloromethane (DCM). Importantly, among the catalysts tested **PC3** did not contain metal. Different



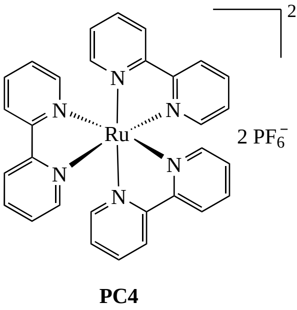
PC1



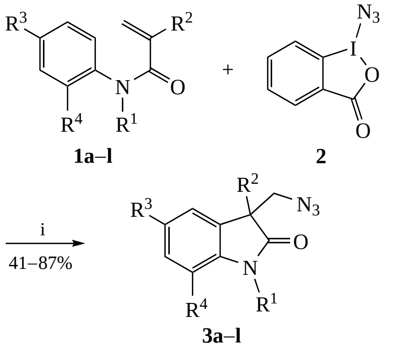
PC2



PC3



PC4



a $R^1 = R^2 = Me, R^3 = R^4 = H$
b $R^1 = R^2 = R^3 = Me, R^4 = H$
c $R^1 = R^2 = Me, R^3 = OMe, R^4 = H$
d $R^1 = R^2 = Me, R^3 = Bu^t, R^4 = H$
e $R^1 = R^2 = Me, R^3 = OCF_3, R^4 = H$
f $R^1 = R^2 = Me, R^3 = F, R^4 = H$
g $R^1 = R^2 = Me, R^3 = NO_2, R^4 = H$
h $R^1 = R^2 = Me, R^3 = H, R^4 = Ph$
i $R^1 = Pr^i, R^2 = Me, R^3 = R^4 = H$
j $R^1 = Bn, R^2 = Me, R^3 = R^4 = H$
k $R^1 = Ph, R^2 = Me, R^3 = R^4 = H$
l $R^1 = Me, R^2 = Bn, R^3 = R^4 = H$

Scheme 1 *Reagents and optimized conditions*: i, substrate **1** (0.2 mmol), **2** (0.4 mmol), catalyst **PC3** (2 mol%), K_2CO_3 (0.4 mmol), DCE (2 ml), sealed Schlenk tube, irradiated by a 2 × 3 W Blue LED, N_2, room temperature, 12 h.

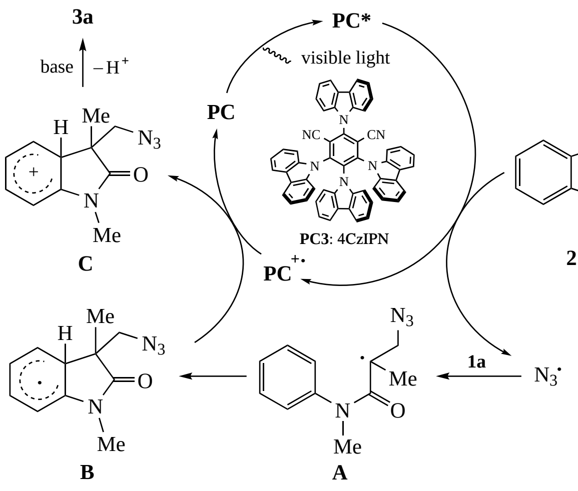
Table 1 Optimization of carboazidation of compound **1a** with N_3-Togni reagent **2**.[a]

Entry	Catalyst	Base	Solvent	Yield of **3a** (%)[b]
1	**PC1**	K_2CO_3	DCM	51
2	**PC2**	K_2CO_3	DCM	68
3	**PC3**	K_2CO_3	DCM	74
4	**PC4**	K_2CO_3	DCM	< 5
5	**PC3**	K_2CO_3	MeCN	37
6	**PC3**	K_2CO_3	DMF	25
7	**PC3**	K_2CO_3	THF	42
8	**PC3**	K_2CO_3	DCE	81 (53,[c] 80,[d] 0[e])
9	**PC3**	Cs_2CO_3	DCE	77
10	**PC3**	K_3PO_4	DCE	69
11	**PC3**	$KOBu^t$	DCE	messy
12	**PC3**	Na_2CO_3	DCE	62

[a] *Reaction conditions*: **1a** (0.2 mmol), **2** (0.4 mmol), catalyst (2 mol%), base (0.4 mmol), solvent (2 ml), 12 h, in a sealed Schlenk tube, irradiated by a 2 × 3 W Blue LED, N_2, room temperature, 12 h. [b] Isolated yield. [c] With 0.2 mmol of **2**. [d] With 0.6 mmol of **2**. [e] Without catalyst or K_2CO_3 or blue LEDs.

solvents were then tried, and the yield of **3a** was further improved to 81% in dichloroethane (DCE) (entry 8). Relatively lower yields were obtained when switching the base to Cs_2CO_3, K_3PO_4 or Na_2CO_3, while messy products were observed in the presence of $KOBu^t$ (entries 9–12). Reducing the dosage of azide reagent **2** to 1 equiv. led to a decrease in the yield, while further increasing the dosage of azide reagent **2** was not beneficial to the reaction (entry 8). Control experiment showed that the reaction did not occur in the absence of either base or photocatalyst (entry 8).

The substrate scope was then explored (Scheme 1).[†] Both electron-withdrawing and electron-donating groups in the benzene ring of *N*-arylacrylamides **1a–g** showed good compatibilities, the corresponding products **3a–g** being formed in moderate to good yields (53–81%). Obvious steric hindrance was observed for *ortho*-phenyl substituted arylacrylamide **1h** (yield of **3h** was 41%). Azidation of substrates with other substituents R^1/R^2 **1i–l** also afforded products **3i–l** in good yields.



Scheme 2

Some control experiments were then performed. No desired product **3a** was observed in the presence of either 2 equiv. of 2,2,6,6-tetramethylpiperidine *N*-oxide (TEMPO), 1,1-diphenylethylene or 2,6-di-*tert*-butyl-4-methylphenol (BHT). These results demonstrate that this reaction probably proceeds *via* a radical mechanism. Based on the above mechanistic studies and related literature reports,[15–17] a plausible mechanism is outlined in Scheme 2. Initially, photocatalyst **PC3** is excited to **PC3*** under blue LED irradiation. Then a single electron transfer from **PC3*** to N_3-Togni reagent **2** would generate azide radical $N_3^{\cdot}$ and radical cation $\mathbf{PC3}^{+\cdot}$. Radical $N_3^{\cdot}$ attacks *N*-methyl-*N*-phenylmethacrylamide **1a** to give the radical intermediate **A**. Next, intramolecular cyclization of intermediate **A** provides the radical intermediate **B**, which is oxidized with $\mathbf{PC3}^{+\cdot}$ to result in intermediate **C** and recovers **PC**. Finally, the deprotonative aromatization of **C** delivers product **3a**.

In summary, a visible-light-promoted intamolecular carboazidation of *N*-arylacrylamides with the N_3-Togni reagent at room temperature has been developed. The reactions proceeded smoothly to provide the desired azide oxindoles in good yields. No extra oxidants or metal catalysts were required in the reaction system.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2024.10.021.

References

1 K. Matcha, R. Narayan and A. P. Antonchick, *Angew. Chem., Int. Ed.*, 2013, **52**, 7985; https://doi.org/10.1002/anie.201303550.

2 M. Kaur, M. Singh, N. Chadha and O. Silakari, *Eur. J. Med. Chem.*, 2016, **123**, 858; https://doi.org/10.1016/j.ejmech.2016.08.011.

3 A. D. Marchese, E. M. Larin, B. Mirabi and M. Lautens, *Acc. Chem. Res.*, 2020, **53**, 1605; https://doi.org/10.1021/acs.accounts.0c00297.

4 W. C. Sumpter, *Chem. Rev.*, 1945, **37**, 443; https://doi.org/10.1021/cr60118a003.

5 S. Bräse, C. Gil, K. Knepper and V. Zimmermann, *Angew. Chem., Int. Ed.*, 2005, **44**, 5188; https://doi.org/10.1002/anie.200400657.

6 P. Thirumurugan, D. Matosiuk and K. Jozwiak, *Chem. Rev.*, 2013, **113**, 4905; https://doi.org/10.1021/cr200409f.

7 W. Song, S. I. Kozhushkov and L. Ackermann, *Angew. Chem., Int. Ed.*, 2013, **52**, 6576; https://doi.org/10.1002/anie.201302015.

8 S. Z. Zard, *Chem. Soc. Rev.*, 2008, **37**, 1603; https://doi.org/10.1039/B613443M.

9 W. Kong, E. Merino and C. Nevado, *Angew. Chem., Int. Ed.*, 2014, **53**, 5078; https://doi.org/10.1002/anie.201311241.

10 Z. Liu and Z.-Q. Liu, *Org. Lett.*, 2017, **19**, 5649; https://doi.org/10.1021/acs.orglett.7b02788.

11 J. Qiu and R. Zhang, *Org. Biomol. Chem*., 2014, **12**, 4329; https://doi.org/10.1039/C4OB00720D.

12 X.-H. Wei, Y.-M. Li, A.-X. Zhou, T.-T. Yang and S.-D. Yang, *Org. Lett*., 2013, **15**, 4158; https://doi.org/10.1021/ol402138y.

13 Y. Yuan, T. Shen, K. Wang and N. Jiao, *Chem. – Asian J*., 2013, **8**, 2932; https://doi.org/10.1002/asia.201300960.

14 D. Zhao, K. Kang, W. Wan, H. Jiang, H. Deng, Y. Chen and J. Hao, *Org. Chem. Front*., 2017, **4**, 1555; https://doi.org/10.1039/C7QO00217C.

15 C. Pei, Y. Liu, X. Chen, J. Li, D. Zou, Y. Wu and Y. Wu, *Adv. Synth. Catal*., 2023, **365**, 860; https://doi.org/10.1002/adsc.202201201.

16 C.-M. Chan, Q. Xing, Y.-C. Chow, S.-F. Hung and W.-Y. Yu, *Org. Lett*., 2019, **21**, 8037; https://doi.org/10.1021/acs.orglett.9b03020.

17 D. Maiti, K. Mahanty and S. De Sarkar, *Chem. – Asian J*., 2021, **16**, 748; https://doi.org/10.1002/asia.202100121.

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