# Iodobenzene diacetate (PIDA)/Zn(II)-mediated oxidation and cleavage of C–C bond: formation of substituted N-aryl carbamoyl methyl diacetates and derivatives from 3-oxo-butanamides

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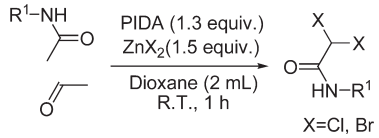
Various substituted N-aryl carbamoyl methyl diacetates have been synthesized from N-aryl-3-oxobutanamides via a diacetoxylation mediated by the combination of iodobenzene diacetate (PIDA)/$Zn(OAc)_2$. This provides a new convenient method to form C–O bonds and cleave C–C bonds. Ten examples were obtained from easily available materials in good to excellent yields.

**Keywords**: cleave C–C bond, acetoxylation, oxidation of (N-aryl substituted-carbamoyl) methyl diacetates

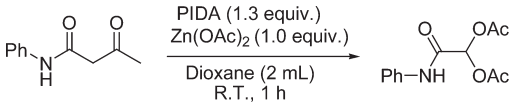
Hypervalent iodine(III) reagents[1,14] have received considerable attention in the literature.[15,17] We have developed novel reactions by using hypervalent iodine(III) reagents, especially iodobenzene diacetate (PIDA), and have applied them to synthesise new compounds, such as polysubstituted pyrroles, 1,2-diheteroatom-substituted (*E*)-alkenes and tetrasubstituted (*E*)-alkenes.[18,19] Recently, we have reported an efficient oxidative approach to the synthesis of 2,2-dihalo-N-phenylacetamides by using PIDA (Scheme 1).[20] In order to understand the mechanism and the scope of this reaction, we replaced the halogen anion of the zinc salt with acetate ion and surprisingly found that (phenylcarbamoyl)methyl diacetate was produced as the major product (Scheme 2).

Subsequently, we used a range of 3-oxo-N-phenylbutanamides, under the same conditions (Table 1), to test this strategy for the synthesis of (N-aryl substituted-carbamoyl)methyl diacetate derivatives. From the results we can see that the yield was decreased when the phenyl ring was substituted by electron-donating groups, such as halogen (Cl) (**1c**, **ld**), methyl (**1b**), methoxyl group (**1e**, **1f**). The positions of substituents on the benzene ring had little effect on this transformation. A *para*-substituent was more effective than an *ortho*-substitutent, as shown by their corresponding yields. For example, N-(4-chlorophenyl)-3-oxobutanamide (**1c**) and N-(4-methoxyphenyl)-3-oxobutanamide (**1e**) were better substrates compared to their *ortho*-substituted partners (**1c**, **1f**) in this method and gave the corresponding product in higher yield (Scheme 3, **2c**, **2d**, **2e** and **2f**). Additionally, 3-oxo-N-alkylbutanamides were also suitable substrates for this protocol. For instance, N-methyl-3-oxobutanamide (**1j**) reacted under the same conditions to give (methylcarbamoyl)methyl acetate (**2j**) in 77% isolated yield.

Based on our previous report,[20] a mechanistic proposal for this transformation, exemplified by the formation of **2a**, is outlined in Scheme 3. In this process, the first step involves the activation of 3-oxo-N-phenylbutanamide by Zn(II) to form **3**.




**Scheme 1** Synthesis of 2,2-dihalo-N-phenylacetamides.




**Scheme 2** Synthesis of (phenylcarbamoyl)methyl diacetate.

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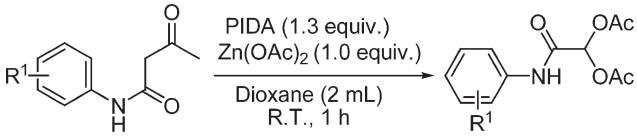
This is followed by diacetoxylation of the activated methylene of 3-oxo-N-phenylbutanamide in the presence of PIDA and leads to the diacetylated product **4**. Subsequent nucleophilic attack of acetate ion on the carbon atom of the carbonyl group affords intermediate **5**. Then, the carbon–carbon bond cleavage of the labile intermediate **5** by a retro-Claisen condensation reaction[22] generates intermediate **6**. Finally, the electrophilic attack of proton on carbon–carbon double bond affords the final product (phenylcarbamoyl)methyl diacetate (**2a**).

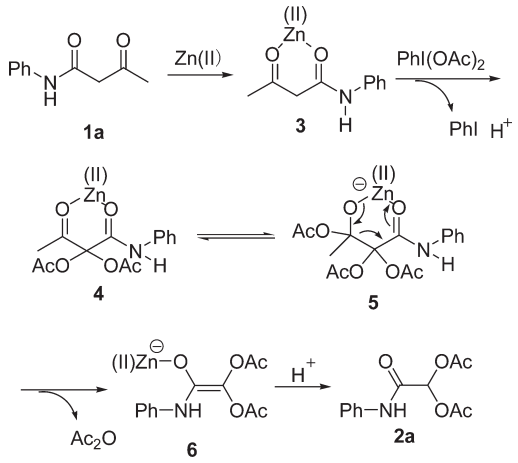
**Table 1** Synthesis of (N-aryl substituted-carbamoyl)methyl diacetate derivatives[a]




1 2

| Entry | 1 | Product | Yields/%[b] |
|---|---|---|---|
| 1 | R=H (**1a**) | **2a** | 80 |
| 2 | R=*o*-methyl (**1b**) | **2b** | 72 |
| 3 | R=*o*-chloro (**1c**) | **2c** | 76 |
| 4 | R=*p*-chloro (**1d**) | **2d** | 79 |
| 5 | R=*p*-methoxyl (**1e**) | **2e** | 71 |
| 6 | R=*o*-methoxyl (**1f**) | **2f** | 69 |
| 7 | R=*p*-oxethyl (**1g**) | **2g** | 67 |
| 8 | R=2,5-dimethoxyl (**1h**) | **2h** | 63 |
| 9 | R=2,5-dimethoxyl-4chloro (**1i**) | **2i** | 61 |
| 10 | N-methyl-3-oxobutanamide (**1j**) | **2j** | 77 |

[a] All the reactions were carried out: 1 (1.0 mmol), dioxane (2 mL), DIB (1.3 equiv.), $Zn(OAc)_2$(1.0 equiv.).
[b] Isolated yields.




**Scheme 3** Possible reaction mechanism.

In conclusion, we have developed an efficient method for the synthesis of substituted N-aryl carbamoyl methyl diacetate derivatives via an activated acetonylation process of a methylene followed by a C–C bond cleavage using the combination of PIDA/$Zn(OAc)_2$. This protocol provides a new, useful route to activate a methylene and construct C–O bonds. The two acetoxyl groups of the resultant products are ready to be converted into other functional groups, such as, hydroxyl and carbonyl. The current direction of our future research is aimed at extending the scope and potential synthetic applications of this reaction.

## Experimental

All the reactions were carried out at room temperature in a Schlenk tube equipped with magnetic stirrer bar. Solvents and reagents were used as received. $^1$H NMR spectra was recorded in $CDCl_3$ at 400 MHz and $^{13}$C NMR spectra was recorded in $CDCl_3$ at 100 MHz. GC–MS were obtained using electron ionisation (EI). IR spectra were obtained as potassium bromide pellets or as liquid films between two potassium bromide pellets with a Bruker Vector 22 spectrometer. TLC was performed using commercially prepared 100–400 mesh silica gel plates (GF254), and visualisation was effected at 254 nm. All the other chemicals were purchased from Aldrich Chemicals.

*Synthesis of 2, 2-dichloro-N-phenylacetamide* (**2a**)*; typical procedure* Iodobenzene diacetate (PIDA) (419 mg, 1.3 mmol), dioxane (2 mL), 3-oxo-N-phenylbutanamide (**1a**) (177 mg, 1.0 mmol) and $Zn(OAc)_2$ (183 mg, 1.0 mmol) were added to a 10 mL Schlenk tube. The mixture was stirred at room temperature for 1 h. The solution was directly subjected to separation by PTLC (GF254), and eluted with a 10:2 petroleum ether / ethyl acetate mixture, to furnished **2a** (201 mg, 80%) as a pale yellow oil.

*(Phenylcarbamoyl)methyl diacetate* (**2a**): Pale yellow oil; IR $\nu_{max}$ (KBr): 3273, 1691, 1600, 1544, 1442, 1298, 1174, 968, 860, 810, 756 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 Hz) δ 8.17 (s, 1H), 8.07 (s, 1H), 7.50–7.48 (d, *J* = 8.0 Hz, 2H), 7.27–7.23 (t, *J* = 8.0 Hz, 2H), 7.15–7.11 (t, *J* = 8.0 Hz, 1H), 5.61 (s, 1H), 2.42 (s, 3H), 2.26 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 Hz) δ 168.7, 161.1, 136.4, 129.1, 125.3, 120.3, 79.3, 27.6, 20.5; MS (EI) *m/z* (%): 127.00 (100.00). Anal. Calcd for $C_{12}H_{13}NO_5$: C, 57.37; H, 5.22; N, 5.58. Found: C, 57.55; H, 5.19; N, 5.71%.

*(o-Tolylcarbamoyl)methyl diacetate* (**2b**): Pale yellow oil; IR $\nu_{max}$ (KBr): 3273, 1691, 1600, 1544, 1442, 1298, 1174, 968, 860, 810, 756 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 Hz) δ 8.08 (s, 1H), 7.73–7.71 (d, *J* = 8.0 Hz, 1H), 7.20–7.18 (t, *J* = 8.0 Hz, 2H), 7.10–7.08 (d, *J* = 8.0 Hz, 1H), 5.64 (s, 1H), 2.43 (s, 3H), 2.26 (s, 3H) , 2.23 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 Hz) δ 168.7, 161.2, 134.2, 130.9, 129.5, 127.2, 126.0, 122.9, 79.2, 27.7, 20.4, 17.4; MS (EI) *m/z* (%): 108.00 (100.00). Anal. Calcd for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28. Found: C, 58.77; H, 5.59; N, 5.45%.

*(2-Chlorophenylcarbamoyl)methyl diacetate* (**2c**): Pale yellow oil; IR $\nu_{max}$ (KBr): 3273, 1691, 1600, 1544, 1442, 1298, 1174, 968, 860, 810, 756 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 Hz) δ 8.66 (s, 1H), 8.21-8.19 (d, *J* = 8.0 Hz, 1H), 7.30–7.28 (d, *J* = 8.0 Hz, 1H), 7.20–7.16 (t, *J* = 8.0 Hz, 1H), 7.01–6.97 (t, *J* = 8.0 Hz, 1H), 5.59 (s, 1H), 2.37 (s, 3H), 2.21 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 Hz) δ 168.4, 161.2, 133.3, 129.2, 127.8, 125.6, 123.4, 121.5, 79.1, 27.7, 20.4; MS (EI) *m/z* (%): 43.00 (100.00). Anal. Calcd for $C_{12}H_{12}ClNO_5$: C, 50.45; H, 4.23; N, 4.90. Found: C, 50.63; H, 4.09; N, 5.07%.

*(4-Chlorophenylcarbamoyl)methyl diacetate* (**2d**): Pale yellow oil; IR $\nu_{max}$ (KBr): 3273, 1691, 1600, 1544, 1442, 1298, 1174, 968, 860, 810, 756 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 Hz) δ 8.24 (s, 1H), 7.46–7.44 (d, *J* = 8.0 Hz, 2H), 7.28–7.24 (t, *J* = 8.0 Hz, 2H), 5.60 (s, 1H), 2.43 (s, 3H), 2.26 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 Hz) δ 168.6, 161.0, 134.9, 130.3, 129.0, 121.4, 79.0, 27.6, 20.4; MS (EI) *m/z* (%): 43.00 (100.00). Anal. Calcd for $C_{12}H_{12}ClNO_5$: C, 50.45; H, 4.23; N, 4.90. Found: C, 50.50; H, 4.32; N, 5.01%.

*(4-Methoxyphenylcarbamoyl)methyl diacetate* (**2e**): Pale yellow oil; IR $\nu_{max}$ (KBr): 3273, 1691, 1600, 1544, 1442, 1298, 1174, 968, 860, 810, 756 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 Hz) δ 8.17 (s, 1H), 7.42–7.40 (d, *J* = 8.0 Hz, 2H), 6.87–6.85 (d, *J* = 8.0 Hz, 2H), 5.63 (s, 1H), 3.79 (s, 3H), 2.45 (s, 3H), 2.27 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 Hz) δ 168.7, 161.0, 157.0, 129.4, 122.1, 114.2, 79.2, 55.4, 27.6, 20.5; MS (EI) *m/z* (%): 149.00 (100.00). Anal. Calcd for $C_{13}H_{15}NO_6$: C, 55.51; H, 5.38; N, 4.98. Found: C, 55.33; H, 5.29; N, 5.14%.

*(2-Methoxyphenylcarbamoyl)methyl diacetate* (**2f**): Pale yellow oil; IR $\nu_{max}$ (KBr): 3273, 1691, 1600, 1544, 1442, 1298, 1174, 968, 860, 810, 756 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 Hz) δ 8.72 (s, 1H), 7.06–7.04 (d, *J* = 8.0 Hz, 1H), 694–6.85 (m, 3H), 5.63 (s, 1H), 3.86 (s, 3H), 2.43 (s, 3H), 2.27 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 Hz) δ 168.6, 160.8, 148.3, 126.2, 125.9, 124.8, 121.0, 119.9, 110.1, 79.4, 55.8, 27.6, 20.5; MS (EI) *m/z* (%): 149.00 (100.00). Anal. Calcd for $C_{13}H_{15}NO_6$: C, 55.51; H, 5.38; N, 4.98. Found: C, 55.59; H, 5.21; N, 5.07%.

*(4-Ethoxyphenylcarbamoyl)methyl diacetate* (**2g**): Pale yellow oil; IR $\nu_{max}$ (KBr): 3273, 1691, 1600, 1544, 1442, 1298, 1174, 968, 860, 810, 756 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 Hz) δ 8.05 (s, 1H), 7.37–7.35 (d, *J* = 8.0 Hz, 2H), 6.83–6.81 (d, *J* = 8.0 Hz, 2H), 5.59 (s, 1H), 4.00–3.95 (q, *J* = 8.0 Hz, 2H), 2.42 (s, 3H), 2.24 (s, 3H), 1.38–1.34 (t, *J* = 8.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 100 Hz) δ 168.7, 160.9, 156.4, 129.3, 122.1, 114.9, 79.2, 63.7, 27.6, 20.5, 14.7; MS (EI) *m/z* (%): 163.08 (100.00). Anal. Calcd for $C_{14}H_{17}NO_6$: C, 56.94; H, 5.80; N, 4.74. Found: C, 56.77; H, 5.88; N, 4.83%.

*(2,4-Dimethoxyphenylcarbamoyl)methyl diacetate* (**2h**): Pale yellow oil; IR $\nu_{max}$ (KBr): 3273, 1691, 1600, 1544, 1442, 1298, 1174, 968, 860, 810, 756 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 Hz) δ 8.47 (s, 1H), 6.48–6.40 (m, 3H), 5.61 (s, 1H), 3.82 (s, 3H), 3.74 (s, 3H), 2.42 (s, 3H), 2.25 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 Hz) δ 168.6, 160.4, 157.2, 149.7, 120.9, 119.7, 103.8, 98.7, 79.3, 55.8, 55.5, 27.6, 20.5; MS (EI) *m/z* (%): 123.00 (100.00). Anal. Calcd for $C_{14}H_{17}NO_7$: C, 54.02; H, 5.50; N, 4.50. Found: C, 54.07; H, 5.66; N, 4.71%.

*(2,5-Dimethoxy-4-chlorophenylcarbamoyl)methyl diacetate* (**2i**): Yellow oil; IR $\nu_{max}$ (KBr): 3273, 1691, 1600, 1544, 1442, 1298, 1174, 968, 860, 810, 756 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 Hz) δ 8.71 (s, 1H), 8.07 (s, 1H), 6.87 (s, 1H), 5.61 (s, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 2.43 (s, 3H), 2.27 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 Hz) δ 168.5, 160.8, 149.0, 142.2, 125.5, 116.9, 112.4, 104.9, 79.0, 56.6, 56.5, 27.6, 20.4; MS (EI) *m/z* (%): 153.00 (100.00). Anal. Calcd for $C_{14}H_{16}ClNO_7$: C, 48.64; H, 4.66; N, 4.05. Found: C, 48.66; H, 4.49; N, 4.11%.

*(Methylcarbamoyl)methyl acetate* (**2j**): Pale yellow oil; IR $\nu_{max}$ (KBr): 3273, 1691, 1600, 1544, 1442, 1298, 1174, 968, 860, 810, 756 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 Hz) δ 6.49 (s, 1H), 5.46 (s, 1H), 2.37 (s, 3H), 2.18 (s, 3H), 2.02 (s, 3H); $^{13}$C NMR ($CDCl_3$, 100 Hz) δ 168.6, 163.7, 79.1, 27.7, 26.1, 20.4; MS (EI) *m/z* (%): 193.05 (100.00). Anal. Calcd for $C_7H_{11}NO_5$: C, 44.45; H, 5.86; N, 7.40. Found: C, 44.31; H, 5.97; N, 7.45%.

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## References

1 V.V. Zhdankin and P.J. Stang, *Chem. Rev.*, 2008, **108**, 5299.
2 T. Dohi and Y. Kita, *Chem. Commun.*, 2009, 2073.
3 M.S. Yusubov and V.V. Zhdankin, *Mendeleev Commun.*, 2010, **20**, 185.
4 M. Uyanik and K. Ishihara, *Chem. Commun.*, 2009, 2086.
5 M. Ngatimin and D.W. Lupton, *Aust. J. Chem.*, 2010, **63**, 653.
6 M.S. Yusubov, V.N. Nemykin and V.V. Zhdankin, *Tetrahedron*, 2010, **66**, 5745.
7 V. Satam, A. Harad, R. Rajule and H. Pati, *Tetrahedron*, 2010, **66**, 7659.
8 M. Uyanik and K. Ishihara, *Aldrichim. Acta.*, 2010, **43**, 83.
9 E.A. Merritt and B. Olofsson, *Angew. Chem. Int. Ed.*, 2009, **48**, 9052.
10 E.A. Merritt and B. Olofsson, *Synthesis*, 2011, 517.
11 S. Desjardins, J.C. Andrez and S. Canesi, *Org. Lett.*, 2011, **13**, 3406.
12 F.V. Singh and T. Wirth, *Org. Lett.*, 2011, **13**, 6504.
13 X. Wang, W.X. Ye, S.N. Zhang, J.J. Feng, Y. Xu, Y. Zhang and J.B. Wang, *J. Am. Chem. Soc.*, 2011, **133**, 16410.
14 A.A. Guilbault and C.Y. Legault, *ACS Catal.*, 2012, **2**, 219.
15 J.P. Brand, D.F. González, S. Nicolai and J. Waser, *Chem. Commun.*, 2011, **47**, 102.
16 K. Niedermann, N. Früh, E. Vinogradova, M.S. Wiehn and A. Moreno, *Angew. Chem. Int. Ed.*, 2011, **50**, 1059.
17 M. Uyanik, T. Yasui and K.Ishihara, *Angew. Chem. Int. Ed.*, 2010, **49**, 2175.
18 W.B. Liu, and H.F. Jiang, *Org. Lett.*, 2010, **12**, 312.
19 W.B. Liu, C. Chen and Q. Zhang, *Org. Biomol. Chem.*, 2011, **9**, 4684.
20 W.B. Liu, C. Chen, Q. Zhang and Z.B. Zhu, *Beilstein J. Org. Chem.*, 2012, **8**, 344..
21 J. Christoffers, *Chem. Commun.*, 1997, 943.
22 S. Biswas, S. Maiti and U. Jana, *Eur. J. Org. Chem.*, 2010, 2861.