Pergamon

*Tetrahedron Letters*, Vol. 37, No. 1, pp. 69-72, 1996
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0040-4039/96 $15.00 + 0.00

0040-4039(95)02104-3

# A Novel Reaction of Benzoyl Chloride Adduct of Aromatic *N*-Oxide with Carbonitrile via a Carbene Intermediate

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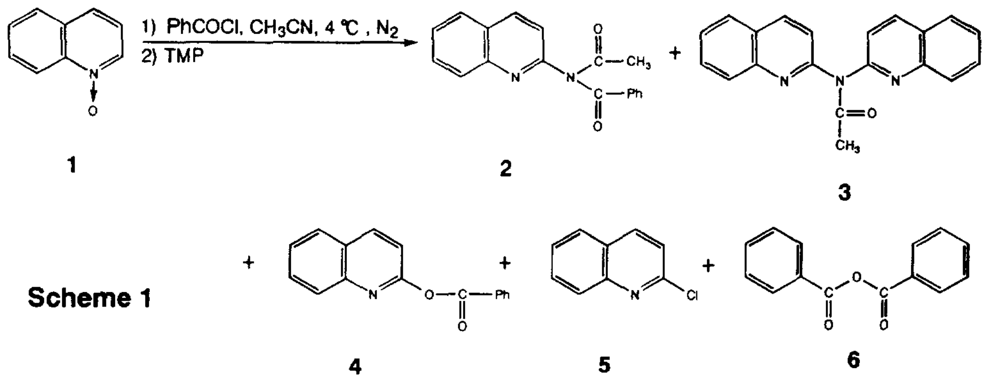
***Abstract***: A carbene intermediate is proposed as a reactive species in the base-induced reaction of benzoyl chloride adducts of pyridine and quinoline *N*-oxides with carbonitriles to give 2-pyridyl- and 2-quinolyl diacylamine as main products.

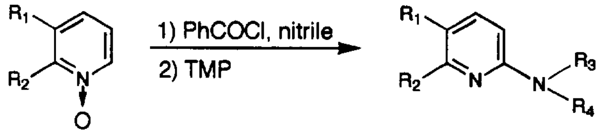
In the course of our investigation of electrophilic reactions of aromatic *N*-oxides through base-induced deprotonation,[1] we found that successive treatment of quinoline 1-oxide **1** (10 mmol) with benzoyl chloride (10 mmol or 12 mmol) and 2,2,6,6-tetramethylpiperidine (TMP, 10 mmol or 12 mmol) in acetonitrile (MeCN) afforded *N*-2-quinolyl-*N*-benzoyl-acetamide[2] (**2**, 30%) and *N*, *N*-bis(2-quinolyl)-acetamide[3] (**3**, 22%) as main products along with 2-benzoyloxyquinoline (**4**, 10%), 2-chloroquinoline (**5**, 12%) and benzoic anhydride (**6**, 47%)(Scheme 1).



**Scheme 1**

Apparently, **2** and **3** evolved from the participation of MeCN in the reaction. The reaction using benzonitrile (PhCN) instead of MeCN proceeded similarly to give *N*, *N*-dibenzoyl-2-aminoquinoline[4] (**7**, 12%) corresponding to **2**. However, participation of the solvent was not apparent in the reaction when THF, benzene, dichloromethane or acetone was used as the solvent instead of MeCN, only small amounts of **4** and **5** being formed. The presence of TMP as a base is essential for the reaction and no reaction occurred without TMP. Triethylamine was shown to be equally effective as TMP giving **2**, **3**, **4**, **5** and **6** in 21, 18, 9, 11 and 51% yields, respectively, but no satisfactory results were obtained with pyridine, *t*-BuOK, NaOEt, DBU and piperidine. It was further found that pyridine 1-oxide also reacts with benzoyl chloride and TMP in MeCN or PhCN; *N*-2-pyridyl-*N*-benzoylacetamide[5] (**8**), 2-benzoylaminopyridine (**9**), or *N*,*N*-dibenzoyl-2-aminopyridine[6] (**10**) and *N*,*N*-bis(2-pyridyl)-benzamide[7] (**11**) were obtained together with other products(Table1).

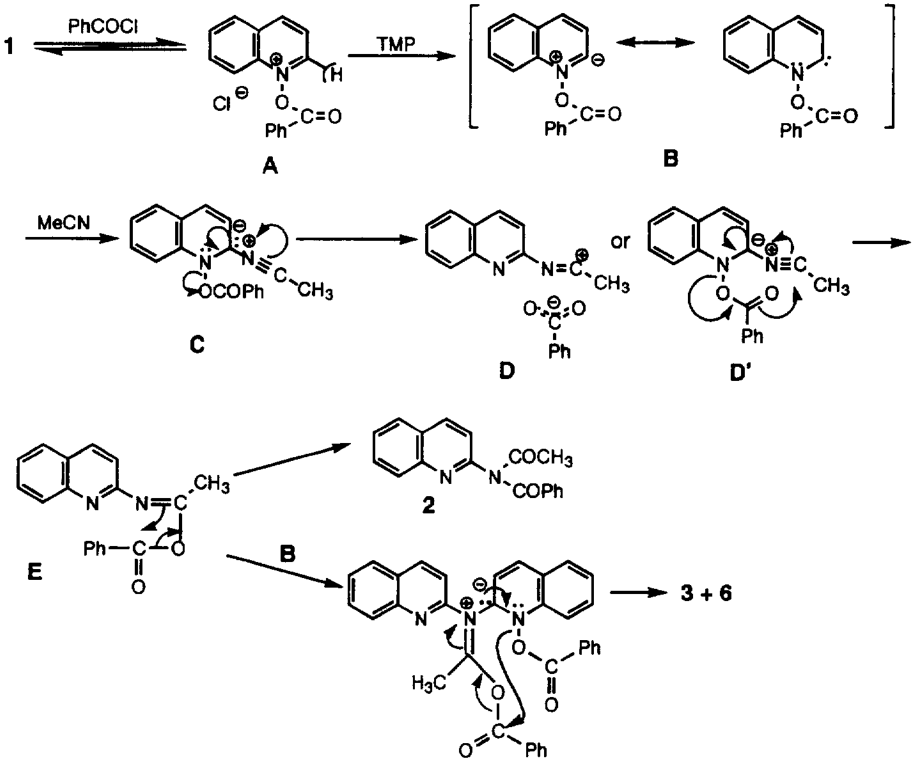
**Table 1**



| Entry | Nitrile | $R_1$ | $R_2$ | $R_3$ | $R_4$ | Compd. No | Yield(%) |
|---|---|---|---|---|---|---|---|
| 1[a] | acetonitrile | $-(CH)_4-$ | | acetyl | benzoyl | 2 | 30 |
| | | | | acetyl | 2-quinolyl | 3 | 22 |
| 2[b] | acetonitrile | H | H | acetyl | benzoyl | 8 | 4 |
| | | H | H | H | benzoyl | 9 | 35 |
| 3[c] | benzonitrile | $-(CH)_4-$ | | benzoyl | benzoyl | 7 | 12 |
| 4[b] | benzonitrile | H | H | benzoyl | benzoyl | 10 | 22 |
| | | H | H | H | benzoyl | 9 | 10 |
| | | H | H | 2-pyridyl | benzoyl | 11 | 4 |

a : In Entry 1, compounds 4(10%), 5(12%) and 6(47%) are obtained as the other products.
b : In Entry 2 and 4, compound 6(50%) is obtained as the other product.
c : In Entry 3, compounds 5(26%) and 6(49%) are obtained as the other products.

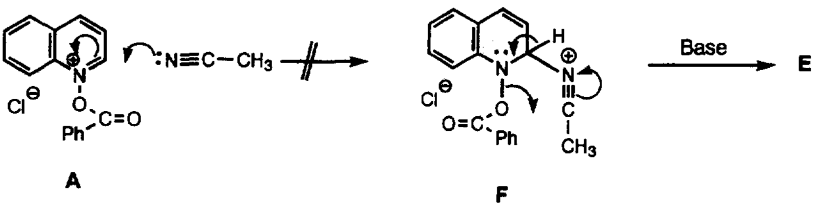
**Scheme 2**



The formation of 2 and 3 may be most likely explained by the following pathway. The initial step is the formation of *N*-benzoyloxyquinolinium chloride **A**, quinoline 1-oxide-benzoyl chloride adduct. Deprotonation of **A** at the 2-position by TMP leads to an intermediate **B**, better represented by the carbene form. The carbene **B** is electrophilic and reacts with MeCN to give a nitrilium ylide **C**. An intramolecular shift of benzoyloxy anion in **C** can be expected to give a benzoyloxyimine derivative **E**. An intramolecular transfer of the benzoyl group from O to N in **E** leads to **2**. The formation of 3 can be rationalized by the reaction of an intermediate **B** with **E**. This process accounts for a fairly good yield of benzoic anhydride 6 (Scheme 2).

As an alternative path from **A** to **E**, while a process involving nucleophilic attack of the nitrogen of MeCN at the 2-position of **A** followed by elimination of benzoic acid from the thus-formed 1,2-dihydroquinoline intermediate **F** may be conceivable, this is nonetheless unreasonable for the following reasons: 1) the nucleophilicity of MeCN or PhCN is extremely low and there is no known precedent of such reaction of aromatic *N*-oxide with carbonitrile, 2) the NMR spectral examination of **A** prepared in MeCN-$d_3$ gave no evidence of the formation of **F** (Scheme 3).

**Scheme 3**



In regard to the mechanism of the transformation of **C** to **E**, we studied the reaction using $^{18}O$-labelled benzoyl chloride (enriched with 97 atom% of $^{18}O$), and found that product **2** contains an almost equal concentration of $^{18}O$ in both the acetyl and the benzoyl oxygens. This finding indicates that this transformation proceeds via ion pair **D** in a similar manner with the reaction of 2-picoline 1-oxide with acetic anhydride,[8] and rules out the path via a cyclic transition state **D'**.

Although the detailed mechanism of the formation of **4** and **5**, which are commonly observed products in the reaction of **1** with benzoyl chloride, is not clear, it is likely that these products would be obtained from the reaction of benzoyloxy anion or chloride anion with an intermediate **B**. While the nucleophilic reactions through a carbene intermediate have been known with *N*-fluoropyridinium salts,[9] very few reports[10] are available so far as regards examples with aromatic *N*-oxides like the above-mentioned reactions. These results are of major theoretical significance, leading to a diversity of synthetic procedures of aromatic *N*-oxide. Further work is in progress to examine the reaction conditions in detail and to extend the scope of the reaction by using various weak nucleophiles.

## References and Notes

1) a) Y. Tagawa, K. Hama, Y. Goto, and M. Hamana, *Heterocycles*, **1992**, *34*, 2243. b) *ibid.*, **1995**, *40*, 809.

2) Compound **2** : colorless prisms(ether), mp 141°C ; $^1$H-NMR(400MHz, $CDCl_3$) δ 2.53(3H,s,$CH_3$), 7.23-7.27(2H,m,Ar-H), 7.32-7.36(1H,m,Ar-H), 7.47-7.51(2H,m,Ar-H), 7.59-7.63(1H,m,Ar-H), 7.67-7.70(2H,m,Ar-H), 7.76(1H,d,J=8.1Hz,Ar-H), 7.83(1H,d,J=8.3Hz,Ar-H), 8.16(1H,d,J=8.3Hz,Ar-H). $^{13}$C-NMR(100MHz,$CDCl_3$) δ 25.5(q,$CH_3$), 120.2(d,Ar), 126.7(s,Ar), 127.0(d,Ar), 127.3(d,Ar), 128.3(d,Ar), 128.9(d,Ar), 129.2(d,Ar), 129.8(d,Ar), 132.2(d,Ar), 134.8(s,Ar), 138.1(d,Ar), 147.0(s,Ar), 151.9(s,Ar), 172.6(s,C=O), 173.2(s,C=O). MS

m/z(rel.int.) 290($M^+$,12), 262(16), 247(28), 219(25), 171(42), 128(15), 105(100), 77(72). Anal.calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65; Found: C, 74.52; H, 5.01; N, 9.66. IR (KBr) ν 1710, 1703, 1595, 1504, 1427, 1370, 1309, 1261, 1248, 1223, 968, 821, 763, 720 $cm^{-1}$. The structure of **2** was further confirmed by its synthesis in 29% yield from 2-benzoylaminoquinoline with trimethylsilylurethane-acetylchloirde ( a) N. Ya. Derkach and N. P. Smetankina, *Zhurnal Obshchei Khimii*, **1964**, *34*, 3613 . b) L. M. Weinstock, S. Karady, F. E. Roberts, A. M. Hoinowski, G. S. Brenner, T. B. K. Lee, W. C. Lumma and M. Sletzinger, *Tetrahedron Letters*, **1975**, 3979 ).

3) F. M. Hamer, *J. Chem. Soc.*, **1924**, *125*, 1348 .

4) Compound **7** : colorless needles(ether-acetone), mp 214-215 °C ; $^1$H-NMR(400MHz, $CDCl_3$) δ 7.30-7.34(4H,m,Ar-H), 7.41-7.45(3H,m,Ar-H), 7.46-7.50(1H,m,Ar-H), 7.57-7.62(1H,m,Ar-H), 7.76-7.83(6H,m,Ar-H), 8.17(1H,d,J=8.3Hz, Ar-H). $^{13}$C-NMR(100MHz, $CDCl_3$) δ 119.5(d,Ar), 126.6(s,Ar), 126.8(d,Ar), 127.3(d,Ar), 128.5(d,Ar), 128.9(d,Ar), 129.2(d,Ar), 129.8(d,Ar), 132.4(d,Ar), 134.8(s,Ar), 138.3(d,Ar), 147.1(s,Ar), 152.9(s,Ar), 173.2(s,C=O). MS m/z(rel.int.) 352($M^+$,5), 324(7), 296(6), 247(16), 219(5), 128(5), 105(100), 77(63). Anal. calcd for $C_{23}H_{16}N_2O_2$ : C, 78.39; H, 4.58; N, 7.95; Found: C, 78.61; H, 4.54; N, 8.02. IR (KBr) ν 1686, 1597, 1504, 1427, 1288, 1249, 1126, 726 $cm^{-1}$.

5) Compound **8** : colorless prisms(n-hexane-ether), mp 63-64 °C ; $^1$H-NMR(400MHz, $CDCl_3$) δ 2.48(3H,s,$CH_3$), 7.11-7.15(1H,m,Ar-H), 7.26-7.35(3H,m,Ar-H), 7.38-7.43(1H,m,Ar-H), 7.63-7.66(2H,m,Ar-H), 7.70(1H,dd,J=7.3Hz, Ar-H), 8.36(1H,dd,J=2.0 and 4.9Hz,Ar-H). $^{13}$C-NMR(100MHz, $CDCl_3$) δ 25.5(q,$CH_3$), 122.5(d,Ar), 122.6(d,Ar), 128.3(d,Ar), 129.4(d,Ar), 132.3(d,Ar), 134.7(s,Ar), 138.0(d,Ar), 149.1(d,Ar), 152.7(s,Ar), 172.5(s,C=O), 173.0(s,C=O). MS m/z(rel.int.) 240($M^+$,3), 212(11), 197(25), 170(12), 121(24), 105(100), 77(65). Anal.calcd for $C_{14}H_{12}N_2O_2$ : C, 69.99; H, 5.03; N, 11.66; Found: C, 70.28; H, 4.96; N, 11.51. IR (KBr) ν 3378, 3064, 1713, 1707, 1586, 1469, 1431, 1365, 1200-1300, 1023, 790, 714, 667 $cm^{-1}$.

6) E. H. Huntress and H. C. Walter, *J. Org. Chem.*, **1948**, *13*, 735.

7) D. St. C. Black and R. C. Srivastava, *Aust. J. Chem.*, **1971**, *24*, 287. Whereas D. St. C. Black reported that the melting point of *N, N* -bis(2-pyridyl)-benzamide is 89-90 °C, the compound we prepared according to their synthetic method indicates the melting point of 160-161 °C, which completely coincided with the melting point of our product obtained in the present experiment.

8) a) S. Oae and S. Kozuka, *Tetrahedron*, **1964**, *20*, 2671 . b) S. Oae and K. Ogino, *Heterocycles*, **1977**, *6*, 583 .

9) a) T.Umemoto and G.Tomizawa, *Tetrahedron Lett.*, **1987**, *28*, 2705. b) T. Umemoto and G. Tomizawa, *J. Org. Chem.*, **1989**, *54*, 1726 . c) A. S. Kiselyov and L. Strekowski, *Terahedron Lett.*, **1994**, *35*, 207 .

10) For example, M. Van Der Puy, D. Nalewajek, and G. E. Wicks, *Tetrahedron Lett.*, **1988**, *29*, 4389 and references cited therein.

(*Received in Japan* 8 *September* 1995; *revised* 27 *October* 1995; *accepted* 2 *November* 1995)