W. H. Pirkle, *Bull. Kor. Chem. Soc.*, **8**, 45 (1987).
8. (a) W. H. Pirkle and M. H. Hyun, *J. Org. Chem.*, **49**, 3043 (1984); (b) W. H. Pirkle, M. H. Hyun, and B. Bank, *J. Chromatogr.*, **316**, 585 (1984); (c) M. H. Hyun, Y.-W. Park, and I.-K. Baik, *Tetrahedron Lett.*, **29**, 4735 (1988); (d) M. H. Hyun, J.-J. Ryoo, C.-S. Min, and W. H. Pirkle, *Bull. Kor. Chem. Soc.*, **13**, 407 (1992).
9. D. G. Kaiser, G. J. Vangiessen, R. J. Reisher, and W. J. Wechter, *J. Pharm. Sci.*, **65**, 269 (1976).
10. (a) G. Helmchen, H. Volter, and W. Schuhle, *Tetrahedron Lett.*, 1417 (1977); (b) G. Helmchen, G. Nill, D. Flockerzi, W. Schuhle, Mand M. S. K. Youssef, *Angw. Chem. Int. Ed. Engl.*, **18**, 62 (1979).
11. (a) S. K. Burley and G. A. Petsko, *Science*, **229**, 23 (1985); (b) A. V. Muehldorf, D. Van Engen, J. C. Warner, and A. D. Hamilton, *J. Am. Chem. Soc.*, **110**, 6561 (1988); (c) P. Linse, *J. Am. Chem. Soc.*, **114**, 4366 (1992).

4-Quinolones by Unusual Cyclocondensation of *o*-Imidophenacyl Bromides and Azides

Seong Heon Kim, Jae Uk Jeong, Dae Ock Choi, and Kee-Jung Lee*

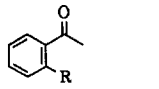
Division of Chemistry, Korea Institute of Science and Technology, Seoul 130-650

Received September 25, 1992

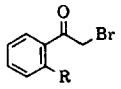
Azido functionality is very useful in the synthesis of various types of nitrogen heterocycles.[1] Recently, we reported[2] the synthesis of 5-hydroxy-1,3-benzoxazepines based on the Staudinger reaction followed by an intramolecular aza-Wittig reaction of *o*-acyloxyphenacyl azides. In this connection, we were interested in the synthesis of their nitrogen homologues, 1,3-benzodiazepines by the similar manner because it might provide a convenient route to two nitrogen containing heterocycles.[3] We describe herein unusual, useful method for the synthesis of 4-quinolones from the *o*-imidophenacyl bromides and azides.

The starting compounds, *o*-imidophenacyl bromides **2a-c**,[4] were readily obtained from the reactions of corresponding *N*-(2-acetylphenyl)imides **1a-c**[5] with copper(II) bromide in refluxing chloroform-ethyl acetate (1/1) according to King *et al.*[6] However, unexpectedly, we have found a conversion of *N*-(2-bromoacetylphenyl)maleimide (**2b**) into 4-bromo-1,5-dihydropyrrolo[1,2-a]quinoline-1,5-dione (**5**)[7] by the column chromatographic separation (silica gel, EtOAc/*n*-Hex=1/4, 68 %). On the other hand, *N*-(2-bromoacetylphenyl)phthalimide (**2a**) was converted into 6-bromo-5,11-dihydroisoindolo[2,1-a]quinoline-5,11-dione (**4a**)[8] in 62% yield in the presence of an equimolecular amount of triethylamine in dichloromethane at room temperature for 4 h, but *N*-(2-bromoacetylphenyl)succinimide (**2c**) was not participated.

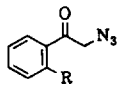
The reactions of *o*-imidophenacyl bromides **2a** and **2c** with sodium azide were carried out in acetone-water at room temperature and gave *o*-imidophenacyl azides **3a** (76%) and **3c** (92%), respectively.[9] Interestingly again, the crude *N*-(2-bromoacetylphenyl)phthalimide (**3a**) was cyclized directly to 6-azido-5,11-dihydroisoindolo[2,1-a]quinoline-5,11-dione (**4b**)[10] by the column chromatographic purification (silica gel, CH_2Cl_2, 70%). But, in case of **3c** was cyclized to 4-azido-1,2,3,5-tetrahydropyrrolo[1,2-a]quinoline-1,5-dione (**6a**)[11] only in the presence of an equimolecular amount of 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) in chloroform at 0℃ within 5 min (40% yield). The reaction of the crude *N*-(2-bromoacetylphenyl) maleimide (**2b**) with sodium azide was unsuccessful under various reaction conditions, and only gave complex mixture.



1a-c

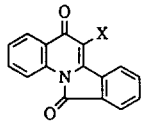


2a-c

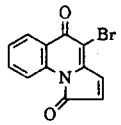


3a-c

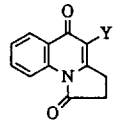
a, R=phthalimide **b**, R=maleimide **c**, R=succinimide



4a, X=Br
4b, X=N_3
4c, X=N=PPh_3
4d, X=NH_2
4e, X=H



5



6a, Y=N_3
6b, Y=N=PPh_3
6c, Y=H

Treatment of *N*-(2-azidoacetylphenyl)phthalimide (**3b**) with an equimolecular amount of triphenylphosphine in chloroform at reflux temperature for 1 h gave anormalous 6-[(triphenylphosphoranylidene)amino]-5,11-dihydroisoindolo[2,1-a]quinoline-5,11-dione (**4c**, 41%) and 6-amino-5,11-dihydroisoindolo[2,1-a]quinoline-5,11-dione (**4d**, 29%).[12] Alternatively, the same compounds, **4c** (90%) and **4d** (8%) could also be obtained from the reaction of 3-azidoquinoline-4-one (**4b**) with triphenylphosphine for 4 h at room temperature, and **4d** (62%) from the pyrolysis of **4b** in refluxing toluene for 15 min, respectively. Similarly, treatment of *N*-(2-azidoacetylphenyl)-succinimide (**3c**) with triphenylphosphine resulted in only low yield of 6-[(triphenylphosphoranylidene)amino]-1,2,3,5-tetrahydropyrrolo[1,2-a]quinoline-1,5-dione (**6b**, 38%).[13]

Finally, the reaction of *N*-(2-bromoacetylphenyl)phthalimide (**2a**) with triphenylphosphine and triethylamine in acetonitrile at room temperature for 2 h yielded 3-bromoquinoline-4-one (**4a**, 63%) and the Wittig reaction product **4e** (34%),[14] and *N*-(2-bromoacetylphenyl)succinimide (**2c**) gave only the known 1,2,3,5-tetrahydropyrrolo[1,2-a]quinoline-1,5-dione (**6c**)[15] in 77 % yield at reflux temperature for 6 h.

Further studies on the preparation of 5-hydroxy-1,3-benzodiazepines by other intramolecular condensation reaction method and some remaining mechanistic problems are underway.

Acknowledgement. We wish to thank the Korea Minister of Science and Technology for financial support.

References

1. For recent general reviews, see: (a) E. F. V. Scriven and K. Trunbull, *Chem. Rev.*, **88**, 298 (1988); (b) *Azides and*

Nitrenes, E. F. V. Scriven, Ed.; Academic Press; New York, 1984; (c) H. Takeuchi, S. I. Yanagida, T. Ozaki, S. Hagiwara, and S. Eguchi, *J. Org. Chem.*, **54**, 431 (1989) and references cited therein; (d) A. N. Luheshi, S. M. Salem, and R. K. Smalley, *Tetrahedron Lett.*, **31**, 6561 (1990) and references cited therein.

2. K.-J. Lee, D. O. Choi, S. Kim, J. U. Jeong, and H. Park, *Synthesis* 455 (1990).
3. During our studies on the synthesis of 1,3-benzodiazepines, a very similar method was reported, see: J. Kurita, T. Iwata, W. Yasuike, and T. Tsuchiya, *J. Chem. Soc. Chem. Commun.*, 81 (1992).
4. Selected data for **2a** (89%): mp. 195-196℃ (EtOAc); ^{1}H-NMR ($CDCl_3$/DMSO-d_6) δ 4.86 (s, 2H, CH_2), 7.60-8.20 (m, 8H, Ar); **2b** (62%): mp. 89℃ (Et_2O); ^{1}H-NMR ($CDCl_3$) δ 4.47 (s, 2H, CH_2), 6.88 (s, 2H, vinyl H), 7.20-8.40 (m, 4H, Ar); **2c** (87%): mp. 151℃ (Et_2O); ^{1}H-NMR ($CDCl_3$/DMSO-d_6) δ 2.82 (s, 4H, CH_2CH_2), 4.73 (s, 2H, CH_2Br), 7.26-8.23 (m, 4H, Ar).
5. The compounds **1a-c** were prepared conventionally from the *o*-aminoacetophenone with the corresponding anhydride, and selected data for **1a** (84%): mp. 134℃ (Et_2O); ^{1}H-NMR ($CDCl_3$) δ 2.50 (s, 3H, CH_3), 7.30-8.10 (m, 8H, Ar); **1b** (84%): mp. 112℃ (Et_2O); ^{1}H-NMR ($CDCl_2$) δ 2.50 (s, 3H, CH_3), 6.85 (s, 2H, vinyl H), 7.20-8.00 (m, 4H, Ar); **1c** (82%): mp. 212℃ (EtOAc); ^{1}H-NMR ($CDCl_3$) δ 2.53 (s, 3H, CH_3), 2.85 (s, 4H, CH_2CH_2), 7.13-8.02 (m, 4H, Ar).
6. L. C. King and G. K. Ostrum, *J. Org. Chem.*, **29**, 3459 (1964).
7. For the different synthetic method of 1,5-dihydropyrrolo [1,2-a]quinoline-1,5-diones, see: L. W. Deady and D. M. Werden, *J. Org. Chem.*, **52**, 3930 (1987); selected data for **5**: mp. 218-219℃ (Et_2O); ^{1}H-NMR ($CDCl_3$) δ 6.48 and 7.37 (two d, each 1H, J=6.1 vinyl H), 7.42-8.82 (m, 4H, Ar).
8. For the different synthetic method of 6-chloro-5,11-dihydroisoindolo[2,1-a]quinoline-5,11-dione, see: H. Vorbruggen, B. D. Bohn, and K. Krolikiewicz, *Tetrahedron* **46**, 3489 (1990); selected data for **4a**: mp. 234-235℃; ^{1}H-NMR ($CDCl_3$/DMSO-d_6) δ 7.30-8.30 (m, 8H, Ar); MS (relative intensity) m/z 327 ($M+2^+$, 19), 325 (M^+, 22), 297 (17), 246 (12), 190 (100).
9. Selected data for **3a**: mp. 137-139℃ (Et_2O); ^{1}H-NMR ($CDCl_3$/DMSO-d_6) δ 4.48 (s, 2H, CH_2), 7.50-8.20 (m, 8H, Ar); **3c**: mp. 101-102℃ (Et_2O); ^{1}H-NMR ($CDCl_3$/DMSO-d_6) δ 2.85 (s, 4H, CH_2CH_2), 4.53 (s, 2H, CH_2N_3), 7.22-7.92 (m, 4H, Ar).
10. For the different synthetic method of same heterocyclic system, see: (a) reference 8; (b) Y. Ishihara, Y. Kiyota, and G. Goto, *Chem. Pharm. Bull.*, **38**, 3024 (1990); (c) G. Goto and Y. Ishihara, JP 90 42,078 (1990); C. A. 1990, **113**, 40431z; selected data for **4b**: mp. 122-124℃ (dec); ^{1}H-NMR ($CDCl_3$) δ 7.30-9.20 (m, 8H, Ar); MS (relative intensity) m/z 288 (M^+, 2), 260 (76), 205 (11), 204 (100), 203 (30), 177 (29), 102 (43); IR (KBr) ν_{N_3} (cm^{-1}) 2124.
11. For the different synthetic method of 1,2,3,5-tetrahydropyrrolo[1,2-a]quinoline-1,5-diones, see: L. W. Deady and D. M. Werden, *Synth. Commun.*, **17**, 319 (1987) and reference 7; selected data for **6a**: mp. 139℃ (dec); ^{1}H-NMR ($CDCl_3$) δ 2.92 (m, 2H, CH_2), 3.14 (m, 2H, CH_2), 7.45-9.06 (m, 4H, Ar).
12. Selected data for **4c**: mp. 308-310℃; ^{1}H-NMR ($CDCl_3$) δ 7.15-9.24 (m, 23H, Ar); ^{31}P-NMR ($CDCl_3/H_3PO_4$) δ 17.6; MS (relative intensity) m/z 522 (M^+, 97), 470 (30), 469 (32), 207 (29), 183 (100); **4d**: mp. 255-256℃ (toluene); ^{1}H-NMR (DMSO-d_6) δ 5.89 (s, 2H, NH_2), 7.37-9.15 (m, 8H, Ar); MS (relative intensity) m/z 262 (M^+, 100), 234 (27), 178 (38), 103 (33), 76 (40).
13. Selected data for **6b**: mp. 250-251℃ (dec); ^{1}H-NMR ($CDCl_3$) δ 2.93 (m, 2H, CH_2), 3.47 (m, 2H, CH_2), 7.25-9.14 (m, 19H, Ar); ^{31}P-NMR ($CDCl_3/H_3PO_4$) δ 9.94: MS (relative intensity) m/z 474 (M^+, 27), 288 (25), 184 (27), 183 (100), 130 (28).
14. Selected data for **4e**: mp. 249-251℃; ^{1}H-NMR ($CDCl_3$) δ 6.74 (s, 1H, CH), 7.27-9.12 (m, 8H, Ar); MS (relative intensity) m/z 247 (M^+, 40), 219 (100), 190 (47), 163 (22), 101 (17).
15. Mp. 190-192℃ (EtOH, lit.[11] 192-193℃).

The Effect of Medium on the α-Effect for the Reaction of *p*-Nitrophenyl Acetate with Benzohydroxamates

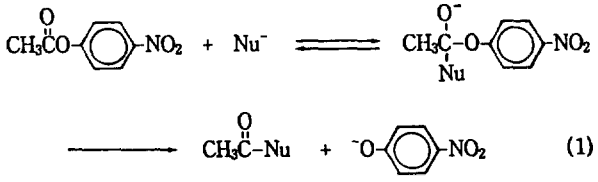
Ik-Hwan Um*, Jin-Kyung Jung, and Dong-Sook Kwon

Department of Chemistry, Ewha Womans University, Seoul 120-750

Received September 28, 1992

The term α-effect has been given to a positive deviation on a Broensted plot which is often observed in the reaction of the nucleophile containing a hetero atom adjacent to the reaction center (the α-position).[1] Although, numerous studies have been performed to investigate the origin of the α-effect, it has not been completely understood.[2]

Recently, a series of systematic studies has demonstrated that the effect of medium on the α-effect is significantly important for the acyl-transfer reaction of *p*-nitrophenyl acetate (PNPA) with anionic nucleophiles in various reaction medium, such as aqueous dimethyl sulfoxide (DMSO),[3] aqueous acetonitrile (MeCN),[4] and aqueous micellar solutions.[5] In our preceding paper on this series, we reported that benzohydroxamate (**1**) shows a large α-effect in pure H_2O, but the α-effect nucleophile (**1**) becomes less reactive than the corresponding normal-nucleophile (**4**) upon the addition of cethyltrimethylammonium bromide (CTAB) in H_2O.[6] Some explanations were suggested for the disappearance of the α-effect, but they were speculative and not conclusive.[6] Thus, we have now performed a systematic study for the following reactions in order to obtain some solid evidences.



(1)