Pergamon

Tetrahedron Letters 43 (2002) 6209–6211

TETRAHEDRON LETTERS

Synthesis of quinolines from the Baylis–Hillman acetates via the oxidative cyclization of sulfonamidyl radical as the key step

Jae Nyoung Kim,* Yun Mi Chung and Yang Jin Im

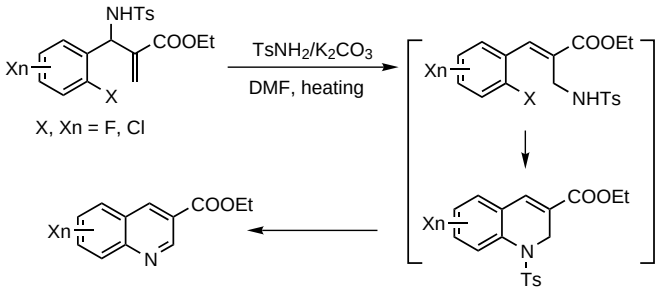
Department of Chemistry and Institute of Basic Science, Chonnam National University, Kwangju 500-757, Republic of Korea

Received 9 May 2002; revised 27 June 2002; accepted 28 June 2002

Abstract—Ethyl 3-quinolinecarboxylates **5** were synthesized in good to moderate yields from the Baylis–Hillman acetates **1** via the oxidative cyclization reaction of the *N*-tosylamidyl radical, which was generated from the rearranged tosylamide derivatives **2** by iodobenzene diacetate and iodine.

Recently, we have reported on the synthesis of quinolines from the Baylis–Hillman adducts of *N*-tosylimines derived from *ortho*-halobenzaldehydes.[1] In the reaction, there must be an *ortho*-halogen atom inevitably at the benzaldehyde portion in order to generate the quinoline backbone by S_NAr mechanism (Scheme 1). Thus, the usefulness of the reaction was limited. In this regard we intended to search for another procedure without the S_NAr step. Oxidative coupling reaction of the *N*-tosylamidyl radical might provide the route for the formation of the dihydroquinoline backbone.

It has been well recognized that radical reactions are quite useful for organic synthesis. However, study on the radical cyclization via nitrogen-centered radicals is somewhat limited. Fortunately, some papers on the oxidative coupling of aminyl radicals were reported in a similar system.[2] Togo and Yokoyama have reported many brilliant papers on the reaction of *N*-centered- and *O*-centered radicals generated by using iodobenzene diacetate and related reagents.[3] Thus our rationale, intramolecular oxidative cyclization reaction of the *N*-tosylamidyl radical to dihydroquinoline backbone, seemed plausible.



Scheme 1.

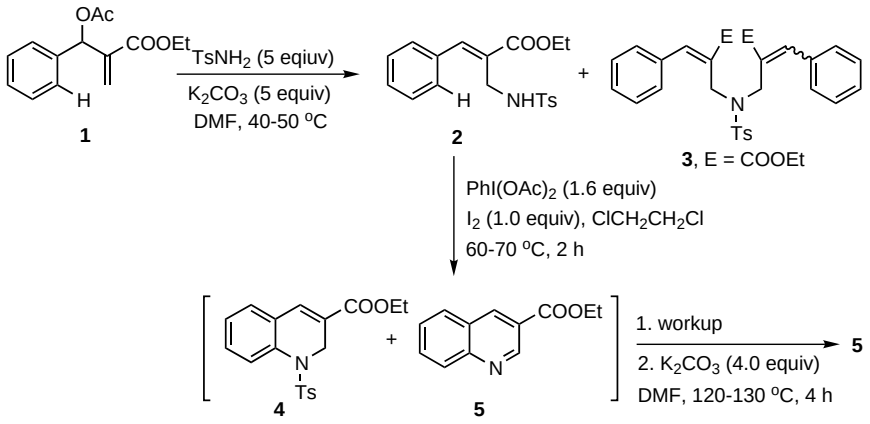
The Baylis–Hillman acetate **1** was prepared as previously from benzaldehydes and ethyl- or methyl acrylate followed by acetylation with acetic anhydride in the presence of DMAP.[1] The reaction of **1** and tosylamide in the presence of K_2CO_3 in DMF gave the rearranged tosylamide derivatives **2** in moderate yields (48–76%). In the reaction side product **3**, a 2:1 product of **1** and tosylamide, was generated in variable amounts (Scheme 2).[4] Thus, we performed the reaction with excess use of tosylamide (5.0 equiv.). The reaction of **2** in the presence of iodobenzene diacetate (1.6 equiv.) and iodine (1.0 equiv.) in dichloroethane afforded a mixture of *N*-tosyl dihydroquinolines **4** and quinolines **5** in variable ratios depending on the substrate. As shown in Table 1 (entry 1), two components **4a** and **5a** were isolated. Dihydroquinoline **4a** could be converted into **5a** quantitatively in the normal elimination reaction conditions (K_2CO_3, DMF, 120–130°C) by the elimination of *p*-toluenesulfinic acid.[1] Thus, in other cases we did not isolate the dihydroquinolines **4**. Instead, the next elimination step was performed directly after usual aqueous workup. The representative results are shown in Table 1.[5]

It is noteworthy to compare that 5,7-dichloro derivative **5e** was synthesized in 80% (entry 6), whereas 7-monochloro derivative was obtained in 70% from the

Keywords: quinolines; Baylis–Hillman acetates; sulfonamidyl radical; iodobenzene diacetate.

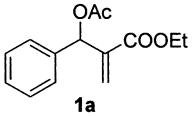
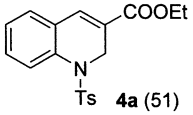
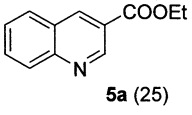
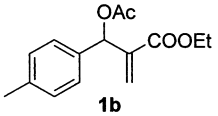
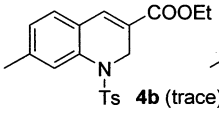
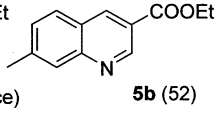
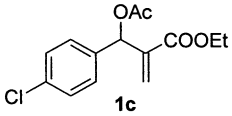
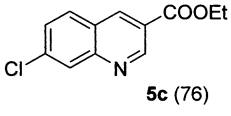
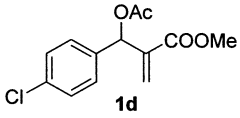
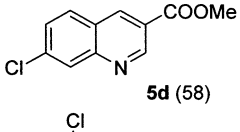
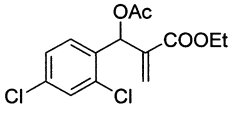
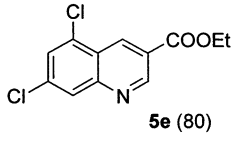
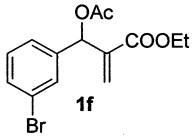
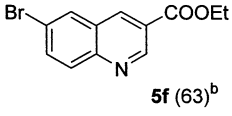
* Corresponding author. Fax: +82-62-530-3389; e-mail: kimjn@chonnam.chonnam.ac.kr

0040-4039/02/$ - see front matter
PII: S0040-4039(02)01314-X



Scheme 2.

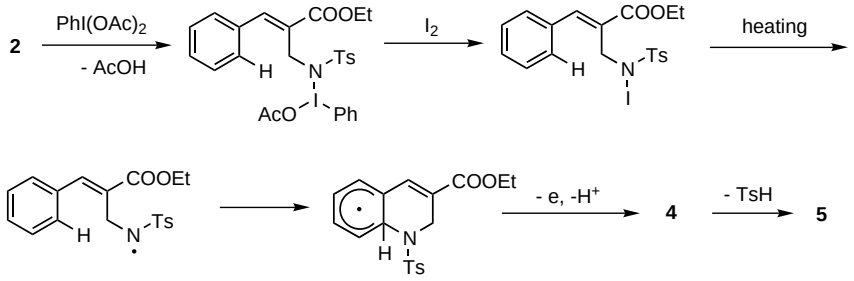
Table 1. Synthesis of quinolines **5**

entry	1	2 (%)	conditions[a]	products (%)	
1	 **1a**	**2a** (76)	A	 **4a** (51)	 **5a** (25)
2	**1a**	**2a** (76)	B	—	**5a** (75)
3	 **1b**	**2b** (76)	A	 **4b** (trace)	 **5b** (52)
4	 **1c**	**2c** (48)	B	—	 **5c** (76)
5	 **1d**	**2d** (70)	B	—	 **5d** (58)
6	 **1e**	**2e** (61)	B	—	 **5e** (80)
7	 **1f**	**2f** (57)	B	—	 **5f** (63)[b]

[a]Conditions: A: $PhI(OAc)_2$ (1.6 equiv), I_2 (1.0 equiv), $ClCH_2CH_2Cl$, 60-70 °C, 2 h
B: (i) $PhI(OAc)_2$ (1.6 equiv), I_2 (1.0 equiv), $ClCH_2CH_2Cl$, 60-70 °C, 2 h, (ii) workup, (iii) K_2CO_3 (4 equiv), DMF, 120-130 °C, 4 h. [b]The corresponding 8-bromo analog was not observed.

same starting material **1e** by adopting the method in our previous paper.[1]

The plausible reaction mechanism is shown in Scheme 3 as reported in a similar case.[2,3] In our case, the reaction proceeded without irradiation with tungsten lamp. It is interesting to note the regioselective formation of product **5f** in the case of entry 7. Radical cyclization toward 6-bromodihydroquinoline, the precursor of **5f**, is easier than the corresponding 8-bromo analog pre-



Scheme 3.

sumably due to the unfavorable steric hindrance during the radical cyclization stage.

In conclusion we disclosed herein the facile synthesis of ethyl 3-quinolinecarboxylates from the Baylis–Hillman acetates via the oxidative cyclization reaction of *N*-tosylamidyl radical as the key step.

Acknowledgements

This work was supported by the grant (No. R02-2000-00074) from the Basic Research Program of the Korea Science and Engineering Foundation.

References

1. (a) Kim, J. N.; Lee, H. J.; Lee, K. Y.; Kim, H. S. *Tetrahedron Lett*. **2001**, *42*, 3737; (b) Chung, Y. M.; Lee, H. J.; Hwang, S. S.; Kim, J. N. *Bull. Korean Chem. Soc*. **2001**, *22*, 799.
2. (a) Togo, H.; Hoshina, Y.; Yokoyama, M. *Tetrahedron Lett*. **1996**, *37*, 6129; (b) Togo, H.; Hoshina, Y.; Muraki, T.; Nakayama, H.; Yokoyama, M. *J. Org. Chem*. **1998**, *63*, 5193; (c) Togo, H.; Katohgi, M.; Yokoyama, M. *Synlett* **1998**, 131; (d) Tsuritani, T.; Shinokubo, H.; Oshima, K. *Org. Lett*. **2001**, *3*, 2709; (e) Togo, H.; Harada, Y.; Yokoyama, M. *J. Org. Chem*. **2000**, *65*, 926; (f) Togo, H.; Katohgi, M. *Synlett* **2001**, 565 and references cited therein.
3. (a) Togo, H.; Muraki, T.; Hoshina, Y.; Yamaguchi, K.; Yokoyama, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 787; (b) Togo, H.; Muraki, T.; Yokoyama, M. *Tetrahedron Lett*. **1995**, *36*, 7089; (c) Muraki, T.; Togo, H.; Yokoyama, M. *Tetrahedron Lett*. **1996**, *37*, 2441; (d) Kita, Y.; Tohma, H.; Hatanaka, K.; Takada, T.; Fujita, S.; Mitoh, S.; Sakurai, H.; Oka, S. *J. Am. Chem. Soc*. **1994**, *116*, 3684.
4. Lee, H. J.; Kim, H. S.; Kim, J. N. *Tetrahedron Lett*. **1999**, *40*, 4363.
5. The compounds **4a**, **5a** and **5c** were reported in our previous paper.[1] Other products were also easily characterized by their ^{1}H and ^{13}C NMR spectrum. As an example, typical procedure for the synthesis of **5e** is as follows. To a stirred solution of **1e** (317 mg, 1.0 mmol) and *p*-toluenesulfomamide (855 mg, 5.0 mmol) in DMF (5 mL) was added K_2CO_3 (690 mg, 5.0 mmol) and stirred at 40–50°C for 3 h. After the usual workup process and column chromatographic purification (hexanes/ether, 1:2), pure **2e** was obtained as a white solid, 262 mg (61%): mp 94–96°C; ^{1}H NMR ($CDCl_3$) δ 1.32 (t, $J=7.1$ Hz, 3H), 2.43 (s, 3H), 3.78 (d, $J=6.7$ Hz, 2H), 4.24 (q, $J=7.1$ Hz, 2H), 5.25 (brs, 1H), 7.26–7.78 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 14.16, 21.54, 40.74, 61.67, 127.18, 127.51, 129.03, 129.54, 129.76, 131.01, 131.56, 134.83, 135.95, 136.22, 138.77, 143.66, 166.58. A stirred mixture of **2e** (128 mg, 0.3 mmol), iodobenzene diacetate (155 mg, 0.48 mmol) and iodine (77 mg, 0.3 mmol) in dichloroethane (5 mL) was heated to 60–70°C during 2 h. After usual aqueous workup process the obtained crude mixture of **4e** and **5e** was dissolved in DMF. To the solution K_2CO_3 (166 mg, 1.2 mmol) was added and the reaction mixture was heated to 120–130°C for 4 h. After usual workup process and column chromatographic purification (hexanes/ether, 1:4) pure **5e** was obtained as a white solid, 65 mg (80%): mp 128–129°C; IR (KBr) 1709, 1264 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.49 (t, $J=7.1$ Hz, 3H), 4.51 (q, $J=7.1$ Hz, 2H), 7.67 (d, $J=2.0$ Hz, 1H), 8.06 (m, 1H), 9.13 (m, 1H), 9.46 (d, $J=2.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.32, 60.88, 122.78, 123.14, 126.78, 127.27, 132.52, 134.25, 136.11, 149.28, 150.75, 163.66; Mass (70 eV) m/z (rel. intensity) 161 (18), 196 (53), 198 (34), 224 (100), 226 (63), 241 (51), 243 (33), 269 (M^+, 55), 271 (M^++2, 34).