Pergamon

Tetrahedron Letters 42 (2001) 3351–3354

TETRAHEDRON
LETTERS

Synthesis of naphthalenes using acid-catalyzed ring-opening and recyclization of 3-acetyl-5,5-diaryl-2-methyl-4,5-dihydrofurans. Isolation of intermediates

Shougo Kajikawa,[a] Hiroshi Nishino[b,*] and Kazu Kurosawa[c]

[a] *Department of Environmental Science, Graduate School of Science and Technology, Kumamoto University, Kurokami 2-39-1, Kumamoto 860-8555, Japan*

[b] *Institute for Fundamental Research of Organic Chemistry (IFOC), Kyushu University, Hakozaki 6-10-1, Higashi-ku, Fukuoka 812-8581, Japan*

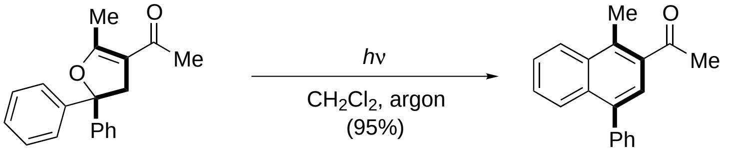
[c] *Department of Environmental Science, Faculty of Science, Kumamoto University, Kurokami 2-39-1, Kumamoto 860-8555, Japan*

Received 29 January 2001; revised 12 March 2001; accepted 14 March 2001

Abstract—3-Acetyl-5,5-diaryl-2-methyl-4,5-dihydrofurans were heated in concentrated hydrochloric acid to give the 4-aryl-1-methylnaphthalenes in high yields. The same reaction was carried out in hydrochloric acid diluted with acetonitrile to give the 5,5-diaryl-4-penten-2-ones (87–96%), while treatment of the dihydrofurans with *p*-toluenesulfonic acid in acetonitrile afforded the 3-(2,2-diarylethenyl)-4-hydroxy-3-penten-2-ones (73–91%) which were transformed in diluted hydrochloric acid into the 5,5-diaryl-4-penten-2-ones. It was demonstrated that the 3- and 4-penten-2-ones were intermediates of the 4-aryl-1-methylnaphthalenes since the 3- and 4-penten-2-ones were easily converted into the corresponding naphthalenes in concentrated hydrochloric acid. The UV irradiation of the dihydrofurans in the presence of hydrochloric acid quantitatively gave the 2-acetyl-4-aryl-1-methylnaphthalenes (94–97%) via the same 3-penten-2-one intermediates. © 2001 Elsevier Science Ltd. All rights reserved.

In previous studies,[1] we reported the convenient 3-acetyl-5,5-diaryl-2-methyl-4,5-dihydrofuran synthesis using tris(2,4-pentanedionat irradiation of the dihydrofurans in dichloromethane gave the 2-acetyl-4-aryl-1-methylnaphthalenes (Scheme 1 for **1a**, Table 1, entry 1).[2] Highly-substituted naphthalenes are common features of numerous biologically significant natural products and pharmaceuticals,[3] and improved methods for their construction are highly desired.[4] Although the benzannulation is a worthwhile synthetic method in view of both the unique reaction mode and the practical method providing a variety of substituted aromatic compounds, the mechanism of the photo-induced benzannulation was not obvious at that time. In order to ascertain the mechanism, we scrutinized the acid-catalyzed reaction of the 3-acetyl-5,5-diaryl-2-methyl-4,5-dihydrofurans since we knew by intuition that the hydrogen chloride generated in situ by the photoreaction of dichloromethane might promote the photo-induced benzannulation. As a result, we could show the optimum benzannulation conditions and the exact reaction pathway by the isolation of the reaction intermediates. Herein we briefly describe the results.

Many experiments involving the photo-induced benzannulation of dihydrofurans **1a**–**d** were carried out, and



1a **5a**

Scheme 1.

Keywords: acid-catalyzed transformation; dihydrofurans; pentenones; naphthalene synthesis; photocyclization.

* Corresponding author. Fax: +81-96-342-3374; e-mail: nishino@aster.sci.kumamoto-u.ac.jp

0040-4039/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(01)00431-2

Table 1. Reactions of dihydrofurans **1a–d** and their products **2a**, **3a**, and **5a**[a]

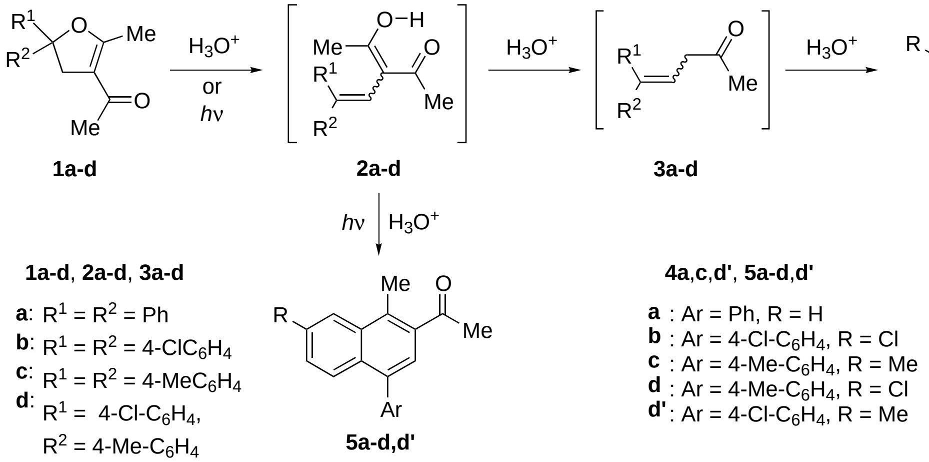
Entry	Substrate	Reaction conditions[b]	Temp (°C)	Time (h)	Product (yield/%)[c]			
1	**1a**	UV irrad., CH_2Cl_2	23	4				**5a** (95)
2	**1a**	UV irrad., 2 M HCl–MeCN	23	3				**5a** (97)
3	**1b**	UV irrad., 2 M HCl–MeCN	23	3				**5b** (96)
4	**1c**	UV irrad., 2 M HCl–MeCN	23	3				**5c** (97)
5	**1d**	UV irrad., 2 M HCl–MeCN	23	3				**5d** (47) **5d′** (47)
6	**1a**	Conc. HCl–MeCN	100	12	**2a** (1)	**3a** (94)		
7	**1b**	Conc. HCl–MeCN	100	15		**3b** (96)		
8	**1c**	Conc. HCl–MeCN	100	12		**3c** (87)	**4c** (10)	
9	**1d**	Conc. HCl–MeCN	100	12		**3d** (94)	**4d′** (2)	
10	**1a**	Conc. HCl	100	8	**2a** (<1)	**3a** (4)	**4a** (94)	
11	**1b**	Conc. HCl	100	8		**3b** (93)		
12	**1c**	Conc. HCl	100	8			**4c** (98)	
13	**1d**	Conc. HCl	100	8			**4d′** (92)	
14	**1a**	*p*-TsOH–MeCN	80	36	**2a** (73)	**3a** (21)		
15	**1b**	*p*-TsOH–MeCN	80	36	**2b** (91)	**3b** (4)		
16	**1c**	*p*-TsOH–MeCN	80	36	**2c** (65)	**3c** (24)	**4c** (3)	
17	**1d**	*p*-TsOH–MeCN	80	36	**2d** (88)	**3d** (10)	**4d′** (<1)	
18	**2a**	Conc. HCl–MeCN	100	6		**3a** (99)		
19	**2a**	Conc. HCl	100	6			**4a** (92)	
20	**3a**	Conc. HCl	100	4			**4a** (94)	
21	**5a**	Conc. HCl	100	8	No reaction			
22	**2a**	UV irrad., MeCN	23	72				**5a** (87)
23	**2a**	UV irrad., CH_2Cl_2	23	2				**5a** (97)
24	**2a**	UV irrad., 2 M HCl–MeCN	23	1.5				**5a** (98)
25	**3a**	UV irrad., 2 M HCl–MeCN	23	6	Intractable mixture			

[a] The substrate (0.2 mmol) was stirred in solvent under an argon atmosphere (1 atm).

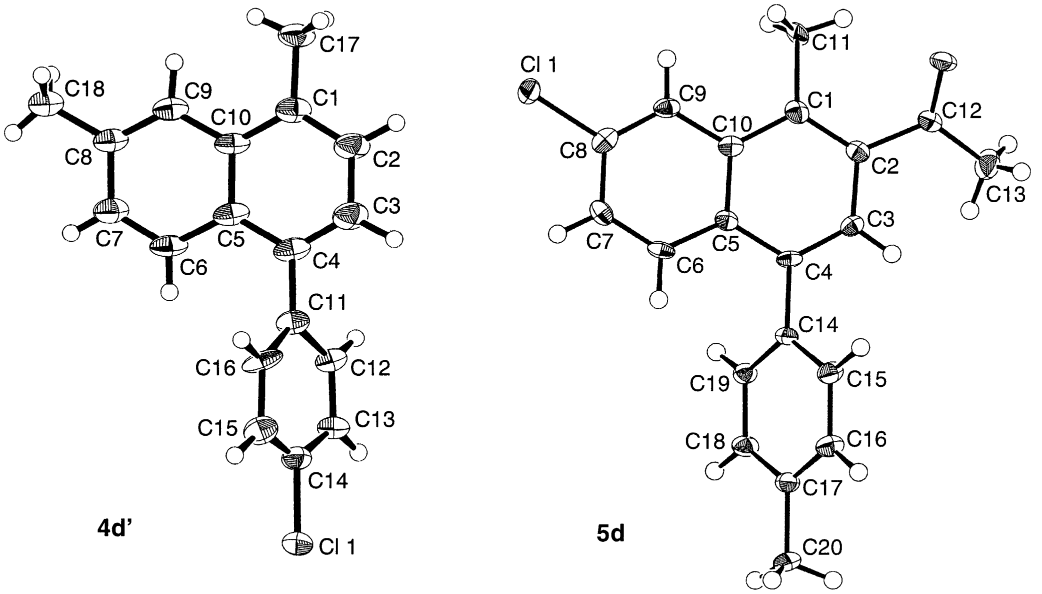
[b] Dichloromethane (10 mL), 2 M hydrochloric acid (1 mL)–acetonitrile (9 mL), concentrated hydrochloric acid (1 mL)–acetonitrile (9 mL), concentrated hydrochloric acid (10 mL), and *p*-toluenesulfonic acid (2.0 mmol)–acetonitrile (10 mL) were used as the solvent system. The UV irradiation was carried out in a 12 mL quartz cell using a 100 W high-pressure mercury lamp.

[c] Isolated yield based on the amount of the substrate used.

we found that the best solvent system was acetonitrile (9 mL) containing 2 M hydrochloric acid (1 mL). The corresponding naphthalenes **5a–d,d′** were then obtained in high yields (Scheme 2 and Table 1, entries 2–5). The photoreaction of dihydrofuran **1d** (R^1=4-Cl-C_6H_4, R^2=4-Me-C_6H_4) at 23°C for 3 h gave 2-acetyl-7-chloro-4-(4-methylphenyl)-1-mehylnaphthalene (**5d**)[5] and 2-acetyl-4-(4-chlorophenyl)-1,7-dimethylnaphthalene (**5d′**)[6] in the same yields. The structures of **5d** and **5d′** were established by spectroscopic methods and



Scheme 2.



4d' **5d**

Figure 1. ORTEP view of **4d**′ and **5d**.

elemental analyses, and the structure of **5d** was finally determined by an X-ray crystallographic method (Fig. 1).[5]

Stirring dihydrofuran **1a** ($R^1 = R^2 = Ph$) under similar reaction conditions without UV irradiation did not give any products. A mixture of **1a** (0.2 mmol) and concentrated hydrochloric acid–acetonitrile (1:9 v/v) was heated at 100°C for 12 h, and water (30 mL) was then added to the reaction mixture, followed by extraction with dichloromethane (20×3 mL), giving 5,5-diphenyl-4-penten-2-one (**3a**: $R^1 = R^2 = Ph$)[7] in 94% yield along with a small amount of 4-hydroxy-3-(2,2-diphenylethenyl)-3-penten-2-one (**2a**: $R^1 = R^2 = Ph$)[8] (entry 6). A similar reaction of **1b** ($R^1 = R^2 = 4\text{-Cl-}C_6H_4$) gave the corresponding 4-penten-2-one **3b** as the sole product (entry 7). The reactions of **1c** ($R^1 = R^2 = 4\text{-Me-}C_6H_4$) and **1d** led to the ring-opening reaction, and the 4-penten-2-ones **3c** and **3d** were produced in 87 and 94% yield, respectively, together with small amounts of the deacetylated naphthalenes **4c** (10%) and **4d**′ (2%) (entries 8 and 9). Since it was anticipated that these reactions clearly depended on the strength of the acid, the reaction of the dihydrofurans **1a**–**d** was carried out in concentrated hydrochloric acid at 100°C for 8h. As a result, it was found that the corresponding deacetylated naphthalenes **4a**,**c**,**d**′ were produced in high yields except for the reaction of **1b** which gave **3b** (entries 10–13). The reaction of **1d** did not give 7-chloro-4-(4-methylphenyl)-1-methylnaphthalene (**4d**: $Ar = 4\text{-Me-}C_6H_4$, $R = Cl$), but 4-(4-chlorophenyl)-1,7-dimethylnaphthalene (**4d**′) as the sole product (entry 13). The structure of **4d**′ was established by spectroscopic methods, elemental analysis, and finally by X-ray crystallography (Fig. 1).[9] On the other hand, the treatment of the dihydrofurans **1a**–**d** with *p*-toluenesulfonic acid in acetonitrile afforded the 3-(2,2-diarylethenyl)-4-hydroxy-3-penten-2-ones **2a**–**d** in moderate to good yields (entries 14–17).

In order to clarify the relationship of the products **2**, **3**, **4**, and **5**, the acid-catalyzed reaction of each product was examined. The 3-penten-2-one **2a** was quantitatively transformed into **3a** in concentrated hydrochloric acid–acetonitrile (1:9 v/v) (entry 18). The treatment of both **2a** and **3a** with concentrated hydrochloric acid resulted in the production of the deacetylated naphthalene **4a** (entries 19, 20). However, 2-acetylnaphthalene **5a** could not be converted into **4a** in hot concentrated hydrochloric acid (entry 21). It was interesting that the UV irradiation of **2a** in 2 M hydrochloric acid–acetonitrile (1:9 v/v) quantitatively gave 2-acetylnaphthalene **5a** and no deacetylated naphthalene **4a** was detected (entry 24). A similar UV irradiation of **3a** gave only intractable oily materials and no products were isolated (entry 25). It was suggested that the 3-penten-2-one **2a** should be an intermediate in the photo-induced benzannulation of **1a**. Therefore, it was proved that the generation of hydrogen chloride was essential for the photo-induced benzannulation of the dihydrofurans **1** in dichloromethane.[2,10] In fact, stirring of **1a** at 23°C for 24 h in dichloromethane which was beforehand UV irradiated for 4 h gave **2a** (2%).

On the basis of the transformation mentioned above, it was concluded that the UV irradiation or the presence of acid caused the ring-opening of the 4,5-dihydrofurans **1** to generate the 3-penten-2-one intermediates **2**. The photocyclization of the intermediates **2** accelerated by the presence of a catalytic amount of acid produced the 2-acetylnaphthalenes **5** (entries 22–24), whilst the presence of a strong acid without UV irradiation promoted the deacetylation of **2** to form the 4-pente-2-one intermediates **3** which were intramolecularly cyclized to finally give the naphthalenes **4** (Scheme 2).

The present photo-induced and/or acid-catalyzed benzannulation of the 4,5-dihydrofurans are very simple and convenient, and the substituted naphthalenes as well as their intermediates can be selectively obtained in high yields by controlling of the reaction conditions. We are still investigating the acid-catalyzed reaction in order to control the substituent on the naphthalene ring, and apply it to the synthesis of ring-assembling aromatic compounds and polycyclic aromatic hydrocarbons.

Acknowledgements

We thank Dr. Mikio Yasutake, Institute for Fundamental Research of Organic Chemistry, Kyushu University, Japan, for crystallographic assistance.

References

1. (a) Nishino, H. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1922–1927; (b) Nishino, H.; Tategami, S.; Yamada, T.; Korp, J. D.; Kurosawa, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1800–1809; (c) Kajikawa, S.; Nishino, H.; Kurosawa, K. *Heterocycles* **2001**, *54*, 171–183.
2. Nishino, H.; Kajikawa, S.; Hamada, Y.; Kurosawa, K. *Tetrahedron Lett.* **1995**, *36*, 5753–5756.
3. (a) Whiting, D. A. *Nat. Prod. Rep.* **1985**, *2*, 191–211; (b) Ward, R. S. *Nat. Prod. Rep.* **1995**, *12*, 183–205; (c) Eich, E.; Pertz, H.; Kaloga, M.; Schulz, J.; Fesen, M. R.; Mazumder, A.; Pommier, Y. *J. Med. Chem.* **1996**, *39*, 86–95; (d) Smyth, M. S.; Stefanova, I.; Horak, I. D.; Burke, Jr., T. R. *J. Med. Chem.* **1993**, *36*, 3015–3020; (e) Zhao, H.; Neamati, N.; Mazumder, A.; Sunder, S.; Pommier, Y.; Burke, Jr., T. R. *J. Med. Chem.* **1997**, *40*, 1186–1194; (f) Ukita, T.; Nakamura, Y.; Kubo, A.; Yamamoto, Y.; Takahashi, M.; Kotera, J.; Ikeo, T. *J. Med. Chem.* **1999**, *42*, 1293–1305.
4. (a) Charlton, J. L.; Oleschuk, C. J.; Chee, G.-L. *J. Org. Chem.* **1996**, *61*, 3452–3457; (b) Katritzky, A. R.; Zhang, G.; Xie, L. *J. Org. Chem.* **1997**, *62*, 721–725; (c) Nishii, Y.; Yoshida, T.; Tanabe, Y. *Tetrahedron Lett.* **1997**, *38*, 7195–7198; (d) Cotelle, P.; Catteau, J.-P. *Tetrahedron Lett.* **1997**, *38*, 2969–2972; (e) de Koning, C. B.; Michael, J. P.; Rousseau, A. L. *J. Chem. Soc., Perkin Trans. 1* **2000**, 787–797; (f) Kao, C.-L.; Yen, S. Y.; Chern, J.-W. *Tetrahedron Lett.* **2000**, *41*, 2207–2210.
5. **2-Acetyl-7-chloro-4-(4-methylphenyl)-1-methylnaphthalene (5d)**: $R_f = 0.54$ (3:7 diethyl ether–hexane); light yellow microcrystals (from methanol); mp 61.5–63.0°C; IR ($CHCl_3$) ν 1688 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16–7.23 (8H, m, arom. H), 2.75 (3H, s, CH_3), 2.63 (3H, s, $COCH_3$), 2.45 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.1 (C=O), 138.7, 137.7, 137.6, 136.7, 134.2, 132.7, 131.6, 130.8 (arom. C), 129.8 (2C), 128.2 (2C), 128.5, 127.7, 124.9, 124.5 (arom. CH), 30.9 ($CO\underline{C}H_3$), 21.2, 15.7 (CH_3); MS *m*/*z* (rel intensity), 308 (M^+, 96), 293 (100), 265 (48), 229 (32), 215 (60); HR MS found *m*/*z* 308.1015, calcd for $C_{20}H_{17}{}^{35}ClO$ M, 308.0968. Anal. calcd for $C_{20}H_{17}ClO$: C, 77.79; H, 5.55. Found: C, 78.04; H, 5.68. X-ray crystallographic data of **5d** (Ar = 4-Me-C_6H_4, R = Cl): empirical formula $C_{20}H_{17}ClO$; formula weight 308.81; colorless prism; crystal dimensions 0.20×0.05×0.50 mm; orthorhombic; space group $Pna2_1$ (no. 33); $a = 22.9004(8)$, $b = 6.0532(2)$, $c = 22.4819(6)$ Å, $V = 3116.5(5)$ Å^3, $Z = 8$; $D_{\text{calcd}} = 1.316$ g/cm^3; $F(000) = 1296.00$; $(\mu \text{MoK}_\alpha) = 2.44$ cm^{-1}; $2\theta_{\max} = 55.0°$; no. of reflections measured 21932; no. of observations ($I > 3.00\sigma(I)$) 3637; no. of variables 398; reflection/parameter ratio was 5.32; $R = 0.039$; $R_w = 0.046$; GOF = 1.00.
6. **2-Acetyl-4-(4-chlorophenyl)-1,7-dimethylnaphthalene (5d′)**: $R_f = 0.50$ (3:7 diethyl ether–hexane); colorless needles (from hexane); mp 82.0–84.0°C; IR ($CHCl_3$) ν 1685 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98–7.24 (8H, m, arom. H), 2.79 (3H, s, CH_3), 2.64 (3H, s, $COCH_3$), 2.56 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.3 (C=O), 138.8, 137.1, 136.8, 136.4, 133.52, 133.48, 132.5, 130.4 (arom. C), 131.3 (2C), 129.5, 128.5 (2C), 126.1, 124.8, 124.0 (arom. CH), 31.0 ($CO\underline{C}H_3$), 22.0, 15.9 (CH_3); MS *m*/*z* (rel intensity), 308 (M^+, 94), 293 (100), 265 (34), 229 (28), 215 (56); HR MS found *m*/*z* 308.0942, calcd for $C_{20}H_{17}{}^{35}ClO$ M, 308.0968. Anal. calcd for $C_{20}H_{17}ClO$: C, 77.79; H, 5.55. Found: C, 78.01; H, 5.74.
7. **5,5-Diphenyl-4-penten-2-one (3a)**: $R_f = 0.61$ (3:7 diethyl ether–hexane); yellow liquid; IR ($CHCl_3$) ν 1713 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.14 (10H, m, arom. H), 6.28 (1H, t, $J = 7.34$ Hz, CH), 3.25 (2H, d, $J = 7.34$ Hz, CH_2), 2.12 (3H, s, $COCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.7 (C=O), 144.8 (>C=), 141.9, 139.5 (arom. C), 129.7 (2C), 128.4 (2C), 128.1 (2C), 127.41 (2C), 127.37 (2C) (arom. CH), 120.5 (=CH-), 44.7 (CH_2), 29.9 (CH_3); MS *m*/*z* (rel intensity) 236 (14), 193 (87), 178 (29), 115 (100), 91 (53); HR MS found *m*/*z* 236.1205, calcd for $C_{17}H_{16}O$ M, 236.1201.
8. **4-Hydroxy-3-(2,2-diphenylethenyl)-3-penten-2-one (2a)**: $R_f = 0.66$ (3:7 diethyl ether–hexane); yellow liquid; IR ($CHCl_3$) ν 1596 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 16.51 (1H, s, OH), 7.32–7.08 (10H, m, arom. H), 6.54 (1H, s, =CH-), 1.95 (6H, s, CH_3×2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.0 (2C) (C=O), 146.0 (>C=), 142.9, 140.0 (arom. C), 129.9 (2C), 128.3 (2C), 128.22 (2C), 128.18 (2C), 127.8, 127.5 (arom. CH), 122.2 (=CH-), 110.6 (C-3), 24.1 (2C) (CH_3); MS *m*/*z* (rel intensity) 278 (100), 191 (44), 105 (58), 77 (42), 44 (87); HR MS found *m*/*z* 278.1300, calcd for $C_{19}H_{18}O_2$ M, 278.1307. Anal. calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 81.93; H, 6.71.
9. **4-(4-Chlorophenyl)-1,7-dimethylnaphthalene (4d′)**: $R_f = 0.82$ (3:7 diethyl ether–hexane); colorless microcrystals (from hexane); mp 95.0–96.0°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81–7.17 (9H, m, arom. H), 2.70 (3H, s, CH_3), 2.54 (3H, s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.6, 137.1, 135.4, 133.5, 133.01, 132.96, 129.6 (arom. C), 131.4 (2C), 128.4 (2C), 128.0, 126.2, 126.1, 125.7, 123.6 (arom. CH), 21.9, 19.6 (CH_3); MS *m*/*z* (rel intensity) 266 (100), 228 (22), 215 (31), 196 (41). Anal. calcd for $C_{18}H_{15}Cl$: C, 81.04; H, 5.67. Found: C, 81.23; H, 5.91. X-ray crystallographic data of **4d′** (Ar = 4-Cl-C_6H_4, R = Me): empirical formula $C_{18}H_{15}Cl$; formula weight 266.77; colorless platelet; crystal dimensions 0.05×0.35×0.10 mm; orthorhombic; space group *Fdd*2 (no. 43); $a = 19.702(2)$, $b = 51.114(3)$, $c = 5.3845(3)$ Å, $V = 5422.5(6)$ Å^3, $Z = 16$; $D_{\text{calcd}} = 1.307$ g/cm^3; $F(000) = 2240.00$; $(\mu \text{MoK}_\alpha) = 2.63$ cm^{-1}; $2\theta_{\max} = 55.0°$; no. of reflections measured 10424; no. of observations ($I > 3.00\sigma(I)$) 1450; no. of variables 285; reflection/parameter ratio was 5.09; $R = 0.035$; $R_w = 0.043$; GOF = 1.18.
10. (a) Ohkura, K.; Noguchi, Y.; Seki, K. *Chem. Lett.* **1997**, 99–100; (b) Matohara, K.; Lim, C.; Yasutake, M.; Nogita, R.; Koga, T.; Sakamoto, Y.; Shinmyozu, T. *Tetrahedron Lett.* **2000**, *41*, 6803–6807.