Synthesis of Some Substituted Dimethyl and Diethyl 4-(Phenylethynyl)-2,6-pyridinedicarboxylates

Harri Takalo,* Jouko Kankare and Elina Hänninen*

Department of Chemistry, University of Turku, SF-20500 Turku, Finland

Takalo, H., Kankare, J. and Hänninen, E., 1988. Synthesis of Some Substituted Dimethyl and Diethyl 4-(Phenylethynyl)-2,6-pyridinedicarboxylates. – Acta Chem. Scand., Ser. B 42: 448–454.

Substituted dimethyl and diethyl 4-(phenylethynyl)-2,6-pyridinedicarboxylates were prepared by coupling reactions between dialkyl 4-halo-2,6-pyridinedicarboxylates and terminal arylacetylenes in the presence of an organopalladium catalyst and copper(I) iodide in a suitable solvent system. The terminal acetylenes needed in this work were synthesized from the corresponding aryl halides using either (trimethylsilyl)acetylene or 2-methyl-3-butyn-2-ol followed by deprotection of the triple bond, depending on the nature of the compound in question.

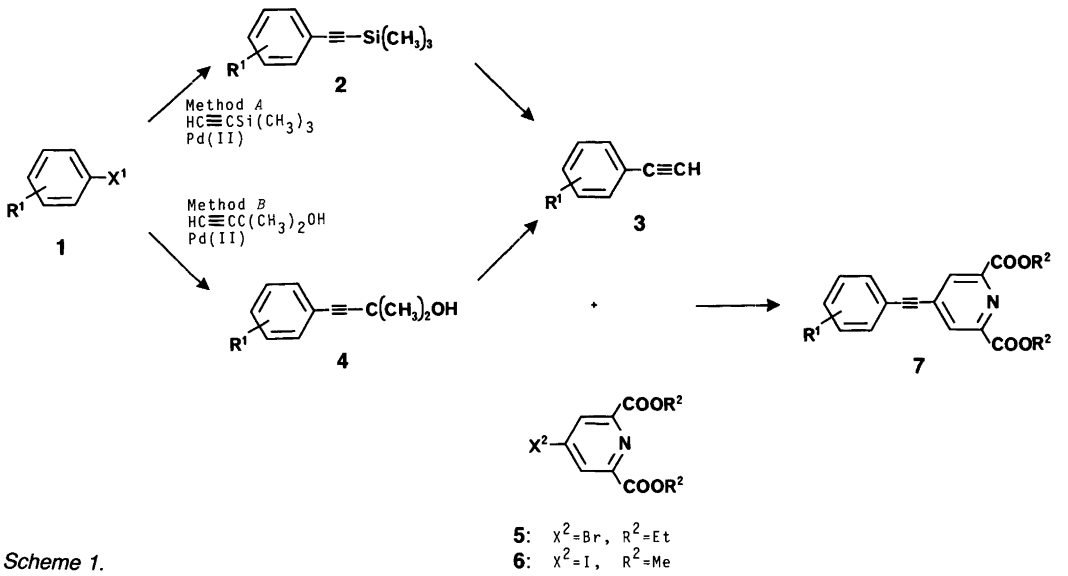
We have been interested in the properties of metal complexones of 4-substituted 2,6-pyridinedicarboxylic acids, and have recently reported the synthesis of dimethyl and diethyl 4-(phenylethynyl)-2,6-pyridinedicarboxylate (**7**, R^1=H and R^2=Me or Et in Scheme 1) from dialkyl 4-halo-2,6-pyridinedicarboxylate (**5** or **6**) and phenylacetylene in the presence of an organopalladium catalyst and copper(I) iodide in triethylamine.[1] Terminal acetylenes are valuable intermediates in these coupling reactions. In recent years much attention has been paid to a convenient two-step synthesis of these compounds.[1–16] In the first step an aromatic halide reacts with a protected acetylenic compound. After this, the removal of the protecting group generates a terminal arylacetylene.

Aryl halides react with (trimethylsilyl)acetylene in the presence of a small amount of a palladium catalyst and copper(I) iodide in secondary or tertiary amine as solvent to give (trimethylsilyl)ethynylarenes in high yields (Scheme 1, method *A*).[2–11] Aryl iodides react easily at room temperature, but bromides and especially chlorides must be activated, and in some cases also higher reaction temperatures are needed. The protecting group can be easily removed by treatment with dilute potassium or sodium hydroxide,[2,4,8,12] under milder conditions by treatment with potassium carbonate,[3,5,7] sodium bicarbonate,[11] potassium fluoride[9] or by passing compound **2** through an alumina column.[4] The yields of unpurified arylacetylenes are almost quantitative. This method is very useful if the molecule contains base-sensitive groups because of the mild desilylation conditions. However, a disadvantage of this method is the high cost of (trimethylsilyl)acetylene.

Aryl halides also react with the relatively inexpensive 2-methyl-3-butyn-2-ol under conditions similar to those described above for (trimethylsilyl)acetylene to yield the corresponding 4-aryl-2-methyl-3-butyn-2-ols (Scheme 1, method *B*).[7,9,13–16] The protecting group can usually be removed by treatment with alkali-metal hydroxides,[7,13,14,16] but also with sodium hydride[15] and potassium tert-butoxide[9] at elevated temperatures. A disadvantage of using alkali-metal hydroxides is that ester groups are usually not stable under these conditions, although it has been shown that the use of powdered potassium hydroxide in a vacuum or the use of sodium hydride has no effect on the ester groups.[15] Nevertheless, this method requires a rather high temperature which may lead to polymerization or other side reactions.

Terminal arylacetylenes react with aryl halides

*Present address: Wallac Oy, PL 10, SF-20101 Turku, Finland.



Scheme 1.

in the presence of an organopalladium catalyst and copper(I) iodide so that the final products are unsymmetric or symmetric diarylacetylenes.[1,8,11,17–20] As mentioned above, we have recently reported that the acetylenic hydrogen of phenylacetylene can be readily substituted by reaction with **5**[1] and **6**[25] to give dialkyl 4-(phenylethynyl)-2,6-pyridinedicarboxylate. In this paper we report the synthesis of some new substituted dimethyl and diethyl 4-(phenylethynyl)-2,6-pyridinedicarboxylates via terminal arylacetylenes which we synthesized using (trimethylsilyl)acetylene or 2-methyl-3-butyn-2-ol.

Results and discussion

Table 1 shows the conditions and results of the two-step synthesis of terminal arylacetylenes (**3a–f**) via 2-methyl-3-butyn-2-ol. In all cases the coupling reaction occurred at low temperatures within a few hours, generally giving reasonable yields. Some of the intermediates (**4**) were puri-

Table 1. Synthesis of terminal arylacetylenes (**3a–f**) from aryl halides (**1a–f**) by method *B*.

Aryl halide (**1a–f**)	1st step				2nd step	
	Reaction temp./°C	Reaction time/h	Yield/%	M.p./°C	Product (**3a-f**)	Yield/%
4-Iodoaniline (**1a**)	40	1–2	51–72($CHCl_3$-hexane)	85	**3a**[a]	46–57
3-Iodoaniline (**1b**)	40	1–2	69–72($CHCl_3$-hexane)	120–121	**3b**[b]	56
4-Iodo-*N*-methylaniline (**1c**)	40	4	–	–	**3c**[c]	60
4-Iodo-*N,N*-dimethylaniline (**1d**)	20–25	1–2	76(hexane)	85–86	**3d**[d]	44
4-Iodo-*O*-(tetrahydropyran-2-yl)-phenol (**1e**)	20–25	1–2	68(EtOH)	93–94	**3e**	52(EtOH)
4-Iodobenzophenone (**1f**)	40	4	65(CH_3CN)	116–117	**3f**	86(MeOH)

[a]M.p. 99.5–101.0 °C (lit. 99–100 °C).[27] [b]B.p. 122–124 °C/0.24 kPa (lit. 78–80 °C/0.2 mmHg).[32] [c]The liquid product was purified by chromatography on silica using petroleum ether (50–70 °C) – ethyl acetate (10:1) as eluent. [d]M.p. 54–56 °C (lit. 51–52 °C).[27]

fied, although it is not necessary for the next step.[14] On the other hand, according to our experiments the purification of these coupling products (**4**) ensures better results in the next step by shortening the induction period of the deprotection reaction. Yet the yields of the second step were only moderate. However, by this method we managed to synthesize 4- and 3-ethynylanilines (**3a–b**) with total yields of 41 % and 40 %, respectively. Although **3a** has been prepared earlier in better yield (66 %) via (trimethylsilyl)acetylene,[2] the use of 2-methyl-3-butyn-2-ol offers a less costly alternative. Also **3b** has been made earlier using the three-step synthesis, but the yield was not mentioned.[21] Compounds **1c–f** gave similar results.

As mentioned above, this method is not suitable for compounds containing base-sensitive ester groups. Since the desilylation step can be performed under milder conditions, e.g. by treatment with potassium carbonate, we synthesized the ester group containing terminal arylacetylenes (**3g–k**) using (trimethylsilyl)acetylene (Table 2). The organometallic coupling reactions also took place at low temperatures and within rather short times, with the exception of the reaction of **1j**. In every case the yield of the triethylamine hydrohalide formed during the reaction was almost quantitative. The reaction time for the first step was usually shorter than that for the second step. According to our experiments the desilylation reaction sometimes stopped prematurely when only a catalytic amount of potassium carbonate was used. In such cases the addition of an equivalent amount of the base completed the reaction. Since we used only unpurified (trimethylsilyl)ethynylarenes (**2**) immediately for the second step, the system may contain trace amounts of catalysts which enhance the formation of diarylbutadiynes.[22–24] This oxidative coupling reaction of terminal arylacetylenes could decrease the total yield of the products. As shown in Table 2, the hydroxy group of benzoic acids did not need any protection. This may be due to the chelating hydrogen bond between the carbonyl and the hydroxy group. On the other hand, 4-iodophenol (**1k**), which has no possibility of giving rise to such effects, gave only a polymer. Much better yields were obtained by using protected 4-iodophenol (**1e**) and 2-methyl-3-butyn-2-ol. The work-up procedure for **1j** induced ester exchange, which may explain the lower yield of **3j**.

The conditions and results of the coupling reactions between **3a–j** and **5** or **6** are given in Table 3. In most cases we used solvent systems which besides triethylamine also contained tetrahydrofuran or *N,N*-dimethylformamide to dissolve all starting materials. Although other solvents (e.g. methanol, piperidine and toluene) were also tried, tetrahydrofuran was found to be the best choice in these reactions. According to our experiments piperidine was not suitable as solvent because it reacted with both halides.

Experimental

*4-Iodo-*N*-methylaniline* (**1c**). Iodine (48.2 g, 0.190 mol) was added in small portions during 45 min to a cold (12–15 °C) solution of sodium hy-

Table 2. Synthesis of terminal arylacetylenes (**3g–k**) from aryl halides (**1g–k**) by method *A*.

Aryl halide (**1g–k**)	1st step		2nd step		Total yield/%
	Reaction temp./°C	Reaction time/h	Product (**3g–k**)	Reaction time/h	
Methyl 2-hydroxy-5-iodobenzoate (**1g**)	20–25	1	**3g**	48	65(petr. ether 50–70 °C)
Methyl 2-hydroxy-5-iodo-3-methylbenzoate (**1h**)	45	1	**3h**	26	70(hexane)
Methyl 2-amino-5-iodobenzoate (**1i**)	20–25	1	**3i**	5	50–55(hexane)
Ethyl 6-bromo-3-coumarincarboxylate (**1j**)	100	22	**3j**[a]	6	39(1-PrOH)
4-Iodophenol (**1k**)	20–25	4	**3k**	48	[b]

[a]The product was methyl ester. [b]We obtained only a polymer.

Table 3. Synthesis of substituted dialkyl 4-(phenylethynyl)-2,6-pyridinedicarboxylates (**7a–j**).

Arylacetylene (**3a–j**)	Halide (**5** or **6**)	Product (**7a–j**)	Solvent (ml)	Reaction temp./°C	Reaction time/h	Yield/%
3a	**6**	**7a**	Et_3N (5)	40	4	88
3b	**6**	**7b**	Et_3N (5)	30	1.5	67
3c	**6**	**7c**	Et_3N/DMF (8/2)	40	1	45
3d	**6**	**7d**	Et_3N (5)	40	5	48
3e	**6**	**7e**	Et_3N (5)	40	8	80
3f	**6**	**7f**	Et_3N/DMF (6/2.5)	40	3	71
3g	**5**	**7g**	Et_3N/THF (5/2)	45–50	5	80
3h	**5**	**7h**	Et_3N/THF (5/1)	50	4	54
3i	**5**	**7i**	Et_3N/THF (5/2)	50	3	69
3j	**5**	**7j**	Et_3N/THF (5/2)	45–50	3	32

drogen carbonate (23.5 g, 0.280 mol in 160 ml of water) and *N*-methylaniline (20.0 g, 0.187 mol). After stirring for 45 min the product was extracted with ether (50 ml), and the ether phase was washed with water (2×10 ml) and dried with sodium sulfate. After evaporation *in vacuo* the material was purified by chromatography on silica using petroleum ether (b.p. 50–70 °C)/ethyl acetate(5:3) as eluent, giving 27.2 g (63 %) of an easily decomposed liquid which was used without further purification. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.70 (3H, s), 3.65 (1H, s), 6.30 (2H, d), 7.35 (2H, d).

4-Iodo-N,N-*dimethylaniline* (**1d**) was prepared using the same method as for **1c**, giving a solid (33–45 %) which crystallized from petroleum ether (b.p. 50–70 °C); m.p. 81–82 °C (lit. 78.5 °C).[26]

4-Iodo-O-*(tetrahydropyran-2-yl)-phenol* (**1e**). A mixture of 4-iodophenol (0.44 g, 2.0 mmol), 3,4-dihydro-2*H*-pyran (0.19 g, 2.2 mmol) and one drop of 10 % HCl in ether was stirred for 4 h at room temperature. The mixture was diluted with ether (20 ml), washed with 20 % NaOH (2×5 ml) and then water (2×5 ml), and dried with sodium sulfate. Evaporation *in vacuo* gave a product which was crystallized from ethanol. The yield was 0.54 g (89 %), m.p. 65–66 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.55–2.02 (6H, m), 3.56–3.62 (1H, m), 3.83–3.89 (1H, m), 5.37 (1H, t), 6.83 (2H, d), 7.55 (2H, d).

4-Iodobenzophenone (**1f**). Sodium nitrite (1.7 g, 25 mmol) in water (6 ml) was added to a cold (<5 °C) mixture of 4-aminobenzophenone (4.9 g, 25 mmol) and 2M H_2SO_4 (50 ml) during 0.5 h. After stirring for 0.5 h below 5 °C, potassium iodide (6.2 g, 38 mmol) in 2M H_2SO_4 (20 ml) was added during 0.5 h. After further stirring for 0.5 h below 5 °C the ice bath was removed and stirring was continued for 1.5 h. The product was filtered off, washed with water and crystallized from ethanol. The yield was 4.9 g (64 %), m.p. 102–104 °C (lit. 102–103 °C).[27]

Methyl 2-hydroxy-5-iodobenzoate (**1g**). A mixture of 2-hydroxy-5-iodobenzoic acid (10.6 g, 40 mmol), methanol (40 ml) and concentrated H_2SO_4 (2 ml) was heated under reflux for 6 h. The reaction mixture was poured into ice-cold water (250 ml), which was then extracted with chloroform (3×100 ml). The combined organic solutions were washed with 5 % sodium hydrogen carbonate (100 ml) and water (100 ml), and dried with sodium sulfate. The solution was evaporated *in vacuo* and the residue was crystallized from ethanol. The yield was 5.7 g (51 %), m.p. 74–75 °C (lit. 75–76 °C).[28]

Methyl 2-hydroxy-5-iodo-3-methylbenzoate (**1h**). Iodine (2.54 g, 10 mmol) and potassium iodide (3.32 g, 20 mmol) in water (15 ml) were slowly added to a cold (0 °C) mixture of 2-hydroxy-3-methylbenzoic acid (3.04 g, 20 mmol) in 10 % potassium hydroxide solution (25 ml). The mixture was acidified with 10 % HCl and the solid was filtered off and washed with water. The dry material was heated under reflux for 6 h with methanol (20 ml) containing concentrated H_2SO_4

(1 ml). The product was treated as above and finally crystallized from methanol. The yield was 2.05–2.40 g (35–41 %), m.p. 93–94 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.22 (3H, s), 3.94 (3H, s), 7.62 (1H, d), 7.99 (1H, d), 10.97 (1H, s).

Methyl 2-amino-5-iodobenzoate (**1i**). A dry 20 % solution of HCl in methanol (40 ml) was added to a mixture of 2-amino-5-iodobenzoic acid (11.6 g, 44 mmol) in methanol (50 ml). After heating under reflux for 24 h, the solution was poured into cold water (150 ml) and the mixture was neutralized with solid sodium carbonate. The product was filtered off, washed with water and finally crystallized from petroleum ether (b.p. 50–70 °C) after removal of the insoluble acid by filtration. The yield was 6.5 g (53 %), m.p. 82.5–83.0 °C (lit. 83–85 °C).[29]

Ethyl 6-bromo-3-coumarincarboxylate (**1j**) was prepared as described previously.[30]

Preparation of terminal arylacetylenes (**3**). *Method A.* A mixture of **1g–k** (10 mmol), bis-(triphenylphosphine)palladium(II) chloride (140 mg, 0.2 mmol) and copper(I) iodide (76 mg, 0.4 mmol) in dry triethylamine (40 ml) was deaerated with nitrogen. (Trimethylsilyl)acetylene (1.0 g, 10 mmol) was added and the reaction mixture was heated to the desired temperature. After the reaction was complete, the mixture was filtered and the filtrate was evaporated *in vacuo*. The residue was dissolved in dichloromethane (75 ml), and the solution was washed with water (2×30 ml) and dried with sodium sulfate. After evaporation *in vacuo* the remaining material was dissolved in methanol (28 ml); the solution was deaerated with nitrogen, and potassium carbonate (1–10 mmol) was added to the reaction vessel. The mixture was stirred until the reaction was complete. The solution was filtered and the filtrate was evaporated *in vacuo* without heating. The residue was dissolved in dichloromethane (60 ml), and the solution was washed with 5 % sodium hydrogen carbonate (30 ml) and water (30 ml), and dried with sodium sulfate. The solution was evaporated *in vacuo* and the residue was crystallized from a suitable solvent (Table 2).

Methyl 5-ethynyl-2-hydroxybenzoate (**3g**). M.p. 86 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.99 (1H, s), 4.00 (3H, s), 6.94 (1H, d), 7.56 (1H, dd), 8.01 (1H, d), 10.92 (1H, s). IR (KBr): 3265 cm^{-1} (C≡C–H), 2110 cm^{-1} (C≡C), 1680 cm^{-1} (C=O).

Methyl 5-ethynyl-2-hydroxy-3-methylbenzoate (**3h**). M.p. 79–80 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.24 (3H, s), 2.96 (1H, s), 3.95 (3H, s), 7.44 (1H, d), 7.87 (1H, d), 11.17 (1H, s). IR (KBr): 3280 cm−1 (C≡C–H), 2105 cm^{-1} (C≡C), 1670 cm^{-1} (C≡O).

Methyl 2-amino-5-ethynylbenzoate (**3i**). M.p. 117–119 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.94 (1H, s), 3.87 (3H, s), 5.93 (2H, s), 6.59 (1H, d), 7.36 (1H, dd), 8.04 (1H, d). IR (KBr): 3480, 3370 cm^{-1} (N–H), 3285 cm^{-1} (C≡C–H), 2100 cm^{-1} (C≡C), 1685 cm^{-1} (C≡O).

Methyl 6-ethynyl-3-coumarincarboxylate (**3j**). M.p. 196–197 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 3.17 (1H, s), 3.96 (3H, s), 7.33–8.52 (4H, m). IR (KBr): 3230 cm^{-1} (C≡C–H), 2100 cm^{-1} (C≡C), 1745, 1700, 1250 cm^{-1} (C=O and C–O).

Method B. A mixture of **1a–f** (10 mmol), bis-(triphenylphosphine)palladium(II) chloride (140 mg, 0.2 mmol), copper(I) iodide (38 mg, 0.2 mmol) and 2-methyl-3-butyn-2-ol (1.01 g, 12 mmol) in dry triethylamine (20–40 ml) was deaerated with nitrogen and the reaction mixture was heated to the desired temperature. After the reaction was complete, the mixture was filtered and the filtrate was evaporated *in vacuo*. The residue was dissolved in ether (60 ml), and the solution was washed with water (3×20 ml) and dried with sodium sulfate. Evaporation *in vacuo* gave a crude material which was further purified by crystallization or was used as such. This material was heated under distillation conditions in the presence of three pellets of sodium hydroxide in toluene (30 ml). After the reaction was complete (1–2 h), the hot mixture was filtered and the filtrate was evaporated *in vacuo*. The crude material was crystallized from a suitable solvent, or used in the next step without further purification (Table 1).

4-Ethynyl-N-methylaniline (**3c**). ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.75 (3H, s), 2.95 (1H, s), 3.80 (1H, s), 6.44 (2H, d), 7.25 (2H, d). IR (KBr): 3420 cm^{-1} (N–H), 3290 cm^{-1} (C≡C–H), 2100 cm^{-1} (C≡C).

4-Ethynyl-O-(tetrahydropyran-2-yl)phenol (**3e**). M.p. 68 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.40–2.10 (6H, m), 2.79 (1H, s), 3.37–3.70 (2H, m), 5.22 (1H, m), 6.79 (2H, d), 7.21 (2H, d). IR (KBr): 3280 cm^{-1} (C≡C–H), 2110 cm^{-1} (C≡C), 1240, 1115 cm^{-1} (C–O–C).

4-Ethynylbenzophenone (**3f**). M.p. 48 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 3.10 (1H, s), 7.00–7.87 (9H, m). IR (KBr): 3290 cm^{-1} (C≡C–H), 2100 cm^{-1} (C≡C), 1656 cm^{-1} (C=O).

General method for the coupling reaction of 3a–j to 5[1] *or 6*[25]. A mixture of **5** or **6** (1.25 mmol), bis(triphenylphosphine)palladium(II) chloride (18 mg, 0.025 mmol) and copper(I) iodide (10 mg, 0.050 mmol) in dry triethylamine (5 ml) was deaerated with nitrogen compound. **3a–j** (1.25 mmol) was added to the reaction mixture and heated to the desired temperature. After the reaction was complete, the mixture was filtered and the filtrate was evaporated *in vacuo*. The residue was dissolved in chloroform (30 ml), and the solution was washed with water (3×10 ml) and dried with sodium sulfate. Evaporation *in vacuo* gave a crude material which was further purified by crystallization from methanol (Table 3).

Dimethyl 4-(4-aminophenylethynyl)-2,6-pyridinedicarboxylate (**7a**). M.p. 213 °C. ^{1}H NMR (60 MHz, CD_3COCD_3): δ 3.96 (6H, s), 5.25 (2H, broad s), 6.71 (2H, d), 7.20 (2H, d), 8.20 (2H, s). IR (KBr): 3480, 3382 cm^{-1} (N–H), 2195 cm^{-1} (C≡C), 1735, 1262 cm^{-1} (C=O and C–O). Anal. $C_{17}H_{14}N_2O_4$: C, H, N.

Dimethyl 4-(3-aminophenylethynyl)-2,6-pyridinedicarboxylate (**7b**). M.p. 183 °C. ^{1}H NMR (60 MHz, CD_3COCD_3): δ 4.00 (6H, s), 4.88 (2H, broad s), 6.80–7.15 (4H, m), 8.20 (2H, s). IR (KBr): 3450, 3380 cm^{-1} (N–H), 2210 cm^{-1} (C≡C), 1740, 1265, 1244 cm^{-1} (C=O and C–O). Found: C 65.05; H 4.51; N 8.94. Calc. for $C_{17}H_{14}N_2O_4$: C 65.81; H 4.54; N 9.03.

Dimethyl 4-(N-methyl-4-aminophenylethynyl)-2,6-pyridinedicarboxylate (**7c**). M.p. 191–192 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.90 (3H, s), 4.05 (6H, s), 6.55 (2H, d), 7.40 (2H, d), 8.25 (2H, s). IR (KBr): 3425 cm^{-1} (N–H), 2200 cm^{-1} (C≡C), 1720, 1270 cm^{-1} (C=O and C–O). Found: C 65.43; H 4.99; N 8.43. Calc. for $C_{18}H_{16}N_2O_4$: C 66.67; H 4.96; N 8.64.

Dimethyl 4-(N,N-dimethyl-4-aminophenylethynyl)-2,6-pyridinedicarboxylate (**7d**). M.p. 215–216 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 3.05 (6H, s), 4.02 (6H, s), 6.60 (2H, d), 7.45 (2H, d), 8.25 (2H, s). IR (KBr): 2205 cm^{-1} (C≡C), 1756, 1715, 1283, 1246 cm^{-1} (C=O and C–O). Anal. $C_{19}H_{18}N_2O_4$: C, H, N.

Dimethyl 4-[O-(tetrahydropyran-2-yl)hydroxyphenylethynyl]-2,6-pyridinedicarboxylate (**7e**). M.p. 149 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.47–2.05 (6H, m), 3.61–3.65 (1H, m), 3.85–3.91 (1H, m), 4.04 (6H, s), 5.48 (1H, t), 7.07 (2H, d), 7.51 (2H, d), 8.34 (2H, s). IR (KBr): 2210 cm^{-1} (C≡C), 1753, 1720, 1280, 1245 cm^{-1} (C=O and C–O). Found: C 64.17; H 5.23; N 3.84. Calc. for $C_{22}H_{21}NO_6$: C 66.83; H 5.34; N 3.54.

Dimethyl 4-(4-benzoylphenylethynyl)-2,6-pyridinedicarboxylate (**7f**). M.p. 165–166 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 4.05 (6H, s), 7.05–8.00 (9H, m), 8.40 (2H, s). IR (KBr): 2215 cm^{-1} (C≡C), 1755, 1722, 1655, 1270 cm^{-1} (C=O and C–O). Anal. $C_{24}H_{17}NO_5$: C, H, N.

Diethyl 4-(3-carbomethoxy-4-hydroxyphenylethynyl)-2,6-pyridinedicarboxylate (**7g**). M.p. 52.0–52.5 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.47 (6H, t), 4.00 (3H, s), 4.51 (4H, q), 7.03 (1H, d), 7.65 (1H, dd), 8.12 (1H, d), 8.31 (2H, s), 11.05 (1H, s). IR (KBr): 2210 cm^{-1} (C≡C), 1745, 1720, 1680, 1240 cm^{-1} (C=O and C–O). Anal. $C_{21}H_{19}NO_7$: C, H, N.

Diethyl 4-(3-carbomethoxy-4-hydroxy-5-methylphenylethynyl)-2,6-pyridinedicarboxylate (**7h**). M.p. 116–120 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.47 (6H, t), 2.29 (3H, s), 3.99 (3H, s), 4.50 (4H, q), 7.53 (1H, s), 7.98 (1H, s), 8.30 (2H, s), 11.31 (1H, s). IR (KBr): 2210 cm^{-1} (C≡C), 1745, 1720, 1285, 1238 cm^{-1} (C=O and C–O). Anal. $C_{22}H_{21}NO_7$: C, H, N.

Diethyl 4-(4-amino-3-carbomethoxyphenylethynyl)-2,6-pyridinedicarboxylate (**7i**). M.p. 173 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.47 (6H, t), 3.91 (3H, s), 4.50 (4H, q), 6.67 (1H, d), 7.46 (1H, d), 8.16 (1H, s), 8.28 (2H, s). IR (KBr): 3465, 3360

cm^{-1} (N−H), 2215 cm^{-1} (C≡C), 1745, 1695, 1245 cm^{-1} (C≡O and C−O). Anal. $C_{21}H_{20}N_2O_6$: C, H, N.

Diethyl 4-[6-(3-carbomethoxycoumaryl)ethynyl]-2,6-pyridinedi-carboxylate (**7j**). M.p. 206–207 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 1.48 (6H, t), 3.99 (3H, s), 4.52 (4H, q), 7.41 (1H, d), 7.80–7.85 (2H, m), 8.35 (2H, s), 8.55 (1H, s). IR KBr): 2220 cm^{-1} (C≡C), 1760, 1719, 1255 cm^{-1} (C=O and C−O). Anal. $C_{24}H_{19}NO_8$: C, H, N.

References

1. Takalo, H. and Kankare, J. *Acta Chem. Scand., Ser. B 41* (1987) 219.
2. Takahashi, S., Kuroyama, Y., Sanogashira, K. and Hagihara, N. *Synthesis* (1980) 627.
3. Austin, W. B., Bilow, N., Kelleghan, W. J. and Lau, K. S. Y *J. Org. Chem. 46* (1981) 2280.
4. Sakamoto, T., Shiraiwa, M., Kondo, Y. and Yamanaka, H. *Synthesis* (1983) 312.
5. Lau, K. S. Y., Kelleghan, W. J., Boschan, R. H. and Bilow, N. *J. Polym. Sci., Polym. Chem. Ed. 21* (1983) 3009.
6. Sakamoto, T., Kondo, Y. and Yamanaka, H. *Heterocycles 22* (1984) 1347.
7. Havens, S. J. *J. Polym. Sci., Polym. Chem. Ed. 22* (1984) 3011.
8. Diercks, R. and Vollhardt, K. P. C. *Angew. Chem. Int. Ed. Engl. 25* (1986) 266.
9. Diercks, R., Armstrong, J. C., Boese, R. and Vollhardt, K. P. C. *Angew. Chem. Int. Ed. Engl. 25* (1986) 268.
10. Tischler, A. N. and Lanza, T. J. *Tetrahedron Lett. 27* (1986) 1653.
11. Undheim, K. and Solberg, J. *Acta Chem. Scand., Ser. B 40* (1986) 381.
12. Eaborn, C. and Walton, D. R. M. *J. Organomet. Chem. 4* (1965) 217.
13. Ames, D. E., Bull, D. and Takundwa, C. *Synthesis* (1981) 364.
14. Sabourin, E. T. and Onopchenko, A. *J. Org. Chem. 48* (1983) 5135.
15. Havens, S. J. and Hergenrother, P. M. *J. Org. Chem. 50* (1985) 1763 and references therein.
16. Cianna, L. D. and Haim, A. *J. Heterocycl. Chem. 21* (1984) 607.
17. Sonogashira, K., Todha, Y. and Hagihara, N. *Tetrahedron Lett.* (1975) 4467.
18. Dieck, H. A. and Heck, F. R. *J. Organomet. Chem. 93* (1975) 259.
19. Cassar, L. *J. Organomet. Chem. 93* (1975) 253.
20. Cabrita, A., Lessi, A. and Rossi, R. *Synthesis* (1984) 571.
21. Onopchenko, A., Sabourin, E. T. and Selwitz, C. M. *J. Org. Chem. 44* (1979) 1233.
22. Fritzsch, V. and Hunig, S. *Tetrahedron Lett.* (1972) 4831.
23. Rossi, R., Carpita, A. and Bigelli, C. *Tetrahedron Lett. 26* (1985) 523.
24. Carpita, A., Rossi, R. and Varacini, C. A. *Tetrahedron 41* (1985) 1919.
25. Graf, R. *J. Prakt. Chem. 148* (1937) 13.
26. Reade, T. H. and Sim, S. A. *J. Chem. Soc. 125* (1924) 157.
27. Hoffmann, E. *Liebigs Ann. Chem. 264* 160.
28. Immerwahr, W. A. *Pharm. J. 159* (1947) 182.
29. Petyunin, P. A. and Konshin, M. E. *Zh. Obshch. Khim. 27* (1957) 475; *Chem. Abstr. 51* (1957) 15523a.
30. Clinton, R. O. and Laskowski, S. C. *J. Am. Chem. Soc. 71* (1949) 3602.
31. Dawson, D. A. and Reynolds, W. F. *Can. J. Chem,. 53* (1975) 373.
32. Onoipchenko, A., Sabourin, E. T. and Selwitz, C. M. *J. Org. Chem. 44* (1979) 3671.

Received December 22, 1987.