January, 1985] © *1985 The Chemical Society of Japan* *Bull. Chem. Soc. Jpn., 58, 181—184 (1985)* 181

Synthesis of 5-(Substituted Styryl)-2-aminotropones

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(Received July 23, 1984)

The methylation of 4-styryltropolones with diazomethane afforded 2-methoxy-4-styryltropones (**2a—g**) and 2-methoxy-6-styryltropones. The reactions of **2a—g** with hydrazine gave 2-hydrazino derivatives, which were converted to 2-chloro derivatives **5a—g**. Ammonolysis of **5a—g** afforded 2-amino-5-styryltropones (**7a—g**) by *ciné* substitution reaction. The compounds **7a—g** were hydrolyzed to give the corresponding 5-styryltropolones. Some interesting by-products were also found in these synthetic processes.

Previously, we have studied long-range substituent effects on dissociation constants of some series of styryltropolone derivatives and transmission of the electronic effects between two aromatic rings which were connected by vinylene linkage.[1-4] In connection with these studies, the dissociation constants of some 5-(substituted styryl)-2-aminotropones were discussed.[5] This paper deals with their synthesis.

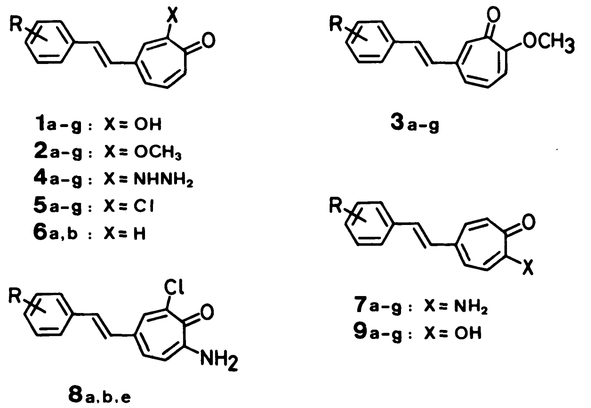
Results and Discussion

The condensations of 3-carboxy-4-carboxymethyltropolone with some substituted benzaldehydes gave 3-carboxy-4-styryltropolones, which were converted to 4-styryltropolones (**1a—g**) with carbon dioxide elimination.[6] Now, two new 4-styryltropolones (**1b**: R=*m*-CH_3 and **1d**: R=*m*-OCH_3) were obtained.

The methylations of **1a—g** with diazomethane afforded two isomeric 2-methoxy-4-styryl- (**2a—g**) and 2-methoxy-6-styryltropones (**3a—g**), which were previously reported[7] except for the new compounds **2b**, **d** and **3b**, **d**. Furthermore, treatments of **2a—g** with hydrazine gave 2-hydrazino-4-styryltropones (**4a—g**). The yields and characteristic data are summarized in Table 1.

Oxidative decompositions of **4a—g** in concentrated hydrochloric acid in the presence of copper(II) sulfate afforded 2-chloro-4-styryltropones (**5a—g**). The structures were confirmed by their analytical and spectral data, which are listed in Table 1. Further, in this reaction a trace amount of by-products were isolated. We could confirm structures of only two products from **4a** and **4b** to be 4-styryl- (**6a**)[8] and 4-(*m*-methylstyryl)tropone (**6b**). Other isolated ones were too small to analyze.

Reactions of 2-chloro-4-styryltropones (**5a—g**) with ammonia afforded 2-amino-5-styryltropones (**7a—g**) by *ciné* substitution reaction. These reactions also gave a new type of compounds, 2-amino-7-chloro-5-styryltropones (**8a, b, e**). These results were summarized in Table 1. Although some by-products were isolated in the cases of the ammonolysis of **5c**, **d**, **f**, **g**, their amounts were too small to establish their structures.



Scheme 1.
a R=H, **b** R=*m*-CH_3, **c** R=*p*-CH_3, **d** R=*m*-OCH_3, **e** R=*p*-OCH_3, **f** R=*m*-Cl, **g** R=*p*-Cl

The infrared spectra of the compounds **8a**, **b**, **e** are very similar to those of 2-amino-5-styryltropones **7** but show a little difference in the finger-print region. Their electronic spectra are also similar to those of **7** but show slightly bathochromic shift. These spectral data suggest that **8a**, **b**, **e** have a tropone ring and styryl group. The structure of **8a** was also confirmed by the fragmentation analysis in the mass spectrum.

In addition, 2-amino-5-styryltropones (**7a—g**) were hydrolyzed to afford 5-styryltropolones (**9a—g**).[9]

Experimental

The melting points were determined with a Yanagimoto MP-S2 apparatus and are uncorrected. The IR and UV spectra were taken on a JASCO IRA-1 and a Hitachi EPS-3T spectrophotometer, respectively. The NMR spectra were recorded with a Hitachi-Perkin-Elmer R-24 spectrometer (60 MHz). The mass spectrum was run on a JEOL JMS-01-SG2 apparatus.

4-Styryltropolones (1a—g). 4-Styryltropolones (**1a—g**) were prepared according to a previous work.[6]

2-Methoxy-4-styryltropones (2a—g) and 2-Methoxy-6-styryltropones (3a—g). An excess of diazomethane ethereal

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TABLE 1. CHARACTERISTIC DATA

Compd	Yield	Mp	IR ($CHCl_3$)	UV (CH_3OH)	NMR ($CDCl_3$)	Formula	Found (Calcd) (%)		
	%	θ_m/°C	cm^{-1}	λ/nm (log ε)	δ		C	H	N
1b	48	93— 94	1600 (C=O)	315 (4.25) 402 (4.22)	2.33 (3H, s, CH_3) 6.9—7.3 (9H, m) 7.46 (1H, s, H-3)	$C_{16}H_{14}O_2$	80.49 (80.60	5.88 5.92)	
1d	22	106—107	1600 (C=O)	218 (4.30) 314 (sh, 4.33)	3.76 (3H, s, OCH_3) 6.8—7.4 (9H, m) 7.50 (1H, s, H-3) 8.73 (1H, br, OH)	$C_{16}H_{14}O_3$	75.40 (75.57	5.47 5.55)	
2b	40	Oil	1595 (C=O)	313 (4.41)	2.40 (3H, s, CH_3) 4.03 (3H, s, OCH_3) 6.9—7.4 (10H, m)	$C_{23}H_{19}N_3O_9$ a)	57.35 (57.38	3.94 3.98	8.42 8.73)
2d	28	107	1590 (C=O)	282 (4.13) 396 (4.16)	3.86 (3H, s, OCH_3) 4.02 (3H, s, OCH_3) 6.8—7.4 (10H, m)	$C_{17}H_{16}O_3$	75.85 (76.10	6·03 6.01)	
3b	45	150—152	1590 (C=O)	314 (4.41)	2.34 (3H, s, CH_3) 3.88 (3H, s, OCH_3) 6.5—7.4 (10H, s)	$C_{17}H_{16}O_2$	80.62 (80.92	6.37 6.39)	
3d	35	140—141	1585 (C=O)	309 (4.47)	3.86 (3H, s, OCH_3) 3.94 (3H, s, OCH_3) 6.6—7.3 (9H, m) 7.40 (1H, s, H-3)	$C_{17}H_{16}O_3$	76.07 (76.10	6.21 6.01)	
4a	68	195 (189—190) b)	3305 (NH) 3270 (NH) 1630 (C=O)	238 (4.09) 330 (4.56) 444 (3.92)	7.3—8.2 (m) c)				
4b	89	163—164	3310 (NH) 3270 (NH) 1640 (C=O)	239 (4.08) 332 (4.56) 442 (3.73)	2.40 (3H, s, CH_3) 3.84 (2H, m, NH_2) 6.5—7.6 (10H, m) 8.0—8.1 (1H, m, H-3)	$C_{16}H_{16}N_2O$	76.08 (76.16	6.31 6.39	11.37 11.10)
4c	80	212	3310 (NH) 3265 (NH) 1630 (C=O)	240 (4.31) 334 (4.75) 442 (4.15)	2.40 (3H, s, CH_3) c) 7.4—8.4 (10H, m)	$C_{16}H_{16}N_2O$	75.96 (76.16	6.44 6.39	11.23 11.10)
4d	99	173—174	3300 (NH) 3255 (NH) 1630 (C=O)	216 (4.39) 331 (4.50) 442 (3.98)	4.06 (3H, s, OCH_3) c) 7.0—8.5 (10H, m)	$C_{16}H_{16}N_2O_2$	71.47 (71.62	5.94 6.01	10.35 10.44)
4e	64	198—200	3310 (NH) 3270 (NH) 1650 (C=O)	242 (4.10) 340 (4.50) 440 (4.04)	4.04 (3H, s, OCH_3) c) 7.0—8.5 (10H, m)	$C_{16}H_{16}N_2O_2$	71.51 (71.62	5.94 6.01	10.24 10.44)
4f	86	191—192	3300 (NH) 3255 (NH) 1625 (C=O)	236 (4.15) 329 (4.58) 446 (3.96)	7.3—8.2 (9H, m) c) 8.35 (1H, s, H-3)	$C_{15}H_{13}ClN_2O$	66.02 (66.06	4.74 4.80	10.14 10.27)
4g	95	223	3310 (NH) 3270 (NH) 1635 (C=O)	237 (4.13) 334 (4.55) 445 (3.94)	7.0—8.2 (9H, m) c) 8.24 (1H, s, H-3)	$C_{15}H_{13}ClN_2O$	65.79 (66.06	4.80 4.80	10.08 10.27)
5a	32	110 (111—111.5) b)	1615 (C=O)	242 (4.03) 282 (4.09) 276 (4.26)	6.9 (10H, m) 8.04 (1H, s, H-3)				

Table 1. (Continued)

Compd	Yield	Mp	IR ($CHCl_3$)	UV (CH_3OH)	NMR ($CDCl_3$)	Formula	Found (Calcd) (%)		
	%	θ_m/°C	cm^{-1}	λ/nm (log ε)	δ		C	H	N
5b	37	130—131	1610 (C=O)	243 (4.12) 284 (4.01) 380 (4.33)	2.28 (3H, s, CH_3) 6.9—7.5 (9H, m) 8.18 (1H, s, H-3)	$C_{16}H_{13}ClO$	74.54 (74.85	5.12 5.10)	
5c	52	140	1620 (C=O)	246 (4.14) 263 (4.12) 325 (4.02) 382 (4.17)	2.34 (3H, s, CH_3) 6.8—7.2 (5H, m) 7.23 (2H, d, J=8 Hz, H-3′,5′) 7.41 (2H, d, J=8 Hz, H-2′,6′) 8.09 (1H, s, H-3)	$C_{16}H_{13}ClO$	74.83 (74.85	5.19) 5.10)	
5d	37	118—119	1610 (C=O)	280 (4.28) 383 (4.39)	3.84 (3H, s, OCH_3) 6.6—7.4 (9H, m) 8.13 (1H, s, H-3)	$C_{16}H_{13}ClO_2$	70.20 (70.46	4.83 4.80)	
5e	45	111—112	1615 (C=O)	249 (4.23) 400 (4.38)	3.83 (3H, s, OCH_3) 6.6—7.3 (5H, m) 6.84 (2H, d, J=9 Hz, H-3′,5′) 7.48 (2H, d, J=9 Hz, H-2′,6′) 8.13 (1H, s, H-3)	$C_{16}H_{13}ClO_2$	70.28 (70.46	4.78 4.80)	
5f	36	182	1615 (C=O)	245 (4.14) 284 (4.17) 369 (4.26)	6.9—7.9 (9H, m) 8.12 (1H, s, H-3)	$C_{15}H_{10}Cl_2O$	64.78 (65.00	3.67 3.64)	
5g	28	146—147	1620 (C=O)	246 (4.12) 380 (4.43)	6.9 (9H, m) 8.11 (1H, s, H-3)	$C_{15}H_{10}Cl_2O$	64.79 (65.00	3.65 3.64)	
7a	43	207—208 (205—206)[b]	3510 (NH) 3360 (NH) 1595 (C=O)	236 (4.36) 242 (4.45) 285 (4.34) 389 (4.58)	5.8 (2H, br, NH_2) 7.0—7.6 (11H, m)				
7b	8	172	3510 (NH) 3350 (NH) 1595 (C=O)	237 (4.36) 244 (4.36) 285 (4.34) 391 (4.58)	2.37 (3H, s, CH_3) 5.88 (2H, br, NH_2) 6.5—7.8 (10H, m)	$C_{16}H_{15}NO$	80.79 (80.98	6.37 6.37	5.86 5.90)
7c	48	237	3510 (NH) 3360 (NH) 1585 (C=O)	244 (4.45) 288 (4.37) 394 (4.58)	2.35 (3H, s, OCH_3) 5.8 (2H, br, NH_2) 6.5—7.7 (10H, m)	$C_{16}H_{15}NO$	80.89 (80.98	6.36 6.37	5.63 5.90)
7d	24	162	3500 (NH) 3350 (NH) 1595 (C=O)	243 (4.48) 280 (4.34) 392 (4.58)	3.84 (3H, s, OCH_3) 5.9 (2H, br, NH_2) 6.7—7.5 (10H, m)	$C_{16}H_{15}NO_2$	75.62 (75.87	6.02 5.97	5.40 5.53)
7e	15	244—245	3510 (NH) 3360 (NH) 1595 (C=O)	245 (4.41) 295 (4.32) 398 (4.55)	3.83 (3H, s, OCH_3) 5.9 (2H, br, NH_2) 6.8—7.9 (10H, m)	$C_{16}H_{15}NO_2$	75.82 (75.87	6.02 5.97	5.25 5.53)
7f	20	244—246	3510 (NH) 3360 (NH) 1590 (C=O)	243 (4.45) 285 (4.35) 391 (4.58)	6.00 (2H, br, NH_2) 6.7—7.7 (10H, m)	$C_{15}H_{12}ClNO$	70.10 (69.91	4.57 4.69	5.35 5.43)
7g	22	231—232	3500 (NH) 3350 (NH) 1590 (C=O)	244 (4.54) 289 (4.50) 393 (4.69)	5.95 (2H, br, NH_2) 6.9—7.5 (10H, m)	$C_{15}H_{12}ClNO$	69.85 (69.91	4.76 4.69	5.26 5.43)

a) Picrate. b) H. Matsumura, *Nippon Kagaku Zasshi*, **81**, 1763 (1960). c) In CF_3COOH.

solution was added to a solution of 4-styryltropolone (**1a**—**g**) (1.0 g, 3.3—4.2 mmol) in chloroform (10 ml), and the mixture was allowed to stand for 2 d in a refrigerator. After removal of the solvents, the residue was chromatographed on three Wakogel B-10 plates (30×30 cm) with ethyl acetate. 2-Methoxy-4-styryltropones (**2a**—**g**) and 2-methoxy-6-styryltropones (**3a**—**g**) were obtained from the upper and lower band, respectively. Each methyl ether was recrystallized from benzene.

2-Hydrazino-4-styryltropones (4a—g). To a solution of 2-methoxy-4-styryltropone (**2a**—**g**) (1.0 g, 3.7—4.2 mmol) in ethanol (5 ml) was added 80% hydrazine hydrate (1.0 ml). The mixture was allowed to stand overnight at room temperature. The precipitate was collected and recrystallized from methanol to give 2-hydrazino-4-styryltropones (**4a**—**g**).

2-Chloro-4-styryltropones (5a—g). A hot solution of copper(II) sulfate pentahydrate (5 g) in water (6 ml) was added to a hot suspended solution of 2-hydrazino-4-styryltropones (**4a**—**g**) (500 mg) in concentrated hydrochloric acid (5 ml). The mixture was immediately cooled, diluted with water, and extracted with chloroform. The extract was dried over sodium sulfate, concentrated, and chromatogrpahed on a Wakogel C-100 column (50 g) with chloroform to afford 2-chloro-4-styryltropones (**5a**—**g**) (from methanol).

4-Styryltropones (6a, b). In the preparation of 2-chloro-4-styryltropones (**5a**, **b**), the second band in the chromatography gave 4-styryltropones (**6a**, **b**).

6a: Yellow crystals. Yeild, 9%. Mp 89—92 °C (lit,[8] 89—91 °C).

6b: Oil. Yield, 19%. IR ($CHCl_3$) 1625 (C=O), 1565 (C=C), 960 cm^{-1} (CH). Found: C, 86.23; H, 6.39%. Calcd for $C_{16}H_{14}O$ C, 86.45; H, 6.35%.

2-Amino-5-styryltropones (5a—g). A suspended solution of 2-chloro-4-styryltropone (**5a**—**g**) (100 mg) in ammonia-saturated absolute ethanol (6 ml) in a sealed tube was allowed to stand for 2 d at room temperature. After removal of the ammonia and ethanol, the residue was chromatographed on a Wakogel B-10 plate (20×20 cm) with ethyl acetate to give 2-amino-5-stytyltropones (**7a**—**g**) (from ethanol).

2-Amino-7-chloro-5-styryltropones (8a, b, e). In the preparation of 2-amino-5-styryltropones (**7a**, **b**, **e**), the upper fraction in the chromatography gave 2-amino-7-chloro-5-styryltropones (**8a**, **b**, **e**), respectively.

8a: Yellow needles (from benzene). Yield, 35%. Mp 186 °C. IR ($CHCl_3$) 3510 (NH), 3360 (NH), 1590 (C=O), 950 cm^{-1} (CH); UV (CH_3OH) 251 (log ε 4.24), 289 (5.32), 392 nm (4.46); MS *m/z* (%) 259 (M', 38), 257 (M, 100), 231 (M'−CO, 14), 229 (M−CO, 40), 194 ([231 and 229]-Cl, 25), 193 ([231 and 229]-HCl, 42). Found: C, 69.86; H 4.92; N, 5.31%. Calcd for $C_{15}H_{12}NOCl$: C, 69.90; H, 4.70; N, 5.44%.

8b: Yellow prisms (from benzene). Yield, 3%. Mp 177 °C. IR ($CHCl_3$) 3510 (NH), 3350 (NH), 1595 (C=O), 970 cm^{-1} (CH); NMR ($CDCl_3$) δ=2.36 (3H, s, CH_3), 6.12 (2H, br, NH_2), 6.8—7.5 (9H, m). Found: C, 70.75; H, 5.23; N, 5.10%. Calcd for $C_{16}H_{14}NOCl$: C, 70.72; H, 5.19; N, 5.15%.

8e: Yellowish brown needles (from benzene). Yield, 30%. Mp 208—210 °C. IR ($CHCl_3$) 3500 (NH), 3340 (NH), 1600 (C=O), 960 cm^{-1} (CH). Found: C, 66.73; H, 4.96; N, 4.63%. Calcd for $C_{16}H_{14}NO_2Cl$: C, 66.78; H, 4.96; N, 4.87%.

We wish to thank Professor Hitoshi Takeshita, Kyushu University, for his kind measurement of the mass spectrum.

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