SYNTHESES OF PYRANO[4,3-*b*]BENZODIAZEPINE AND PYRANO-[4,3-*b*]QUINOLINE USING 4-CHLORO-3-(1-CHLOROVINYL)-6-METHYL-2*H*-PYRAN-2-ONE AND 4-CHLORO-3-ETHYNYL-6-METHYL-2*H*-PYRAN-2-ONE

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Abstract- Reaction of dichloropyrone (**1**) and chloroethynylpyrone (**2**) with *o*-phenylenediamine and *m*-phenylenediamine give pyranobenzodiazepine (**3**) and pyranoquinoline (**5**), respectively. Treatment of **1** and **2** with *p*-phenylenediamine yield aminoethynylpyrone (**6**), which is a key product in the reaction of **1** and **2** with phenylenediamines.

Moreno-Manas and his co-workers reported[1] that the reaction of 4-chloro-3-(1-chlorovinyl)-6-methyl-2*H*-pyran-2-one (**1**) with hydrazines gave pyranopyrazole derivatives. It seems that dichloropyrone (**1**) is potentially useful for the synthesis of heterocyclic compounds containing pyrane ring. Few reports, however, have been published on the reactivity of dichloropyrone (**1**) except their reports. In the previous papers, we reported[2] that dichloropyrone (**1**) was treated with primary and secondary amines to afford aminopyrone derivatives, and with tertiary amines to afford 4-chloro-3-ethynyl-6-methyl-2*H*-pyran-2-one (**2**). In the course of our continuing study, it was found that both dichloropyrone (**1**)[3] and chloroethynylpyrone (**2**)[4] were treated with phenylenediamines to afford pyrano[4,3-*b*]diazepine (**3**) and pyrano[4,3-*b*]quinoline (**5**), which is described in the communication here. These products (**3** and **5**) are expected to possess pharmacological activities.

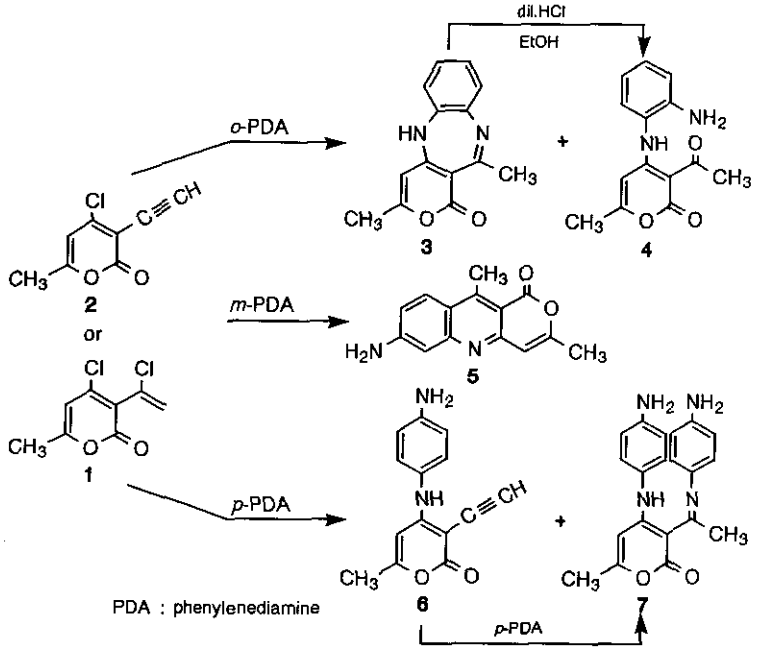
A mixture of chloroethynylpyrone (**2**, 5.9 mmol), *o*-phenylenediamine (6.6 mmol), and Et_3N (12.4 mmol) in 98 % EtOH (50 ml) was heated under reflux for 1 h. The precipitate was collected by filtration,

Dedicated to Prof. E. C. Taylor on the occasion of his 70th birthday.

and was recrystallized from 98 % EtOH to give pyranobenzodiazepine (**3**) in 75 % yield, and the concentrated filtrate was purified by column chromatography on silica gel to give 3-acetyl-4-(2-aminoanilino)-6-methyl-2*H*-pyran-2-one (**4**) in 8 % yield. Pyranobenzodiazepine (**3**) was quantitatively converted into **4** by treatment with a small amount of 10 % HCl in EtOH.

In the same procedure as previously, the reaction of chloroethynylpyrone (**2**) with *m*-phenylenediamine gave pyranoquinoline (**5**), in 82 % yield, of which ^{1}H-nmr spectra showed three typical signals of a *meta*-coupled proton at 6.91 ppm, an *ortho*- and *meta*-coupled proton at 7.02 ppm, and an *ortho*-coupled proton at 8.03 ppm. Furthermore, irradiation of methyl proton at 3.27 ppm of **5** gives NOE on an *ortho*-coupled proton at 8.03 ppm.

On the other hand, a mixture of chloroethynylpyrone (**2**), *p*-phenylenediamine, and Et$_3$N in 98 % EtOH was stirred at room temperature for 30 min to afford aminoethynylpyrone (**6**), in 68 % yield, which was treated with *p*-phenylenediamine to give imine (**7**, 82 %). The structures of all products were determined by the spectral and analytical evidences (Table 1).



Scheme 1

In addition, dichloropyrone (**1**) also reacted with phenylenediamines in the presence of 3.5 mole eq. amount of Et$_3$N to yield the corresponding products (**3**, **4**, **5**, **6** and **7**), respectively. In the same procedure, for example, a mixture of dichloropyrone (**1**, 4.9 mmol), *o*-phenylenediamine (5.9 mmol), and

Table 1. Products by reaction of **1** and **2** with phenylenediamines

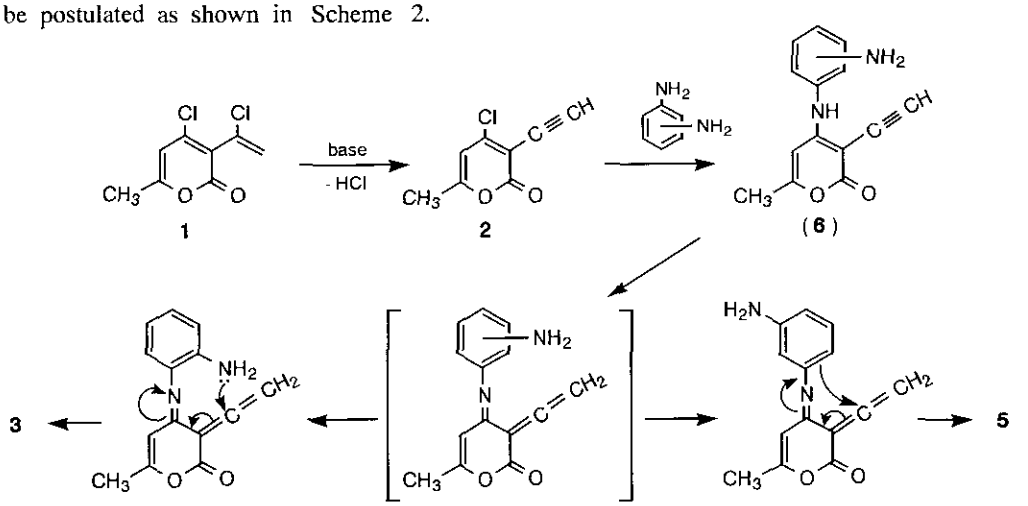
Compd. No.	Yield (%) Method A [a] (Method B [b])	mp (℃)	Formula	Analysis (%) Calcd (Found) C	H	N	ir (KBr) cm^{-1}	^{1}H-nmr δ (ppm)
3	75 (58)	245 (decomp.)	$C_{14}H_{12}N_2O_2$	70.00 (69.95	5.00 4.94	11.67 11.60)	1670	2.14 (3H, s), 2.34 (3H, s), 5.86 (1H, s), 6.64 -6.99 (4H, m), 8.06 (1H, br s)
4	8 (12)	188 – 189 (decomp.)	$C_{14}H_{14}N_2O_3$	65.12 (65.16	5.43 5.43	10.85 10.81)	1720	2.12 (3H, s), 2.67 (3H, s), 3.87 (2H, br s), 5.66 (1H, s), 6.77 - 7.20 (4H, m),12.57 (1H, br s)
5	82 (65)	299 (decomp.)	$C_{14}H_{12}N_2O_2$	70.00 (69.96	5.00 4.95	11.67 11.58)	1715	2.49 (3H, s), 3.27 (3H, s), 6.33 (2H, br s), 6.40 (1H, s), 6.91 (1H, d, J=2Hz), 7.02 (1H, dd, J=9 and 2Hz), 8.03 (1H, d, J=9Hz)
6	68 (3)	195 (decomp.)	$C_{14}H_{12}N_2O_2$	70.00 (69.76	5.00 5.01	11.67 11.72)	2100, 1700	2.13 (3H, s), 3.63 (1H, s), 3.83 (2H, br s), 5.73 (1H, s), 6.60 - 7.17 (4H,m), 7.09 (1H, br s)
7	60 (45)	170 – 171 (decomp.)	$C_{20}H_{20}N_4O_2$	68.97 (68.90	5.75 5.74	16.09 15.85)	1680	2.08 (3H, s), 2.43 (3H, s), 3.73 (4H, br s), 5.87 (1H, s), 6.63 - 7.05 (8H, m), 14.43 (1H, br s)

a) Method A : using chloroethynylpyrone (**2**)

b) Method B : using dichloropyrone (**1**)

Et_3N (14.7 mmol) in 98 % EtOH (50 ml) was heated under reflux for 1 h to give pyranobenzodiazepine (**3**) in 58% yield.

The use of chloroethynylpyrone (**2**) instead of dichloropyrone (**1**) resulted in far more yield to afford the corresponding products (Method A in Table 1). A probable route of the ring formation of pyranobenzodiazepine (**3**) and pyranoquinoline (**5**) by the reaction of **1** and **2** with phenylenediamines can be postulated as shown in Scheme 2.



Scheme 2

REFERENCES AND NOTES

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2. Y. Azuma, A. Sato, K. Tanno, M. Madarame, and S. Hisamichi, *Annu. Rep. Tohoku Coll. Pharm.* 1988, **35**, 221 [*Chem. Abstr.*, 1990, **112**, 178560b] ; *Idem*, *ibid.*, 1989, **36**, 219 [*Chem. Abstr.*, 1991, **114**, 143052b].
3. Preparation of **1** : A mixture of dehydroacetic acid (100 g, 0.6 mol), phosphorus pentachloride (250 g, 1.2 mol), and phosphorus oxychloride (185 g, 1.2 mol) in $CHCl_3$ (1000 ml) was heated under reflux for 1.5 h. The reaction mixture was slowly poured into an ice-water. The resulting mixture was neutralized with a concentrated aqueous ammonia. The organic layer was separated, and the aqueous layer was extracted with $CHCl_3$. The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed *in vacuo*. The residue was purified by column chromatography on alumina with $CHCl_3$ elution to give a crude product (**1**), which was recrystallized from a mixture of CH_2Cl_2 - cyclohexane to afford **1** (92 g, 75 %) ; mp 101 – 102 ℃ (lit.,[1] mp 100 ℃).
4. Preparation of **2** : A mixture of dichloropyrone (**1**, 49 g, 0.24 mol) and Et_3N (60 g, 0.6 mol) in $CHCl_3$ (1000 ml) was heated under reflux for 6 h. The reaction mixture was washed with 10 % HCl and water. After the solvent was removed *in vacuo*, the residue was purified by column chromatography on silica gel with $CHCl_3$ elution to give a crude product (**2**), which was recrystallized from Et_2O to afford **2** (37 g, 92 %) ; mp 145 ℃ (decomp.) ; ir (KBr) 3260, 2110, 1725 cm^{-1} ; ^1H nmr ($CDCl_3$) : δ 2.30 (3H, s), 3.63 (1H, s), 6.19 (1H, s).

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