The Condensation of Cyclic Anhydrides with Schiff Bases. A Convenient Synthesis of 1,4,6-Triaryl-5-carboxy-2-oxo-1,2-dihydropyridines and 2,3-Diaryl-4-carboxy-1-oxo-1,2-dihydroisoquinolines

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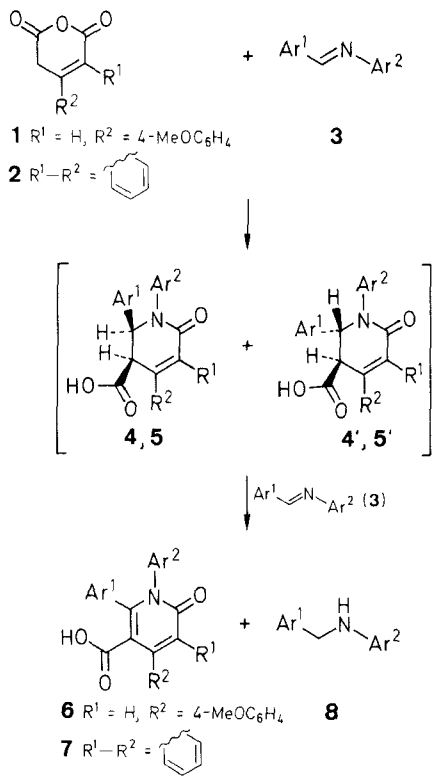
Condensation of Schiff bases of *o*-hydroxyarenecarboxaldehydes with 3-arylpentenedioic or homophthalic acid anhydrides was found to give 1,4,6-triaryl-5-carboxy-2-oxo-1,2-dihydropyridines and 2,3-Diaryl-4-carboxy-1-oxo-1,2-dihydroisoquinolines, respectively, instead of the expected tetrahydro products. The Schiff bases (used in excess) oxidize the intermediate tetrahydro products to the title compounds.

Pyridones and isoquinolinones constitute two important groups of heterocyclic compounds. Some of the substituted 2-pyridinones are known to possess anticonvulsant, hypnotic, and analgesic activity,[1-5] while some 1-isoquinolinones possess antitumor and antiallergic activity[6,7] etc. These biological activities have been related to some common structural moieties present in the molecules.

A series of new substituted 2-pyrrolidones and 2-piperidones has been synthesised by condensation of various imines and cyclic anhydrides.[8,9] In a project requiring some substituted 2-pyridones and 1-isoquinolinones and derivatives thereof, we tried reaction of 3-(4-methoxyphenyl)pentenedioic anhydride (**1**) and homophthalic anhydride (**2**) with various Schiff bases **3** using the reported methods. Thus, the reaction of anhydrides **1** and **2** with aldimines **3** gave rise to 1,4,6-triaryl-5-carboxy-2-oxo-1,2-dihydropyridines **6** and 2,3-diaryl-4-carboxy-1-oxo-1,2-dihydroisoquinolines **7**, respectively, instead of the corresponding tetrahydro products **4** and **5**. It was also observed that only half the amount anhydrides **1** and **2** is consumed in reactions with equimolecular amounts of aldimines **3**. Another isolable product being the tetrahydro derivative **4** or **5**, respectively. The same reaction using a 1:2 molecular ratio of anhydride to imine was



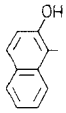
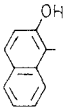
3-8	Ar¹	Ar²	3-8	Ar¹	Ar²
a	2-HOC₆H₄	4-ClC₆H₄	d	2-HOC₆H₄	4-MeC₆H₄
b	2-OH-6-MeOC₆H₃	3-NO₂C₆H₄			
c		3-NO₂C₆H₄	e		4-MeC₆H₄

Table. Compounds **6** and **7** Prepared

Product	Yield[a] (%)	mp (°C)	Molecular Formula[b]	MS (70 eV)[c] *m/z* (%)	IR (KBr)[d] ν(cm^{-1})	^{1}H-NMR (CDCl$_3$/TMS)[e] δ
6a	62	205 (MeOH)	$C_{25}H_{18}ClNO_5$ (447.5)	447 (M^+, 6); 315 (100)	1680, 1720	3.8 (s, 3H, *p*-OCH_3), 5.7 (br s, 1H, OH), 6.4 (s, 1H, H-3); 6.8–7.6 (m, 12H_{arom})
6b	58	177 (MeOH)	$C_{26}H_{20}N_2O_8$ (488.0)	488 (M^+, 7); 310 (100)	1670, 1720	3.85 (s, 3H, *p*-OCH_3), 3.95 (s, 3H, *o*-OCH_3), 6.45 (s, 1H, H-3), 6.8–7.5 (m, 11H_{arom})
6c	56	210 (MeOH)	$C_{29}H_{20}N_2O_7$ (508.0)	508 (M^+, 6); 335 (100)	1680, 1725	3.85 (s, 3H, *p*-OCH_3), 6.5 (s, 1H, H-3), 6.85 (m, 14H_{arom})
7b	59	195 (MeOH)	$C_{23}H_{16}N_2O_7$ (432.0)	432 (M^+, 7); 300 (100)	1660, 1720	3.90 (s, 3H, *m*-OCH_3), 6.85–8.25 (m, 11H_{arom})
7d	57	239 (EtOH)	$C_{23}H_{17}NO_4$ (371.0)	371 (M^+, 6); 225 (100)	1680, 1720	1.25 (s, 3H, *p*-CH_3), 7.25–8.25 (m, 12H_{arom})
7e	55	160 (MeOH)	$C_{27}H_{19}NO_4$ (421.0)	421 (M^+, 7); 255 (100)	1660, 1700	1.25 (s, 3H, *p*-CH_3), 6.90–8.5 (m, 14H_{arom})

[a] Yield of pure isolated product.

[b] Satisfactory microanalyses obtained: C ±0.29, H ±0.28, N ±0.36.

[c] Recorded on a Varian MAT-112S DCMS spectrometer.

[d] Recorded on a Perkin-Elmer 683 Infrared spectrophotometer.

[e] Recorded on a Varian FT-80 spectrometer.

found to go to completion with respect to the anhydride; under these conditions, the intermediate tetrahydro products **4** and **5** underwent dehydrogenation by the Schiff bases **3** which act as oxidizing agents. Such observations in other reactions of Schiff bases have been reported earlier.[10-12] The secondary amines **8** thus obtained as by products were found to be identical in all respects with authentic samples[13] of compounds **8**.

The same reactions in the absence of triethylamine were found to give pentenedioic amides.

1,4,6-Triaryl-5-carboxy-2-oxo-1,2-dihydropyridines 6 and 2,3-Diaryl-4-carboxy-1-oxo-1,2-dihydroisoquinolines 7; General Procedure:

A mixture of the anhydride[10] **1** or **2** (0.01 mol), the aldimine **3** (0.02 mol), and Et_3N (0.506 g, 0.005 mol) in CH_2Cl_2 (15–20 mL) is stirred for 6–8 h at room temperature. It is then extracted with 10% aq. HCl (3 × 15 mL) and with H_2O (2 × 10 mL). The combined organic layers are dried (Na_2SO_4) and the solvent is removed by distillation. The residue is dissolved in sat. aq. $NaHCO_3$ (30 mL). This solution is filtered, the filtrate neutralised with 10% aq. HCl and evaporated, and the residue is crystallized from an appropriate solvent (Table) to give the product **6** or **7**.

The combined acid extract is basified with 20% aq. NaOH and extracted with CH_2Cl_2 (2 × 20 mL) to remove Et_3N. The alkaline aqueous layer is carefully neutralised (to pH 6.5) with AcOH, then extracted with CH_2Cl_2 (2 × 15 mL). The organic layer is washed with H_2O (2 × 10 mL), dried (Na_2SO_4), and distilled to remove the solvent. The residue is crystallized from EtOAc to give the pure amine **8** (found to be identical with authentic samples[13]).

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(1) Scudi, J.V.; Childress, J.; Reisner, D.B. *British Patent* 851 033 (1960), Wallace and Tiernan Inc.; *C.A.* **1961**, *55*, 8440.
(2) Scudi, J.V.; Childress, J.; Reisner, D.B. *British Patent* 851 033 (1960), Wallace and Tiernan Inc.; *C.A.* **1961**, *55*, 114639.
(3) Raczka, A.; Swirska, A.; Bojarska, H. *Acta Pol. Pharm.* **1963**, *20*, 155; *C.A.* **1961**, *62*, 1630.
(4) Kubo, K.; Masuo, M.; Isao, S.; Noriki, I.; Hideki, A.; Hiroshige, H. *Jpn. Kokai Tokkyo Koho* 78 34 777 (1978), Yamanouchi Pharmaceutical Co. Ltd.; *C.A.* **1979**, *90*, 87279.
(5) Nippon Synthetic Chemical Industry Co. Ltd., *Jpn. Kokai Tokkyo Koho* 80 136 206 (1980); *C.A.* **1981**, *94*, 59774.
(6) Eisaku, H.; Takeo, H.; Etsuo, O.; Chihoko, I.; Masaki, Y.; Chieko, O.; Yoshio, M.; At Suko, N.; Shigeko, I. *Yakugaku Zasshi* **1978**, *98*, 1560; *C.A.* **1979**, *90*, 152111.
(7) Masayasu, K.; Isami, W.; Yaji, D.; Kouji, A.; Tetsuya, M. *Chem. Pharm. Bull.* **1983**, *31*, 1277; *C.A.* **1983**, *99*, 139728.
(8) Castagnoli, N. Jr.; Cushman, M. *J. Org. Chem.* **1971**, *36*, 3404.
(9) Cushman, M.; Madaj, E.J. *J. Org. Chem.* **1987**, *52*, 907.
(10) Kamath, S.D. *Ph.D. Thesis*, University of Bombay, **1984**.
(11) Singh, S.; Kaur, U. *Indian J. Chem. Sect. B.* **1987**, *26*, 199.
(12) Veerangaiah, V.; Ratnam, K.V.; Rao, N.V.S. *Indian J. Chem. Sect. B* **1972**, *10*, 133.
(13) Samant, S.D.; Joglekar, S.J. *J. Indian Chem. Soc.* **1988**, *65*, 110.