BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 40 1695—1697 (1967)

Some 4(1*H*)-Pyridylidene Compounds. Synthesis and Structure

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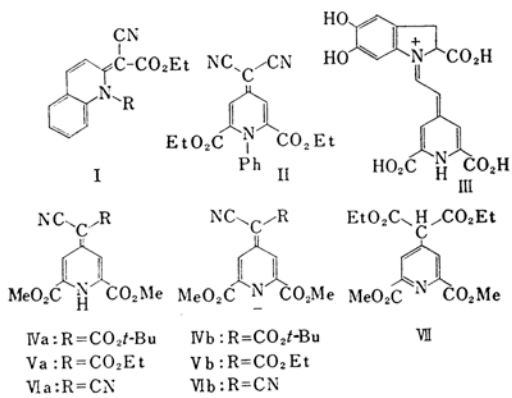
(Received January 10, 1967)

The reaction of methyl 4-chloro-pyridine-2,6-dicarboxylate with a sodium compound of *t*-butyl cyanoacetate, ethyl cyanoacetate, or malononitrile, followed by acidification, gives the corresponding 4(1*H*)-pyridylidene compound, *t*-butyl cyano-4(1*H*)-(2,6-bismethoxy-carbonyl-pyridylidene)-acetate (IVa), ethyl cyano-4(1*H*)-2,6-bismethoxycarbonyl-pyridylidene)acetate (Va), or 4(1*H*)-(2,6-bismethoxy-carbonyl-pyridylidene)malononitrile (VIa). The structures assigned to these compounds are based on the UV, IR and NMR spectra. In an alkaline solution, IVa, Va and VIa change into the anion forms. The elimination reaction of IVa and Va is also examined.

In 1961 Bredereck[1] reported the *N*-methyl-2(1*H*)-quinolylidene compound (I, R=CH_3), and recently Borror and Haeberer[2] reported another 2(1*H*)-quinolylidene compound (I, R=H). However, the analogous 4(1*H*)-pyridylidene compounds have not been reported except for such *N*-substituted pyridylidene compounds as *N*-phenyl-4(1*H*)-(2,6-bismethoxycarbonyl-pyridylidene)malononitrile (II).[3] The novel 4(1*H*)-pyridylidene compound without *N*-substitution is also interesting because of its similarity with the neobetanidin (III) derived from betanidin.[4]



IVa: R=CO_2*t*-Bu
Va: R=CO_2Et
VIa: R=CN
IVb: R=CO_2*t*-Bu
Vb: R=CO_2Et
VIb: R=CN
VII

We have found that methyl 4-chloro-pyridine-2,6 dicarboxylate[5] reacts with *t*-butyl cyanoacetate,

1) H. Bredereck and K. Bredereck, *Chem. Ber.*, **94**, 2278 (1961).
2) A. L. Borror and A. F. Haeberer, *J. Org. Chem.*, **30**, 243 (1965).
3) F. Eiden and P. Peter, *Arch. Pharmaz.*, **297**, 1 (1964).
4) H. Wyler and A. S. Dreiding, *Helv. Chim. Acta*, **45**, 638 (1962).
5) E. Köning and W. Jäschke, *Ber.*, **54**, 1352 (1921).

ethyl cyanoacetate, or malononitrile, to give *t*-butyl cyano-4 (1*H*)-(2, 6-bismethoxycarbonyl-pyridylidene)-acetate (IVa), ethyl cyano-4(1*H*)-(2,6-bismethoxycarbonyl-pyridylidene)-acetate (Va), or 4-(1*H*)-(2, 6-bismethoxycarbonyl-pyridylidene) malononitrile (VIa) respectively, after the acidification of the corresponding condensation product.

The absorption maxima of the UV spectra indicate that IVa, Va, and VIa exist in the 4(1*H*)-pyridylidene form in an acidic solution, but that they change into 4(1*H*)-pyridylidene anions, IVb, Vb, and VIb respectively, in a basic solution (Table 1). The b form returns to the a form upon the addition of acid. Both forms are stable in an ethanol solution. On the contrary, ethyl 4-(2,6-bismethoxycarbonyl-pyridyl)malonate[5] (VII) shows no shift in UV spectrum in either acid or a basic solution. This fact seems to indicate that a nitrile group in IVa, Va, or VIa stabilizes the 4(1*H*)-pyridylidene form by conjugation in an acid solution, while a nitrile group in IVb, Vb, or VIb stabilizes the 4(1*H*)-pyridylidene anion form by conjugation in a basic solution.

TABLE 1. ULTRAVIOLET AND VISIBLE SPECTRA OF IVa, Va AND VIa

Compound	λ_{max}^{EtOH} nm (ε)	$\lambda_{max}^{EtOH-0.1NNaOH}$ (ε)
IVa	405 (18500)	365 (18100)
	242 (21700)	248 (26000)
Va	405 (16600)	360 (16800)
	241 (19600)	246 (24600)
VIa	395 (25000)	355 (21200)
	237 (21200)	242 (26100)

The IR spectra of IVa, Va, VIa, IVb, Vb, and VIb in potassium bromide pellets are consistent with each structure assigned on the basis of the UV spectra. A conjugated ester carbonyl band at 1680 cm^{-1} overlaps with the aromatic ester carbonyl band. Nitrile bands of IVa and Va are shown at nearly the same position, 2200 cm^{-1}, as has been found for I,[1] while VIa shows two nitrile bands, at 2250 and 2170 cm^{-1}. The ester carbonyl bands of IVa, Va, and VIa are normal and are free from intermolecular hydrogen bonding with the imino group in the pyridylidene ring.

The NMR spectra of Va in deuterochloroform show a signal attributable to the methyl group at 5.95 (s) and typical ethyl signals at 5.45 (q) and 8.54 (t). Two protons, at 3-C and 5-C, show their peaks at 2.45 (d) and 1.1 (d) respectively, with $J=5$ cps. IVa shows a NMR spectrum similar to that of Va. Moreover, the NMR spectrum of IVb in trifluoroacetic acid is consistent with that of IVa. This fact indicates that IVb changes the IVa structure in an acidic medium. The UV, IR, and NMR spectra support the 4(1*H*)-pyridylidene structure for IVa, Va, and VIa, as well as the change in the structure between the a form and the b form. In order to compare the reactivity of elimination between the nitrile group and the ester group at the carbon atom bonded to the 4(1*H*)-pyridylidene group, IVa and Va were treated under the conditions of decarboxylation. The conditions used were similar to those which have been found to be suitable for the decarboxylation without the elimination of a nitrile group. It was found that IVa loses a nitrile group upon treatment with cold concentrated hydrochlroic acid or Va loses a nitrile group *p*-toluenesulfonic acid, and that upon heating with or without ethanolic potassium hydroxide. When Va is heated with 10% hydrobromic acid, it loses a nitrile group and then ester group to form the corresponding picoline derivative. Consequently, it can be concluded that a nitrile group of IVa and Va is more easily eliminated than a malonic ester group.

Experimental

All melting points are uncorrected.

***t*-Butyl Cyano-4 (1*H*)-(2, 6-bismethoxycarbonyl-pyridylidene)acetate Anion (IVb).** About 1.5 g of a 50% sodium hydride dispersion in oil was placed in a flask. The oil was removed by washing with dry petroleum ether. The sodium hydride dispersion in petroleum ether was transferred into a 100 m*l* three-necked flask fitted with a reflux condenser, a stirrer, and a dropping funnel. A nitrogen stream was passed into the flask. After removing the petroleum ether under reduced pressure, anhydrous dimethylformamide (10 m*l*) was added. The flask was placed in an ice bath, while 3.4 g of *t*-butyl cyanoacetate was stirred in drop by drop. Then the mixture was heated to 50°C, and a 2 g portion of methyl 4-chloropyridine-2,6-dicarboxylate dissolved in 10 m*l* of dimethylformamide was added, drop by drop. The temperature was raised slowly to 120°C and maintained at this temperature for 4.5 hr. The reaction mixture was cooled, the excess sodium hydride was decomposed with water, and then the mixture was concentrated under reduced pressure. By adding water to the concentrate, 2.5 g of a precipitate were obtained; recrystallized from ethanol to give pale yellow needles, 1.5 g, mp 247°C (decomp.).

***t*-Butyl Cyano-4(1*H*)-(2,6-bismethoxycarbonyl-pyridylidene)acetate (IVa).** IVb was acidified with hydrochloric acid in ethanol, and recrystallized from ethanol or dimethylformamide and water, to afford yellow needles, 70 mg from 100 mg of IVb, mp 175°C (decomp.).

Found: C, 57.40; H, 5.53; N, 8.46%. Calcd for $C_{16}H_{18}O_6N_2$: C, 57.48; H, 5.43; N, 8.38%.

IR: ν^{KBr} cm^{-1} 3450, 3370, 2200 (CN), 1730 (CO), 1680 (CO), 1630, 1500.

NMR: $\tau(CDCl_3)$ 0.3 (m) 1H, 1.1 (d) 1H, 2.45 (d) 1H, 5.95 (s) 6H, 8.45 (s) 9H.

Ethyl Cyano-4(1*H*)-(2,6-bismethoxycarbonyl-pyridylidene)acetate (Va). In 5 m*l* of ethanol 0.2 g of sodium was dissolved, and then 2.5 g of ethyl cyanoacetate were added slowly. The mixture was heated on water bath for 30 min, and then cooled to room temperature. Methyl 4-chloropyridine-2,6-dicarboxylate

(2 g) was added, and the mixture was heated on a water bath for 30 min. After the evaporation of the ethanol, water was added to the concentrate, the solution was acidified with diluted hydrochloric acid, and extracted with ether, and the ethereal solution was evaporated. The crude product was recrystallized from ethanol to give yellow needles, mp 149°C.

Found: C, 55.66; H, 4.98; N, 8.80%. Calcd for $C_{14}H_{14}O_6N_2$: C, 54.90; H, 4.61; N, 9.15%.

IR: ν^{KBr} cm^{-1} 3350, 3300, 2250 (CN), 1725 (CO), 1685 (CO), 1625, 1500.

NMR: $\tau(CDCl_3)$ 1.1(d)1H (J=5 cps), 2.45(d)1H (J=5 cps), 5.45(q)2H, 5.95(s)6H, 8.54(t)3H.

Ethyl Cyano-4(1*H*)-(2,6-bismethoxycarbonyl-pyridylidene)acetate Anion (Vb). Va was dissolved in ethanol, and ethanolic potassium hydroxide was added until the solution showed the UV spectrum of Vb. After extraction with ether and recrystallization from ethanol, pale yellow needles were obtained, mp 207—208°C (decomp.).

IR: ν^{KBr} cm^{-1} 3420, 2250(CN), 1720(CO), 1560, 1520.

4 (1*H*)-(2, 6-Bismethoxycarbonyl-pyridylidene)-malononitrile Anion (VIb). Methyl chloro-pyridyl-2,6-dicarboxylate (1 g) was reacted with 0.5 g of malononitrile in 1 m*l* of dimethylformamide by a procedure similar to that used for the preparation of IVa. The crude product was recrystallized to give green-yellow needles, mp 291°C.

IR: ν^{KBr} cm^{-1} 3550, 3420, 2200(CN), 2150(CN), 1730, 1705, 1640, 1580.

4 -(1*H*) - (2, 6-Bismethoxycarbonyl-pyridylidene)-malononintrile (VIa). VIb was acidified with hydrochloric acid in an ethanol solution and then recrystallized from ethanol to afford VIa as yellow needles, mp 218—219°C (decomp.).

Found: C, 55.27; H, 3.68; N, 15.99%. Calcd for $C_{12}H_9O_4N_3$: C, 55.60; H, 3.50; N, 16.21%.

IR: ν^{KBr} cm^{-1} 3450, 3300, 2250(CN), 2170(CN), 1740(CO), 1630, 1590, 1500.

Methyl 4-Chloropyridine-2,6-dicarboxylate. Prepared according to the method of Köning,[5] mp 142°C.

Found: Cl, 15.48%. Calcd for $C_7H_8O_4NCl$: Cl, 15.43%.

NMR: $\tau(CDCl_3)$ 1.40(s) 2H, 5.95(s) 6H.

Attempted Decarboxylation of IVa and Va. The conditions used were similar to those which had been found suitable for the decarboxylation without the elimination of the nitrile group. It was proved that Va lost the nitrile group by reaction with concentrated hydrochloric acid or *p*-toluenesulfonic acid, while IVa lost the nitrile group when heated with ethanolic potassium hydroxide or by thermal decomposition. When Va was heated with 10% hydrobromic acid, it lost the nitrile group and then the ester group to form the corresponding picoline derivative. To 100 mg of Va dissolved in cold ethanol, 10 mg of sodium was added, and after 10 min, the precipitate separated, this precipitate was then filtered. By adding water to the filtrate, the precipitate was recrystallized from ethanol to give colorless crystals, mp 90°C.

Found: C, 51.28; H, 4.69; N, 4.68%. Calcd for $C_{14}H_{15}O_8N$: C, 51.69; H, 4.65; N, 4.31%.

This was proved to be the monoester from 4-(2,6-bismethoxycarbonyl-pyridyl)malonate.