forded the analytical sample, m.p. 142.8–143.7°. An infrared spectrum of a 10% chloroform solution of the product revealed peaks at 3400 (enolic O–H) and 1700–1725 cm.$^{-1}$ (broad, due to three carbonyl absorptions).

Anal. Calcd. for $C_{12}H_{13}NO_7S$: C, 45.71; H, 4.15; N, 4.44. Found: C, 45.58; H, 4.02; N, 4.23.

2,5-Dicarbethoxythieno[3,2-*b*]pyrrole (XII).—To a solution containing 18 g. of stannous chloride dihydrate, 150 ml. of 95% ethanol, and 50 ml. of concentrated hydrochloric acid was added 3.15 g. (0.01 mole) of ethyl 5-carbethoxy-3-nitro-2-thienylpyruvate. The mixture was stirred for 8 hr. while the temperature was kept between 40–50°. The deep red reaction mixture was placed in a dropping funnel and was slowly added to 150 ml. of 50% potassium hydroxide. The temperature of the strongly alkaline solution was not allowed to exceed 10°. After the addition was completed, the mixture which contained a yellow precipitate was extracted with several portions of ether. The ether extracts were combined, dried over anhydrous magnesium sulfate, and filtered to remove the drying agent. The solvent was removed from the filtrate to yield a solid residue. The residue was dissolved in a boiling methylcyclohexane–benzene mixture, and the solution was treated with Darco and filtered. The filtrate was allowed to cool in the refrigerator for several hours. The slightly yellow crystals which had precipitated were collected and dried. The yield of 2,5-dicarbethoxythieno[3,2-*b*]pyrrole was 1.70 g. (64%), m.p. 156–158°. Two additional recrystallizations from benzene-methylcyclohexane afforded the analytical sample, m.p. 158.3–159°. An infrared spectrum of a 5% chloroform solution of the product revealed peaks at 3430 and 3280 (pyrrole N–H and hydrogen-bonded pyrrole N–H) and 1680–1705 cm.$^{-1}$ (broad, carbonyl absorption).

Anal. Calcd. for $C_{12}H_{15}NO_4S$: C, 53.92; H, 4.90; N, 5.24. Found: C, 53.72; H, 4.81; N, 5.18.

6-Bromo-2,5-dicarbethoxythieno[3,2-*b*]pyrrole (XIII).—To a solution of 267 mg. (1.0 mmole) of 2,5-dicarbethoxythieno[3,2-*b*]pyrrole in 30 ml. of chloroform was added 160 mg. (2.0 mmoles) of bromine. At the end of 3 hr. the reaction mixture was concentrated to dryness on a rotary evaporator. A solid residue was obtained which was dissolved in a boiling mixture of methylcyclohexane–benzene, and the solution was treated with Darco and filtered. The filtrate was stored in the refrigerator overnight. The white crystals which had formed were collected and dried. The yield of 6-bromo-2,5-dicarbethoxythieno[3,2-*b*]pyrrole was 306 mg. (88%), m.p. 178.7–179.8°. One additional recrystallization from benzene–methylcyclohexane afforded the analytical sample, m.p. 179.1–179.9°.

An infrared spectrum of a 5% chloroform solution of the product revealed peaks at 3450 and 3300 (pyrrole N–H and hydrogen-bonded pyrrole N–H) and 1690–1705 cm.$^{-1}$ (broad, carbonyl absorption).

Anal. Calcd. for $C_{12}H_{12}NO_4S$: C, 41.63; H, 3.50; N, 4.05. Found: C, 41.32; H, 3.37; N, 3.86.

6-Dimethylaminomethyl-2,5-dicarbethoxythieno[3,2-*b*]pyrrole (XIV).—To 3.0 ml. of glacial acetic acid were added 85 mg. (1.89 mmoles) of dimethylamine (as a 40% aqueous solution) and 470 mg. (1.76 mmoles) of 2,5-dicarbethoxythieno[3,2-*b*]pyrrole. The temperature was kept between 0–5° while the components were added. The reaction mixture was heated on the steam bath for 1 hr. and then allowed to stand at room temperature for 12 hr. The mixture was poured into 25 ml. of ice–water, and the resulting solution was brought to pH 10 by the slow addition of 10% sodium hydroxide. The temperature was not allowed to exceed 10° while the base was added. The white solid which precipitated was filtered and washed freely with ice–water. The solid was dried *in vacuo* over anhydrous calcium sulfate for 24 hr. The yield of the crude Mannich base was 518 mg. (89%), m.p. 120–123°. The material was dissolved in a boiling mixture of benzene–methylcyclohexane, and the solution was treated with Darco and filtered. The filtrate was allowed to cool overnight in the refrigerator. The white crystals which had formed were collected and dried. The yield of 6-dimethylaminomethyl-2,5-dicarbethoxythieno[3,2-*b*]pyrrole was 460 mg. (79%), m.p. 124.3–124.9°. An analytical sample was prepared by one recrystallization from benzene–methylcyclohexane, m.p. 124.3–124.9°. An infrared spectrum of a 5% chloroform solution of the product revealed peaks at 3470 and 3330 (pyrrole N–H and hydrogen-bonded pyrrole N–H) and 1680–1720 cm.$^{-1}$ (broad, carbonyl absorptions).

Anal. Calcd. for $C_{15}H_{20}N_2O_4S$: C, 55.53; H, 6.21; N, 8.64. Found: C, 55.41; H, 6.20; N, 8.69.

Preparation and Reductive Cyclization of Some Carbon-Alkylated Derivatives of Ethyl 3-Nitro-2-thienylpyruvate[1]

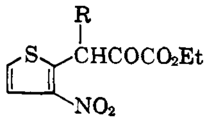
Alan N. Scott,[2] Bernard E. Hoogenboom, and H. R. Snyder

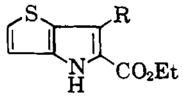
The Noyes Chemical Laboratory, University of Illinois, Urbana, Illinois

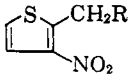
Received March 10, 1964

Alkylation reactions of the ambident anion of ethyl 3-nitro-2-thienylpyruvate were studied. The C-allyl and C-benzyl derivatives were prepared and converted in poor yields to the corresponding 6-alkylated 5-carbethoxythieno[3,2-*b*]pyrroles.

Condensation of 2-methyl-3-nitrothiophene (IIIa) with diethyl oxalate affords ethyl 3-nitro-2-thienylpyruvate (Ia), which can be reduced and cyclized to 5-carbethoxythieno[3,2-*b*]pyrrole (IIa).[3] In this paper we described the behavior of the pyruvic ester Ia toward certain alkylating agents; reductive cyclization of carbon-alkylated derivatives of Ia offers one route to 6-substituted 5-carbethoxythieno[3,2-*b*]pyrroles of type II. These studies were part of a program directed toward synthesis of 6-substituted thieno[3,2-*b*]pyrroles analogous to biologically active indole compounds.


Ia, R = H
b, R = $CH_2CH{=}CH_2$
c, R = $CH_2C_6H_5$
d, R = Br


IIa, R = H
b, R = $CH_2CH{=}CH_2$
c, R = $CH_2C_6H_5$


IIIa, R = H
b, R = CH_3
c, R = $CH_2C_6H_4NO_2$-*p*
d, R = CH_2CN
e, R = $CH_2CH{=}CH_2$

In the solid state and in fresh solutions the pyruvate Ia exists predominantly as the enol, as indicated by strong infrared peaks at 3400 cm.$^{-1}$ for the enolic hydroxyl absorption, and at 1700 cm.$^{-1}$ for the hydrogen-bonded ester carbonyl absorption. In the nuclear magnetic resonance (n.m.r.) spectrum of Ia in chloroform,

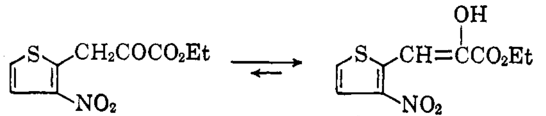
---

[1] (a) Supported in part by a grant (C3969-Bio) from the National Cancer Institute, U. S. Public Health Service; (b) abstracted in part from the thesis submitted by A. N. Scott, to the Graduate College of the University of Illinois in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1964.

[2] National Science Foundation Summer Fellow, 1962.

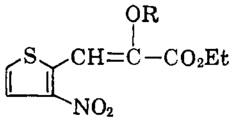
[3] W. W. Gale, A. N. Scott, and H. R. Snyder, *J. Org. Chem.*, **29**, 2160 (1964).

only peaks due to the enol form are detectable. Undoubtedly the enol owes its stability to its extended π-conjugated system. A similarly high degree of enolization has been noted in methyl 2-thienylpyruvate and methyl phenylpyruvate.[4]


Ia Ia

Pyruvate Ia readily loses a proton to form an intensely red anion, the negative charge of which is shared by the enol oxygen, the carbon adjacent to the ring, and the nitro oxygens. Alkylation could conceivably occur at any of these three sites, but only carbon alkylation would afford a pyruvate of type I which might be converted to a 6-alkylated thienopyrrole.

Through reactions of Ia, alkyl bromides, and alkali metal carbonates in refluxing acetone, two carbon-alkylated pyruvates were prepared: the allyl compound Ib (93% yield), and the benzyl compound Ic (*ca.* 45% yield). No oxygen alkylation was detected with allyl bromide, but in certain experiments using benzyl bromide some benzyl enol ether (IVa) was produced along with the C-benzyl derivative. In many other attempts, carbon alkylated pyruvates could not be isolated. For example, reaction of Ia with methyl iodide and potassium carbonate in acetone afforded only the O-methyl derivative IVb (24% yield) and a trace of 2-ethyl-3-nitrothiophene (IIIb). Similarly, alkylation with *p*-nitrobenzyl chloride in ethanolic sodium ethoxide gave principally the ether IVc and in smaller yield the deacetylated product IIIc. A small amount of 3-(3-nitro-2-thienyl)propionitrile (IIId) was obtained from reaction with chloroacetonitrile. Knoevenagel condensations with aromatic aldehydes and Michael addition to electrophilic olefins did not occur.

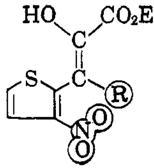


IVa, R = $CH_2C_6H_5$
b, R = CH_3
c, R = $CH_2C_6H_4NO_2$-*p*

Although the alkali metal enolate was readily soluble in acetone, its poor solubility in ethanol, *t*-butyl alcohol, and tetrahydrofuran impeded alkylations attempted in these solvents.

The structures of the alkylated pyruvates were deduced chiefly from n.m.r. spectra.[5] The carbon-alkylated pyruvates Ib and Ic were predominantly ketonic oils. The internal methylene of the allyl group and the benzyl methylene appeared as multiplets at δ = 2.8 and *ca.* 3.3 p.p.m., respectively. The multiplicity of the benzyl methylene peak may be attributed to the asymmetry of an adjacent carbon and to conformational effects.[6] The benzyl methylene of the ether IVa and O-methyl group of IVb gave n.m.r. singlets at 5.2 and 4.0 p.p.m., respectively. The proton at the tertiary carbon of Ic produced a triplet (apparently a coalesced quartet) at 5.9 p.p.m. In Ib this resonance appeared at 5.7 p.p.m. Triplets in this region did not appear in the spectra of the ethers IVa and IVb, but a singlet at 8.1 p.p.m. in each spectrum was assigned to the proton on the carbon adjacent to the ring. The main product from reaction of Ia with *p*-nitrobenzyl chloride was thought to be the enol ether IVc because of infrared peaks at 1708 (α,β-unsaturated ester carbonyl), and 1620 and 1605 cm.$^{-1}$ (doublet due to enol carbon–carbon double bond[7]). Thiophenes of type III were assigned structures on the basis of infrared spectra.

Steric hindrance is probably responsible, at least in part, for the ketonic character of the C-alkylated pyruvates, Ib and Ic. Molecular models of V show that when R is hydrogen, coplanarity and therefore π-interaction are possible between the atoms of the nitrothienyl group and the appropriate atoms of the enolic side chain. Because of the many resonance possibilities afforded by enolization, the keto–enol equilibrium shifts in favor of the enol form. When R is alkyl as in Ib and Ic such coplanarity is prohibited by the crowding between R and the nitro group. Conjugation is not greatly extended through enolization and the molecule tends to be ketonic.


V

The products of type III probably arose through basic cleavage of C-alkylpyruvates. Attack of base at the 2-keto group of a type I molecule could lead to two cleavage fragments, an oxalic acid derivative and a resonance-stabilized anion of III. When the weak base, sodium bicarbonate, was employed in the alkylation with allyl bromide, little or no cleavage occurred, but with potassium carbonate, a stronger base, there was extensive cleavage of the desired product Ib to IIIe. In the reaction of Ia, benzyl bromide and lithium carbonate, the yield of C-benzylpyruvate probably suffered owing to cleavage. The facile cleavage of C-alkylpyruvates stands in contrast to the relative stability to base of the simple pyruvate Ia. In the C-alkylated compounds, the steric crowding that suppresses enolization is relieved through cleavage. The simple pyruvate, on the other hand, tends to form the stable enolate ion, which is safe from destruction by base.

From our limited data, little can be said concerning the factors that influence the ratio of carbon to enolic oxygen alkylation (C–O ratio) in Ia. Of the alkylating agents examined, only allyl and benzyl bromide produced C–O ratios greater than one. These halides are known to effect carbon alkylation of phenoxides more readily than do saturated halides.[8] It also has been noted that under some conditions a smaller cation will associate in solution with the oxygen of phenoxide, thus

---

(4) A. M. Stock, W. E. Donahue, and E. D. Amstutz, *J. Org. Chem.*, **23**, 1840 (1958).

(5) Chemical shifts are expressed in units of δ, parts per million downfield from internal tetramethylsilane. The spectra were obtained by Mr. D. H. Johnson and associates on a Varian A-60 n.m.r. spectrometer.

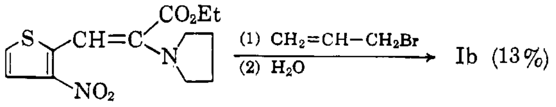
(6) H. S. Gutowsky, *J. Chem. Phys.*, **37**, 2196 (1962); *Pure Appl. Chem.*, **7**, 93 (1963).

(7) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, p. 41.

(8) D. Y. Curtin, R. J. Crawford, and M. Wilhelm, *J. Am. Chem. Soc.*, **80**, 1391 (1958).

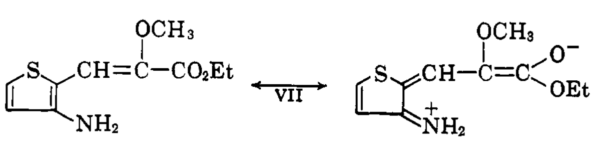
blocking O-alkylation and promoting C-alkylation, while a larger cation will tend to dissociate from the anion and expose it to O-alkylation.[8,9] In reactions of Ia and benzyl bromide in acetone we obtained a C–O ratio of 3:1with sodium bicarbonate and at least 10:1 (from n.m.r. data) with lithium carbonate.

The Stork enamine method for the α-alkylation of ketones[10] was investigated as a possible route to C-alkylated derivatives of Ia. In this method a ketone is converted to a tertiary enamine, which is treated with an electrophilic alkylating agent in the absence of catalyst. Acid hydrolysis of the alkylated enamine affords the α-alkylated ketone. If this method could be applied to Ia, enol ethers could not form and the product would not be exposed to cleavage by base. Although Ia was converted by pyrrolidine to the enamine VI, alkylations of this enamine proved difficult. The allyl compound Ib was obtained under forcing conditions in only 13% yield. Attempted alkylations of VI with ethyl bromoacetate and acrylonitrile failed completely and Ia was recovered as the result of hydrolysis of VI during the work-up.



VI

Stannous chloride in hydrochloric acid converted Ia to IIa in 55% yield.[3] The same reductant mainly gave resinous materials from the C-alkylpyruvates Ib and Ic; the 6-allylthienopyrrole IIb was obtained in yields up to 7% while the 6-benzylthienopyrrole IIc was formed in 11% yield. The yields were not improved by conducting the reactions under nitrogen. These poor results may be due to steric hindrance to cyclization. Also, the intermediate amines from the predominantly ketonic pyruvates may undergo rapid resinification if they, too, are ketonic. Free aminothiophenes, if not stabilized by electron-withdrawing groups, rapidly polymerize under normal conditions.[11] It is of interest in this connection that a stable free amine (VII) was obtained from the stannous chloride reduction of the methyl enol ether IVb. The satisfactory conversion of Ia to IIa may depend upon similar stabilization of the intermediate enolic amine.



VII

Ethyl 3-nitro-2-thienylbrompyruvate (Id) was prepared by the action of bromine on Ia. When Id was reduced in the usual way[3] with stannous bromide in hydrobromic acid, the only product was 5-carbethoxythieno[3,2,-*b*]pyrrole, unsubstituted in position 6. The facile reduction of the carbon–bromine bond in Id also was exemplified by the immediate release of iodine upon treatment of Id with potassium iodide.

Experimental[12]

Ethyl 2-Keto-3-(3-nitro-2-thienyl)-5-hexenoate (Ib).—Ethyl 3-nitro-2-thienylpyruvate[3] (4.86 g., 0.020 mole), 10 ml. of allyl bromide, and 1.85 g. (0.22 mole) of sodium bicarbonate in 40 ml. of acetone were heated together under reflux for 14 hr. The mixture was diluted with ether, filtered to remove inorganic salts, and dried over sodium sulfate. The solvent and excess allyl bromide were removed *in vacuo*. There remained 5.29 g. (93%) of dark orange oil which, according to spectra, was relatively pure hexenoate. An analytical sample, prepared by chromatography on alumina and molecular distillation, was a yellow oil which darkened on standing.

An infrared spectrum of a liquid film of the compound revealed a peak at 1730 with a shoulder at 1700 (carbonyl groups) and a peak at 1640 cm.$^{-1}$ (olefinic carbon–carbon double bond). A very weak band appeared at 3450 cm.$^{-1}$ (enolic hydroxyl).

Anal. Calcd. for $C_{12}H_{13}NO_4S$: C, 50.87; H, 4.62; N, 4.94. Found: C, 50.89; H, 4.60; N, 5.03.

6-Allyl-5-carbethoxythieno[3,2-*b*]pyrrole (IIb).—Ethyl 2-keto-3-(3-nitro-2-thienyl)-5-hexenoate (500 mg.) dissolved in 6 ml. of absolute ethanol was added slowly with cooling to a solution of 4 g. of stannous chloride dihydrate in 6 ml. of concentrated hydrochloric acid. As the mixture was stirred without external temperature control, the temperature rose spontaneously to 35°. After being stirred for 75 min., the mixture was cooled and was added slowly to a mixture of 20 ml. of saturated aqueous potassium carbonate solution, 10 ml. of water, and 20 ml. of ether, with swirling in an ice bath. The ether layer was decanted and the aqueous layer was extracted twice with ether. The combined ether solution was washed with aqueous potassium carbonate and with saturated potassium chloride solution, then was filtered and dried over sodium sulfate. The red oil which remained upon removal of the ether was placed on a 2 × 2 in. chromatographic column of acid-washed alumina and eluted with benzene–cyclohexane (2:1). The second and third liters of eluent contained 31 mg. (7%) of the allylcarbethoxythienopyrrole, m.p. 80–94°. Two recrystallizations from petroleum ether (40–60°) afforded an analytical sample of white prisms, m.p. 97–98°.

An infrared spectrum of a 5% chloroform solution of the compound contained a carbonyl absorption at 1690 and a pyrrole N-H absorption at 3500 cm.$^{-1}$.

Anal. Calcd. for $C_{12}H_{13}NO_2S$: C, 61.26; H, 5.57; N, 5.95. Found: C, 60.84; H, 5.49; N, 5.90.

Ethyl 2-Keto-3-(3-nitro-2-thienyl)-4-phenylbutyrate (Ic).—A mixture of 1.944 g. (0.008 mole) of ethyl 3-nitro-2-thienylpyruvate, 1.370 g. (0.008 mole) of benzyl bromide, and 0.296 g. (0.004 mole) of lithium carbonate in 10 ml. of acetone was heated under reflux for 38 hr. A dark, viscous oil remained after removal of the solvent. The oil was chromatographed on silica gel with cyclohexane as eluent. The first band to be eluted contained 1.21 g. of orange oil, mainly the C-benzylated pyruvate (45%) according to n.m.r. and infrared spectra. The material was employed without further purification in the synthesis of 6-benzyl-5-carbethoxythieno[3,2-*b*]yprrole.

6-Benzyl-5-carbethoxythieno[3,2-*b*]pyrrole (IIc).—Ethyl 2-keto-3-(3-nitro-2-thienyl)-4-phenylbutyrate (1.00 g., 0.003 mole) was dissolved in 9 ml. of ethanol and treated under nitrogen with a solution of 5.5 g. of stannous chloride dihydrate in 9 ml. of concentrated hydrochloric acid. The procedure was that outlined above for the preparation of 6-allyl-5-carbethoxythienopyrrole. A nearly white product weighing 76 mg. (11% yield) was obtained by chromatography and recrystallization from hexane-benzene. Three more crystallizations from hexane–benzene gave analytically pure 6-benzyl-5-carbethoxythienopyrrole as white needles, m.p. 126–129°. An infrared spectrum of the product in chloroform showed peaks at 1690 (carbonyl), 3300 and 3450 cm.$^{-1}$ (bonded and free N–H).

Anal. Calcd. for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30; N, 4.91. Found: C, 67.47; H, 5.38; N, 4.89.

---

(9) N. Kornblum, R. Seltzer, and P. Haberfield, *J. Am. Chem. Soc.*, **85**, 1148 (1963).

(10) G. Stork, A.Brizzolara, A. Landesman, H. Szmuszkovicz, and R. Terrel, *ibid.*, **85**, 207 (1963).

(11) H. D. Hartough, "Thiophene and Its Derivatives," Interscience Publishers, Inc., New York, N. Y., 1952, p. 233; S. Gronowitz, "Advances in Heterocyclic Chemistry," A. R. Katritzky, Ed., Associated Publishers, New York, N. Y., 1963, p. 85.

(12) Melting points are uncorrected. Microanalyses were performed by Mr. Josef Nemeth and his associates, University of Illinois. Infrared spectra were obtained from a Perkin-Elmer Model 21 spectrophotometer by Mr. D. H. Johnson and associates.

Methylation of Ethyl 3-Nitro-2-thienylpyruvate.—A mixture of 4.24 g. (0.017 mole) of ethyl 3-nitro-2-thienylpyruvate, 2.60 g. of anhydrous potassium carbonate, 15 ml. of methyl iodide, and 300 ml. of acetone was heated at reflux for 12 hr. During the reflux period, the initially red mixture became light orange. The mixture then was cooled and filtered to remove inorganic salts. After removal of the acetone, the residual oil was chromatographed on alumina with benzene as eluent. The first band to be eluted contained 3.58 g. of an oil which slowly crystallized. Recrystallization from ethanol–water afforded 1.06 g. (24%) of the enol methyl ether, ethyl 2-methoxy-3-(3-nitro-2-thienyl)acrylate (IVb). A second recrystallization gave an analytical sample of yellow needles, m.p. 74.5–75.5°. The material failed to give a ferric chloride test for enols. An infrared spectrum (KBr pellet) contained peaks at 1725 (ester carbonyl) and 1612 cm.$^{-1}$ (enol C=C).

Anal. Calcd. for $C_{10}H_{11}NO_5S$: C, 46.70; H, 4.28; N, 5.45. Found: C, 46.67: H, 4.36; N, 5.30.

The filtrate from the first recrystallization of IVb was evaporated and again chromatographed on alumina. Fractionation of the benzene eluent afforded a trace of crystalline solid, m.p. 40–42°, which was assigned the structure of 2-ethyl-3-nitrothiophene (IIIb) on the basis of infrared spectra.

Reduction of Ethyl 2-Methoxy-3-(3-nitro-2-thienyl)acrylate (IVb).—Reduction of IVb under conditions employed for the reductive cyclization of Ib to IIb, afforded ethyl 2-methoxy-3-(3-amino-2-thienyl)acrylate (VII), a yellow solid, which was purified by recrystallization from benzene–petroleum ether (30–60°), m.p. 89.5–90.5°.

Anal. Calcd. for $C_{10}H_{13}NO_3S$: C, 52.91; H, 5.73; N, 6.17. Found: C, 52.75; H, 5.88; N, 5.97.

Reaction of Ethyl 3-Nitro-2-thienylpyruvate with *p*-Nitrobenzyl Chloride.—To a stirred solution of 0.1 g. (0.0043 g.-atom) of sodium metal in 15 ml. of absolute ethanol was added a solution of 1.0 g. (0.0041 mole) of the pyruvate Ia in 25 ml. of ethanol. The mixture was brought to reflux temperature and a solution of 0.71 g. (0.0041 mole) of *p*-nitrobenzyl chloride in 20 ml. of ethanol then was added over a 10-min. period. The resulting mixture was refluxed for 19 hr. Most of the ethanol was evaporated, and the solution was diluted with water and acidified with hydrochloric acid. The brown solid which precipitated was collected, dried, and recrystallized from absolute ethanol. A yellow solid, 0.354 g. (24%), which separated from the solution was identified through analysis and infrared spectroscopy as ethyl 2-(*p*-nitrobenzoxy)-3-(3-nitro-2-thienyl)acrylate (IVc). Another recrystallization from ethanol provided an analytical sample, m.p. 168.5–169°.

Anal. Calcd. for $C_{16}H_{14}N_2O_7S$: C, 50.80; H, 3.73; N, 7.40. Found: C, 50.98; H, 3.69; N, 7.44.

The filtrate from the first recrystallization of IVc yielded 0.185 g. (12%) of another yellow solid identified as 1-(3-nitro-2-thienyl)-2-(*p*-nitrophenyl)ethane (IIIc). An analytical sample from ethanol–water melted at 120–121°.

Anal. Calcd. for $C_{12}H_{10}N_2O_4S$: C, 51.80; H, 3.62; N, 10.08. Found: C, 51.63; H, 3.61; N, 10.35.

Cyanomethylation of Ethyl 3-Nitro-2-thienylpyruvate.—The pyruvate Ia (0.50 g.), sodium iodide (0.31 g.), and chloroacetonitrite (0.156 g.) were dissolved in 25 ml. of absolute ethanol. To this solution at reflux temperature was added a solution of sodium metal (0.051 g.) in 25 ml. of absolute ethanol. The mixture was heated at reflux for 24 hr., then reduced in volume, acidified with dilute hydrochloric acid, and extracted with ether. An oil which remained after removal of the ether was taken up in cyclohexane, treated with Darco, filtered, and chilled. 3-(3-Nitro-2-thienyl)propionitrile (IIId) was obtained in 15% yield as white needles, m.p. 77.5–78.3°. In the infrared (KBr pellet) the material does not absorb in the carbonyl region but exhibits a nitrile absorption at 2240 cm.$^{-1}$.

Anal. Calcd. for $C_7H_6N_2O_2S$: C, 46.20; H, 3.32; N, 15.40. Found: C, 45.94; H, 3.12; N, 15.18.

Ethyl 1-Pyrrolidino-2-(3-nitro-2-thienyl)acrylate (VI).—In a two-necked 100-ml. flask were placed 55 ml. of dry benzene, 2.00 g. (0.0082 mole) of ethyl 3-nitro-2-thienylpyruvate, 0.62 g. (0.0088 mole) of dry redistilled pyrrolidine, and 40 mg. of *p*-toluenesulfonic acid monohydrate. The flask was fitted with a nitrogen inlet and with a Soxhlet extractor containing a thimble filled with molecular sieve, as recommended by Stork[9] for the efficient removal of water in conversions of ketones to enamines. The mixture was refluxed vigorously under nitrogen. After 12 hr., the reaction was shown to be complete by infrared analysis. The mixture absorbed strongly at 1730 (ester carbonyl of enamine), while peaks due to unchanged pyruvate at 1700 (bonded ester carbonyl) and 3400 cm.$^{-1}$ (enolic hydroxyl) were weak or absent. Removal of the benzene and excess pyrrolidine *in vacuo* afforded a viscous, dark red oil, principally the enamine, which was used directly in attempted alkylations.

When the sulfonic acid catalyst was omitted, considerable cleavage of the pyruvate to 2-methyl-3-nitrothiophene occurred.

Ethyl 3-Nitro-2-thienylbromopyruvate (Id).—A solution of 3.35 g. (0.021 mole) of bromine in 80 ml. of chloroform was added slowly to a stirred solution of 5.00 g. (0.020 mole) of ethyl 3-nitro-2-thienylpyruvate in 100 ml. of chloroform. The temperature of the reaction mixture was held between −5 and −10° with an ice–salt bath. Moist litmus paper indicated the evolution of hydrogen bromide. When the addition was complete, the chloroform was removed *in vacuo*. The residue was dissolved in ethyl ether and treated with Darco. The ether solution was reduced in volume and hot petroleum ether (b.p. 30–60°) was added to effect crystallization. A yield of 5.4 g. (82%) of light yellow crystals was obtained, m.p. 66–68°. For analysis, the material was recrystallized twice from ethyl ether–petroleum ether (b.p. 30–60°), m.p. 67–68°.

An infrared spectrum of a 10% chloroform solution of the product exhibited a carbonyl absorption at 1730 cm.$^{-1}$. There was no band for enolic hydroxyl in the region 3200–4000 cm.$^{-1}$.

Anal. Calcd. for $C_9H_8BrNO_6S$: C, 33.55; H, 2.50; N, 4.35. Found: C, 33.44; H, 2.48; N, 4.38.

Arylboronic Acids. VII. Some Reactions of *o*-Formylbenzeneboronic Acid[1]

PAUL TSCHAMPEL AND H. R. SNYDER

Noyes Chemical Laboratory, University of Illinois, Urbana, Illinois

Received February 11, 1964

The behavior of *o*-formylbenzeneboronic acid towards various aldehyde reagents is described. Reaction with secondary diamines, malononitrile, sodium bisulfite, and Girard's reagent T provides the usual products, while the 2,4-dinitrophenylhydrazone is isolated as the diethyl boronate ester. The boronic acid function participates in condensation reactions with semicarbazide and *p*-carboxyphenylhydrazine hydrochlorides to give the corresponding 4-hydroxyborazaroisoquinolines. α-Substituted boronophthalides are formed with isopropylidene malonate, nitromethane, and sodium cyanide.

The formation of the stable boron-containing compounds, bis(4,3-borazaro-4-isoquinolinyl) ether (Ia) and bis(3-phenyl-4,3-borazaro-4-isoquinolinyl) ether (Ib), from the reaction of *o*-formylbenzeneboronic acid (II) with hydrazine and phenylhydrazine hydrochloride, respectively, was recently reported by Dewar.[2] Although II also reacted with hydroxylamine to form a cyclic derivative (III), the aldehyde appeared to be

---

[1] This work was supported by a grant [AT(11-1)-314] from the Atomic Energy Commission; report COO-314-8.

[2] M. J. S. Dewar and R. C. Dougherty, *J. Am. Chem. Soc.*, **84**, 2648 (1962); **86**, 433 (1964).