enter the flask, and the contents were shaken vigorously for 3–5 minutes. Liberated nitric acid was titrated to the methyl purple end point with 0.1*N* NaOH.

$$\text{Titration (c) Acidity meq./g.} = \frac{\text{ml. NaOH} \times N}{\text{Sample (g.)}}$$

$$\text{Thus: \% Sodium acetylide} = \frac{(a + b + c) \times 100}{2 \times 20.83}$$

$$\text{\% Sodium carbonate} = \frac{2b}{18.86} \times 100$$

$$\text{Free alkalinity as \% Na} = \frac{a - \left(b - \frac{a + b + c}{2}\right)}{43.48} \times 100$$

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MURRAY HILL, N. J.

[CONTRIBUTION FROM THE INSTITUTE OF CHEMISTRY, FACULTY OF SCIENCES, BELGRADE, AND THE INSTITUTE OF CHEMISTRY, BELGRADE]

Chemistry of Thiophene. I. Derivatives of 3-Thiophenecarboxaldehyde

MIHAILO LJ. MIHAILOVIĆ[1] AND MARGITA TOT

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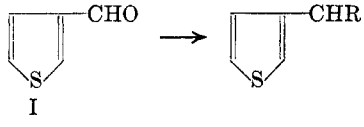
The preparation of several new derivatives of 3-thiophenecarboxaldehyde is described.

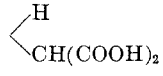
3-Thiophenecarboxaldehyde (I), which was practically unknown until 1948 when Campaigne and LeSuer[2] developed a convenient method for its preparation, starting from 3-methylthiophene through 3-thenyl bromide, so far has been studied only to a limited extent. However, many derivatives of this aldehyde might be of interest as starting products for various syntheses of 3-substituted thiophene compounds. In this paper are described the preparations of several derivatives of 3-thiophenecarboxaldehyde, which were carried out by applying some typical aromatic aldehyde condensations.



I

II, R = $(NHCOCH_3)_2$; III, R = $(NHCOC_6H_5)_2$
IV, R = NC_6H_4OH-*p*; V, R = $CHCOC_6H_5$
VI, R = C—CO—C=CHC_4H_3S; VII, R = C—C_6H_5
$-(CH_2)_3-$ CN

VIII, R = CHCOOH; IX, R = 

X, R = 

3-Thiophenecarboxaldehyde (I) reacted with benzamide or acetamide in acetic anhydride to yield the corresponding well crystallized *N,N'*-(3-thenylidene)bisamides (II and III). Bisamides, in general, can be used for the characterization of aldehydes;[3] besides they react with most compounds containing active hydrogen atoms giving unsaturated or acylamino compounds.[4]

With *p*-aminophenol, 3-thiophenecarboxaldehyde (I) gave the corresponding Schiff base IV. In alkaline solution, I reacted with acetophenone to yield the α,β-unsaturated ketone V. The condensation of cyclohexanone with two molecules of 3-thiophenecarboxaldehyde afforded 2,6-dithenylidenecyclohexanone (VI). From I and phenylacetonitrile, in the presence of sodium methoxide, α-phenyl-β-(3-thienyl)acrylonitrile (VII) was obtained.

The Doebner modification of the Perkin reaction with malonic acid in the presence of pyridine and piperidine gave very good yields of 3-(3-thienyl)-acrylic acid (VIII). Upon reduction of VIII with sodium-amalgam, by the usual procedure, 3-(3-thienyl)propionic acid (IX) was obtained. The same acid has been previously prepared by Campaigne and McCarthy[5] from 3-thenylmalonic acid (X). If the condensation of I with malonic acid was carried out in ethanolic ammonia at 70–75°, with subsequent reduction with sodium-amalgam in the presence of carbon dioxide,[6] 3-thenylmalonic acid (X) was obtained, in 72% yield. Esterification of X with ethanol afforded the corresponding diethyl ester. Both the acid X and its ester have been previ-

(1) Requests for reprints should be addressed to Dr. M. Lj. Mihailović, Institute of Chemistry, Faculty of Sciences, 1, Studentski trg, Belgrade, Yugoslavia.

(2) Campaigne and LeSuer, *J. Am. Chem. Soc.*, **70**, 1555 (1948); Campaigne, Bourgeois, and McCarthy, *Org. Syntheses*, **33**, 93 (1953).

(3) Stefanović, Bojanović, and Vandjel, *Bull. soc. chim. Belgrade*, **18**, 579 (1953); Stefanović, Mihailović, Bojanović, and Vandjel, *Bull. soc. chim. Belgrade*, **20**, 417 (1955).

(4) Stefanović and Stefanović, *J. Org. Chem.*, **21**, 161 (1956). This communication contains references to previous papers about reactions of bisamides.

(5) Campaigne and McCarthy, *J. Am. Chem. Soc.*, **76**, 4466 (1954).

(6) Owen and Nord, *J. Org. Chem.*, **15**, 988 (1950).

ously synthesized by another route:[5,7] diethyl malonate and 3-thenylbromide reacted to give the diethyl ester of X, which upon saponification was converted to 3-thenylmalonic acid (X).

Campaigne *et al.*[8] have reported the formation of 3-thiophenecarboxaldehyde thiosemicarbazone, melting at 151–152°. However, the thiosemicarbazone that we prepared from 3-thiophenecarboxaldehyde and thiosemicarbazide, in the cold, crystallized in white needles, m.p. 160°. Upon standing it turned yellow.

EXPERIMENTAL[9,10]

N,N'-(3-Thenylidene)bisbenzamide (III). A mixture of 1.12 g. (0.01 mole) of 3-thiophenecarboxaldehyde,[2] 3.63 g. (0.03 mole) of benzamide, and 2.5 ml. of acetic anhydride was heated on the water bath for 4 hr. The reaction mixture was cooled in ice and the white crystalline solid that separated was filtered and washed with small amounts of cold diethyl ether. There was obtained 1.72 g. (51.2%) of bisamide III, m.p. 213°. Recrystallization from ethanol did not raise the melting point.

Anal. Calcd. for $C_{19}H_{16}N_2O_2S$: N, 8.33. Found: N, 8.19.

N,N'-(3-Thenylidene)bisacetamide (II). A mixture of 1.12 g. (0.01 mole) of 3-thiophenecarboxaldehyde, 2.36 g. (0.04 mole) of acetamide, and 1 ml. of acetic anhydride was treated as above. The crude bisacetamide II, m.p. 228°, was obtained in a yield of 61.3% (1.3 g.). After 3 crystallizations from acetone the product melted at 231°.

Anal. Calcd. for $C_9H_{12}N_2O_2S$: N, 13.19. Found: N, 13.30.

p-(3-Thenylideneamino)phenol (IV). In a three-necked flask fitted with a mercury sealed mechanical stirrer and a reflux condenser were placed 16 ml. of ethanol and 2.18 g. (0.02 mole) of *p*-aminophenol. The mixture was heated to boiling and 2.24 g. (0.02 mole) of 3-thiophenecarboxaldehyde was added in small portions, during 15 min. The mixture was then stirred for another 20 min., but without heating. After standing for 5 hr. at −5°, the brown crystalline precipitate was separated by filtration and washed with cold 50% ethanol. There was obtained 1.75 g. (43.1%) of crude IV, m.p. 197°. Treatment with decolorizing charcoal and 2 crystallizations from ethanol afforded drab needles, m.p. 202.5°.

Anal. Calcd. for $C_{11}H_9NOS$: C, 64.99; H, 4.46; N, 6.89. Found: C, 65.18; H, 4.58; N, 7.03.

1-Phenyl-3-(3-thienyl)-2-propene-1-one (V). To a solution of 1.0 g. (0.025 mole) of sodium hydroxide in 9.3 ml. of water and 4.6 ml. of ethanol, 2.4 g. (0.02 mole) of acetophenone and 2.24 g. (0.02 mole) of 3-thiophenecarboxaldehyde were added with stirring. The temperature, during the addition, was maintained by external cooling at 10–12°. The reaction mixture was then stirred for a further 3 hr. at 25°, and allowed to stand overnight at 0°. The white crystals were separated by filtration, washed with water until neutral and then with aqueous ethanol. There was obtained 2.95 g. (68.9%) of crude V, m.p. 77°, which after one crystallization from ethanol melted at 88°.

Anal. Calcd. for $C_{13}H_{10}OS$: C, 72.86; H, 4.70. Found: C, 72.66; H, 4.90.

2,6-Dithenylidenecyclohexanone (VI). To a solution of 1.12 g. (0.01 mole) of 3-thiophenecarboxaldehyde in 7 ml. of ethanol, 0.98 g. (0.01 mole) of freshly distilled cyclohexanone, followed by 5–6 drops of 10% aqueous sodium hydroxide were slowly added, with stirring. After heating for 15 min. on the water bath, the mixture was cooled to 0°, and the yellow needles which soon separated were filtered off. The yield of crude 2,6-dithenylidenecyclohexanone (VI), m.p. 130°, was 1.0 g. (69.9%). Recrystallized twice from ethanol the pure compound melted at 139°.

Anal. Calcd. for $C_{16}H_{14}OS_2$: C, 67.09; H, 4.93. Found: C, 66.82; H, 5.10.

α-Phenyl-β-(3-thienyl)acrylonitrile (VII). This compound was prepared according to the procedure of Castle and Seese.[11] From 2.24 g. (0.02 mole) of 3-thiophenecarboxaldehyde there was obtained 2.27 g. (53.8%) of colorless VII, m.p. 65–66°. Two crystallizations from methanol raised the m.p. to 68°.

Anal. Calcd. for $C_{13}H_9NS$: C, 73.89; H, 4.29; N, 6.63. Found: C, 73.83; H, 4.39; N, 6.81.

3-(3-Thienyl)acrylic acid (VIII). A mixture of 3.36 g. (0.03 mole) of 3-thiophenecarboxaldehyde, 6.24 g. (0.06 mole) of malonic acid, 15 ml. of dry pyridine (distilled over potassium hydroxide), and 0.5 ml. of piperidine was heated on a water bath for 2 hr. and then heated to boiling for 5–10 min. After cooling, the resulting solution was poured, with stirring, into 75 ml. of water and treated with excess 25% hydrochloric acid. Filtration of the white flaky precipitate yielded 3.94 g. (85.2%) of 3-(3-thienyl)acrylic acid (VIII), m.p. 146°, which after recrystallization from 45% ethanol (twice) had m.p. 151°.

Anal. Calcd. for $C_7H_6O_2S$: C, 54.53; H, 3.92. Found: C, 54.72; H, 4.04.

3-(3-Thienyl)propionic acid (IX). 3-(3-Thienyl)acrylic acid (VIII) (1.54 g., 0.01 mole) was neutralized with 2% aqueous sodium hydroxide, diluted with 10 ml. of water, and reduced in the usual manner with 2% sodium-amalgam (at 15°). After recrystallization from water there was obtained 1.3 g. (83.3%) of white needles of the acid IX, m.p. 62–62.5° (reported[5] m.p. 61–62°).

Anal. Calcd. for $C_7H_8O_2S$: C, 53.82; H, 5.16. Found: C, 53.80; H, 5.00.

3-Thenylmalonic acid (X). This acid was obtained according to the procedure described by Owen and Nord[7] for the preparation of 2-thenylmalonic acid. After removing the ether the solidified residue was recrystallized from benzene, affording 4.3 g. (71.5%) of 3-thenylmalonic acid (X), in the form of white needles, m.p. 140° (reported[5] m.p. 139–140°).

Anal. Calcd. for $C_8H_8O_4S$: C, 47.99; H, 4.03. Found: C, 48.06; H, 4.06.

By heating X and recrystallizing the resulting product from water, 75% of 3-(3-thienyl)propionic acid (IX), m.p. 62°, was obtained.[5]

Diethyl 3-thenylmalonate. The esterification was carried out by gently refluxing for 4 hr. a mixture of 4.0 g. (0.02 mole) of 3-thenylmalonic acid, 35 ml. of anhydrous ethanol, and 1 ml. of concentrated sulfuric acid. After removing the excess ethanol *in vacuo*, the residue was treated with 30 ml. of water, and the resulting solution extracted with ether (twice with 25 ml. portions). The usual procedure yielded 4.3 g. (83.7%) of diethyl 3-thenylmalonate, b.p. 146–150° (6 mm.), n_D^{20} 1.4950, d_4^{20} 1.1428 (reported[5,6] b.p. 146°/3 mm., 141–147°/4 mm., n_D^{20} 1.4960, d_4^{20} 1.142).

Anal. Calcd. for $C_{12}H_{16}O_4S$: C, 56.22; H, 6.29. Found: C, 56.15; H, 6.39.

3-Thiophenecarboxaldehyde thiosemicarbazone. To 0.56 g. (0.005 mole) of 3-thiophenecarboxaldehyde dissolved in 6 ml. of ethanol and containing 0.5 ml. of glacial acetic acid was added a warm solution of 0.46 g. (0.005 mole) of thiosemicarbazide in 9 ml. of water, with constant stirring. A white crystalline precipitate was immediately formed.

(7) Campaigne and Patrick, *J. Am. Chem. Soc.*, **77**, 5425 (1955).

(8) Campaigne, Monroe, Arnwine, and Archer, *J. Am. Chem. Soc.*, **75**, 988 (1953).

(9) All melting points are uncorrected.

(10) The microanalyses were performed by Mrs. R. Tasovac, Microanalytical Laboratory, Institute of Chemistry, Faculty of Sciences, Belgrade.

(11) Castle and Seese, *J. Org. Chem.*, **20**, 987 (1955).

Stirring was continued at room temperature for another 2 hr. Upon standing for several hours at 0°, the solid was collected by filtration and washed with ice cold 50% ethanol. There was obtained 0.77 g. (82.8%) of thiosemicarbazone, m.p. 159°. Recrystallized from 25% ethanol it melted at 160° (reported[8] m.p. 151–152°).

Anal. Calcd. for $C_6H_7N_3S_2$: C, 38.89; H, 3.80; N, 22.68. Found: C, 38.69; H, 3.88; N, 22.55.

The freshly prepared compound was white, but on standing turned yellow.

BELGRADE, YUGOSLAVIA

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF DEPAUL UNIVERSITY AND PURDUE UNIVERSITY]

Synthesis and Isomerization of Substituted 5-Amino-1,2,3-triazoles[1]

EUGENE LIEBER,[2] TAI SIANG CHAO,[3] AND C. N. RAMACHANDRA RAO[4]

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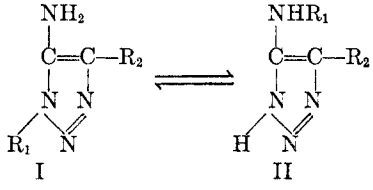
A series of 1,4-disubstituted-5-amino-1,2,3-triazoles were prepared by reactions involving the base-catalyzed condensation of alkyl- and aryl-azides with malonic ester, cyanoacetic ester and phenylacetonitrile. The latter proved advantageous for preparing a series of 1-substituted-4-phenyl-5-amino-1,2,3-triazoles. A mechanism is proposed for the base-catalyzed condensation of azides with phenylacetonitrile which accounts for the resistance of the electropositively substituted azides to form vicinal triazoles. The 1,4-disubstituted-5-amino-1,2,3-triazoles were irreversibly isomerized to a series of 4-phenyl-5-(substituted)anilino-1,2,3-triazoles by refluxing in pyridine-type bases. The comparative rate of irreversible isomerization of a selected group of 1-substituted-4-phenyl-5-amino-1,2,3-triazoles to 4-phenyl-5-(substituted)anilino-1,2,3-triazoles in boiling pyridine was found to depend on the electrical effect of the substituent in the 1-position in a manner comparable to that found for 1-substituted-5-aminotetrazoles. The isomerization of 1-substituted-4-phenyl-5-amino-1,2,3-triazoles to 4-phenyl-5-(substituted)anilino-1,2,3-triazoles, or *vice versa*, at 184–185° in homogeneous melts has been investigated and found to reach an equilibrium. The position of equilibrium shifts to the acidic isomer as the electronegativity of the substituent is increased, yielding an approximately linear relationship between the logarithm of the equilibrium constant and Hammett's σ-value for groups.

The discovery that 1-substituted-5-amino-1,2,3-triazoles undergo a rather facile and apparently reversible isomerization to 5-substituted amino-1,2,3-triazoles:



I II

was made by Dimroth.[5] The examples reported[5] were:

$R_1 = C_6H_5$; $R_2 = CO_2Et$ (1)

$R_1 = C_6H_5$; $R_2 = H$ (2)

$R_1 = C_6H_5$; $R_2 = C_6H_5$ (3)

$R_1 = C_6H_5$; $R_2 = CH_3$ (4)

All except example (1) were carried out under non-equilibrium conditions, *i.e.*, by use of a basic solvent which favors the acidic isomer II, or by allowing the higher melting isomer (usually II) to crystallize out from the melt. Example (1) was run in absolute ethanol and in benzene, in sealed tubes at 150° for 3 hrs. (unfortunately the tubes were cooled under ambient conditions) approaching equilibrium from either pure III or IV:

III ($R_1 = C_6H_5$; $R_2 = CO_2Et$) $\rightleftharpoons$ IV ($R_1 = C_6H_5$; $R_2 = CO_2Et$)

Dimroth's titration data[25] enable an estimation of the positions of equilibrium to be calculated. The results of these calculations are summarized in Table I. It thus appears that the reversible nature of I $\rightleftharpoons$ II has been established, although from limited data, and that the shift in the position of equilibrium with the type of solvent is in the same order as predicted by Henry, Finnegan, and Lieber[6] for substituted 5-aminotetrazoles. However, the magnitude in the shift of the position of equilibrium in a Lewis type of basic solvent appears (Table I) to be abnormally large considering the very weak basic properties of ethanol. The data for the homogeneous melt, while showing perfect coincidence regardless of the direction from which the reaction is initiated, need verification due to the questionable analytical technique[7,25] employed. Further, the limited amount

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(2) DePaul University, Chicago 14, Ill., to whom all requests for reprints and additional information should be addressed.

(3) Present address: Archer Daniel Midland Corp., Minneapolis, Minn.

(4) Department of Chemistry, Purdue University.

(5) O. Dimroth, *Ann.*, **364**, 183 (1909).

(6) R. A. Henry, W. G. Finnegan, and E. Lieber, *J. Am. Chem. Soc.*, **76**, 88 (1954).

(7) A study of the determination of the weak bases and acids represented by I and II by titration in nonaqueous media has been submitted for publication elsewhere. (*Anal. Chem.*, in press.) Briefly, the determination of the acidic isomer was generally used for estimation of purity and for the determination of the positions of equilibrium. Anhydrous dimethyl formamide was used as solvent, with sodium methoxide as titrant and azoviolet as the visual indicator. The method was tested with the pure isomers of type I giving an average deviation from 100% recovery of $\pm 0.03\%$.