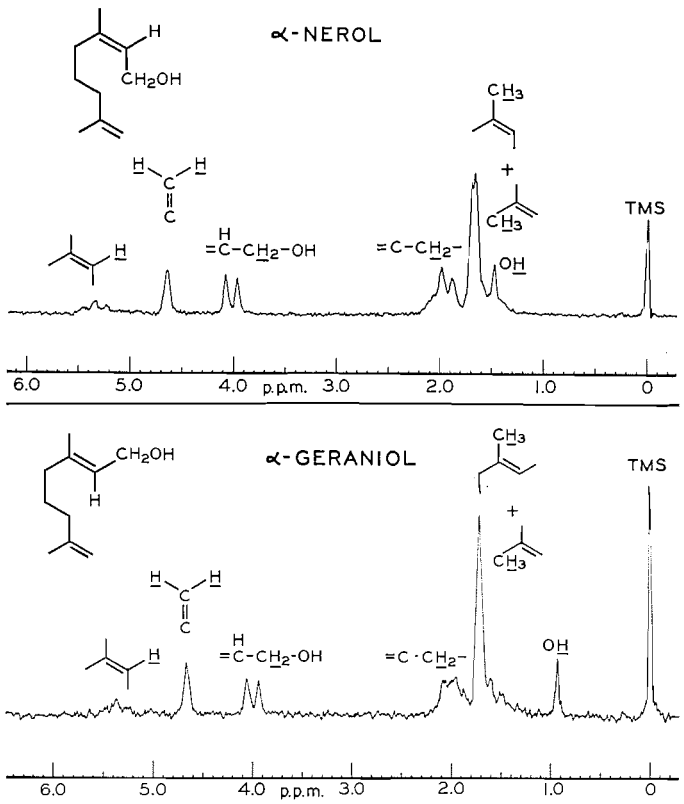

FIG. 2. TMS = tetramethylsilane.

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RECEIVED FEBRUARY 21, 1966.
INTERNATIONAL FLAVORS & FRAGRANCES (U.S.),
NEW YORK, NEW YORK.

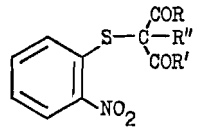
ORGANIC SULFUR COMPOUNDS
III. CONDENSATIONS INVOLVING *o*-NITROBENZENESULFENYL CHLORIDE[1]

R. T. COUTTS, K. W. HINDMARSH, AND N. J. POUND

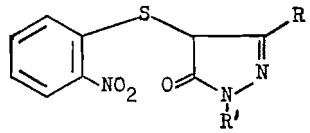
o-Nitrobenzenesulfenyl chloride, 2,4-dinitrobenzenesulfenyl chloride, and 4-chloro-2-nitrobenzenesulfenyl chloride are known to react with ketones possessing an active methylene group to yield α-(*o*-nitrophenylthio), α-(2,4-dinitrophenylthio), and α-(4-chloro-2-nitrophenylthio) ketones, respectively (1–3). Typical of this reaction is the condensation of *o*-nitrobenzenesulfenyl chloride with ethyl acetoacetate, which gives rise

[1]*For part II in this series, see R. T. Coutts, D. L. Barton, and E. M. Smith, Can. J. Chem., 44, 1733 (1966).*

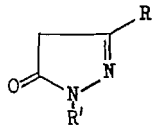
to ethyl α-(*o*-nitrophenylthio)acetoacetate (I*a*). When, however, 4-chloro-2-nitrobenzenesulfenyl chloride was reacted with diethyl malonate, the expected product, diethyl α-(4-chloro-2-nitrophenylthio)malonate, was not produced (3). The major product in this case was bis(4-chloro-2-nitrophenyl) disulfide. *o*-Nitrobenzenesulfenyl chloride also reacts atypically with diethyl malonate, with malonic acid, and with ethylmalonic acid. The products identified by us were bis(*o*-nitrophenyl) disulfide and the *S*-*o*-nitrophenyl ester of *o*-nitrothiobenzenesulfonic acid; α-(*o*-nitrophenylthio)butyric acid was an additional product in the reaction with ethylmalonic acid which yielded none of the desired compound (I*e*).



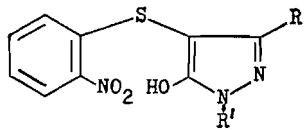
	R	R'	R''
Ia	Me	OEt	H
Ib	OH	OH	H
Ic	NH_2	NH_2	H
Id	NH-CO-NH		H
Ie	OH	OH	Et



	R	R'
IIa	Me	H
IIb	Me	Ph
IIc	Ph	Ph



III

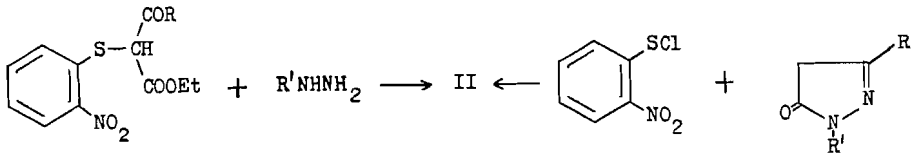


IV

In contrast with these results, when malonamide was reacted at room temperature with *o*-nitrobenzenesulfenyl chloride in acetonitrile, an almost quantitative yield of α-(*o*-nitrophenylthio)malonamide (I*c*) was obtained. As expected, this compound is a weak acid and is insoluble in sodium bicarbonate solution but readily soluble in aqueous sodium hydroxide, giving an orange solution from which I*c* is reprecipitated when acid is added. When the aqueous sodium hydroxide solution was heated, ammonia was rapidly evolved, but no α-(*o*-nitrophenylthio)malonic acid (I*b*) was isolable. An obvious extension of the above successful condensation was the interaction of *o*-nitrobenzenesulfenyl chloride with barbituric acid. This reaction occurred readily, and 5-(*o*-nitrophenylthio)barbituric acid (I*d*) was isolated in excellent yield. It is a relatively strong acid which dissolves in sodium bicarbonate solution. Also, it is stable in hot concentrated sulfuric acid. After such a solution was heated at 80–100° for 6 h, the addition of water precipitated the unchanged acid, almost quantitatively.

Our attention was then directed towards the preparation of 4-(*o*-nitrophenylthio)-2-pyrazolin-5-ones (II), which were required for our reductive cyclization studies (4). The initial method chosen to prepare the 4-(*o*-nitrophenylthio)-2-pyrazolin-5-ones was by the interaction of hydrazine or phenylhydrazine with ethyl α-(*o*-nitrophenylthio)acetoacetate or ethyl α-(*o*-nitrophenylthio)benzoylacetate. The action of phenylhydrazine on ethyl

α-(*o*-nitrophenylthio)acetoacetate gave the expected product (II*b*) in poor yield; however, when ethyl α-(*o*-nitrophenylthio)acetoacetate was treated with hydrazine hydrate, hydrolysis occurred and the only product isolated was the hydrazide of (*o*-nitrophenylthio)acetic acid. The action of phenylhydrazine on ethyl α-(*o*-nitrophenylthio)benzoylacetate was more complex; once again, the expected product (II*c*) was not obtained.



Instead, two red products were isolated in poor yields. The first contained sulfur and melted at 158°; the second product, m.p. 173°, was sulfur-free. Because neither product was the desired one, these compounds were not identified at this time. In view of these results, this synthetic approach was abandoned.

The fact that *o*-nitrobenzenesulfenyl chloride readily reacts with malonamide suggested that it might also condense with the active methylene group of the structurally related 2-pyrazolin-5-ones (III). Thus, *o*-nitrobenzenesulfenyl chloride was reacted in acetonitrile with 3-methyl-2-pyrazolin-5-one, with 3-methyl-1-phenyl-2-pyrazolin-5-one, and with 1,3-diphenyl-2-pyrazolin-5-one; in each case the reaction proceeded as expected, yielding the corresponding 4-(*o*-nitrophenylthio) derivatives (II*a*, II*b*, and II*c*, respectively).

The infrared spectra of the pyrazolones (II*a*–II*c*) in potassium bromide were of interest. They showed no carbonyl absorption, whereas absorption attributable to the hydroxyl group was present, which indicated that, in the solid state, the pyrazolones are better represented in the tautomeric form (IV). This conclusion is in agreement with the findings of Katritzky and Maine (5), who have studied in detail the tautomerism of pyrazolin-5-ones.

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra (KBr disks) were recorded on a Unicam SP 200 spectrophotometer. Palladium–charcoal refers to 10% palladium on charcoal.

Ethyl 2-(*o*-nitrophenylthio)acetoacetate (1) and *o*-nitrobenzenesulfenyl chloride (6), which was obtained by the action of chlorine on bis(*o*-nitrophenyl) disulfide (7), were prepared by previously reported methods.

Reaction of o-Nitrobenzenesulfenyl Chloride with Ethylmalonic Acid

A solution of *o*-nitrobenzenesulfenyl chloride (3.0 g) and ethylmalonic acid (2.5 g) in acetonitrile (60 ml) was heated under reflux for 6 h; then the solution was concentrated to ca. 30 ml, from which, when it was allowed to stand, bis(*o*-nitrophenyl) disulfide (0.72 g), m.p. 195–200° (decomp.), precipitated and was filtered off. A yellow solid (0.82 g), m.p. 125–130°, slowly precipitated from the mother liquors over a period of 48 h. Crystallization of this solid from methanol gave the *S*-*o*-nitrophenyl ester of *o*-nitrothiobenzenesulfonic acid (0.54 g), m.p. 140–142° (lit. (8) m.p. 142–143°), the infrared spectrum of which was superimposable on that of an authentic sample. The mother liquors remaining were evaporated to dryness, and the resulting waxy solid was treated with 5% aqueous sodium hydroxide (50 ml). The solution was filtered and the filtrate, on acidification, gave α-(*o*-nitrophenylthio)butyric acid (0.39 g), m.p. 105–108°, as a yellow solid, the melting point of which was raised to 112–114° on crystallization from aqueous ethanol. Infrared spectrum: broad absorption from 2 100 to 3 400 with maxima at 2 970 (m) and 2 910 (m) (OH); 1 702 (s) (C=O); 1 520 (s), 1 338 (s), and 868 (m) (NO_2) cm^{-1}.

Anal. Calcd. for $C_{10}H_{11}NO_4S$: C, 49.78; H, 4.59; S, 13.29. Found: C, 49.75; H, 4.40; S, 12.66.

(o-Nitrophenylthio)malonamide (Ic)

Malonamide (1.0 g) was added to a solution of *o*-nitrobenzenesulfenyl chloride (1.9 g) in acetonitrile (60 ml), and the resulting suspension was stirred at room temperature for 24 h. The yellow solid which formed (2.48 g), m.p. 222–225° (decomp.), dissolved completely in aqueous sodium hydroxide or sodium carbonate to give an orange solution. The title compound was reprecipitated when hydrochloric acid was

added. Infrared spectrum: broad absorption from 2 900 to 3 500 (s) with maxima at 3 400, 3 280, and 3 200 (amide NH_2); 1 665 (s) (C=O); 1 515 (s), 1 345 (s), and 865 (w) (NO_2) cm^{-1}.

Anal. Calcd. for $C_9H_9N_3O_4S$: C, 42.35; H, 3.55; N, 16.47; S, 12.56. Found: C, 42.16; H, 3.58; N, 16.08; S, 12.41.

Hydrolysis of (o-Nitrophenylthio)malonamide

The title compound (8 g) was dissolved in 10% aqueous sodium hydroxide (200 ml), and this solution was gently boiled until the evolution of ammonia ceased (90 min). The solution was cooled, acidified with hydrochloric acid, and extracted with ether. The dried ether solution, on evaporation, gave a brown oil (1.2 g) which was only partially soluble in sodium bicarbonate solution and was therefore not further investigated.

5-(o-Nitrophenylthio)barbituric Acid (Id)

Barbituric acid (2.56 g) was added to a solution of *o*-nitrobenzenesulfenyl chloride (3.8 g) in acetonitrile (100 ml), and the resulting suspension was stirred at room temperature for 30 h. The yellow solid (5.23 g), m.p. 243° (decomp.), was removed. This was the title compound. Crystallization from acetonitrile did not raise the melting point. Infrared spectrum: broad absorption from 2 100 to 3 350 (m) with maxima at 2 600, 2 680, 3 120, and 3 280 (cyclic ureide); 1 728 (s) (C=O); 1 525 (s), 1 375 or 1 345 (s), and 865 (w) (NO_2) cm^{-1}.

Anal. Calcd. for $C_{10}H_7N_3O_5S$: C, 42.70; H, 2.51; N, 14.95; S, 11.40. Found: C, 42.47; H, 2.58; N, 14.54; S, 11.06.

Crystallization from water gave the monohydrate as a yellow solid, m.p. 244–246° (decomp.).

Anal. Calcd. for $C_{10}H_7N_3O_5S \cdot H_2O$: C, 40.13; H, 3.03. Found: C, 40.38, 40.21; H, 3.14, 3.12.

The acid (I*d*) was soluble, with vigorous effervescence, in aqueous sodium bicarbonate, giving an orange solution, from which the acid was reprecipitated when hydrochloric acid was added. A suspension of the acid (I*d*) (2.2 g) in 80% sulfuric acid (250 ml) was heated on a boiling water bath for 6 h, during which time the acid dissolved completely. The orange solution was poured into water (500 ml); the resulting yellow crystalline precipitate (1.7 g) melted at 248° (decomp.). An infrared spectrum confirmed that I*d* had been recovered.

3-Methyl-4-(o-nitrophenylthio)-1-phenyl-2-pyrazolin-5-one (IIb)

Method a

When a solution of *o*-nitrobenzenesulfenyl chloride (3.0 g) in acetonitrile (20 ml) was added to a suspension of 3-methyl-1-phenyl-2-pyrazolin-5-one (3.0 g) in acetonitrile (20 ml), the latter dissolved and a yellow precipitate formed almost immediately. The mixture was heated under reflux for 4 h (during which time hydrochloric acid was evolved), cooled, and filtered to give the title compound (4.6 g) as a bright-yellow solid, m.p. 209–211° (decomp.) when crystallized from aqueous ethanol (lit. (9) m.p. 207°). Infrared spectrum: broad absorption from 2 000 to 3 200 with a broad maximum centered at 2 600 (m) (OH); 1 520 (s), 1 340 (s), and 855 (w) (NO_2) cm^{-1}; carbonyl absorption absent.

Anal. Calcd. for $C_{16}H_{13}N_3O_3S$: C, 58.70; H, 4.00; N, 12.84; S, 9.80. Found: C, 58.68; H, 4.20; N, 12.10; S, 10.21.

Method b

A solution of phenylhydrazine (2.1 g) and ethyl 2-(*o*-nitrophenylthio)acetoacetate (3.0 g) in acetonitrile (30 ml) was heated under reflux for 5 h. When the red solution was allowed to cool and stand, the title compound (1.35 g) precipitated out, m.p. 200–202°, raised to 208–210° (decomp.) when crystallized from ethanol. The infrared spectrum was identical with that of the product obtained by method *a*.

3-Methyl-4-(o-nitrophenylthio)-2-pyrazolin-5-one (IIa)

Method a

This pyrazolone was obtained by the method used in the preparation of II*b* (method *a*). The bright-yellow solid (91% yield) was dissolved in 10% sodium hydroxide solution, this solution was extracted with ether, and the ether extract was rejected. The aqueous layer was acidified with hydrochloric acid; the resulting yellow solid had m.p. 273–274° (decomp.) when crystallized from ethanol. Infrared spectrum: 3 390 (m) (NH); broad absorption from 3 300 to 2 000 with a maximum at 2 600 (w) (OH); 1 525 (s), 1 345 (s), and 855 (w) (NO_2) cm^{-1}; carbonyl absorption absent.

Anal. Calcd. for $C_{10}H_9N_3O_3S$: C, 47.81; H, 3.61; N, 16.72; S, 12.76. Found: C, 47.40; H, 3.60; N, 16.89; S, 13.09.

Method b

Hydrazine hydrate (2.1 g) was added to a solution of ethyl (*o*-nitrophenylthio)acetoacetate (4.0 g) in acetonitrile (25 ml), and the resulting deep-red solution was stirred for 2 h. The crystalline yellow precipitate (2.7 g), m.p. 163–165°, which formed was the hydrazine of (*o*-nitrophenylthio)acetic acid (lit. (10) m.p. 164°). The infrared spectrum was identical with that of an authentic sample.

Anal. Calcd. for $C_8H_9N_3O_3S$: C, 42.28; H, 3.99; N, 18.50. Found: C, 42.59; H, 3.76; N, 18.25.

4-(o-Nitrophenylthio)-1,3-diphenyl-2-pyrazolin-5-one (IIc)

Using essentially the conditions described for the preparation of II*b* (method *a*), we obtained the title compound (8.9 g), initially as a brown oil which quickly solidified, from *o*-nitrobenzenesulfenyl chloride (4.6 g) and 1,3-diphenyl-2-pyrazolin-5-one (5.8 g). Crystallization from anhydrous benzene gave a yellow solid, m.p. 182–183° (decomp.) after preliminary softening around 110°. Infrared spectrum: broad absorption from 2 100 to 3 200 with maxima at 3 080 (w) and 2 260 (w) (OH); 1 525 (s), 1 340 (m), and 860 (w) (NO_2) cm^{-1}; carbonyl absorption absent.

Anal. Calcd. for $C_{21}H_{15}N_3O_3S$: C, 64.76; H, 3.88; N, 10.79; S, 8.23. Found: C, 64.46; H, 3.84; N, 10.64; S, 8.27.

ACKNOWLEDGMENTS

The financial support of the National Research Council of Canada is gratefully acknowledged. The authors also thank H. W. Peel, M.Sc., for his assistance in this project.

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Received April 13, 1966.
College of Pharmacy,
University of Saskatchewan,
Saskatoon, Saskatchewan.

ON THE FORMATION OF A PEROXY PHTHALAZINE COMPOUND BY THE AUTOXIDATION OF 1-METHYL-1,2-DIHYDROPHTHALAZINE

Arthur Hirsch and Demetrius G. Orphanos

It was recently shown (1) that autoxidation of 1-methyl-1,2-dihydrophthalazine (I), prepared by the reaction of phthalazine with methyllithium, yields a mixture of 1-methylphthalazine (III) and an organic peroxide. The isolation of III has been successful. However, the peroxy compound, although it was the main reaction product, could not be obtained in a pure state. Formation of an organic peroxide in the phthalazine series, as far as we are aware, has not been reported previously.

However, it has now been possible, by applying the chromatographic technique of Milas *et al.* (2), to isolate such a substance and to determine its structure.

The elemental analysis, molecular weight and active oxygen determinations, and infrared and nuclear magnetic resonance spectra of this compound were compatible with a structure such as II. Additional support for II was obtained by the fact that the organic peroxide, on reduction with Na_2SO_3, was quantitatively converted into the known 1-methylphthalazine (III) (1). The conversion of II into III could proceed by a mechanism involving the unstable intermediate IV (Reaction Scheme 1).