

REACTION OF THIOSEMICARBAZIDE WITH ACETYLENIC KETONES AND ESTERS

AHMED SAID AHMED YOUSSEF

Chemistry Department, Faculty of Science, Ain Shams University,
Abbassia, Cairo, EGYPT

ABSTRACT

Piperidine - catalysed addition of the thiosemicarbazide (I) to 1-aryl-3-phenylprop-2-yn-1-ones (IIa-c) and methyl 3-arylprop-2-ynoates (II d & e) in ethanol gave a mixture of the monoadducts (IIIa-d) and their cyclised 1,3,4-thiadiazole derivatives (IVa & b). The structural assignments of the products were based on, spectroscopic and analytical data.

INTRODUCTION

Several studies¹⁻⁵ have been reported for the reaction of nucleophilic sulphur compounds with acetylenic ketones and esters. Although the reaction of thiosemicarbazide with acetylenic esters has been described⁶, the reaction with acetylenic ketones is still vague. The present investigation describes the nucleophilic addition of thiosemicarbazide (I) to 1-aryl-3-phenylprop-2-yn-1-ones (IIa-c) and methyl 3-arylprop-2-ynoates (II d & e).

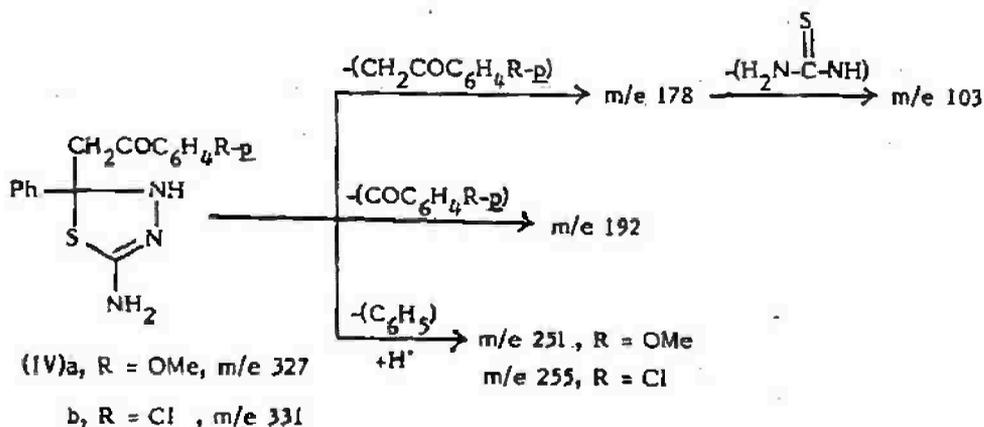
1-(p-Methoxyphenyl)-3-phenylprop-2-yn-1-one (IIb) reacted with thiosemicarbazide (I) using catalytic amount of piperidine in ethanol to give a mixture of 3-(S-thiocarbamoylhydrazono)-1-(p-methoxyphenyl)-3-phenylprop-2-en-1-one (IIIb) and 2-amino-5-(p-methoxybenzoyl)methyl-5-phenyl-4,5-dihydro-1,3,4-thiadiazole (IVa).

The reaction seems to proceed through attack of sulphur atom to the triple bond leading ultimately to the products (III) and (IV). In a previous report⁶, thiosemicarbazide derivative reacted with dimethyl acetylenedicarboxylate to give thiazinone derivative via sulphur attack.

The structure of (III) was established by spectroscopic evidence (cf. Experimental). Thus, the infrared spectra showed absorption bands corresponding to $\nu_{\text{C=O}}$ and ν_{NH} . The mass spectrum of (IIIb) supported the molecular formula as it showed the respective molecular ion beside some of the abundant peaks. A further support was gained from $^1\text{H NMR}$ spectra which showed signals attributable to OMe, NH, vinyl proton and aromatic protons. An alternative structure (V) rises from the attack by nitrogen atom was excluded on the basis of the absence of any absorption correspond to methylene protons in $^1\text{H NMR}$ spectra of (III). However, (III) in the absence of conclusive evidence may tentatively be assigned the Z-configuration on the basis of the rule of trans nucleophilic addition⁷.

Spectroscopic evidence supported the structure of the 1,3,4-thiadiazole derivative (IVa). Thus, its infrared spectrum revealed the presence of bands corresponding to $\nu_{\text{C=O}}$ and ν_{NH} . The low absorption frequency of the carbonyl group may be attributed to the chelation with NH in the ring through hydrogen bonding. The $^1\text{H NMR}$ spectrum (cf. Experimental) showed a two doublets (2H) representing an AB system ($J_{\text{AB}} = 18\text{Hz}$) due to CH_2CO

protons. The fact that the methylene group behaves as an AB system can be attributed to its existence adjacent to an asymmetric centre⁸. The mass spectrum of (IVa) was particularly valuable in assigning its structure as it showed a molecular ion peak at m/e 327 corresponding to $C_{17}H_{17}N_3O_2S$. Conventional simple fragmentation such as loss of $-COC_6H_4OMe-p$ and $-CH_2CO-C_6H_4OMe-p$ confirm the gross structural feature and significant peaks occurred at m/e 192 and 178, respectively (cf. Scheme 1).



However, the treatment of 1,3-diphenylprop-2-yn-1-one (IIa) with thiosemicarbazide (I) gave only the open chain adduct (IIIa). The structure of (IIIa) was established from analytical and spectral data (cf. Experimental).

On the other hand, similar treatment of 1-(p-chloro-phenyl)-3-phenylprop-2-yn-1-one (IIc) with (I) under the same conditions gave

the 1,3,4- thiadiazole derivative (IVb) as the only product. Adequate evidence for its structure was forthcoming from analytical and spectral data (cf. Experimental).

The reaction of methyl 3-arylprop-2-ynoates (IIId&e) with thiosemicarbazide (I) using catalytic amount of piperidine in ethanol afforded only the open chain adducts methyl 3-(S-thiocarbamoylhydrazono)-3-arylacrylates (IIIc&d) as the sole products.

The structure of (IIIc&d) was substantiated from analytical and spectral data (cf. Experimental). Thus, the infrared spectra showed absorption bands characteristic of $\nu_{\text{C=O}}$ (ester) and ν_{NH} . The $^1\text{H NMR}$ spectrum of (IIIc) and the assignment of signals, are reported in the experimental.

EXPERIMENTAL

All melting points were uncorrected. Infrared spectra were recorded on a Unicam SP 1200 spectrophotometer (KBr discs). $^1\text{H NMR}$ spectra were measured on a Bruker, 250 MHz instrument using $\text{DMSO}-d_6$ as a solvent and TMS as an internal reference. The mass spectra were determined on NERMAG R 10.10c mass spectrometer using direct introduction chemical ion technique in (NH_3) .

General Procedure for the Addition of Thiosemicarbazide (I) to 1-Aryl-3-phenylprop-2-yn-1-ones (IIa-c) and methyl 3-aryl-prop-2-ynoates (II&e).

To a solution of (IIa-e) 0.005 mole) in ethanol (20 ml) was added thiosemicarbazide (I) (0.005 mole) followed by 4 drops of piperidine. The mixture was left at room temperature for 72 hrs. The precipitated solid was then filtered off and recrystallised from a proper solvent to give the title compounds (III). Concentration of the mother liquor gave the title compounds (IV).

3-(S-Thiocarbamoylhydrazono)-1,3-diphenylprop-2-en-1-one (IIIa), (55% yield), buff crystals, m.p. 145 - 146°C (ethanol).

I.R.: 1630 (ν C=O), 3150, 3240, 3350, and 3420 cm^{-1} (ν NH).

$\text{C}_{16}\text{H}_{15}\text{N}_3\text{OS}$ requires: C, 64.64; H, 5.05; N, 14.14

Found : C, 63.92; H, 5.00; N, 13.88%

3-(S-thiocarbamoylhydrazono)-1-(p-methoxyphenyl)-3-phenylprop-2-en-1-one (IIIb), (20% yield), buff crystals, m.p. 163 - 165°C (ethanol).

I.R.: 1630 (ν C=O), 3150, 3240 and 3340 cm^{-1} (ν NH).

$^1\text{H NMR}$ (DMSO - d_6): δ 3.37 (s, 3, OCH_3), 3.75 (br., 2, C-NH₂, exchangeable with D_2O), 4.50 (br., 2, =N.NH₂, exchangeable with D_2O) and 6.8 - 8.6 (m, 10, ArH & =CH).

MS:m/e 327 (M^+ , 17%), 251 ($\text{M}-76$, 12), 192 ($\text{M}^+-\text{COC}_6\text{H}_4\text{OMe}$, 2), 135 ($\text{COC}_6\text{H}_4\text{OMe-p}$, 44), 131 (36), 116 (48), 107 ($\text{C}_6\text{H}_4\text{OMe-p}$, 3).

$\text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_2\text{S}$ requires: C, 62.38; H, 5.19; N, 12.84

Found : C, 61.77; H, 4.97; N, 12.53%

Methyl 3-(S-thiocarbamoylhydrazone)-3-phenylacrylate (IIIc), (58% yield), pale yellow crystals, m.p. 158 - 160°C (ethanol).

I.R.: 1725 (ν C=O ester), 3240, 3380 and 3460 cm^{-1} (ν NH).

^1H NMR (DMSO - d_6): δ 3.72 (s, 3, OCH₃), 3.80 (br., 2, =C-NH₂, exchangeable with D₂O), 4.55 (br., 2, =N.NH₂, exchangeable with D₂O), 6.4 - 8.7 (m, 6, ArH & =CH).

$\text{C}_{11}\text{H}_{13}\text{N}_3\text{O}_2\text{S}$ requires: C, 52.58; H, 5.17; N, 16.73

Found : C, 51.89; H, 5.11; N, 16.05%

Methyl 3-(S-thiocarbamoylhydrazone)-3-(p-chlorophenyl)acrylate (III'd), (60% yield), colourless crystals, m.p. 153 - 155°C (ethanol).

I.R.: 1725 (ν C=O ester), 3140, 3230 and 3380 cm^{-1} (ν NH).

$\text{C}_{11}\text{H}_{12}\text{ClN}_3\text{O}_2\text{S}$ requires: C, 46.23; H, 4.20; N, 14.71

Found : C, 45.77; H, 4.13; N, 14.20%

2-Amino-5-(p-methoxybenzoyl)methyl-5-phenyl-4,5-dihydro-1,3,4-thiadiazole (IVa), (40% yield), pale yellow crystals, m.p. 147-148°C (benzene).

I.R.: 1640 (ν C=O), 3150, 3230 and 3330 cm^{-1} (ν NH).

^1H NMR (DMSO - d_6): δ 3.40 (s, 3, OCH₃), 3.54 and 3.82 (dd, 2, -CH₂- \rightarrow J = 18 Hz), 6.8-8.5 (m, 13, ArH, NH & NH₂).

MS: m/e 327 (M^+ , 21%), 251 ($\text{M}-76$, 14), ($\text{M}^+ - \text{COC}_6\text{H}_4\text{OMe-p}$, 13), 178 ($\text{M}^+ - \text{CH}_2\text{COC}_6\text{H}_4\text{OMe-p}$, 100).

$\text{C}_{17}\text{H}_{17}\text{N}_3\text{O}_2\text{S}$ requires: C, 62.38; H, 5.19; N, 12.84

Found : C, 62.11; H, 5.03; N, 12.71%

2-Amino-5-(p-chlorobenzoyl) methyl-5-phenyl-4,5-dihydro-1,3,4-thiadiazole
(IVb), (50% yield), pale yellow crystals, m.p. 155 - 157°C (benzene).

I.R.: 1640 (ν C=O), 3260, 3340 and 3460 cm^{-1} (ν NH).

^1H NMR (DMSO - d_6): δ 3.57 and 3.79 (dd, 2, $-\text{CH}_2-$, $J = 18$ Hz),
6.9 - 8.7 (m, 12, ArH, NH&NH $_2$).

MS: m/e 333/331 (M^+ , 6/19%), 257/255 (M^+-76 , 4/13), 192 (M^+ -
 $\text{COC}_6\text{H}_4\text{Cl-p}$, 3), 141/139 ($\text{COC}_6\text{H}_4\text{Cl-p}$, 8/28), 113/111 ($\text{C}_6\text{H}_4\text{Cl-p}$,
2/6), 103 (5).

$\text{C}_{16}\text{H}_{14}\text{ClN}_3\text{OS}$ requires: C, 57.91; H, 4.22; N, 12.66

Found : C, 57.20; H, 4.17; N, 12.42%

REFERENCES

- (1) F.G. Baddar, F.H. Al-Hajjar and N.R. El-Rayyes, J. Heterocyclic Chem. **13**, 691 (1976).
- (2) G. Dallas, J.W. Lown and J.C.N. Ma, J. Chem. Soc. (C), 2510 (1968).
- (3) M.T. Omar and M.N. Basyouni, Bull. Chem. Soc. Japan **47**, 2325 (1974).
- (4) M.N. Basyouni and M.T. Omar, Aust. J. Chem. **27**, 1585 (1974).
- (5) M.N. Basyouni, M.T. Omar, A.A. El-Khamry and E.A. Ghali Egypt. J. Chem. **23** (4), 237 (1980).
- (6) J.W. Lown and J.C.N. Ma, Canad. J. Chem. **45**, 953 (1967).
- (7) W.E. Truce, "Nucleophilic Reactions of Thiols with Acetylenes and Chloroethylenes", in N. Kharasch, ed, "Organic Sulphur Compounds", Vol. 1, Pergamon Press, Ltd, London (1961).
- (8) D.H. Williams and L. Flening, "Spectroscopic Methods in Organic Chemistry" Third edition, page 93 (1980).

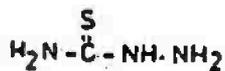
تفاعل الثيوسيمى كرازيد مع الكيتونات
والاسترات الامثليينية

أحمد سعيد أحمد يوسف

قسم الكيمياء - كلية العلوم - جامعة عين شمس - العباسية - القاهرة

يتفاعل الثيوسيمى كرازيد (I) مع ١-أريل-٢-فينيل بروبا-٢-أين-
١-أزوات (IIa-o) وميثيل ٣-أريل-٢-بروميونات (II d&e) في وجود البيريدن
كم.ل.مساعد في الكحول الايثيلى ليعطى مخلوط من النواتج الاحادية المفتوحة
(IIIa-d) مشتقاتها اربعة - ثياديازولات الحلقية (IVa & b) وقد تم التعرف
على تراكيب النواتج باستخدام اطياف الرنين النووي المغناطيسى والكتلة والاشعة
تحت الحمراء بالاضافة الى التحاليل الدقيقة .

=====



(I)



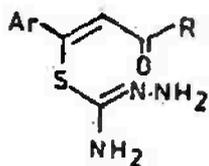
(II) a, Ar = R = Ph

b, Ar = Ph, R = C₆H₄ OMe-p

c, Ar = Ph, R = C₆H₄ Cl-p

d, Ar = Ph, R = OMe

e, Ar = C₆H₄ Cl-p, R = OMe

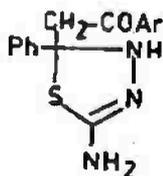


(III) a, Ar = R = Ph.

b, Ar = Ph, R = C₆H₄ OMe p-

c, Ar = Ph, R = OMe

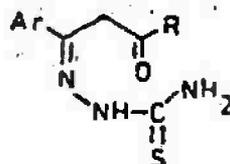
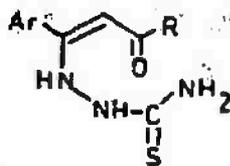
d, Ar = C₆H₄ Cl p-, R = OMe



(IV) a, Ar = C₆H₄ OMe p-

b, Ar = C₆H₄ Cl p-

Scheme 2



(V)