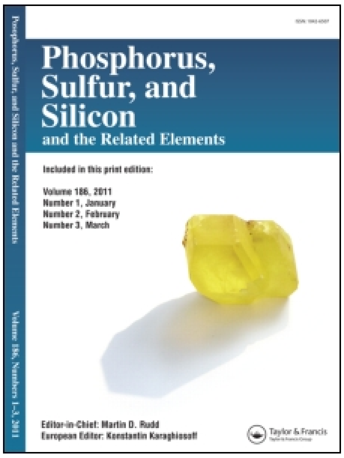

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SYNTHESIS AND C-S BOND FISSION OF 1,3-DIARYL-3-THIOGLYCOLIC ACID-1-PROPANONES

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SYNTHESIS AND C-S BOND FISSION OF 1,3-DIARYL-3-THIOGLYCOLIC ACID-1-PROPANONES

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1,3-Diaryl-3-thioglycolic acid-1-propanones 3a-k have been synthesized by the reaction of either erythro-2,3-dibromo-1,3-diaryl-1-propanones 1a-k or their corresponding trans-chalcones $2_{a\text{-}k}$ with *disodio-thioglycolate* in absolute ethanol. The structure of the products was proven by UV, IR, NMR spectra and elemental analysis. A reaction mechanism leading to the products, and the carbon-sulfur bond fission in alkaline medium were discussed.

Keywords: Chalcone; thioglycolic acid; NMR; IR; C-S bond fission

INTRODUCTION

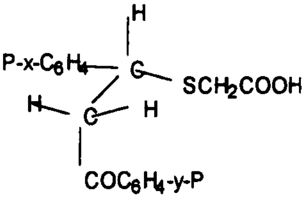
A large number of reports are available on the inhibitory effect of chalcone derivatives on enzymes and their bactereostatic activity[1]. As already sulfur containing compounds are known for their diverse pharmacologic action, the compounds were also screened for antibacterial activity[2]. Thiol nucleophilic reagents are also known to show chemical reactivity towards chalcones, chalcon epoxides, chalcone dibromides and their corresponding propynones. Thus, *trans*-1,3-diaryl-2-propenones $2_{a\text{-}k}$ and their dibromo derivatives $1_{a\text{-}k}$ were reacted with thiosemicarbazide in absolute ethanol and catalytic amount of glacial acetic acid afforded 3,5-diaryl-2-pyrazoline-1-thiocarboxamides[3]. The same α,β-unsaturated ketones and their dibormo derivatives were found to react with thiophenoxide ion in either protic solvent, absolute ethanol, or aprotic one, DMF, to give 1,3-diaryl-3-phenylthio-1-propanones[4]. The reaction of chalcone dibromides[5] and chalcon epoxides[6] with thiourea in presence of potassium hydroxide produced the corresponding 4,6-diaryl-2-imino-1,3-thiazine derivatives. Thioglycolic acid and some of their derivatives showed also a great activity towards the previously reported compounds. When thioglycolinilide was added to 1,3-diphenyl propynone in the presence of lithium hydroxide or triethylamine, the corresponding thioglycolinilide adduct was obtained[7]. The reaction of the same anilide with 3-bromo-1-phenyl propynone resulted in the formation of dithioglycolinilide product[7]. 1,3-Diphenyl propynone was reacted with thioglycolamide in acetonitrile to afford a mixture of *(E)* and *(Z)*-isomers of the corresponding thioglycolamide adduct[8]. Treating the same amide with 3-bromo-1-phenyl propynone in methanol in the presence of triethylamine gave the dithioglycolamide product[8]. Chalcone epoxides were reacted with thioglycolic acid to give the corresponding 1,4-oxathian-2-one derivatives[6]. With chalcones, thioglycolic acid in aprotic solvent, benzene, afforded the corresponding dihydro-3-(2H)-thiophenones[2].

In the present work, it is our interest to carry further investigation of the reaction of chalcones and their diboromo derivatives with thioglycolic acid or *its disodium salt* to find out not only the role of solvent in the reaction pathway but also to show how these compounds would behave under identical experimental conditions as in the case of their reaction with *sodium thiophenoxide*. The work also aimed at studying the effect of sodium hydroxide on the thioglycolic acid reaction product and suggesting a possible mechanism for C-S bond formation and fission.

RESULTS AND DISCUSSION

The reaction of *erythro*-1,3-diaryl-1-propanones $1_{a\text{-}k}$ with *disodiothioglycolate* in 1:3 molar ratio in absolute ethanol produced 1,3-diaryl-3-thioglycolic acid-1-propanones $3_{a\text{-}k}$ as a sole product. The yields were in the range of 82–95% and all the products were crystallized from aqueous ethanol. The structures of the products were identified on the basis of spectral data and elemental analysis for carbon, hydrogen, nitrogen and sulfur which were in excellent agreement with the requirements values. The UV spectra in ethanol exhibited λ max. at 234.3–268.2 nm; $\in$ = 18400–24500. The IR spectra (KBr pellets) indicated the presence of a sharp band at 719–727 cm^{-1} (C-S) and another two sharp bands at 1690–1710 and 1670–1680 cm^{-1} (C=O and COOH, respectively). Another characteristic band was observed at 3419–3427 cm^{-1} (-OH). The NMR spectra ($CDCl_3$)

of all products showed a singlet at δ 2.70–2.95 ppm for the S-CH_2 protons, a doublet at δ 3.33–3.66 ppm (2H, C_2) and a triplet at δ 4.62–4.83 ppm (1H, C_3). The aromatic protons appeared as a multiplet at δ 7.03–8.13 ppm. The para-methyl and methoxy protons for compounds $3_{b,c,g,h}$ appeared as a singlet at δ 2.20–3.75 ppm. The hydroxyl proton appeared as a singlet at δ 10.45–11.23 ppm.



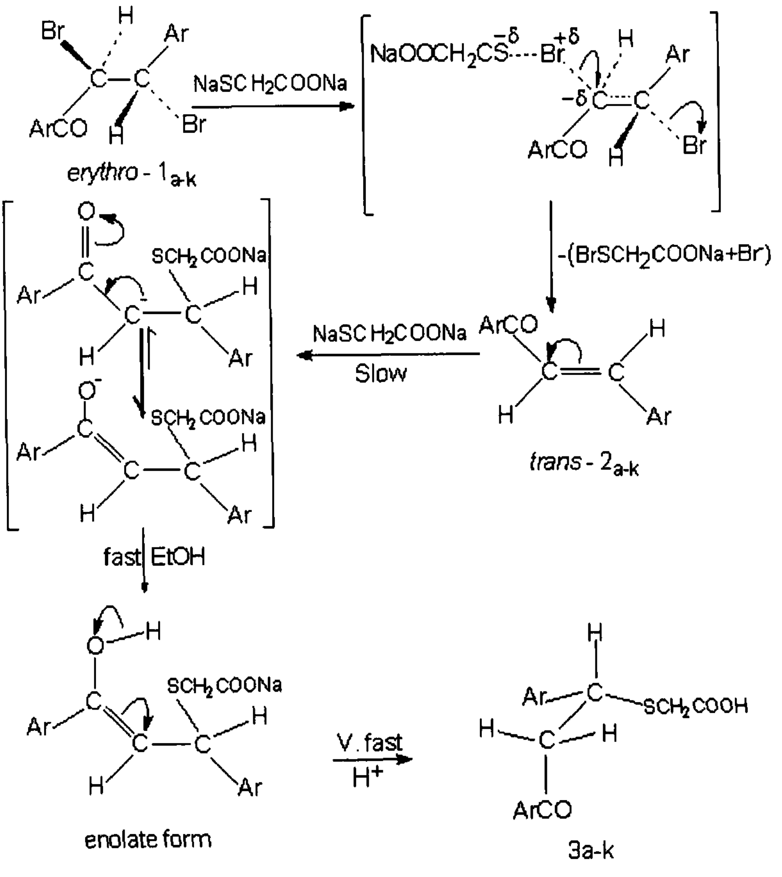
$3_{a\text{-}k}$

Cpd. No.3	Y	X	MP (°C)
a	H	H	135
b	H	OMe	117
c	H	Me	125
d	H	Cl	140
e	H	Br	142
f	H	NO_2	150
g	OMe	H	90
h	Me	H	87
i	Cl	H	105
j	Br	H	109
k	NO_2	H	oil

It is noteworthy, to mention that all of these adducts $3_{a\text{-}k}$ were synthesized by the reaction of 1,3-diaryl-2-propenones $2_{a\text{-}k}$ with two molar equivalents of *disodio-thioglycolate* under similar reaction conditions. The reproducibility of the reaction of thioglycolic acid with 1,3-diaryl-2-propenones $2_{a,b,d,i}$ in 1:1 molar ratio in dry benzene gave the corresponding dihydro-3-(2H)-thiophenones $4_{a,b,d,i}$ as reported before[2].

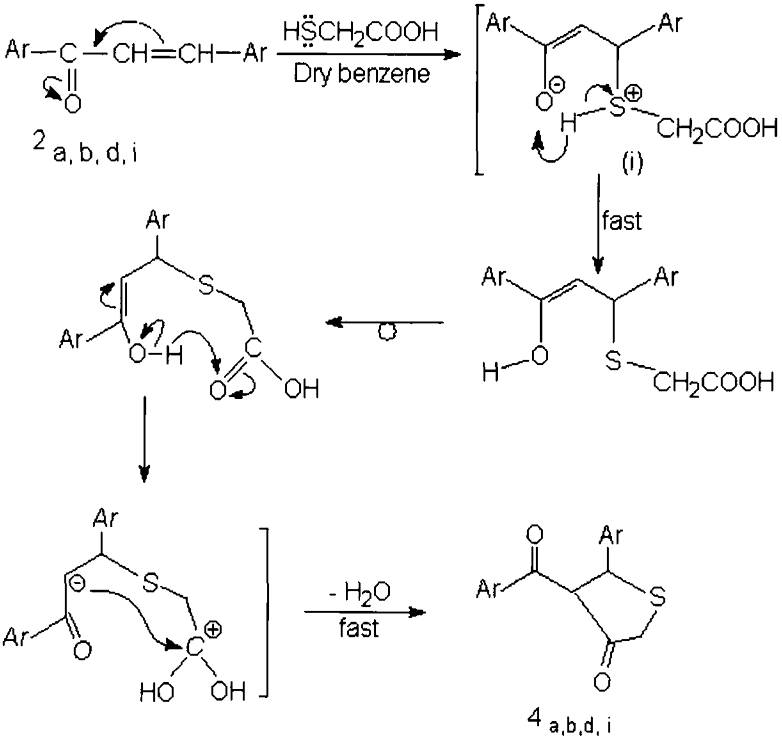
MECHANISM OF THE REACTIONS

On the contrary to the reaction of $1_{a\text{-}k}$ with thiosemicarbazide[3] that depend on the electronic nature of substituents (X) and (Y) of phenyl and benzoyl groups, the reaction of $1_{a\text{-}k}$ with *disodio-thioglycolate* in ethanol is independent of this factor. The latter reaction is proposed to firstly proceed by reductive debromination to give α,β-unsaturated ketones $2_{a\text{-}k}$ as an intermediate[9]. *In the literature many sulfur nucleophiles are cited to undergo similar behavior*[9–13]. This intermediate is then attacked by another molecule of *disodio-thioglycolate* to afford its adduct $3_{a\text{-}k}$, scheme 1.



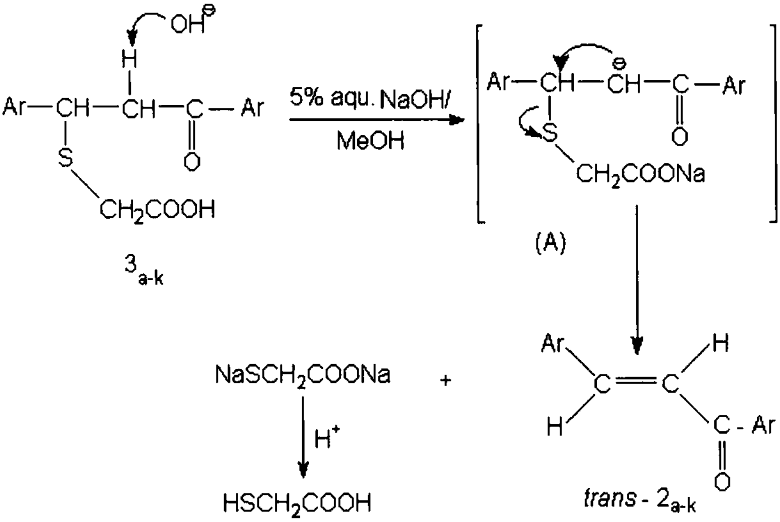
SCHEME 1

The addition reaction of the nucleophile to α,β-unsaturated ketones was found to be reversible[14]. However, during the addition of thioglycolic acid anion to $2_{a\text{-}k}$ the equilibrium shifts largely to the product formation. Since the product does not decompose appreciably under the reaction conditions and its formation is almost quantitative. From this study, it has become evident that the addition of thioglycolic acid to α,β unsaturated ketones $2_{a\text{-}k}$ is dependent on the nature of solvent. In absolute ethanol as protic solvent it gave the corresponding open adducts $3_{a\text{-}k}$ due to the protonation of the enolate intermediate (c.f. Scheme 1). On the other hand, in dry benzene as *aprotic* solvent it produced the cyclic product $4_{a,b,d,i}$ as mentioned before. This result can be attributed to a desolvation effect of the developing carbanion which could be a contributing factor to the enhancement of the chance of cyclization, scheme 2.



SCHEME 2

The alkaline hydrolysis of compounds 3_{a-k} with a few drops of 5% sodium hydroxide in methanol gave 1,3-diaryl-2-propenones 2_{a-k} as the sole product. In the alkaline hydrolysis the C-S bond fission could be rationalized by the attack of the OH ion on the α-acidic hydrogen giving α-carbanion ketone (A) as an intermediate which is followed by C-S bond fission forming the vinylic ketones 2_{a-k} while the remaining moiety producing the *disodio-thioglycolate which upon treatment with dilute hydrochloric acid gave the free acid*, scheme 3.



SCHEME 3

EXPERIMENTAL

Melting points are uncorrected, UV spectra were recorded on Perkin-Elmer Lambada 4B spectrophotometer, IR spectra (KBr pellets) were measured on a perkin-Elmer 1430 ratio recording infrared and ^{1}HNMR spectra in $CDCl_3$ were recorded on a variant EM 90 MHz spectrometer. Elemental analysis of the reaction product were carried out in the Faculty of Science, Cairo University, Egypt.

Starting Materials

erythro-2,3-dibrom-1,3-diaryl-1-propanones $1_{a\text{-}k}$ were prepared by bromination of the corresponding chalcones $2_{a\text{-}k}$ in chloroform following the procedure reported previously[15].

Disodio-thioglycolate

Thioglycolic acid (0.003 mole) was added to a solution of sodium ethoxide (0.002 mole) in absolute ethanol. The disodio-thioglycolate was used immediately after its preparation.

General procedure for the synthesis of compounds $3_{a\text{-}k}$

A solution of the appropriate dibromoketone $1_{a\text{-}k}$ (0.001 mole) in 10 ml absolute ethanol was stirred at room temperature for 4 hr with *disodio-thioglycolate* (0.003 mole). The reaction-mixture was poured onto water and then acidified with dilute hydrochloric acid. The separated solid was filtered, washed thoroughly with water, dried and recrystallized from aqueous ethanol.

Preparation of compounds $4_{a,b,d,i}$

These compounds were prepared by the addition of thioglycolic acid to the desired chalcones $2_{a,b,d,i}$ in dry benzene *using a Dean-stark condenser* as reported before[2].

Action of 5% sodium hydroxide solution

A Few drops of 5% sodium hydroxide solution were added dropwise to a solution of 1,3-diaryl-3-thioglycolic acid-1-prapenones $3_{a\text{-}k}$ in methanol until the mixture alkaline to litmus. The reaction-mixture was refluxed for 1 hr then left to cool at room temperature and the solvent evaporated. The separated solid was washed successively with water and recrystallized from ethanol producing the corresponding 1,3-diaryl-2-propenones $2_{a\text{-}k}$ as the only product. On acidifying the filtrate with dilute hydrochloric acid, a characteristic odor of thioglycolic acid was detected.

References

1. M. Graff and G.J. Martin, Am. J. Digestive diseases **19**, 333 (1952).
2. A.R. Bhat and D. Singh, Indian J. Pharm. Sci., **50** **(3)**, 169 (1988).
3. M.E. Elba, A.I. Darwish and N.M. Mamada, J. Indian Chem. Soc., **74**, 202 (1997).
4. S.M. Sharaf, S.K. El-Sadany, E.A. Hamed and M.E. Elba, Alex. J. Pharm. Sci., **5** **(2)**, 187 (1991).
5. R. Harode and T.C. Sharma, Indian J. Chem., **27 B** **(12)**, 1144 (1988).
6. A.A. Hamed, A. Essawy and M.A. Salem, Indian J. Chem., **16** **(B)**, 693 (1978).
7. R.V. Karnaukhova, A.S. Nakhmanovich, V.N. Elokhina and I.D. Kalikhman, Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk, **4**, 74 (1989).
8. A.S. Nakhmanovich, T.N. Komarova, R.V. Karnaukhova, A.V. Afonin, V.K. Voronov and Yu. A. Mansurov, Izv. Akad, Nauk SSSR, Ser. Khim., **8**, 1805 (1987).
9. M.E. Elba, Alex. J. Pharm. Sci, **7** **(2)**, 142 (1993).
10. K. Fuknaga and H. Yamagushi, Synthesis, 879 (1981).
11. A.G. Doshi and B.J. Ghiya, J. Indian Chem. Soc., 404 (1986).
12. N.J. Reddy and T.C. Sharma, Ind. J. Chem., **17B**, 645 (1979).
13. D. Landini, S. Quici and F. Rolla, synthesis, 397 (1975).
14. F.M. Menger and J.H. Smith, J. Am. Chem. Soc., **91**, 4211 (1969).
15. S.K. El-Sadany, S.M. Sharaf, M.E. Elba and A.A. Youssef, Egypt. J. Chem., **34, No 6**, pp. 467 (1991).