STUDIES ON ACETYLENIC COMPOUNDS

A THESIS

SUBMITTED BY

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B. Sc., M. Sc.

FOR THE DEGREE OF

Ph. D.

FACULTY OF SCIENCE
AIN SHAMS UNIVERSITY

1979

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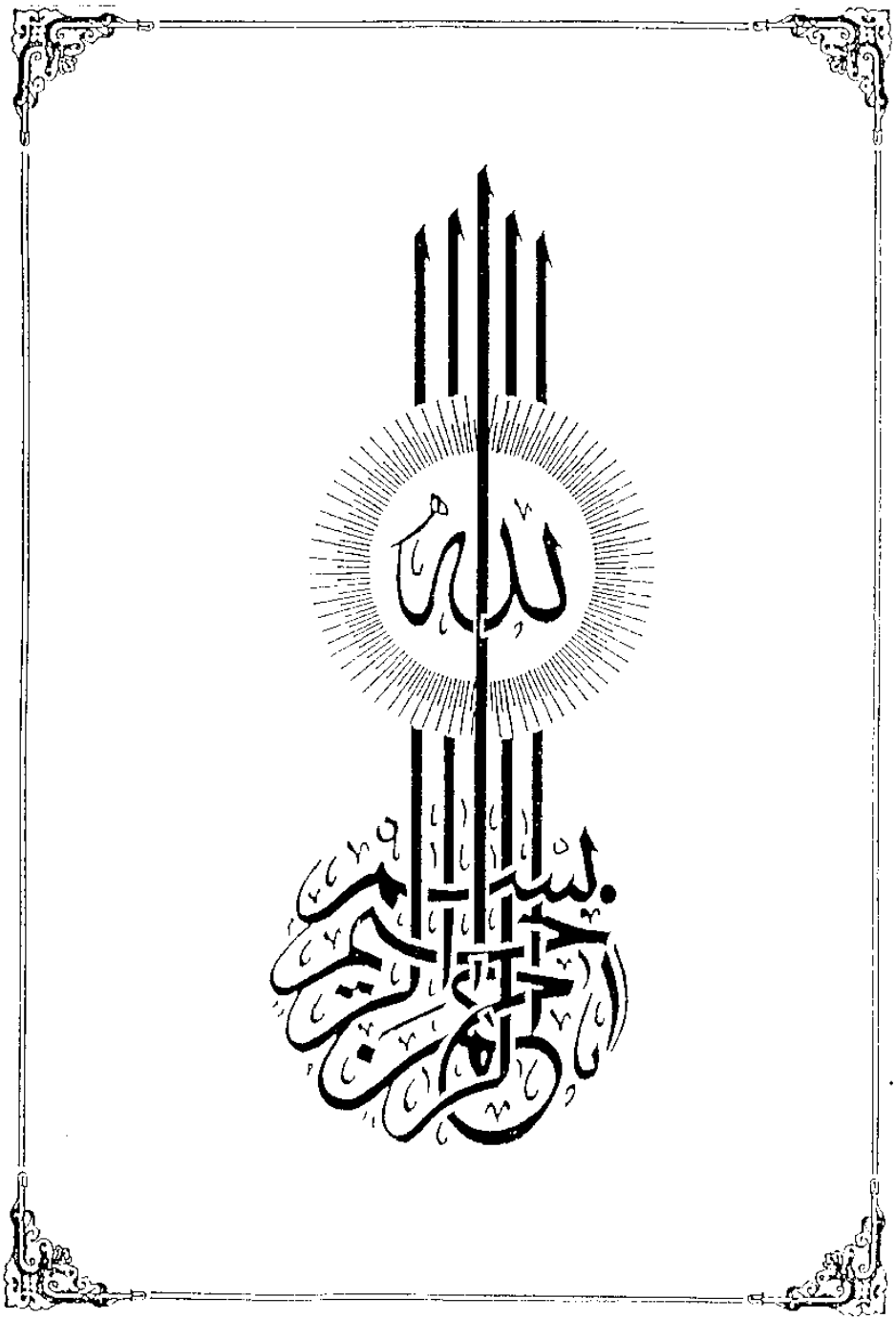

ACKNOWLEDGEMENT

The author wishes to express his gratitude to Drs. M.N. Basyouni and M.T. Omar, Assistant Professors of Organic Chemistry, Faculty of Science, Ain Shams University for suggesting the problem, supervision, advice, criticism and invaluable support.

C O T E N T S

Synopsis

Piperidine-catalysed addition of methyl thioglycollate to benzoyl- and p-chlorobenzoyl-phenylacetylenes (XXXVIa & c) and methyl phenylpropiolate (XXXIIIa) in ethanol gave (Z)-1-aryl-3-(1'-carbomethoxymethylthio)-3-phenyl-2-propen-1-ones (LVIa & c) and methyl (Z)-3-(1'-carbomethoxymethylthio) cinnamate (LIX), respectively. However, p-anisoylphenylacetylene (XXXVIb) gave a mixture of (Z)- (LVIb) and its (E)-isomer (LVII) in the ratio of 4:1. The (Z)-isomers were formed by the usual trans- nucleophilic addition, whereas the (E)- (LVII) was formed by a competing cis-addition and not by the post-isomerisation of the (Z)- (LVIb), since it was independently proved that (Z)- (LVIb) was configurationally stable under the experimental conditions used for the addition. Formation of the (E)-isomer in case of XXXVIb was interpreted in terms of the activating group effect. When dry benzene was used as a solvent in the above addition to XXXVIb the ratio of (Z)-to (E)- was completely reversed (1:4.5) and this was rationalised on the basis of the solvent effect.

S-benzylisothiourea hydrochloride reacted with aroylphenylacetylenes (XXXVIa,b) and methyl phenylpropiolate (XXXIIIa) in the presence of sodium acetate to give (Z)-1-aryl-3-benzylthio-2-propen-1-ones (IXa & b) and methyl (E)-3-benzylthiocinnamate (IXd), respectively. On the other hand, XXXVIc gave 2-benzylthio-4-p-chlorophenyl-6-phenylpyrimidine

LXI. Similarly, XXXIIIa gave with S-methylisothiourea sulphate, 2-methylthio-4(6)-oxo-6(4)-phenylpyrimidine (LXII), whereas XXXVIa gave (Z)-1,3-diphenyl-3-methylthio-2-propen-1-one (LXc).

Imidazolidine thione and XXXVIa gave a mixture of (Z,Z)-(LIa) and (E,Z)- (LIIa)-3,3'-thiodi(1,3-diphenyl-prop-2-ene-1-one), whereas XXXVIb & c gave only the corresponding (E,Z)-isomers. On the other hand, XXXIIIb & c gave 2,3-dihydro-6-p-methoxyphenylimidazo [2,1-b] -thiazine-4-one (LXVI) and 2,3-dihydro-6-imidazolidinethio-6-p-chlorophenylimidazo-[2,1-b] -thiazine-4-one (LXVII), respectively.

Thiourea and XXXIIIa-c gave the corresponding 6-aryl-2,3-dihydro-2-imino-1,3-thiazine-4-ones (LXVa-c).

Isothiocyanic acid and XXXVIa-c gave the corresponding 1-aryl-3-phenyl-3-isothiocyano-2-propen-1-ones (LXVIIIa-c), which failed to react with amines.

Ammonium dithiocarbamate reacted with p-chlorobenzoyl-phenylacetylene (XXXVIc) to give only the (Z,Z)-isomers (LIc), whereas ammonium phenyldithiocarbamate gave a mixture of LIc and (E,Z)-isomer LIIc. p-Anisoylphenylacetylene gave with the latter reagent only (Z,Z)-3,3'-thiodi(1-p-methoxyphenyl-3-phenylprop-2-ene-1-one) (LIb). Phenyl thiourea was isolated from the reactions involving ammonium phenyldithiocarbamate.

Piperidine-catalysed addition of toluene-3,4-dithiol

to XXXVIa gave 2-(phenylcarbonylmethyl)-5-methyl-2-phenyl-benzo-1,3-dithiole (LXXVIa). Similar addition of toluene-3,4-dithiol (Zn salt) in an acetic acid solution to the ketones XXXVIb & c and the esters XXXIIIa & c gave LXXVIb,c and 2-carbomethoxymethyl-5-methyl-2-arylbenzo-1,3-dithiole (LXXVIIa & b), respectively.

The above reactions are summarised in schemes 1 and 2. All the new compounds were analytically pure and their structures and/or configurational assignments were based on IR, UV and NMR spectroscopy.

Introduction

Since this thesis describes the nucleophilic additions of organic sulphur compounds to acetylenic esters and ketones, the following section includes the pertinent literature on such addition reactions to acetylenes. It was, however, found convenient to include, whenever necessary, additions of the same nucleophiles to ethylenic-double bond containing - compounds.

General Introduction :

The interaction of thiols with unsaturated hydrocarbons was first reported by Posner[1] who treated thiophenol and benzyl-thiol with a variety of olefins at room temperature in the presence of acetic and sulphuric acids. With simple olefins, conjugated and non-conjugated, addition of fragments of the thiol produced by scission of the S-H bond proceeded readily and, at an unsymmetrically substituted double bonds, in opposition[1] to Markownikoff's rule, e.g.

$$R^1{}_{R^2}C = CHR^3 + PhSH \xrightarrow{H^+} R^1{}_{R^2}CH-CH(SPh)R^3$$

From an investigation of the reaction between thiophenol or ethanethiol with propylene, isobutylene, trimethylethylene and isopropylethylene at 100-150°C, Ipatieff and others[2,3] found that although addition products "abnormal" with respect to Markownikoff's rule were formed in the absence of catalysts, yet the presence of sulphuric acid, contrary to Posner's findings, reversed the orientation of addition and led to "normal products". Contemporaneously Jones et al.[4] and Kharasch et al.[5] showed that traces of peroxides, either as present normally in unsaturated hydrocarbons or as an added ascaridole, strongly catalyse

the "abnormal" addition and that quinol effectively impedes the reaction. The fact that the "abnormal" addition of thiols to olefins is catalysed by peroxides, oxygen or sunlight and is inhibited by the addition of quinol or piperidine led Mayo and Walling[6] to propose a free-radical chain reaction mechanism for such an addition

$$RSH + O_2 \text{ (or peroxide)} \longrightarrow RS^{\cdot} + HO_2^{\cdot}$$

$$RS^{\cdot} + R'CH{=}CH_2 \longrightarrow R'\dot{C}HCH_2SR \xrightarrow{RSH} R'CH_2CH_2SR + RS^{\cdot}$$

The addition of thiol acids, best exemplified by thiolacetic acid, to isobutylene, isopropylethylene and trimethylethylene at various temperatures, were studied by Ipatieff and Friedmann[3]. They also found that the direction of addition, in this case, being contrary to Markownikoff's rule.

With α,β-unsaturated esters and ketones, the addition of thiols takes place by an ionic mechanism[7], since the addition is accelerated by the addition of basic catalysts. Among the basic catalysts used were sodium alkoxides[8,9], piperidine[10] and potassium carbonate[11]. In this case the sulphur atom becomes attached to the electron deficient β-carbon atom e.g.

$$RCH{=}\overset{\overset{O}{\parallel}}{CH{-}C}{-}OR^1 + R^2SH \longrightarrow RCH(SR^2)\,CH_2CO_2R^1$$

These additions are, therefore, contrary to Markownikoff's rule.

From the above results it was concluded[6] that a thiol, like a halogen acid, when added to an unsymmetrically substituted ethylenic bond, can yield either of two products.

$$R{-}CH{=}CH_2 + R^1SH \longrightarrow RCH_2CH_2SR^1 \quad \text{(abnormal* addition)}$$

$$R{-}CH{=}CH_2 + R^1SH \longrightarrow RCH(CH_3)SR^1 \quad \text{(normal** addition)}$$

The abnormal addition of thiols, i.e. the sulphur becomes attached to the carbon atom carrying the greater number of hydrogen atoms, has been observed in the case of addition to alkene hydrocarbons and is the one commonly observed especially when no catalysts (e.g. sulphuric acid) for the normal addition are employed. The abnormal addition, as has been mentioned previously, are catalysed by peroxides, oxygen or light.

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* Contrary to Markownikoff's rule.

** In accordance with Markownikoff's rule.

Table 1

Normal additions of thiols to alkenes

Alkene	Thiols	Addition product	Evidence of mechanism	Ref
$CH_3CH=CH_2$	C_2H_5SH (a)	i-$C_3H_7SC_2H_5$ (82%) n-$C_3H_7SC_2H_5$ (8 %)	sulphur as catalyst +: no reaction in absence of sulphur	(4)
1-Octene	C_2H_5SH (b)	$C_5H_{13}CHSC_2H_5$ (59%) CH_3	sulphur as catalyst +	(4)
$CH_3CH=CH_2$	C_6H_5SH (b)	i-$C_3H_7SC_6H_5$ (ca 35%)	sulphur as catalyst	(4)
$RCH=CH_2$	$C_{12}H_{25}SH$(b)	Mixture	sulphur as catalyst +	(4)
$(CH_3)_2C=CH_2$	t-C_4H_9SH(c)	$(t\text{-}C_4H_9)_2S$	Nickel, cobalt or iron sulphide as catalyst	(3)
$(CH_3)_2C=CH_2$	C_6H_5SH (a)	t-$C_4H_9SC_6H_5$ (70%)	75% sulphuric acid as solvent and catalyst +	(2)
$(CH_3)_2C=CHCH_3$	C_6H_5SH (a)	t-$C_5H_{11}SC_6H_5$ (60%)	20% sulphuric acid in acetic acid as solvent and catalyst +	(2)

(a) = reaction at room temperature.

(b) = reaction for 10 h in sealed vessel at 150°C in absence of solvent.

(c) = reaction under pressure at 175-200°C (Patent claim).

(+) = A different product obtained without this catalyst.