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Behaviour of α-carbethoxy radical generated from the ester of *N*-hydroxy-2-thiopyridone

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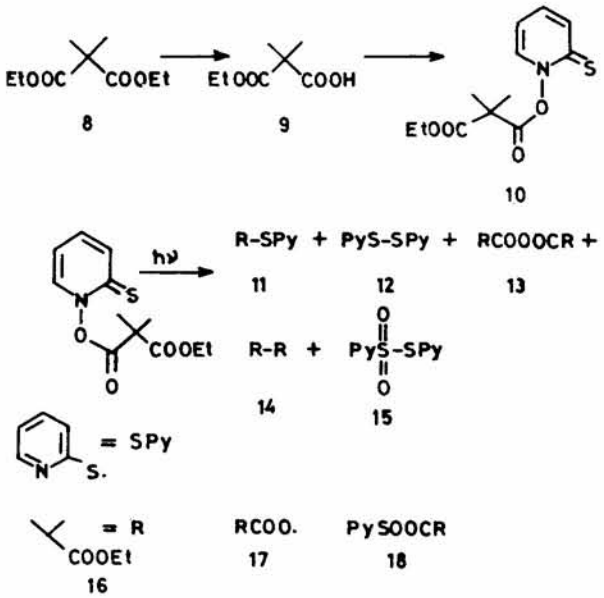
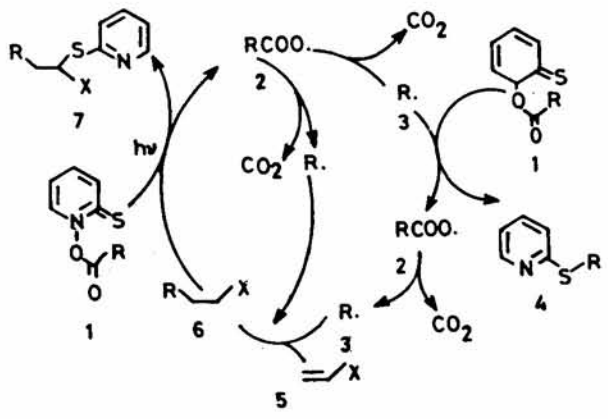
Studies on the behaviour of α-carbethoxy radical generated from the ester of *N*-hydroxy-2-thiopyridone is described.

The generation of free radical by Barton's thiohydroxamic acid method is now a well established phenomenon[1]. The entire process of radical generation and its capture by olefin can be schematically shown in Scheme I. Although there are several reports[2] on the generation and use of alkyl radicals by this method, no study has been done so far on the nature of radicals with α-carbethoxy group generated from the ester of *N*-hydroxy-2-thiopyridone (Barton ester). Herein we wish to present a preliminary report of our work in this area.

Diethyl dimethyl malonate **8** is prepared from diethyl malonate by the usual method. Partial hydrolysis of the diester **8** affords the corresponding monoester **9**[3]. The monoester **9** is transformed into Barton ester **10** by reaction with *N*-hydroxy-2-thiopyridone[1].

Photolysis of the ester **10** in benzene with 200W visible lamp at room temperature or below affords several products **11-15** in varying amounts. If the desired radical **16** is formed in the usual way, we should have got the thiopyridyl compound **11** as the major product along with minor amounts of dipyridyl disulphide **12** and **14**. But analysis of the products shows 14% of **11**, 37% of dipyridyl disulfide **12**, 19% of **14** along with minor amounts of the starting acid **9**, the anhydride **13** and an unstable compound. The unstable compound in its ^{1}H NMR spectrum shows the presence of both the aliphatic and the aromatic peaks of ethoxy and pyridyl groups respectively. On keeping, this compound slowly decomposes to the anhydride **13**, the acid **9**, dipyridyl disulfide **12** and dispyridyl disulfoxide **15**. This is exactly the similar behaviour shown by a non-decarboxylating aromatic radical of the type [PhCOO·][4]. Same explanation may be put forward in this case to justify the formation of the unexpected products.





Scheme I

In this case also the initially formed alkylcarbonyloxy radical **17** does not fully eliminate a CO_2 molecule to generate the substituted alkyl radical **16**. Only half of the radical **17** further transforms into **16** and

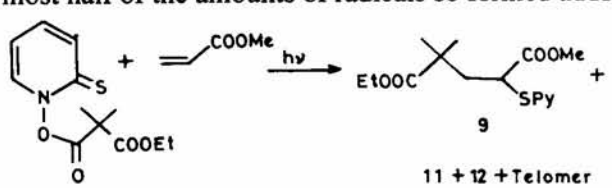
Table I—Effects of solvent, temperature and raction period on the photolysis of the ester **10**.

Solvent	Temp. °C	Reaction period (hr)	Product (%) R-SPy	PyS-SPy	R-R	Unstable Prod. (mg)
C_6H_6	r.t.	2.5	14	37	19	40
$CHCl_3$	r.t.	5	35	9.3	-	80
CH_2Cl_2	r.t.	4.5	37	17	9	70
THF	r.t.	5	15	Complex mixture		
CH_2Cl_2	40	3	55	7	-	27
$CHCl_3$	61	2.5	69	10	-	15
CH_3CN	81	1	66	8	-	25
C_6H_6	80	1	80	6	-	10
Toluene	110	0.5	44	15	-	34

the other half attacks the thiopyridyl radical generating the unstable product **18** which on decomposition gives the products **13**, **15** and the starting acid **9**. In an attempt to expedite the elimination of CO_2 from the sluggish non- decarboxylating radical **17**, different solvents are tried for photolysis at different temperatures. The results show the refluxing benzene as the solvent of choice as the yield of the desired product goes upto 80% in this case (Table I).

After generating the desired radical **16**, its behaviour towards electron deficient olefin has been studied to determine the nature of philicity. As expected the photolysis of the ester **10** at room temperature (r.t.) in the presence of methyl acrylate (5 equiv.) in different solvents affords low yields of the adduct **19**. When the photolysis is carried out in refluxing benzene the adduct **19** is obtained in 37% yield along with compound **11** in 48% and **12** in 6% yield. A small amount of telomeric mixture is also formed. When the amount of methyl acrylate is increased to 7 equivalents the yield of the adduct gets decreased to 25% and the yield of the telomeric mixture increases.

From the above observation it is evident that the radical **16** is not much nucleophilic in nature as compared to simple alkyl radical[5]. Because of this nature the radical does not prefer to add totally to the electron deficient olefin methyl acrylate. Instead almost half of the amounts of radicals so formed adds



to the counter radical. SPy and the other half adds to the olefin[6].

Experimental Section

General Solvents were dried according to standard procedures. ^1H NMR spectra were recorded on a Varian 360L instrument at 60 MHz and 300 MHz in RSIC, Shillong. IR spectral were recorded on a Perkin-Elmer 237B and mass spectra on a Finigan Mat INCOS 50 instrument.

Preparation of Barton ester 10. The acid **9** (240 mg, 1.5 mmoles) was treated with excess of $SOCl_2$ at 0°C and left for overnight at r.t. Excess $SOCl_2$ was removed under reduced pressure and the acid chloride so formed was treated with 190 mg (1.5 mmoles) of *N*-hydroxy-2-thiopyridone and 0.13 mL of pyridine in dry benzene (25 mL). When TLC indicated the completion of the reaction, the mixture was put for photolysis as such. Due to its unstable nature and sensitivity towards visible light, no satisfactory spectral analysis could be done on it.

Photolysis of 10. The ester obtained from the above reaction was subjected to photolysis under nitrogen using a 200W ordinary bulb either at r.t. or under reflux. When TLC indicated the disappearance of the starting ester, the solvent was distilled off and the less polar portion extracted with haxane. Purification of the product mixture by preparative TLC (1:15, EtOAc-hexane) afforded 14% of **11**, 37% of **12**, 19% of **14** and 6 mg of an unstable mixture. Spectral data for compound **11** are as follows: ^1H NMR : δ 7.95 (d, *J*=6Hz, 1H), 7.25-6.45 (m,3H), 3.80 (q, *J*=7Hz,2H), 1,45 (s,6H), 0.95 (t, *J*=7Hz,3H); IR: 2950, 1720,

1580, 1455, 1425, 1275, 1175, 1140 cm^{-1}; MS: m/z 226 (M+1), 225, 180, 152, 112, 111, 83, 78; and that of **14** are: ^1H NMR δ 3.80 (q *J*=7Hz, 4H), 1.05 (s, 12H), 0.95 (t,*J*=7Hz); IR: 2950, 1715, 1555, 1275 cm^{-1}; MS: m/z 231 (M+1), 200, 186, 115, 99, 88, 87, 73, 70, 59, 55. The unstable mixture showed similar behaviour to the polar part of the reaction mixture. It slowly decomposed giving rise to compounds **15, 12** and the unstable anhydride **13** which again transformed into the starting acid **9** during purification by preparative TLC. The more polar part (34 mg) mainly consisted of **12, 13** and **15**.

When photolysis was done in other solvents that acid chloride was prepared in that solvent itself.

Preparation of adduct 19. Photolysis of the ester **10** (1.5 mmoles) was done in the presence of 5 equivalents of methyl acrylate in refluxing benzene following the same procedure as above. Purification of the raction mixture by preparative TLC afforded 37% of the adduct **19** along with 48% of **11**, 6% of **12** and a small amount of telomeric mixture. ^1H NMR (300 MHz) of **19** gave peaks at δ 8.40 (ddd, *J*=0.95, 1.8, 4.9 Hz, 1H), 7.48 (ddd, *J*=1.8, 7.5, 8 Hz, 1H), 7.16 (ddd, *J*=0.7, 0.95, 8 Hz, 1H), 7.00 (ddd, *J*=0.7, 4.9, 7.5, Hz, 1H), 4.67 (dd, *J*=5.8, 8.2 Hz, 1H), 4.10 (q, *J*=7 Hz, 2H), 3.69 (s, 3H), 2.41 (dd, *J*=8.3, 14.5 Hz, 1H), 2.15 (dd, *J*=5.8, 14.5 Hz, 1H), 1.27 (s, 3H), 1.23 (t, *J*=7 Hz, 3H), 1.22 (s, 3H); IR: 2950, 1725, 1575, 1455, 1420, 1270, 1150 cm^{-1}; MS: m/z 312 (M+1), 280, 266, 234, 196, 178, 164, 136, 124, 116, 111, 78, 70, 67.

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6 Work on other monoalkyl and dialkyl derivative of ethyl malonic acid is in progress. Detail will be published as a full paper in due course.