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ALIPHATIC DIAZO COMPOUNDS. XV. FORMATION OF 1,3-DITHIOLANE AND 1,3-DITHIETANE DERIVATIVES BY THE REACTION OF α-DIAZO KETONES WITH CARBON DISULFIDE[1]

PETER YATES* AND J.A. EENKHORN
Lash Miller Chemical Laboratories, University of Toronto, Toronto, Ontario, Canada M5S 1A1

Dedicated to Professor E.C. Taylor on the occasion of his 65th birthday

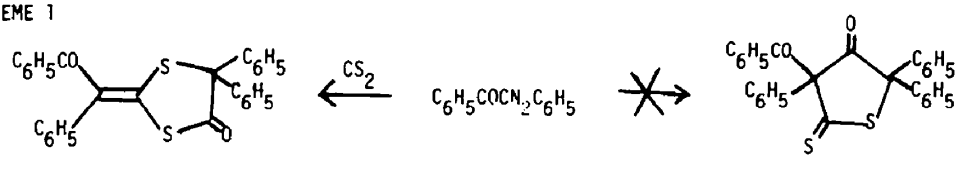
(*Received in USA 7 October* 1987)

Abstract --Reaction of α-diazo ketones, $RCOCN_2R'$, with boiling carbon disulfide can give two major types of product: 2-alkylidene-1,3-dithiolan-4-one derivatives (Type A) and 4-acyl-2-alkylidene-1,-3-dithetane derivatives (type B). When R' = phenyl and R = phenyl or methyl, type A but not type B products are formed. When R' = methyl and R = phenyl or methyl, both types of product are formed; in the case where R' = R = methyl, a small amount of a 4-acyl-2-alkylidene-1,3-dithiolane derivative was isolated in addition to type A and B products. When R' = H and R = phenyl, no product of type A or B could be isolated, but a 1,2,3-thiadiazole derivative was obtained in low yield. These results are interpreted in terms of reaction pathways involving electrophilic addition of carbon disulfide to the diazo carbon of the diazo ketone followed by loss of nitrogen to give an intermediate that reacts electrophilically at the diazo carbon of a second molecule of diazo ketone. It is proposed that this reaction is under kinetic control and gives rise to the less stable E-stereoisomer of the type A product, which can be converted on acid treatment to the more stable Z-stereoisomer.

INTRODUCTION

In 1925, Meyer[2] reported that azibenzil (2-diazo-2-phenylacetophenone; 1) reacts with boiling carbon disulfide to give in high yield a crystalline product, $C_{29}H_{20}O_2S_2$, for which he proposed structure 2. Some thirty years later, Yates and Christensen[3] reinvestigated this reaction and assigned structure 3 ("type A" structure; Scheme 1) to the product, on the basis of degradative and spectroscopic evidence.

SCHEME 1



3 1 2

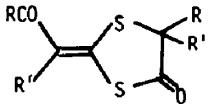
Subsequently, a compound, $C_9H_{12}O_2S_2$, obtained from the reaction between 3-diazo-2-butanone (4) and carbon disulfide, was assigned structure 5.[4] The assignment was made in analogy to that for 3, although the ^1H nmr spectrum of the product showed four methyl signals. However, Kapecki, Baldwin, and Paul[5] showed by an X-ray crystallographic study that this product has structure 6 ("Type B" structure).

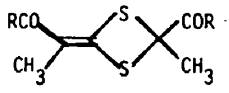
Thereupon, Yates and Williams[6] adduced additional evidence substantiating the assignment of structure 3 to the product from azibenzil (1) and carbon disulfide. Shortly thereafter Baldwin and Kapecki[7] concluded that the major product from 2-(p-fluorophenyl)-2-diazo-p-fluoroacetophenone (7) and carbon disulfide has the type A structure 8. In addition, the product from 2-(p-bromophenyl)-2-diazoacetophenone (9) and carbon disulfide was shown to have the type A structure 10 by X-ray crystallography.[8]

Thus it was established that the reactions of α-diazo ketones with carbon disulfide can result in the formation of products of different types, 1,3-dithiolan-4-one derivatives of type A (3, 8, and 10) and 1,3-dithietane derivatives of type B (6).[9]

The objective of the present work was to investigate the reaction between various α-diazo ketones, $RCOCN_2R'$, and carbon disulfide in order to define the relationship between the products of reaction and the nature of the groups R and R' of the diazo ketones and to interpret its origin in mechanistic terms.

$RCOCN_2R'$





1 R = R' = C_6H_5

4 R = R' = CH_3

7 R = R' = p-FC_6H_4

9 R = C_6H_5, R' = p-BrC_6H_4

11 R = CH_3, R' = C_6H_5

12 R = C_6H_5, R' = CH_3

13 R = C_6H_5, R' = H

3 R = R' = C_6H_5

5 R = R' = CH_3

8 R = R' = p-FC_6H_4

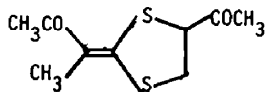
10 R = C_6H_5, R' = p-BrC_6H_4

14,15 R = CH_3, R' = C_6H_5

16 R = C_6H_5, R' = CH_3

6 R = CH_3

17 R = C_6H_5



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RESULTS

Products formed from α-diazo ketones and carbon disulfide

The α-diazo ketones 1, 4, and 11-13 were prepared by standard procedures (see Experimental). Each of these was dissolved in carbon disulfide and the resulting solution was boiled at reflux until reaction was complete, the completion being indicated by the absence of the characteristic α-diazo ketone N=N stretching band at 4.9 μm in the ir spectrum of the reaction mixture. The products that were isolated from each of the reaction mixtures and the reaction times are listed in Table 1. The determination of their structures is discussed subsequently.

Table 1. The reaction between α-diazo ketones and carbon disulfide: reaction products, yields, and reaction times

α-Diazo ketone $RCOCN_2R'$	Products (%) Type A	Type B	Other[b]	Time (days)
$C_6H_5COCN_2C_6H_5$ (1)	3 (90)	-	-	1
$CH_3COCN_2C_6H_5$ (11)	14 (36)[a]	-	-	7
	15 (10)[a]	-	-	7
$C_6H_5COCN_2CH_3$ (12)	16 (34)	17 (4)	-	28
$CH_3COCN_2CH_3$ (4)	5 (6.5)	6 (50)	18 (1.5)	15
$C_6H_5COCN_2H$ (13)	-	-	19 (7)	126

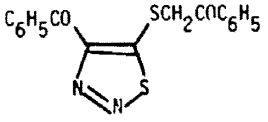
[a] Compounds 14 and 15 are geometrical isomers (see text); other Type A products are single geometrical isomers of undetermined configuration. [b] See text.

As previously reported,[2,3,6] the reaction with azibenzil (1), gave 3 in high yield, as the only product that could be detected. Examination of the spectra of the total crude reaction product gave no evidence for the formation of any other product.

In our first study of the reaction of 1-diazo-1-phenyl-2-propanone (11) with carbon disulfide, two products of type A, the geometrical isomers 14 and 15, were isolated by column chromatography followed by crystallization. However, we were unable to isolate compound 15 from subsequent runs and compound 14 alone was obtained in 70% yield.

The reaction between 2-diazopropiophenone (12) and carbon disulfide afforded compounds of both type A and B, 16 and 17, respectively, in low yield. The poor weight balance of the products is ascribed both to resinification during the reaction and decomposition during their chromatographic separation. No interconversion between compound 16 and 17 was observed in refluxing carbon disulfide, demonstrating that each is formed independently of the other.

The product mixture from 3-diazo-2-butanone (4) and carbon disulfide was found to be more complex than originally reported[4] since it afforded not only compound 6 of type B, but also gave on chromatography on Florisil of the filtrate from crystallization of 6, compound 5 of type A (the structure originally assigned to 6[4]) and compound 18 of another structural type. When compounds 5 and 6 were each stirred at room temperature in a benzene-Florisil slurry they were recovered unchanged and the formation of compound 18 was not detected, indicating that 18 is a product from the original reaction and not an artefact formed during column chromatography.



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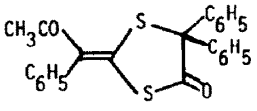

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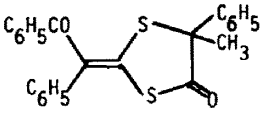

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2-Diazoacetophenone (13) upon reaction with carbon disulfide gave a low yield of a compound 19 of yet another structural type that separated from the mixture during the reaction and was purified by recrystallization. The mother liquor contained a multitude of compounds that could not be separated by column chromatography.

In addition to the reactions shown in Table 1, the reaction of a 1:1 mixture of 1 and 11 with carbon disulfide was investigated. This gave as the major products compounds 3 and 14, which had previously been obtained from the individual diazo ketones, and as minor products the two 'cross-reaction' products 20 and 21. All of these products are of type A.

Structure Determination of Products

Previously, degradative evidence had afforded a structure proof for compound 3[3,6] while X-ray crystallographic studies have established the structures of compounds 6[5] and 10.[8] With the help of these proven assignments, the structures of the other products could be established by spectroscopic methods.

The mass spectra of the products are a very useful means for distinguishing between type A and type B compounds. Examination of the mass spectral fragmentation patterns of the compounds (Table 2) suggests that the processes shown in Schemes 2 and 3 are operative for type A and type B compounds, respectively.

The ketene fragment 22, the hydrocarbon fragment 23, and the thioketone fragment 27 are characteristic of the type A compounds (Scheme 2), except for compound 5, the only compound without phenyl substitutents, which shows no fragment 27. It may be noted also that the abundance of the fragment 23 is exceptionally low in this case.

SCHEME 2

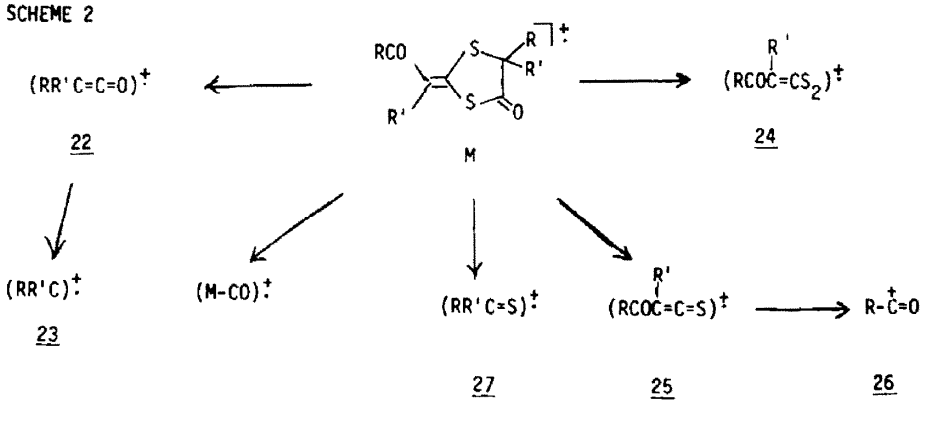
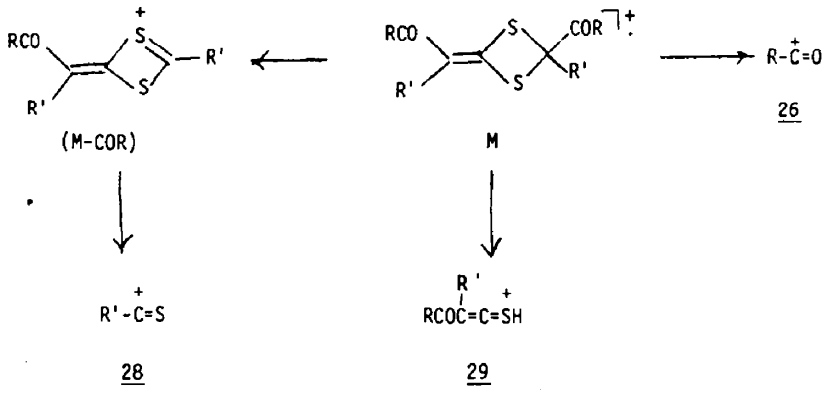


TABLE 2. Mass spectra

Compound and Type	M	(M-CO)	m/z (relative abundance) and assignments 22	23	24	25	26	27	(M-COR)	28	29
3 A	464(24)	-	194(100)	166(33)	-	238(11)	105(65)	198(10)	-	-	-
5 A	216(37)	188(20)	70(16)	46(1)	146(17)	114(37)	43(100)	-	-	-	-
14 A	340(23)	312(5)	132(100)	104(20)	-	176(24)	43(39)	136(5)	-	-	-
15 A	340(24)	312(6)	132(100)	104(21)	-	176(22)	43(37)	137(5)	-	-	-
16 A	340(15)	312(7)	132(100)	104(29)	208(2)	176(2)	105(49)	136(20)	-	-	-
20 A	402(10)	374(2)	194(100)	166(45)	-	176(8)	43(38)	198(19)	-	-	-
21 A	402(7)	-	132(100)	104(17)	-	238(14)	105(100)	136(11)	-	-	-
6 B	216(30)	-	-	-	-	-	43(98)	-	173(100)	59(99)	115(34)
17 B	340(20)	-	-	-	-	176(1)	105(92)	-	235(100)	59(29)	177(22)
18 -	216(34)	-	-	-	146(52)	-	43(100)	-	173(14)	-	115(16)

SCHEME 3



The M-COR fragment, the protonated thioketene fragment 29, and the thioacylium ion 28 are characteristic of the type B compounds (Scheme 3). Although compound 18 shows a fragmentation pattern similar to that of a type B compound, except for the absence of the thioacylium ion 28, its ^{1}H nmr spectrum clearly distinguishes it from the 1,3-dithietane derivatives of type B (vide infra).

The uv spectroscopic data (Table 3) corroborate these structural assignments. Thus, the higher value of the extinction coefficient for the short wavelength band of 17 (type B) (ε = 24,300) relative to that (ε = 10,200) of 16 (Type A) can be attributed to a superimposition of chromophores of the two benzoyl groups in 17. The positions of the maxima of the long wavelength bands allow distinction to be made between acetyl and benzoyl substituents on the ethylenic double bond, the former showing values at 315-323 nm, the latter at 333-347 nm. The structural assignments for 20 and 21 are confirmed in this way.

The ir spectroscopic data for these compounds (Table 3) allow distinction to be made between type A and B compounds and like the uv data, distinguish between acetyl and benzoyl groups in conjugation with the double bond. Values of the shorter wavelength carbonyl band of 5.86-5.90 μm are indicative of the thiolactone carbonyl group in the A-type compounds, while those outside of this range are associated with compounds that lack this group. The band at 5.84 μm of 6 arises from the acetyl group attached to the 4-membered ring, while that of 17 at 5.95 μm arises from the

TABLE 3. UV, IR, and ^{13}C NMR spectra

Compound and Type		Ultraviolet λ_{max} (ε) (MeOH), nm		Infrared $\lambda_{max}(CHCl_3)$, μm		^{13}C nmr δ($CDCl_3$)	
3	A	254 (16,500)	347 (12,400)	5.86	6.17	200.3	191.3
5	A	261 (5,300)	315 (12,100)	5.88	6.06	203.5	195.8
14	A	265 (6,200)	322 (15,900)	5.90	6.08	201.8	195.2
15	A	275 sh (6,000)	323 (15,000)	5.88	6.05	-	
16	A	257 (10,200)	333 (9,600)	5.88	6.16	201.8	193.9
20	A	262 (5,800)	322 (14,100)	5.88	6.09	-	
21	A	255 (14,700)	343 (13,200)	5.88	6.17	-	
6	B	242 (9,400)	316 (16,900)	5.84	6.06	202.9	197.5
17	B	255 (24,300)	341 (18,100)	5.95	6.19	-	
18	-	277 sh (4,900)	320 (13,900)	5.86	6.15	-	
19	-	248 (19,700)	319 (11,700)	5.92	6.12	-	

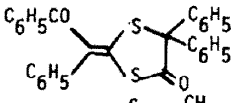
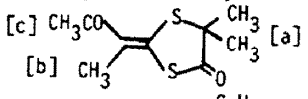
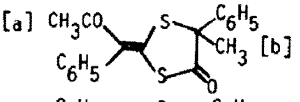
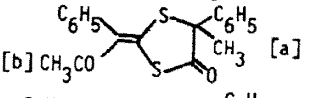
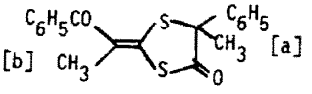
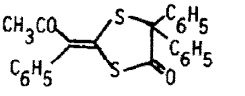
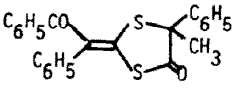
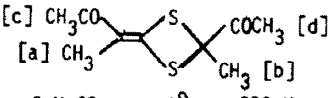
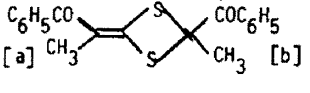
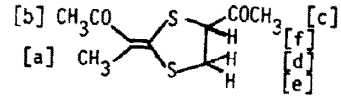
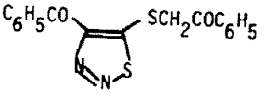
corresponding benzoyl group. The band of 19 at 5.92 μm can readily be assigned to the carbonyl group of the $C_6H_5COCH_2S$ moeity. The longer wavelength bands are associated with the RCOC=C<S-S> system. They occur at 6.05-6.09 μm for the acetyl group and at 6.13-6.17 μm for the benzoyl group of both type A and type B compounds. The longer wavelength band of compound 19 can be assigned to the benzoyl group in conjugation with the 1,2,3-thiadiazole ring.

Table 4 shows the ^1H nmr data for the reaction products with assignments of the signals. These data corroborate the structural assignments, clearly allowing, for example, distinction to be made between compounds 5, 6, and 18. Thus, the spectrum of 5 shows three singlets of intensity ratio 1:1:2, that of 6 shows four singlets of equal intensity while that of 18 shows three singlets of equal intensity, together with a three-proton ABX system for the CH_2CH moeity in the five-membered ring.

In order to assign the aliphatic signals, deuterium exchange reactions were carried out. Acid-catalysed deuteration of compounds 5, 6, 14 and 18 with methanol-O-d and a catalytic quantity of concentrated sulfuric acid resulted in the disappearance of one singlet in the ^1H nmr spectrum of each compound. This signal is assigned to the protons of the acetyl group attached to the ethylenic double bond, the site of deuteration being confirmed by mass spectral fragmentation. It was observed that the acid-catalyzed deuteration of 14 afforded a mixture of the deuterated derivatives of 14 and 15 (*vide infra*). Deuteration of 6 catalyzed by sodium methoxide led to the disappearance of the singlet at δ 2.60 in its ^1H nmr spectrum. Mass spectral evidence confirmed that, as expected, this signal arises from the protons of the acetyl group attached to the four-membered ring.

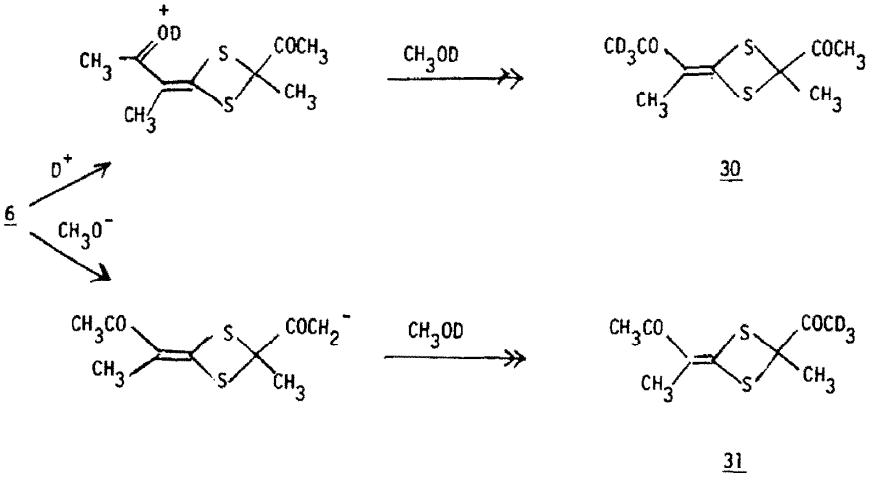
Preferential exchange of the protons of one acetyl group of 6 under acidic reaction conditions and of the protons of the other acetyl group under basic conditions can be interpreted as shown in Scheme 4. The first step in the acid-catalyzed deuteration involves protonation of the conjugated acetyl group, aided by delocalization of the non-bonded electrons of the two sulfur atoms, in preference to protonation of the acetyl group attached to the four-membered ring. This leads to the formation of 30 as the acid-catalyzed deuteration product. On the other hand, the first step in the base-catalyzed deuteration of 6 is proton abstraction from the acetyl group attached to the four-membered ring which is more acidic than the other, cross-conjugated acetyl group. This leads to the formation of 31 as the deuteration product.

TABLE 4. ^{1}H NMR spectra

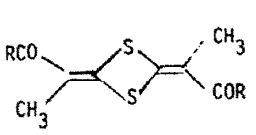
Compound	Structure	$\delta(CDCl_3)$[a]
3		7.0-7.6 (m)
6		1.60 (6H) [a], 2.13 [b], 2.27 [c]
14		2.01 [a], 2.04 [b], 7.2-7.7 (m, 10H)
15		1.93 [a], 2.03 [b], 7.2-7.6 (m, 10H)
16		1.98 [a], 2.16 [b], 7.2-7.8 (m, 10H)
20		2.01, 7.4 (s, 15H)
21		2.04, 7.1-7.7 (m, 15H)
6		1.82 [a], 2.04 [b], 2.18 [c], 2.60 [d]
17		1.91 [a], 2.44 [b], 7.2-8.0 (m, 10H)
18		2.14 [a], 2.24 [b], 2.30 [c], 3.28 (dd, J 5, 10, 1H) [d], 3.75 (dd, J 3.5, 10, 1H) [e], 4.35 (dd, J 3.5, 5, 1H) [f]
19		4.53 (2H), 7.2-7.6 (m, 6H), 7.8-8.4 (m, 4H)

[a]Signals are 3-proton singlets unless otherwise specified; J values are in Hz.

SCHEME 4

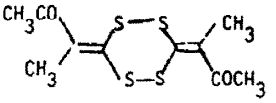


In order to assign the allylic methyl protons in compounds 6 and 17, two model compounds were synthesized. Desaurin 32 was prepared from propiophenone, carbon disulfide, and potassium hydroxide.[10] Desaurin 34 was prepared via the tetrathiin 33.[4] The ^{1}H nmr spectrum of 32 showed a singlet at δ 2.07 and a multiplet at δ 7.3-7.7 with an intensity ratio of 3:5.

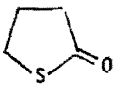


32 R = C_6H_5

34 R = CH_3



33



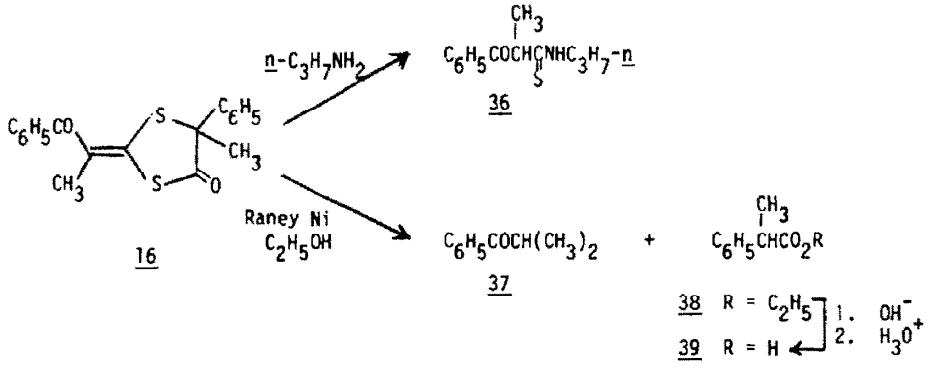
35

Since desaurin 32 contains two $CH_3C{=}C\langle^{S-}_{S-}$ systems and compound 17 only one, the sulfur atoms are expected to exert a smaller conjugative shielding effect on the allylic methyl protons in the former than in the latter compound. Hence the signal for the allylic methyl protons should be at lower field for desaurin 32 than for compound 17. Since the allyl methyl signal of the desaurin occurs at δ 2.07 the signal of 17 at δ 1.91 is assigned to the protons of its allyl methyl group, and the signal at δ 2.44 must then be assigned to the protons of the methyl group attached to the four-membered ring.

The desaurin 34 showed two singlets of equal intensity in its ^{1}H nmr spectrum at δ 2.26 and 1.98. Base-catalysed deuteration caused disappearance of the δ 2.26 signal. This signal is therefore assigned to the protons of the acetyl group, an assignment that is corroborated by the mass spectrum of the deuterated desaurin. Of the two as yet unassigned signals of compound 6 at δ 2.04 and 1.81, the latter is assigned to the protons of the allyl methyl group, since here also a signal at higher field is to be expected for compound 6 than for the desaurin.

It had been expected that the ^{13}C nmr signal of the carbonyl carbon of the thiolactone group in the type A compounds would come at higher field than that of the carbonyl carbon of the saturated ketonic acetyl group of the type B compound 6. However, no distinction was evident (Table 3). Examination of the ^{13}C nmr spectrum of γ-thiobutyrolactone (35)[11] confirmed that the carbonyl carbons of thiolactones are indistinguishable from those of saturated ketones by ^{13}C nmr spectroscopy.

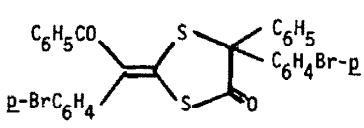
SCHEME 5



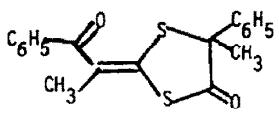
Although our structural assignments rest largely on spectroscopic evidence, confirmatory degradative evidence was obtained in two cases. Compound 16 upon treatment with n-propylamine in chloroform[6] afforded compound 36 (Scheme 5), which was identified on the basis of the relationship of its spectra to those of the analogous product from 3.[6] Treatment of compound 16 with Raney nickel in ethanol afforded a mixture of 2-methylpropiophenone (37) and the ethyl ester of hydratropic acid (38), as evidenced by its ir and ^{1}H nmr spectra. Basic hydrolysis of the mixture afforded hydratropic acid (39), thus confirming the occurrence of rearrangement in the formation of 16. Similarly, hydratropic acid was obtained from the reaction of compound 14 with Raney nickel followed by basic hydrolysis.

Stereoisomerism of Products

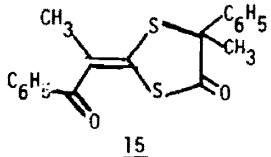
Each of the type A products (and compound 18) can exist as a pair of geometrical isomers. X-ray crystallographic studies showed that compound 10 has the (E)-configuration, 10E. The only other



10E



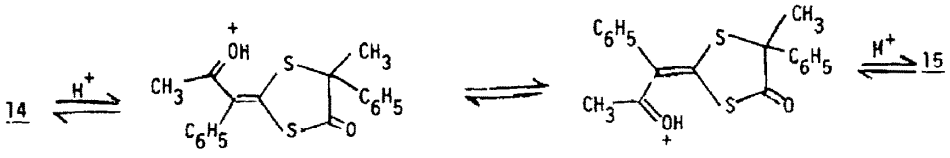
14



15

information garnered on this score is the observation referred to above that one geometrical isomer of the deuterated product from diazo ketone 11 is converted to the other on acid-catalyzed deuteration. Examination of the acid-catalyzed isomerization of the products themselves showed that isomer 14 is converted to a mixture of isomers 14 and 15 on treatment with a catalytic amount of sulfuric acid in methanol, but that 15 is unchanged under these conditions. We conclude that

SCHEME 6



interconversion can occur by rotation about the partial ethylenic double bond (Scheme 6) and that 15 is the thermodynamically favored isomer. The stereostructure 15 is assigned to the latter on the basis that the Z-configuration in 15 will be favored thermodynamically over the E-configuration in 14 because of the greater degree of electrostatic attraction in 15 between the acetyl carbonyl oxygen and the thiolactone sulfur atom versus that between the acetyl carbonyl oxygen and the other sulfur atom in 14. In all but one run of the reaction of diazo ketene 11 with carbon disulfide only isomer 14 was isolated. The isolation of both isomers in one case is ascribable to the adventitious presence of acid, which catalyzed partial equilibration of 14 to a mixture of 14 and 15.

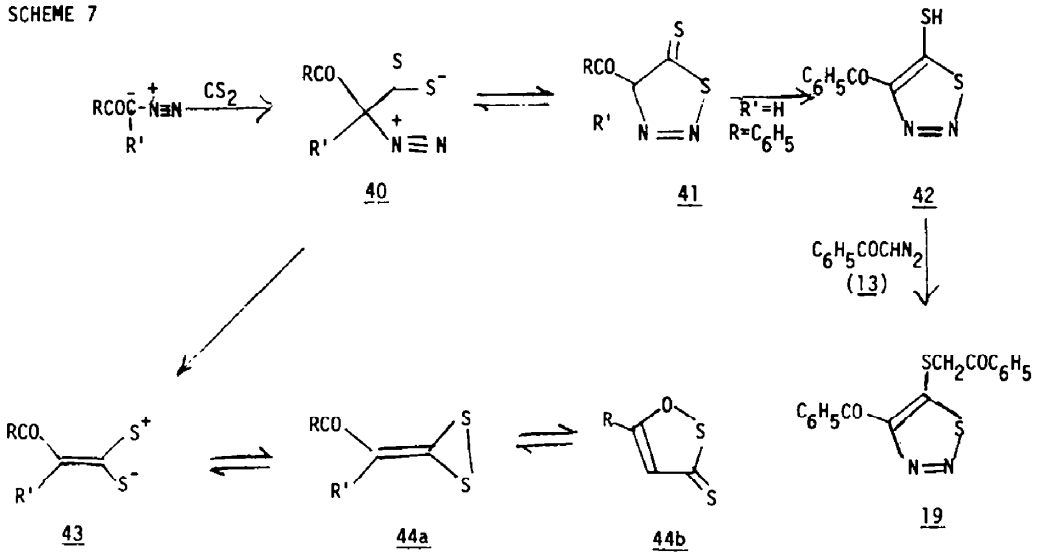
DISCUSSION

The fact that in the cases of the type A products one of the two diazo ketone moeities has undergone a Wolff rearrangement suggests the possibility of carbenoid intermediates. However, this is contraindicated by the observation that when the reaction of 2-diazopropiophenore (12) and carbon disulfide was carried out in the presence of copper bronze the product mixture showned no evidence of the presence of 16 or 17, although the rate of consumption of 12 was increased tenfold. Further, when the uncatalyzed reaction of 12 was carried out at a higher temperature in a mixture of carbon disulfide and benzene, consumption of 12 was accelerated, but again the formation of 16 and 17 could not be detected. We have therefore sought to interpret our observations in terms of ionic rather than carbenoid intermediates.

We propose that the first step involves attack of carbon disulfide as an electrophile at the diazo carbon of the diazo ketone to give an intermediate of type 40 (Scheme 7), in analogous fashion to the attack of other electrophiles, e.g., H^+, on α-diazo ketones. Such an intermediate accounts nicely for the formation of compound 19 from 2-diazoacetophenore (13) and carbon disulfide. If there is an equilibrium between 40 and the heterocyclic isomer 41, thioenolization could occur in this special case where R' = H to give the 1,2,3-thiadiazole 42, which could react with a second molecule of 13 by virtue of the acidity of its aromatic SH group to give the thioether 19.

In the other cases, where R' is a methyl or aryl group, such thioenolization cannot occur and it is postulated that the initial adduct 40 loses nitrogen to give a second zwitterionic intermediate 43 and/or its cyclic valence tautomers 44a and 44b. It is further postulated that 43 or a tautomer

SCHEME 7



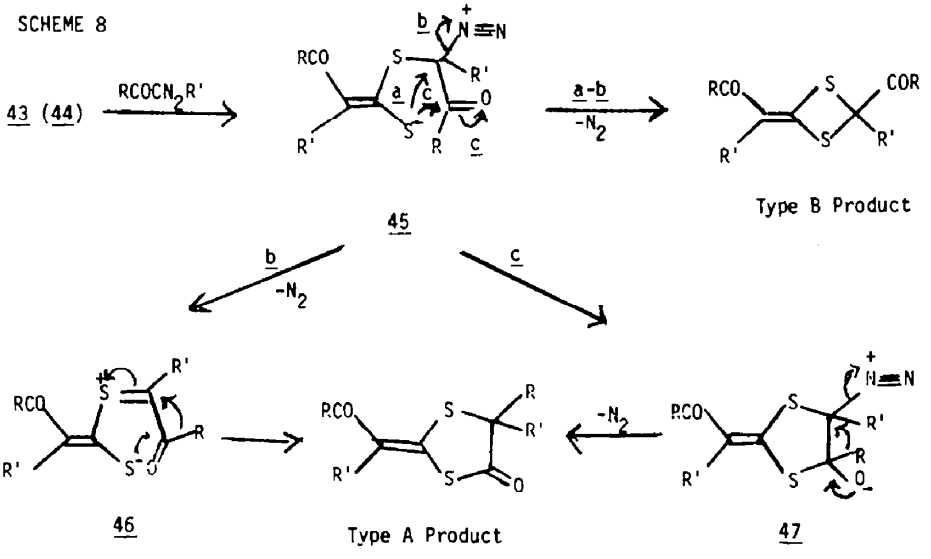
reacts as an electrophile with a second molecule of diazo ketone to give a further intermediate 45 (Scheme 8). Several routes can be envisaged for the conversion of 45 to either type A or type B products. For example, direct displacement of a nitrogen molecule by thiomercaptide ion in 45 would give the type B product, while a stepwise process involving loss of nitrogen to form 46 followed by ring closure could give products of type A. Another variant of these pathways is ring closure in 45 before loss of nitrogen to give 47, followed by loss of nitrogen from this.

Interpretation of the experimental observations concerning the relative amounts of type A and type B products formed must be made cautiously because of the poor weight balances of products isolated in some cases. However, scrutiny of Table 1 leads to the following generalizations:

(i) When R' is an aryl group only products of type A are isolated, but when R' is a methyl group, mixtures of products of both types A and B are obtained.

(ii) For the R' = CH_3 cases, the predominant reaction product is of type B when R is also methyl, while when R is aryl the predominant product is of type A.

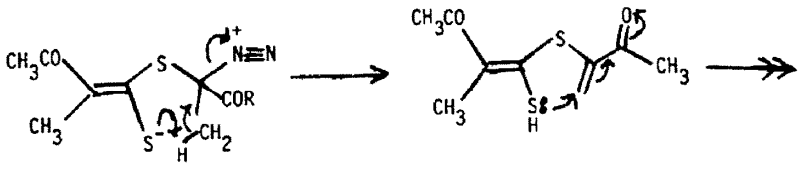
SCHEME 8



The most striking aspect of these observations is that the occurrence of rearrangement leading to type A products is not primarily related to the migratory aptitude of the migrating group R, but to the nature of R', although when R' = CH_3 there is a secondary effect that favors rearrangement when R is a good migrating group.

An interpretation in terms of the reaction pathways in Scheme 8 is that products of type B are formed largely or exclusively from 45 by route a-b and that intermediates 46 and/or 47 give type A and not type B products. Then the formation of type B compounds only when R' = CH_3 can be attributed to steric factors, the direct displacement reaction a-b occurring in this case but not when R' is the larger, aryl group. Further, the secondary effect favoring an increased A:B product ratio for the R' = CH_3 cases when R = aryl can be attributed to the greater migratory aptitude of an aryl versus a methyl group.

SCHEME 9



45 (R = R' = CH_3) 48 18

As shown in Scheme 9, when R = R' = CH_3 the intermediacy of a species of type 45 readily accounts for the formation of 18. Proton transfer from a methyl group concerted with loss of nitrogen would give 48, which could cyclize to 18 via an intramolecular Michael reaction.

EXPERIMENTAL

Melting points were recorded with a Fisher-Johns apparatus and are uncorrected. Spectra are listed in Tables 2-4.

Reaction of 1-Diazo-1-phenyl-2-propanone (11) with Carbon Disulfide. Formation of 14 and 15

(i) A solution of 1-diazo-1-phenyl-2-propanone[12] (1.10 g, 6.9 mmol) in carbon disulfide (20 mL) was boiled under reflux for 7 days. The excess carbon disulfide was removed to give a yellow oil (1.2 g). This was dissolved in 2:1 heptanes-benzene (3 mL) and the solution was added to a column of Florisil (100-200 mesh; 60 g) packed in heptanes. The column was eluted as follows: a mixture of 80 mL of benzene and 160 mL of heptanes, followed by a mixture of 90 mL of benzene and 150 mL of heptanes, etc., until 240 mL of benzene was reached. Fractions of 125 mL were collected and combined on the basis of tlc evidence.

Slow recrystallization of combined fractions 8-16 from ethanol at room temperature gave 14 (0.42 g, 36%), mp 64-66°C. A further recrystallization from ethanol afforded 14, mp 64-66°C. Anal. Calcd. for $C_{19}H_{16}O_2S_2$: C, 67.05; H, 4.75; S, 18.80. Found: C, 66.98; H, 4.79; S, 18.64.

Recrystallization of combined fractions 17-24 from ethanol gave 15 (0.12 g, 10%), mp 116-118°C. A further recrystallization from ethanol afforded 15, mp 117-118°C. Anal. Calcd. for $C_{19}H_{16}O_2S_2$: C, 67.05; H, 4.75; S, 18.80. Found: C, 66.98; H, 4.75; S, 18.96.

(ii) This reaction was carried out in the same manner as above. Compound 14 was obtained directly in 70% yield by recrystallization of the residue after evaporation of the carbon disulfide. Compound 15 could not be detected in this and subsequent runs.

Reaction of 2-Diazopropiophenone (12) with Carbon Disulfide. Formation of 16 and 17

A solution of 2-diazopropiophenone[13] (4.00 g, 25.0 mmol) in carbon disulfide (40 mL) was boiled under reflux for 28 days. The excess carbon disulfide was removed and the resulting brown resin was dissolved in 1:1 benzene-heptanes (5 mL) and the solution was added to a column of Florisil (100-200 mesh; 140 g) packed in heptanes. The column was eluted as follows: 1:1 heptanes-benzene (150 mL), 2:3 heptanes-benzene (250 mL), 3:7 heptanes-benzene (250 mL), 1:4 heptanes-benzene (250 mL) and 1:9 heptanes-benzene (250 mL), benzene (250 mL), and 250-mL portions of benzene containing in order, 1%, 2%, 3%, 55 and 10% ether. Finally the column was washed with ether until no more material was eluted. Fractions, each of 125 mL, were combined on the basis of tlc evidence. Recrystallization of combined fractions 6-15 from ethanol at 0°C gave 16 (1.14 g, 27%) as off-white crystals, mp 99-100°C. Concentration of the filtrate gave an additional 0.30 g of the same material (total yield 34%). A further recrystallization of the first crop from ethanol at room temperature afforded 16, mp 101-102°C. Anal. Calcd. for $C_{19}H_{16}O_2S_2$: C, 67,05; H, 4.75; S, 18.80. Found: C, 66.86; H, 4.88; S, 18.72.

Two recrystallizations of combined fractions 23-24 from ethanol gave 0.16 g (4%) of 17, mp 100-101°C. Anal. Calcd. for $C_{19}H_{16}O_2S_2$: C, 67.05; H, 4.75; S, 18.80. Found: C, 66.98; H, 4.76; S, 18.87.

Reactions of 3-Diazo-2-butanone (4) with Carbon Disulfide. Formation of 5, 6 and 18

A solution of 3-diazo-2-butanone[14] (6.00 g, 61.3 mmol) in carbon disulfide (50 mL) was boilded under reflux for 15 days. The excess carbon disulfide was removed and the remaining yellow solid (6.0 g) was twice recrystallized from ethanol to give 6 (3.18 g, 48%) as yellow crystals, mp 123-124°C (lit[4] mp 126°C). The filtrate was stripped of solvent and the residue (2.76 g) was dissolved in 1:1 (v/v) heptanes-benzene (9 mL), and the solution was added to a column of Florisil (100-200

mesh; 110 g) packed in heptanes. The column was eluted as follows: 400-mL portions of mixtures of 1:1, 2:3, 1:4, and 1:9 heptanes ether-benzene, 400 mL of benzene, followed by 400-mL portions of benzene containing 1%, 2%, 4%, 10%, 25% and 50% of ether. Fractions of 50 mL were collected and combined on the basis of tlc evidence.

Recrystallization of fractions 13-23 from methanol at 0°C gave 5 (0.43 g, 6.5%) as white plates, mp 97-99°C. A further recrystallization from methanol afforded 5, mp 98-99°C. Anal. Calcd. for $C_9H_{12}O_2S_2$: C, 50.00; H, 5.60; S, 29.60. Found: C, 49.98; H, 5.64; S, 29.42.

Recrystallization of fractions 36-51 from ether afforded 6 (0.16 g 2%) as pale yellow crystals, mp 124-125°C (total yield 50%).

Recrystallization of fractions 53-59 from ether at 0°C gave 18 (0.10 g, 1.5%) as white crystals, mp 86-88°C. A further recrystallization from ether afforded 18, mp 87-88°C. Anal. Calcd. for $C_9H_{12}O_2S_2$: C, 50.00 H, 5.60; S, 29.60. Found: C, 49.98; H, 5.76; S, 29.44.

Reaction of 2-Diazoacetophenone (13) with Carbon Disulfide. Formation of 19

A solution of 2-diazoacetophenone (1.46 g, 10.0 mmol) in carbon disulfide (15 mL) was boiled under reflux with stirring for 18 weeks. The solid (0.25 g) that had started to separate after approximately 1 month was collected by filtration after 13 weeks. This solid was recrystallized three times from acetone to give 19 (0.080 g) as a sand-colored solid, mp 158-159PC. An additional 0.040 q of 19, mp 154-156°C, was obtained from the mother liquors, bringing the yield to 7%. Anal. Calcd. for $C_{17}H_{12}O_2N_2S_2$: C, 60.00; H, 3.55; N, 8.23, S, 18.81; M.W. 340. Found: C, 59.89; H, 3.69; N, 8.27; S, 18.89; M.W. 320 (osmometric).

Reaction of a 1:1 Mixture of 1-Diazo-1-phenyl-2-propanone (11) and Azibenzil (1) with Carbon Disulfide. Formation of 3, 14, 20, and 21

A solution of 1-diazo-1-phenyl-2-propanone (1.00 g 6.26 mmol) and of azibenzil (1,38 g, 6.25 mmol) in carbon disulfide (30 mL) was boiled under reflux for 7 days. The carbon disulfide was removed and the resulting yellow resin (2.56 g) was dissolved in a little ether, and the solution was seeded with compound 3 and allowed to crystallize at 0°C, giving 3 (0.80 g), mp undepressed on admixture with authentic material. The filtrate was stripped of solvent and the residue (1.72 g) was dissolved in benzene and added to a column of Florisil (100-200 mesh; 86 g) prepared in heptanes.

The column was eluted as follows: 250 mL of benzene and 250 mL of heptanes, 300 mL of benzene and 200 mL of heptanes, 350 mL of benzene and 150 mL of heptanes, etc. until 500 mL of benzene was reached. Fractions of 125 mL were collected and combined on the basis of ^1H nmr spectroscopic evidence.

Fraction 3 gave further 3 (0.21 g), bringing the total yield to 35%. Fraction 4 gave a yellow resin (0.53 g), which upon crystallization from ether at -20°C afforded 21 (0.22 g, 9%) mp 130-132°C, unchanged on recrystallization. Anal. Calcd for $C_{24}H_{18}S_2O_2$: C, 71.63; H, 4.51; S, 15.91. Found: C, 71.57; H, 4.56; S, 15.76.

Fraction 5 gave a yellow resin (0.30 g), which on crystallization form ether gave a mixture, which after two recrystallizations from acetone afforded 20 (0.040 g, 1.5%), mp 143-154°C. Anal. Calcd for $C_{24}H_{18}S_2O_2$: C, 71.63; H, 4.51; S, 15.91. Found: C, 71.37; H, 4.51; S, 15.74.

Combined fractions 6-10 gave crude compound 14 (0.57 g, 28%).

Deuterium Exchange Reactions

(i) Acid-catalysed Deuteration

(a) Deuteration of 6. Formation of 30. A solution of 6 (0.200 g) in methanol-O-d (10 mL), containing 3 drops of concentrated sulfuric acid, was stirred at room temperature for 1.5 h. The solvent was removed and the residue was washed with ether and recrystallized from methanol-O-d to give 30 (0.080 g), mp 121-122°C. Its ^1H nmr spectrum showed the absence of the δ 2.18 signal of 6. Its mass spectrum showed m/z 219 (6%, M), 176 (34%, M-$COCH_3$), 59 (76%, CH_3CS), 46 (100%, CD_3CO).

(b) Deuteration of 5. A solution of 0.10 g of 5 (0.100 g) in methanol-O-d (5 mL) containing 1 drop of concentrated sulfuric acid was stirred at room temperature for 3 h. The solvent was evaporated to give deuterated 5, whose ^1H nmr spectrum showed the absence of the δ 2.77 signal of 5.

(c) Deuteration of 14. Compound 14 (1.00 g) was dissolved in hot methanol-O-d (15 mL). After the solution had cooled to room temperature, 4 drops of concentrated sulfuric acid were added and the mixture was stirred for 3 h. The solvent was removed and the residue was dissolved in benzene. The solution was washed with aqueous sodium bicarbonate and dried (Na_2SO_4). The solvent was removed to give a yellow oil (1.00 q), whose ^1H nmr spectrum showed the intensity ratio of the δ 1.93 and 2.01 signals to be 1:4. This mixture was chromatographed on Florisil (60 g) with elution with mixtures of heptanes (200 mL) and benzene (100 mL), heptanes (175 mL) and of benzene (125 mL), etc. until 300 mL of benzene was reached. Fractions of 125 mL were collected and combined on the basis of tlc and ^1H nmr spectroscopic evidence. Combined fractions 5-11 (0.75 g) were crystallized from methanol-O-d to give deuterated 14 (0.51 g), mp 62=64°C, whose ^1H nmr spectrum showed the absence of the δ 2.01 signal of 14. Combined fractions 14-18 (0-20 g) gave deuterated 15, whose ^1H nmr spectrum showed the absence of the δ 2.03 signal of 15.

(d) Deuteration of 18. A solution of 8 (0.020 g) in methanol-O-d (2 mL) containing 1 drop of concentrated sulfuric acid was stirred at room temperature for 1 h. The solvent was removed to give deuterated 18, whose ^1H nmr spectrum showed the absence of the δ 2.24 signal and reduction in the intensity of the δ 2.30 signal of 18.

(ii) Base-Catalyzed deuteration

(a) Deuteration of 6. Formation of 31. Compound 6 (0.200 g) was dissolved in methanol-O-d (4 mL) by heating. After the solution had cooled, sodium methoxide (1 mg) was added. After 10 min a precipitate started to form; after 45 min. the mixture was cooled to 0°C and filtered. The resulting white solid (0.110 g) was recrystallized from methanol-O-d to give 31 (60 mg), mp 123-124°C, the ^1H nmr spectrum of which showed the absence of the δ 2.60 signal of 6. It mass spectrum showed m/z 219 (13%, M), 173 (66%, M-CD_3CO), 59 (100%, CH_3CS).

(b) Deuteration of Desaurin 34 A suspension of desaurin - (0.020 g) methanol-O-d (5 mL), containing a catalytic amount of sodium methoxide (1 mg), was stirred at room temperature for 66 h. The solid was collected by filtration to give deuterated 34 as a white solid (0.020 g), mp 230-232°C. Its ^1H nmr spectrum showed 70% deuterium exchange of the methyl protons corresponding to the δ 2.24 signal.

Desaurin 32

Compound 32 was prepared by the method of Kelber and Schwarz.[10] The crude product was recrystallized from xylene to give 32 as yellow crystals, mp 227-229°C (lit[11] mp 225°C); ^{1}H nmr δ: 2.07 (s, 6H), 7.3-7.7 (m, 10H).

Desaurin 34

Tetrathiin 33 was prepared by the method of Kirby[4] and obtained as yellow crystals, mp 168-170°C (lit[4] mp 169-169.5°C); ir λ_{max}: 6.13 μm; uv λ_{max}: 246, 300, 345 nm; ^{1}H nmr δ: 2.33 (s, 6H), 2.36 (s, 6H).

Heating of 33 with triethyl phosphite[4] gave the desaurin 34, mp 232-234°C (lit[4] mp 236-238°C); ir λ_{max}: 6.08 μm; uv λ_{max}: 241 (sh), 257, 370 nm; ^{1}H nmr δ: 1.98 (s, 6H), 2.26 (s, 6H).

Aminolysis of 16 with n-Propylamine. Formation of 36

To a stirred solution of 16 (0.13 g, 0.4 mmol) in chloroform (7 mL) at room temperature was added a solution of n-propylamine (0.07 g, 1.2 mmol) in chloroform (3 mL). After 5 h the solvent was removed to give a pale yellow oil (0.17 g). This was dissolved in a mixture of benzene (2 mL) and heptanes (2 mL) and the solution was added to a column of Florisil (100-200 mesh; 5.1 g) prepared in 1:1 benzene-heptanes. The column was eluted with the same solvent mixture. Fractions of 20 mL were collected and combined on the basis of tlc evidence. Fractions 2-4 gave 36 (0.070 g); λ_{max} 3.18, 5.97, 6.62 and 8.24 μm ^{1}H nmr δ: 0.90 (t, J = 7 Hz, 3H), 1.4 (d, J = 6 Hz, 3H), 1.53 (m, 2H), 3.52 (m, 2H), 5.00 (q, J = 6 Hz, 1H), 7.2-7.5 (m, 3H), 7.8-8.0 (m, 2H), 8.5 (br s, 1H).

Desulfurization of 16 with Raney Nickel followed by Basic Hydrolysis. Formation of 39

Deactivated W-2 Raney nickel catalyst (6.0 g) was suspended in ethanol (50 mL), 0.50 g of 16 was added, and the mixture was boiled under reflux for 65 h. The mixture was filtered and evaporated and the residue was dissolved in ether and the solution was washed with water, dried (Na_2SO_4), and concentrated to give a brown oil (0.25 g), whose ^{1}H nmr spectrum showed signals attributable to 2-methylpropiophenone (37) and ethyl hydratropate (38).

The desulfurization mixture was dissolved in ethanol (5 mL) and the solution was added to a solution of potassium hydroxide (0.25 g) in water (2 mL). The mixture was boiled under reflux for 24 h. The solvent was evaporated and the residue was dissolved in water. The aqueous solution was washed with ether and acidified with concentrated hydrochloric acid. The mixture was extracted with ether and the ethereal extracts were extracted with aqueous sodium bicarbonate. The extracts were acidified and extracted with ether. These extracts were washed with water, dried (Na_2SO_4) and evaporated to give an oil (0.050 g), which was shown to be hydratropic acid (39) by ir and ^{1}H nmr spectroscopic comparison with an authentic sample.

Similar desulfurization of 14 followed by basic hydrolysis also gave 39.

Isomerisation of 14. Formation of 15

A solution of 14 (2.00 g) in methanol (200 mL) containing concentrated sulfuric acid (0.40 mL) was stirred at room temperature for 22 h, after which time the ^{1}H nmr spectrum of the mixture showed a 2:1 ratio of compounds 14 and 15 to be present. Additional concentrated sulfuric acid (0.40 mL) was added and the reaction was allowed to continue for a further 26 h. The ^{1}H nmr spectrum of the product mixture showed compounds 14 and 15 to be present in a 1:2 ratio.

The solvent was evaporated and the oily residue (1.80 g) was purified by chromatography on a Florisil column (90 g). The column was eluted with solvent mixtures as follows: 300 mL of heptanes and 150 mL of benzene, 275 mL of heptanes and 175 mL of benzene, etc. until 450 mL of benzene was reached, followed by 450-mL portions of benzene containing 2%, 5%, 10%, 20% and 50% of ether. Forty-three fractions of 125 mL and 8 fractions of 250 mL were collected and combined on the basis of tlc evidence.

Combined fractions 7-14 were recrystallized from ethanol to give 14 (0.43 g), mp 62-64°C. Combined fractions 16-30 were recrystallized from ethanol to give 15 (0.31 g), mp 115-117°C.

ACKNOWLEDGMENT

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