Gas chromatographic analysis of the resulting mixture showed that all of the starting reagents had reacted and that 5.97 mmoles of acetophenone were formed. Distillation of another reaction mixture consisting of 6.72 g (39.9 mmole) of 2-methanethio-1-phenylethanol and 0.32 g (2.19 mmole) of *t*-butyl peroxide which had been heated for 18 hr at 125° yielded 1.6 g of material identified as acetophenone, collected over the boiling range 83–120° (8 mm) with the bulk distilling at 90° (8 mm). The nmr spectrum of the material was identical with that of acetophenone, melting point of 2,4-dinitrophenyl hydrazone, 245° (lit.[18] mp 250°), melting point of the phenylhydrazone of the material, 102–104° (lit.[18] mp 105°). After removal of the acetophenone, another distillation fraction [0.49 g, bp 120–142° (8 mm)] was collected. The infrared spectra of this material was essentially the same as that of an authentic sample of 1,1-di(methanethio)-1-phenylethane, bp 120° (0.4 mm), the thioketal obtained in 74% yield from acetophenone and methyl mercaptan.

Anal. Calcd for $C_{10}H_{14}S_2$: C, 60.54; H, 7.13; S, 32.33. Found: C, 60.57; H, 6.87; S, 32.55.

The nmr spectra of the authentic sample and the second distillation fraction however, were not the same. Thin layer chromatography on silica gel G of the second distillation fraction using a 2:1 mixture of ethyl acetate and cyclohexane gave a spot identical with that of the authentic sample of thioketal. However, a 10:1 mixture of cyclopentane and diethyl ether did resolve the second distillation fraction into two components, one of which was the same as that of the authentic sample of thioketal. The other component, on the basis of its infrared spectra being similar to that of the thioketal, has been tentatively identified as 1,2-di(methanethio)-1-phenylethane.

ω-Methanethioacetophenone, 2-Butanol, and *t*-Butyl Peroxide.—A reaction mixture consisting of ω-methanethioacetophenone (0.474 g, 2.85 mmoles), 2-butanol (1.81 g, 24.5 mmoles), and *t*-butyl peroxide (0.150 g, 1.02 mmoles) was heated for 18 hr in a sealed Pyrex tube at 125°. Gas chromatographic analysis of the resulting reaction mixture indicated the following amounts of material were present: unreacted ω-methanethioacetophenone, 2.27 mmoles; 2-butanone, 1.12 mmoles; and acetophenone 0.24 mmole. Thin layer chromatographic analysis of the reaction mixture on silica gel G using a 2:1 mixture of ethyl acetate and cyclohexane gave a spot identical with that of 1,1-di(methanethio)-1-phenylethane, the thioketal of acetophenone and methyl mercaptan.

1-Methanethio-3-butanol and *t*-Butyl Peroxide.—A reaction mixture consisting of 1-methanethio-3-butanol (0.606 g, 5.04 mmoles) and *t*-butyl peroxide (0.037 g, 0.025 mmole) was heated in a sealed Pyrex tube at 125° for 18 hr. On opening the tube, no odor of mercaptan was evident. Gas chromatographic analysis of the reaction mixture showed that 4.75 mmoles of the starting hydroxy sulfide had not reacted.

1-Methanethio-2-aminopropane and *t*-Butyl Peroxide.—A mixture of 1-methanethio-2-aminopropane (2.01 g, 19.13 mmoles) and *t*-butyl peroxide (0.15 g, 1.01 mmoles) was heated at 125° for 30 hr in a sealed tube. Both methyl mercaptan and ammonia were detected by their odors when the tube was opened. Examining the mixture by gas chromatography indicated that all of the starting amine was consumed. *t*-Butyl alcohol and dimethyl disulfide were identified from the chromatographic analysis as reaction products by comparison of their retention times with those of authentic samples of these materials. Addition of water to the reaction mixture resulted in evolution of ammonia. Gas chromatographic analysis of the hydrolysis mixture indicated the presence of acetone.

The hydrolysis mixture was dissolved in dioxane and dried, and after the dioxane had been evaporated in a stream of nitrogen, a viscous, red liquid remained. Sulfur was detectable in this material (sodium fusion). Thin layer chromatography on silica gel G using a 2:3 mixture of methanol and chloroform containing a few drops of ammonium hydroxide resolved this mixture into six components, none of which corresponded to that of the starting amine. No further investigations were made of the products of this reaction.

Trichloroacetoacetates. I. Synthesis and Reactions of Ethyl and β,β,β-Trifluoroethyl Trichloroacetoacetates

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A study of the reaction of chloral and ethyl diazoacetate as a potential source of ethyl trichloroacetoacetate (**1**) showed that the main product of this reaction was ethyl 3-(trichloromethyl)glycidate (**2**). The reaction of trichloroacetyl chloride, ketene, and an alcohol in liquid sulfur dioxide was found to be an excellent method to prepare trichloro-β-keto esters. The acid hydrolysis of **1** yielded α,α,α-trichloroacetone, but this reaction could not be utilized as a general synthetic route to trichloromethyl ketones because alkylation of the ester could not be accomplished. The reactions of **1** with amines were studied and the products formed depended on the basicity and structure of the amine. Ammonia reacted with the ester to form ethyl malonamate. Primary aliphatic amines yielded malonamides and secondary amines formed amine salts. Aromatic amines did not react with **1** under similar conditions, but in the presence of polyphosphoric acid they gave 2-trichloromethyl-4-quinolones. These compounds could be hydrolyzed to kynurenic acids, thus providing a new synthetic route to these compounds. The condensation of **1** with *o*-phenylenediamine, under neutral conditions, yielded 4-(trichloromethyl)-1H-1,5-benzodiazepin-2(3H)-one.

While the reactions of ethyl trifluoroacetoacetate have been investigated by several authors[3] the same is not true of the corresponding trichloroacetoacetate (**1**) which is not commercially available.

The Synthesis of 1.—Schlotterbeck first reported to have synthesized **1** by the reaction of chloral with ethyl diazoacetate.[4] Arndt and co-workers prepared the same ester by oxidation of ethyl 4,4,4-trichloro-3-hydroxybutanoate with chromium trioxide.[5] These authors established that the Schlotterbeck method gave a mixture. They attempted to separate the mixture but could not obtain acceptable analytical data for any other product than the acetoacetate. Smrt, Beránek, and Šorm, while studying the reactions of activated acid chlorides with ketene, prepared **1** by treating ketene with trichloroacetyl chloride.[6] We

(1) Abstracted in part from the Ph.D. dissertation of D. K. Wald, University of Pennsylvania, 1965.

(2) Recipient of E. F. Smith Memorial Scholarships, 1962–1964.

(3) (a) F. Swarts, *Bull. Sci. Acad. Roy. Belges*, [5] **12**, 679 (1926); (b) M. M. Joullié, S. Násfay, and L. Rypstat, *J. Org. Chem.*, **21**, 1358 (1956); (c) F. B. Wigton and M. M. Joullié, *J. Am. Chem. Soc.*, **81**, 5212 (1959); (d) A. G. Sorolla and A. Bendich, *ibid.*, **80**, 5744 (1958); (e) S. Inoue, A. J. Saggiomo, and E. A. Nodiff, *J. Org. Chem.*, **26**, 4504 (1961); (f) R. Filler and S. M. Naqvi, *ibid.*, **26**, 2571 (1961); (g) A. S. Dey and M. M. Joullié, *J. Heterocyclic Chem.*, **2**, 113, 120 (1965); (h) A. S. Dey and M. M. Joullié, *J. Org. Chem.*, **30**, 3237 (1965).

(4) F. Schlotterbeck, *Ber.*, **40**, 3000 (1907).

(5) F. Arndt, L. Loewe, and L. Capuano, *Rev. Fac. Sci. Univ. Istanbul*, **8a**, 122 (1943).

(6) J. Smrt, J. Beránek, and F. Šorm, *Collection Czech. Chem. Commun.*, **20**, 285 (1955).

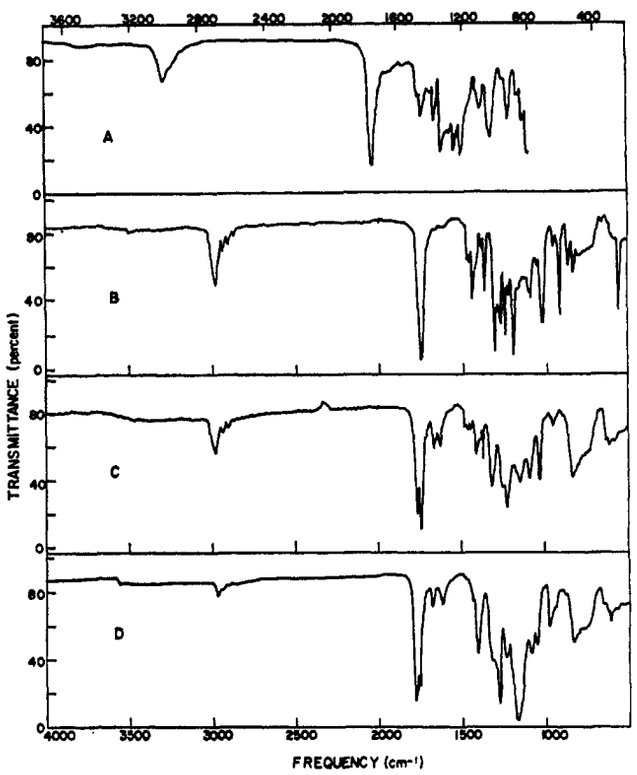
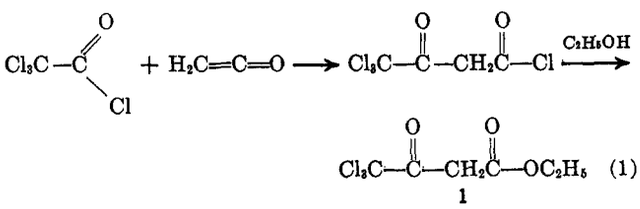
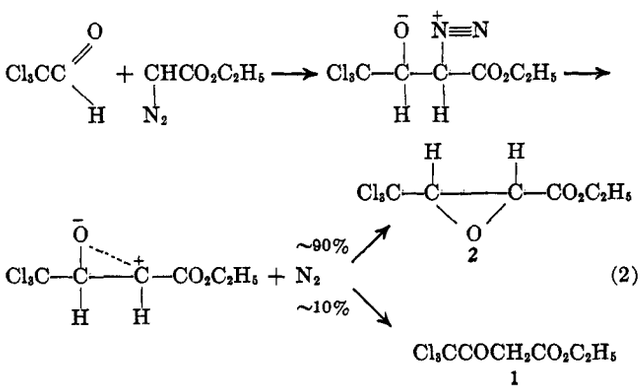


Figure 1.—Infrared spectra of ethyl trichloroacetoacetate as reported by Loos and Herman (A), ethyl 3-(trichloromethyl)-glycidate (B), ethyl trichloroacetoacetate from the ketene synthesis (C), and β,β,β-trifluoroethyl trichloroacetoacetate (D).



found this to be the best method of preparation for this compound as well as other trichloroacetoacetates.

The infrared spectrum of ethyl trichloroacetoacetate had been previously reported by Loos and Herman.[7] These authors used the Schlotterbeck reaction to prepare their ester. Since their data did not agree with our own values, we reinvestigated this reaction. We found, as Arndt and co-workers had postulated, that this reaction was not an adequate method of synthesis for **1** since this product was formed in small amounts and **2** was the predominant product.



(7) H. Loos and M. Herman, *Bull. Soc. Chim. Belges*, **68**, 129 (1959).

A recent investigation of the reaction of an excess of chloral and diazomethane has shown the main product to be 1,1,1,5,5,5-hexachloro-3,4-epoxypentan-2-ol rather than the products originally postulated by Schlotterbeck.[8]

Infrared Spectra.—The infrared spectra of the product obtained by Loos and Herman and of **1** and **2** are shown in Figure 1. The infrared absorption bands of several acetoacetates are shown in Table I. It may be seen from this table that the infrared absorption bands of **1** are comparable with those of similarly substituted acetoacetates.[9] The assignment of the two strong carbonyl bands observed in the spectrum of β,β,β-trifluoroethyl trichloroacetoacetate (**3**) was less obvious than for the ethyl ester. Filler[10] has shown that trifluoroethyl acetates absorb at higher frequencies than the corresponding unfluorinated esters by 21–28 cm^{-1}. The unexpectedly large magnitude of these shifts was explained by the fact that the inductive effect of the trifluoromethyl group, although weakened by the α-methylene group, was still transmitted to a considerable extent by virtue of the polarizability of the intervening C–O linkage. If we assume that fluorine substitution would lead to similar shifts in our system, we can attribute the band at 1777 cm^{-1} to the ester carbonyl of the keto form and the band at 1755 cm^{-1} to the ketone carbonyl. This is supported by the intensities of these bands (see Figure 1), the band at 1777 cm^{-1} being the more intense. As it is the case in all the other trichloroacetoacetates studied,[11] the strongest band is due to the ester carbonyl and the weaker band to the ketone carbonyl.

TABLE I

INFRARED ABSORPTION BANDS OF VARIOUS ACETOACETATES[a]

Ester	C=O	C=O | OR	—OH ⋮ C=O | OR	C=C
Ethyl acetoacetate[b] (keto)	1715	1740	...	...
Ethyl acetoacetate[b] (enol)	...	...	1645	1625
Ethyl γ-chloroacetoacetate[c] (keto)	1726	1745	...	...
Ethyl γ-chloroacetoacetate[c] (enol)	...	...	1656	1632
Ethyl trifluoroacetoacetate[b] (keto)	1775	1740	...	...
Ethyl trifluoroacetoacetate[b] (enol)	...	...	1670	1640 (sh)
Ethyl trichloroacetoacetate[b] (keto)	1767	1741	...	...
Ethyl trichloroacetoacetate[b] (enol)	...	...	1662	1626
Trifluoroethyl trichloroacetoacetate[b] (keto)	1755	1777	...	...
Trifluoroethyl trichloroacetoacetate[b] (enol)	...	...	1683	1626

[a] Bands are in cm^{-1}. [b] In CCl_4. [c] No solvent; see ref 9.

Acid Hydrolysis and Alkylation of 1.—The acid hydrolysis of ethyl acetoacetate is a well-known reaction and the acid hydrolysis of ethyl trifluoroaceto-

(8) R. E. Bowman, A. Campbell, and W. R. N. Williamson, *J. Chem. Soc.*, 3846 (1964).

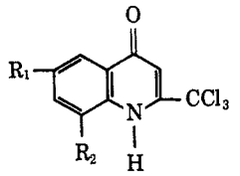
(9) Z. Bánkowska, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, **10**, 401 (1962).

(10) (a) G. Rappaport, M. Hauptschein, J. F. O'Brien, and R. Filler, *J. Am. Chem. Soc.*, **75**, 2695 (1953); (b) R. Filler, *ibid.*, **76**, 1376 (1954).

(11) Unpublished results obtained in this laboratory.

TABLE II

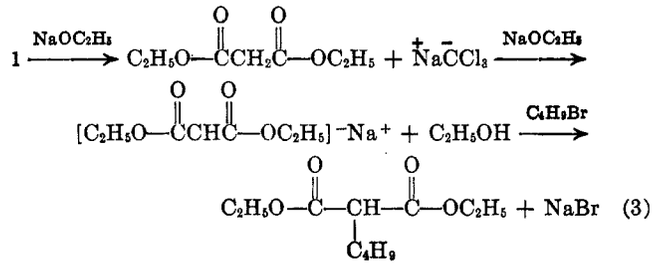
2-TRICHLOROMETHYL-4-QUINOLONES



Compound R_1	R_2	Yield, %	Mp, °C	Formula	Carbon, % Calcd	Carbon, % Found	Hydrogen, % Calcd	Hydrogen, % Found	Nitrogen, % Calcd	Nitrogen, % Found	Chlorine, % Calcd	Chlorine, % Found	λ_{max}^{ethano} mμ (log ε)	$\nu_{C=O}^{KBr}$, cm^{-1}
H	H	66.1	188–189	$C_{10}H_6Cl_3NO$	45.75	45.60	2.30	2.42	5.34	5.15	40.52	40.44	234 (4.46)	1615
Br	H	62.7	229–230	$C_{10}H_5BrCl_3NO$[a]	35.17	35.30	1.48	1.42	4.10	4.15	31.15	31.04	244 (4.51)	1620
H	Br	58.6	194–195	$C_{10}H_5BrCl_3NO$[b]	35.17	35.38	1.48	1.30	4.10	4.16	31.15	31.05	235 (4.53)	1615
Cl	H	68.7	224–225	$C_{10}H_5Cl_4NO$	40.44	40.56	1.70	1.79	4.72	4.90	47.76	47.74	242 (4.50)	1620
H	Cl	43.1	193–194	$C_{10}H_5Cl_4NO$	40.44	40.58	1.70	1.83	4.72	4.91	47.76	47.75	233 (4.58)	1618
CH_3	H	44.4	189–191	$C_{11}H_8Cl_3NO$	47.77	47.91	2.91	2.96	5.07	5.08	38.46	38.45	238 (4.44)	1650, 1630

[a] Calcd for Br: 23.41. Found: 23.25. [b] Calcd for Br: 23.41. Found: 23.34.

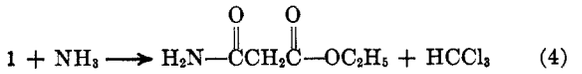
acetate has been studied by Henne and co-workers[12] who used 10% sulfuric acid and by McBee and co-workers[13] who used 30% sulfuric acid. α,α,α-Trifluoroacetone was obtained in both cases. The alkylation of acetoacetates is also a well-known reaction. Because of the therapeutic value of some α,α,α-trichloromethyl ketones,[14] we attempted to utilize the hydrolysis and alkylation of **1** as a new method of preparation for these compounds. The hydrolysis of **1** was accomplished by heating this ester with 50% sulfuric acid. α,α,α-Trichloroacetone was obtained in fair yields. However, the alkylation of **1** did not yield the desired alkylated ester, diethyl *n*-butyl malonate being formed instead. This product resulted from a haloform-type of cleavage on the trichloromethyl carbonyl part of the molecule by the ethoxide ion.



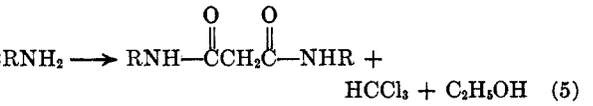
Although this last reaction was undesirable, it illustrated the possibility of a haloform-type of cleavage for this molecule. Since the aminolysis of trihalogenated esters had been previously shown to give rise to two types of cleavage,[15] an investigation of the reactions of **1** with amines offered the opportunity to study a system where a variety of reactions were theoretically possible. The reactions of aliphatic and aromatic amines with ethyl acetoacetate yielded a variety of products depending on the amine used and the conditions of the reaction.

Reactions of 1 with Aliphatic Amines.—Kuckert[16] treated methylamine with ethyl acetoacetate at 0° and obtained ethyl β-hydroxy-β-methylaminobutyrate. Knoevenagel and Reinecke[17] reported that heating a solution of methylamine and the same ester yielded ethyl β-methylaminocrotonate. The reaction of the same compound with aqueous ammonia gave both the crotonate and the anilide.[18] Swarts studied the reaction of ethyl trifluoroacetoacetate with ammonia and reported the formation of a salt.[3a] Amine salts were also formed when this ester was treated with aliphatic primary, secondary, and tertiary amines.[3b]

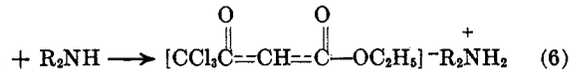
When an excess of anhydrous ammonia was bubbled through a boiling ether solution of **1**, only a haloform-type of cleavage occurred. When **1** was treated with



primary amines under similar conditions, both aminolysis and a haloform-type of cleavage occurred. However, when the ester was treated with an equimolar quantity of amine, a malonamate was obtained.



Secondary amines were treated with an ether solution of **1** at room temperature. These reactions were exothermic and the products formed were found to be amine salts. The high polarity of these compounds was demonstrated by their solubility in water.



Reactions of 1 with Aromatic Amines.—Aniline did not react with **1** under the conditions used for aliphatic amines but when these reagents were mixed in the presence of polyphosphoric acid, 2-trichloromethyl-4-quinolone was obtained. Substituted anilines reacted similarly. The physical and analytical data for the substituted 2-trichloromethyl-4-quinolones prepared in this investigation are shown in Table II.

(12) A. L. Henne, M. S. Newman, L. L. Quill, and R. A. Staniforth, *J. Am. Chem. Soc.*, **69**, 1819 (1947).

(13) E. T. McBee, O. R. Pierce, H. W. Kilbourne, and J. A. Borone, *ibid.*, **75**, 4090 (1953).

(14) R. E. Bowman, A. Campbell, and E. M. Tanner, *J. Chem. Soc.*, 692 (1963).

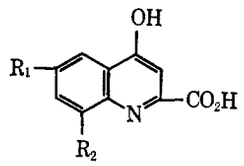
(15) (a) M. M. Joullié and A. R. Day, *J. Am. Chem. Soc.*, **76**, 2990 (1954); (b) A. C. Pierce and M. M. Joullié, *J. Org. Chem.*, **28**, 658 (1953); (c) Y. Ursy and M. Paty, *Compt. Rend.*, **252**, 3812 (1961).

(16) O. Kuckert, *Ber.*, **18**, 618 (1885).

(17) E. Knoevenagel and E. Reinecke, *ibid.*, **32**, 420 (1899).

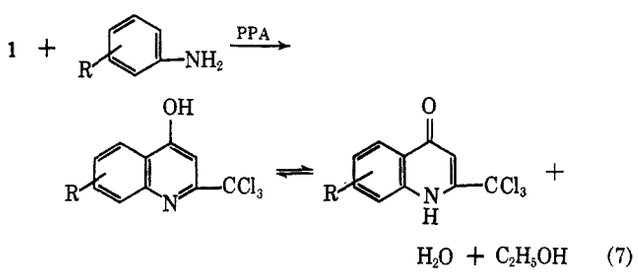
(18) L. Claisen and R. Meyer, *ibid.*, **35**, 583 (1902).

TABLE III
KYNURENIC ACIDS



Compound R_1	R_2	Yield, %	Mp, °C	Formula	—Carbon, %— Calcd	Found	—Hydrogen, %— Calcd	Found	—Nitrogen, %— Calcd	Found	—Bromine, %— Calcd	Found	Infrared bands, cm^{-1}
H	H	57.7	267.5–268.5	...	...	...	...	...	...	...	...	...	1720, 1615, 1590, 1460
Br	H	41.1	287–288	$C_{10}H_6BrNO_3$	44.80	44.78	2.26	2.28	5.23	5.46	29.81	29.75	1730, 1615, 1580, 1460
H	Br	33.6	247.5	$C_{10}H_6BrNO_3$	44.80	44.85	2.26	2.22	5.23	5.04	29.81	29.71	1715, 1610, 1595, 1430
Cl	H	49.2	276–277	$C_{10}H_6ClNO_3$[a]	53.71	53.31	2.71	3.07	6.27	6.16	...	...	1720, 1620, 1590, 1463

[a] Calcd for Cl: 15.86. Found: 15.88.

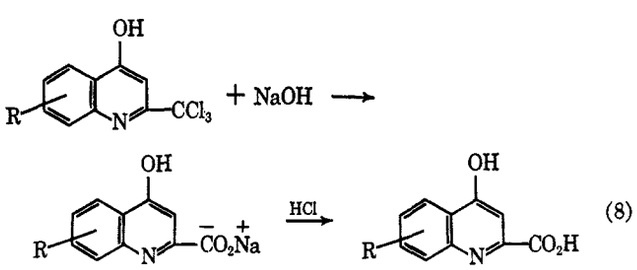


$H_2O + C_2H_5OH$ (7)

Hydroxyquinolines are believed to exist mostly in their tautomeric forms as quinolones. The infrared spectra of 2- and 4-quinolones have been studied by several workers. Ishii reported that the carbonyl absorptions of 4-quinolones were found in the 1630–1617-cm^{-1} region while those of 2-quinolones were in the 1660–1634-cm^{-1} region.[19] Grundon and McCorkindale gave a range of 1630–1620 cm^{-1} for 4-quinolones and 1660–1641 for the 2 isomers.[20] Rapoport and Holden have summarized the criteria for differentiating the 2- and 4-quinolones giving a range of 1660–1650 cm^{-1} for the 2-quinolones and 1630–1620 cm^{-1} for the 4-quinolones.[21] 2-Trifluoromethyl-4-quinolones absorbed between 1628–1600 cm^{-1} while the corresponding 2-quinolones absorbed between 1670–1660 cm^{-1}.[3g] The N–H absorption of 4-quinolones was reported to appear as a broad band between 3300–2500 cm^{-1}.[22] The infrared spectra of the compounds prepared in this investigation showed carbonyl absorptions in the 1620–1615-cm^{-1} region. Bands were also observed at 1590 cm^{-1} and broad bands were observed in the 3600–2600-cm^{-1} region.

Some workers who have studied the condensation of acetoacetates with aromatic amines in the presence of polyphosphoric acid have reported the formation of small amounts of 2-quinolones in some cases.[3g,23] They were able to remove the 2 isomer by washing the mixture with dilute alkali. The 2-quinolones are insoluble in base while the 4-quinolones dissolve and may be reprecipitated with acid. The procedure could not be used in our case because of the susceptibility of the trichloromethyl group to basic conditions. However, the sharp melting points of most of the compounds prepared and the fact that they could be hydrolyzed, in good yields, to known quinoline-2-carboxylic acids suggest that 4-quinolones may have been the only products. Only in the case of the 6-methyl derivative was the presence of a peak at 1650 cm^{-1} noted in the infrared spectra of these compounds. This evidence combined with fact that this compound melted over a 3° range suggested the presence of a small amount of a 2-quinolone. The principal absorption in the ultraviolet spectra of all the quinolones prepared occurred in the 238-mμ region, in agreement with the findings of Ewing and Steck for similar compounds.[24]

The basic hydrolysis of the 2-trichloromethyl-4-quinolones was carried out by heating a mixture of the quinolone and an excess of 10% sodium hydroxide for 15 min. This hydrolysis constituted the last step of a



(8)

new three-step synthetic route to kynurenic acids, the first step being the preparation of **1**, and the second its condensation with an aromatic amine. The entire synthesis may be carried out in about 6 hr and the yields are high in each step. The physical and analytical data for the kynurenic acids prepared in this investigation are shown in Table III.

The condensation of *o*-phenylenediamine with β-keto esters has been the subject of several investigations.[25] The products may be benzodiazepinones, benzimidazole derivatives, or both. The reaction of this amine with ethyl trifluoroacetoacetate has been reported to yield different products according to the conditions used.[3c] In the present investigation the reaction of *o*-phenylenediamine and **1** was carried out under neutral conditions by refluxing the two reagents in xylene and removing the water–alcohol formed. In agreement with the results obtained for ethyl trifluoroacetoacetate, under the same conditions, the only product obtained was 4-(trichloromethyl)-1H-1,5-benzodiazepin-2(3H)-one.

(19) H. Ishii, *Yakugaku Zasshi*, **81**, 248 (1961).
(20) M. F. Grundon and N. J. McCorkindale, *J. Chem. Soc.*, 2177 (1957).
(21) H. Rapoport and K. G. Holden, *J. Am. Chem. Soc.*, **82**, 4395 (1960).
(22) J. R. Price and J. B. Willis, *Australian J. Chem.*, **12**, 589 (1959).
(23) B. Staskun and S. S. Israelstam, *J. Org. Chem.*, **26**, 3191 (1961).
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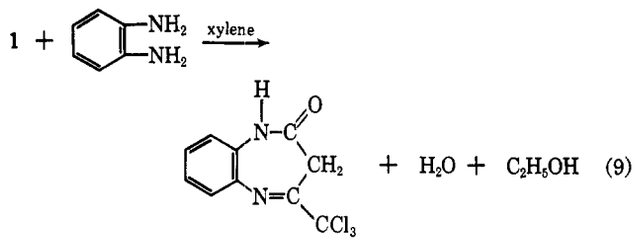

Experimental Section[26]

The Reaction of Chloral and Ethyl Diazoacetate.—Redistilled chloral (59.0 g, 0.4 mole) and ethyl diazoacetate (45.6 g, 0.4 mole) were mixed according to the procedure of Schlotterbeck.[4] The yellow liquid obtained was fractionally distilled under reduced pressure to yield 75 g (80.4%) of a mixture of **1** and **2**, bp 80° (1 mm). This mixture gave a positive ferric chloride test.

Anal. Calcd for $C_6H_7Cl_3O_3$: C, 30.86; H, 3.02; Cl, 45.56. Found: C, 30.64; H, 3.19; Cl, 45.63.

A 1.0-μl sample of this mixture was injected into a column packed with 10% silicone oil on Chromosorb W. The temperature of the column was 145° and the flow rate of helium 60 ml/min. The reaction mixture profile showed the presence of two peaks. Peak A had an area of 13 and a retention time of 0.7 min. Peak B had an area of 109 and a retention time of 5.3 min. Peak A was identified by injecting a sample of pure **1** under the same conditions and observing its retention time and also by addition of an authentic specimen to the reaction mixture, in varying amounts, which resulted in an increase in the area of peak A.

Preparation of Ethyl 3-(Trichloromethyl)glycidate (2).—The yellow liquid obtained by the reaction of chloral and ethyl diazoacetate was dissolved in ether and washed three times with ice-cooled 10% ammonium hydroxide solution. The ether layer was washed with water until the water layer was neutral when tested with litmus paper. The ether layer was dried over anhydrous magnesium sulfate and the ether was removed by distillation. The remaining yellow oil was fractionally distilled *in vacuo* to yield 45 g (48.2% yield based on original starting material) of **2**, bp 85° (1.5 mm), $n^{20}D$ 1.4726. This product gave a negative ferric chloride test. When a 1.0-μl sample of this product was subjected to gas–liquid partition chromatographic analysis under the previously described conditions, the reaction profile showed only peak B. Infrared bands (in CCl_4) were found at 1752, 1278, 1190, 870, and 840 cm^{-1}. The nmr spectrum showed signals at τ +5.69 (2 H), 5.84 (1 H), and 6.09 (1 H) and 8.52 (3 H).

Anal. Calcd for $C_6H_7Cl_3O_3$: C, 30.86; H, 3.02; Cl, 45.56. Found: C, 31.00; H, 3.11; Cl, 45.57.

Ethyl Trichloroacetoacetate (1).—This ester was synthesized by the method of Smrt, Beránek, and Šorm.[6] Redistilled trichloroacetyl chloride (27.3 g, 0.15 mole) was added to 90 ml of anhydrous liquid sulfur dioxide. Ketene was bubbled through the solution at a rate of 4.86 moles/hr for 2 hr, and then 60 ml (1.03 moles) of absolute ethanol was added slowly to the reaction mixture. After 30 min the liquid sulfur dioxide and excess ethanol were removed *in vacuo*. The black, viscous liquid left was fractionally distilled under reduced pressure to yield 30.0 g (85.8%) of **1**, bp 90° (2 mm) [lit.[5] bp 88–89° (2 mm), $n^{25}D$ 1.4681], d^{23}_{23} 1.380. This product gave an intense violet color when treated with ferric chloride solution. Infrared bands (in CCl_4) were found at 1767, 1741, 1662, and 1626 cm^{-1}. Ultraviolet bands (in ethanol) were found at λ_{max}^{EtOH} 246 mμ (ε 886) and λ_{max}^{hexane} 248 mμ (ε 2667). The nmr spectrum showed signals at τ −2.54 (0.1 H), +4.23 (0.1 H), 5.92 (2 H) partially hidden by peak at 6.11, 6.11 (1.8 H), and 8.79 (3 H). The approximate integration values are due to the keto–enol tautomerism exhibited by this ester.

Anal. Calcd for $C_6H_7Cl_3O_3$: C, 30.86; H, 3.02; Cl, 45.56. Found: C, 31.00; H, 3.24; Cl, 45.50.

The copper salt of **1** was prepared by shaking **1** vigorously with 200 ml of a saturated aqueous solution of cupric acetate dihydrate for 15 min; the mixture was allowed to stand for 1 hr. A green solid formed which was collected by filtration, washed twice with water, and air dried to yield 27.5 g (80.2%) of product. The copper salt was recrystallized from low-boiling (30–60°) petroleum ether, mp 124–125° (lit.[5] mp 92–93°). The discrepancy between the melting point obtained and the reported literature value is due to the fact that the melting point obtained is that of thoroughly dried sample. Infrared bands (in CCl_4) were found at 1610 and 1513 cm^{-1}.

Anal. Calcd for $C_{12}H_{12}Cl_6CuO_3$: C, 27.27; H, 2.29; Cl, 40.25. Found: C, 27.23; H, 2.46; Cl, 40.36.

β,β,β-Trifluoroethyl Trichloroacetoacetate (3).—The procedure described for the preparation of **1** was used with the exception that β,β,β-trifluoroethanol (100 g, 1.0 mole) was used instead of ethanol. Fractional distillation yielded 34.0 g (78.8%) of ester, bp 80° (2 mm). The copper salt of this compound was prepared as described for **1**, 78%, mp 77°. This copper salt was hydrolyzed with 50% sulfuric acid to yield pure ester which was purified further by fractional distillation, bp 82° (2.5 mm), $n^{25}D$ 1.4453. Infrared bands (in CCl_4) were found at 1777, 1755, 1683, 1626, 1408, 1322, 1280, 1235, 1166, 1086, 1050, 980, 830, and 610 cm^{-1}. Ultraviolet bands were found at λ_{max}^{EtOH} 252 mμ (ε 774) and λ_{max}^{hexane} 252 mμ (ε 2226). The nmr spectrum showed signals at τ −1.55 (0.05 H), 4.09 (0.05 H), 5.55 (2 H), 5.96 (1.9 H). The approximate integration values are also due to keto–enol tautomerism.

Anal. Calcd for $C_6H_4Cl_3F_3O_3$: C, 25.07; H, 1.40; Cl, 37.00; F, 19.83. Found: C, 25.13; H, 1.33; Cl, 36.85; F, 19.67.

Acid Hydrolysis of 1.—Compound **1** (11.7 g, 0.05 mole) was treated with 20 ml of 50% sulfuric acid added dropwise over a 15-min period. The mixture was heated for 8 hr until the evolution of carbon dioxide ceased. The solution was neutralized with a saturated sodium carbonate solution and extracted with ether. The ether extracts were dried over anhydrous sodium sulfate, the ether was evaporated, and the residue was fractionally distilled to yield 5.1 g (63.2%) of α,α,α-trichloroacetone, bp 132° (lit.[27] bp 134°). Infrared bands were found at 2940, 1758, 1420, 1350, 1230, 1160, 1010, 982, 800, 670, and 560 cm^{-1}. The nmr spectrum of this compound showed a singlet at τ 7.46 (3 H).

Alkylation of 1.—Sodium (4.6 g, 0.2 mole) was dissolved in 116 ml (2.0 mole) of absolute ethanol and the mixture was distilled on a steam bath to yield 60 ml of absolute ethanol which was treated with 2.3 g (0.1 mole) of sodium. Compound **1** (2.34 g, 0.1 mole) was added dropwise to the sodium ethoxide solution and *n*-butyl bromide (15.0 g, 0.11 mole) was then added also dropwise. The reaction mixture was refluxed for 6 hr and was neutral when tested with litmus paper. It was allowed to stand overnight and the sodium bromide formed was removed by filtration. The filtrate was fractionally distilled *in vacuo* to yield 6.2 g of a colorless liquid, bp 75–100° (3.0 mm), which was subjected to gas–liquid partition chromatographic analysis using a column packed with 20% silicone oil on Chromosorb P at a temperature of 165° and a helium flow rate of 40 ml/min. The chromatogram showed the presence of three peaks, A, B, and C. Peak A had a relative area of 16 and a retention time of 0.7 min, peak B had a relative area of 3 and a retention time of 2.4 min, and peak C had a relative area of 95 and a retention time of 4.7 min. Peak A was shown to be **1**, peak B was shown to be diethyl malonate, and peak C was collected using the Aerograph Autoprep (Model A-700) under similar conditions. The analytical data showed this compound to be *n*-butyl diethyl malonate.

Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.08; H, 9.32. Found: C, 61.06; H, 9.14.

The infrared spectrum of this compound was identical with that of an authentic sample of *n*-butyl diethyl malonate.

Reaction 1 with Ammonia.—Compound **1** (5.84 g, 0.025 mole) and 50 ml of anhydrous ether were heated on a water bath and

(26) Liquids were purified by distillation under reduced pressure using a Vigreux column (10 mm i.d. × 12.7 cm). Solids were recrystallized to constant melting point and dried *in vacuo* in an Abderhalden pistol containing phosphorus pentoxide. Melting points were determined in a Thomas-Hoover capillary melting point apparatus. Microanalyses were carried out by Galbraith Laboratories, Knoxville, Tenn., and by Dr. A. Bernhardt, Max Planck Institute, 433 Mülheim (Ruhr), West Germany. Infrared spectra were measured on a Perkin-Elmer 421 recording spectrophotometer. Nmr spectra were run at a frequency of 60 Mc/sec on a Varian nmr spectrometer Model HR-60. A Burrell Kromo-Tog, Model K-I (5 mm i.d. × 250 cm), with integral heating coil and thermal conductivity detector was used for the gas–liquid partition chromatographic analysis. The columns used were packed either with 20% Carbowax 20 M on Chromosorb W or 20% silicone oil on Chromosorb W.

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anhydrous ammonia was bubbled through this solution for 3 hr. The solution was concentrated and a white solid formed. This solid (2.8 g, 85.4%) was distilled *in vacuo*, bp 100° (0.3 mm), and recrystallized from anhydrous ether to yield colorless needles of ethyl malonamate, mp 45–46° (lit.[28] mp 45–47.5°).

Anal. Calcd for $C_5H_9NO_3$: C, 45.79; H, 6.92; N, 10.68. Found: C, 45.70; H, 6.90; N, 10.80.

Reactions of 1 with Primary Amines.—The general procedure for these reactions will be illustrated with *n*-butylamine. Compound **1** (5.84 g, 0.025 mole) in 50 ml of anhydrous ether was treated with *n*-butylamine (1.83 g, 0.025 mole) dissolved in 10 ml of ether. The mixture was stirred and allowed to stand for 1 hr. The ether was removed by distillation and the yellow oil remaining was fractionally distilled *in vacuo* to yield 3.1 g (66.2%) of ethyl N-*n*-butyl malonamate, bp 133° (2.5 mm) [lit.[29] bp 118° (1 mm)], $n^{20}D$ 1.4511.

Anal. Calcd for $C_9H_{17}NO_3$: C, 57.73; H, 9.15; N, 7.48. Found: C, 57.97; H, 9.31; N, 7.27.

This reaction was also performed with an excess of *n*-butylamine (14.6 g, 0.2 mole). The reaction mixture was refluxed for 15 min and the volume of the solution was reduced. A white solid was obtained which was recrystallized from low-boiling petroleum ether (30–60°) to yield 4.2 g (78.5%) of N,N′-di-*n*-butylmalonamide, mp 133–134° (lit.[30] mp 132.5°).

Anal. Calcd for $C_{11}H_{22}N_2O_2$: C, 61.64; H, 10.35; N, 13.07. Found: C, 61.49; H, 10.34; N, 13.25.

Compound **3** under the same conditions yielded 1.5 g (70.1%) of N,N′-di-*n*-butylmalonamide.

When **1** was heated with *n*-propylamine either in an equimolar ratio or with an excess of amine, the only product isolated was N,N′-di-*n*-propylmalonamide which was recrystallized from a methanol–ether–petroleum ether (bp 60–110°) mixture, mp 138° (lit.[30] mp 139°).

Anal. Calcd for $C_9H_{18}N_2O_2$: C, 58.03; H, 9.74; N, 15.04. Found: C, 57.98; H, 9.67; N, 14.94.

Reactions of 1 with Secondary Amines.—The general procedure for these reactions will be illustrated with piperidine. Compound **1** (4.67 g, 0.02 mole) in 50 ml of anhydrous ether was treated with redistilled piperidine (3.41 g, 0.04 mole) in 15 ml of anhydrous ether which was added dropwise over a period of 10 min. The reaction was exothermic and a white precipitate formed at once. The solid was collected by filtration and recrystallized from methanol to yield the piperidine salt (6.5 g, 78.5%), mp 132–133°.

The infrared spectrum of this compound showed a broad band in the 3150–2400-cm^{-1} region with major peaks at 2950, 2860, and 2750 cm^{-1} characteristic of ammonium ions. Peaks were also observed at 1663, 1600, 1550, 1465, 1450, 1380, 1300, 1165, 1090, 1040, 970, 940, and 863 cm^{-1}. The nmr spectrum showed signals at τ −1.29 (2 H), +4.4 (1 H), +5.73 (2 H), +6.62 (4 H), +7.97 (6 H), and +8.33 (3 H).

Anal. Calcd for $C_{11}H_{18}Cl_3NO_3$: C, 41.46; H, 5.69; N, 4.40. Found: C, 41.64; H, 5.54; N, 4.18.

Diethylamine reacted similarly to yield 5.0 g (81.6%) of the diethylamine salt of **1** which was recrystallized from methanol mp 84–85°. The infrared spectrum of this compound showed a broad band in the 3100–2600-cm^{-1} region with major peaks at 2975 and 2770 cm^{-1}. Other peaks were observed at 1665, 1600, 1590, 1550, 1460, 1382, 1315, 1160, 1085, 1035, and 860 cm^{-1}. The nmr spectrum showed signals at τ −1.23 (2 H), +4.50 (1 H), +5.90 (2 H), +6.97 (4 H), +8.62 (6 H), and +8.66 (3 H).

Anal. Calcd for $C_{10}H_{18}Cl_3NO_3$: C, 39.20; H, 5.92; N, 4.57. Found: C, 39.11; H, 5.97; N, 4.51.

Compound **3** reacted with piperidine under similar conditions to yield 5.2 g (69.8%) of the piperidine salt of this ester which was recrystallized from methanol, mp 119°. The infrared spectrum of this compound showed a broad band in the 3200–2500-cm^{-1} region with major peaks at 2950 and 2750 cm^{-1}. Other peaks were observed at 1680, 1600, 1544, 1461, 1448, 1395, 1295, 1277, 1135, 1071, 1025, 985, 958, 850, and 818 cm^{-1}.

Anal. Calcd for $C_{11}H_{15}Cl_3F_3NO_3$: C, 35.46; H, 4.06; Cl, 28.55; F, 15.30; N, 3.76. Found: C, 35.38; H, 4.22; Cl, 28.70; F, 15.23; N, 3.61.

The infrared spectra of these salts are similar to the spectrum of the copper chelate of **1**. The nmr spectra of these compounds show the absence of methylene protons and the presence of a vinyl proton.

Reactions of 1 with Aromatic Amines. Preparation of 2-Trichloromethyl-4-quinolones.—These reactions were carried out according to a modification of the method of Staskun and Israelstam.[23] The general procedure will be illustrated with the condensation of **1** and aniline. Compound **1** (11.67 g, 0.05 mole) and 25.0 g of polyphosphoric acid were placed in a 250-ml, three-necked, round-bottomed flask fitted with a mechanical stirrer, dropping funnel, reflux condenser, and calcium chloride drying tube. The mixture was stirred and redistilled aniline (4.60 g, 0.05 mole) was added to it, dropwise, over a period of 5 min. The reaction mixture was heated for 1 hr. After standing for 1 hr at room temperature the mixture was cooled in an ice bath and diluted with 100 ml of water. A yellow solid formed which was collected by filtration and recrystallized from aqueous ethanol using decolorizing carbon to yield a white solid. The physical and analytical data for all 2-trichloromethyl-4-quinolones prepared are shown in Table II.

Basic Hydrolysis of Some 2-Trichloromethyl-4-quinolones.—This reaction will be illustrated with the preparation of kynurenic acid. Recrystallized 2-trichloromethyl-4-quinolone (2.63 g, 0.01 mole) and 130 ml of 10% sodium hydroxide were mixed and heated for 15 min with occasional shaking. Decolorizing carbon was added to the mixture and heating was continued for another 10 min. The carbon was removed by filtration and the filtrate was acidified with 5% hydrochloric acid to yield a solid which was purified by dissolving it several times in an excess of sodium bicarbonate and reprecipitating it with 5% hydrochloric acid solution. The solid was washed repeatedly with water to remove any inorganic material and dried to yield 1.0 g (57.7%) of kynurenic acid, mp 277° (lit.[31] mp 277°). The physical and analytical data for the kynurenic acids prepared are shown in Table III.

Preparation of 4-(Trichloromethyl)-1H-1,5-benzodiazepin-2-(3H)-one.—*o*-Phenylenediamine (2.7 g, 0.025 mole) was dissolved in 50 ml of xylene in a 250-ml, three-necked, round-bottomed flask fitted with a Dean–Stark tube, reflux condenser, dropping funnel, and calcium chloride tube. The solution was heated to the boiling point of xylene and **1** (7.0 g, 0.03 mole) was added dropwise over a period of 30 min. The mixture was heated for an additional 30 min and half of the xylene was removed by distillation under reduced pressure. The mixture was allowed to stand for 24 hr and the solid which crystallized was collected by filtration, washed with cooled benzene, and recrystallized from benzene to yield 5.2 g (74.9%) of 4-(trichloromethyl)-1H-1,5-benzodiazepin-2(3H)-one, mp 193–194°. The infrared spectrum of this compound showed bands at 2900, 1680, 1637, 1470, 1410, 1335, 1285, 1250, 1100, 960, and 850 cm^{-1}. The nmr spectrum showed signals at τ 6.67 (2 H), 3.30 (4 H), and 1.0 (1 H), which could be assigned to the methylene, benzene, and amide protons, respectively.

Anal. Calcd for $C_{10}H_7Cl_3N_2O$: C, 43.27; H, 2.54; Cl, 38.32; N, 10.09. Found: C, 43.43; H, 2.65; Cl, 38.25; N, 9.95.

The benzodiazepinone gave a negative test when treated with ferric chloride solution. A solution of this product (2.78 g, 0.01 mole) dissolved in 50 ml of absolute ethanol was added to a solution of hydroxylamine hydrochloride (0.7 g, 0.01 mole) and anhydrous sodium acetate (0.82 g, 0.01 mole) dissolved in 10 ml of water. The mixture was refluxed for 5 min. A sample from this mixture gave a positive ferric chloride test.[32]

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