Some of the thiolactams listed in Table I were desulfurized by treatment with Raney nickel, as described in the Experimental section, to give the 2,3-dihydrobenzodiazepines shown in Table II.

Experimental

All melting points are corrected. The infrared and ultraviolet absorption spectra of starting materials and reaction products were compared in order to establish structural changes. The infrared spectra were determined in 3% chloroform solutions or in potassium bromide pellets, using a Perkin-Elmer Model 21 spectrophotometer; the ultraviolet absorption spectra were determined in isopropyl alcohol and in 0.1 *N* hydrochloric acid.

7-Chloro-1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepine-2-thione (II).—A solution of 271 g. of 7-chloro-1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one (I)[12] and 242 g. of phosphorus pentasulfide in 2 l. of anhydrous pyridine was stirred and heated under reflux for 45 min., with protection from atmospheric moisture. The mixture was then rapidly chilled in an ice bath and poured slowly into 5 l. of a well stirred, ice-cold saturated sodium chloride solution. The resulting precipitate was separated by filtration, washed with water, dried *in vacuo*, and dissolved in methylene chloride. The solution was filtered through a bed of activated alumina and concentrated. Addition of petroleum ether (b.p. 40–60°) gave compound II which was recrystallized from alcohol and obtained as pale yellow prisms (40%), m.p. 244–246°.

Anal. Calcd. for $C_{15}H_{11}ClN_2S$: C, 62.82; H, 3.87; S, 11.19. Found: C, 62.55; H, 3.95; S, 11.22.

7-Chloro-2-methylmercapto-5-phenyl-3*H*-1,4-benzodiazepine (IV).—To a stirred solution of 2.87 g. of II in a mixture of 12 ml. of aqueous 1 *N* sodium hydroxide and 15 ml. of methanol was added within 30 min. a solution of 1.39 g. of dimethyl sulfate in 5 ml. of methanol. Stirring was continued for 10 min., then the mixture was diluted with water and made strongly basic with sodium hydroxide solution. The precipitated product was separated by filtration, washed with water, and recrystallized from alcohol, to give pale yellow prisms, m.p. 132–134° (76%).

Anal. Calcd. for $C_{16}H_{13}ClN_2S$: C, 63.88; H, 4.36; S, 10.66. Found: C, 63.52; H, 4.39; S, 10.86.

Acid Hydrolysis to I.—A solution of 1 g. of IV in a mixture of 100 ml. of alcohol and 20 ml. of 1 *N* hydrochloric acid was kept at 20–25° for 6 days. Methyl mercaptan was evolved (detected by its characteristic odor, and yellow coloration with lead acetate paper). The solution was diluted with 100 ml. of water and neutralized (pH 7) with dilute sodium hydroxide. The resulting precipitate was filtered and recrystallized from methylene chloride–hexane to give 0.63 g. (70%) of I, identical[13] with an authentic sample.

7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepine-2-thione (VI).—A solution of 14.3 g. of 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one[12] (V) and 11.1 g. of phosphorus pentasulfide in 100 ml. of anhydrous pyridine was stirred and heated under reflux for 1 hr., with protection from atmospheric moisture. The solution was evaporated *in vacuo*, the resulting tarry residue was dissolved in methylene chloride and filtered through a bed of activated alumina. Concentration of the filtrate and addition of petroleum ether gave the product, which was recrystallized from alcohol and formed pale yellow prisms (73%), m.p. 162–164°.

Anal. Calcd. for $C_{16}H_{13}ClN_2S$: C, 63.88; H, 4.36; S, 10.66. Found: C, 63.96; H, 4.55; S, 10.86.

7-Chloro-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepine (III, $R_1 = CH_3$; $R_2 = H$).—Monomethylamine gas was bubbled slowly through a refluxing solution of 25 g. of IV in a mixture of 300 ml. of alcohol and 50 ml. of dimethyl sulfoxide. After the evolution of methyl mercaptan had ceased (18 hr.), the solution was concentrated *in vacuo*, and the residue dissolved in dilute hydrochloric acid. The aqueous acidic layer was extracted with ether, made basic with sodium hydroxide, and extracted with methylene chloride. The methylene chloride solution was concentrated to give the nearly pure product, which was recrystallized from acetone and formed colorless prisms (91%), m.p. 238–240°, identical[13] with an authentic sample.[7]

(12) L. H. Sternbach and E. Reeder, *J. Org. Chem.*, **26**, 4936 (1961).

(13) Identity was established by comparison of melting points, infrared spectra, and mixture melting point.

7-Chloro-5-phenyl-2-piperidino-3*H*-1,4-benzodiazepine (III, NR_1R_2 = Piperidino). A. From II.—A solution of 28.7 g. of II and 17 g. of piperidine in a mixture of 250 ml. of methanol and 50 ml. of dimethyl sulfoxide was refluxed on the steam bath until evolution of hydrogen sulfide ceased (after 1.5 hr.). The solution was concentrated, and the product isolated in the manner described in the previous experiment. Recrystallization from aqueous alcohol gave colorless prisms (60%), m.p. 115–116°. The yield was not increased by longer reaction periods.

Anal. Calcd. for $C_{20}H_{20}ClN_3$: C, 71.12; H, 5.96; N, 12.44. Found: C, 71.47; H, 6.23; N, 12.47.

B. From IV.—A mixture of 3.01 g. of IV and 21 g. of piperidine was refluxed until evolution of methyl mercaptan ceased (after 1.5 hr.). The resulting solution was concentrated, and the product isolated as previously, to give colorless prisms (89%), m.p. 115–116° (from alcohol), identical[13] with the authentic sample prepared by method A. The yield was unaffected by prolongation of the reaction time.

7-Chloro-2,3-dihydro-1-methyl-5-phenyl-1*H*-1,4-benzodiazepine (VIII).—A mixture of 20 g. of VI, 500 ml. of acetone, and 160 g. of wet Raney nickel was stirred and refluxed for 2 hr. Filtration and evaporation of the filtrate gave the crude product, which was purified by dissolving it in dilute hydrochloric acid and extracting the solution with ether to remove nonbasic impurities. The acidic solution was then made basic with dilute sodium hydroxide and extracted with methylene chloride, to give VIII (69%), which was identical[13] with an authentic sample.[9]

7-Chloro-2,3-dihydro-5-phenyl-1*H*-1,4-benzodiazepine (VII).—Desulfurization of II with Raney nickel, followed by purification of the product in the manner described previously, gave VII as yellow plates (52%), m.p. 166–167° (from aqueous ethanol), identical[13] with an authentic sample.[9]

Acknowledgment.—We are indebted to Dr. A. Motchane, Mr. S. Traiman, and Dr. V. Toome for the infrared and ultraviolet spectra, and to Dr. Al Steyermark and his staff for the microanalyses. Mr. L. A. Dolan was helpful in the preparation of larger amounts of starting materials and intermediates.

Autoradiolysis of 6,7,8,9,10,10-Hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepine 3-Oxide-5a,9a-C^{14}

SYLVAN E. FORMAN AND JACK R. GRAHAM[1]

The FMC Corporation, Chemical Divisions, Central Research and Development Center, Princeton, New Jersey

Received June 13, 1962

The autoradiolysis of compounds containing radioactive isotopes is a well known phenomenon.[2] We wish to report a new and interesting observation of this sort of behavior with C^{14}-labeled samples of the insecticide Thiodan (I).

The infrared spectra of samples of Thiodan-5a,9a-C^{14} (6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepine 3-oxide-5a,9a-C^{14}) taken shortly after preparation[3] showed no indication of the presence of Thiodan ether (II) (4,5,6,7,8,8-hexachloro-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofurane). The radio-Thiodan was stored in vials kept in a desiccator which was placed in a darkened cabinet. About 2.5 years later new infrared spectra showed the presence of Thiodan ether.

(1) Niagara Chemical Division, Middleport, N. Y.

(2) A. Murray, III, and D. L. Williams, "Organic Syntheses with Isotopes," Part I, Interscience Publishers, Inc., New York, N. Y., 1958, p. 19.

(3) S. E. Forman, B. L. Gilbert, G. S. Johnson, C. A. Erickson, and H. Adelman, *J. Agr. Food Chem.*, **8**, 193 (1960).

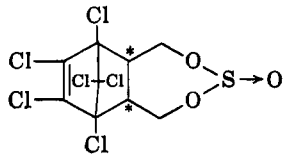
TABLE I

GAS CHROMATOGRAPHIC ANALYSES OF THIODAN SAMPLES

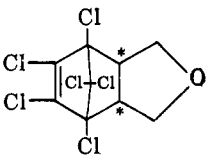
Sample	Activity, μc./mg.	Analyses, %[a] Age, weeks	Ether[b]	L.m.i.[c]	H.m.i.[d]	G(−M)[e]	Age, weeks	Ether[b]	L.m.i.[c]	H.m.i.[d]	G(−M)[e]
1							257	3	67	26	
2A[f]		123[g]	2	39	42						
2B							203	2	61	37	
3							165	1	57	42	
4							134	1	66	33	
5							32	2	57	41	
6A	5.91	129	51	38	12	120	212	75	9	14	100
6B[h]	5.99						199[i]	40	0	0	
7	1.9	129	18	30	53	140					
8A	0.95	119	23	53	21	350	197	45	22	30	430
8B[j]	0.95	1	9	53	35		79	13	56	28	90

[a] Thiodan alcohol was usually present, 0 to 4%, except where noted. [b] Thiodan ether. [c] Lower melting Thiodan isomer. [d] Higher melting Thiodan isomer. [e] Molecules permanently altered per 100 e.v. See J. R. Catch, "Carbon-14 Compounds," Butterworths Inc., Washington, D. C., 1961, p. 69. [f] Samples 2A and 2B were portions of the same commercial preparation. 2A was kept in a tightly sealed drum. [g] Thiodan alcohol, 17%. [h] 6B is a sample of 6A which was recrystallized from hexane shortly after preparation. [i] Thiodan alcohol, 60%. [j] 8B is a column chromatographed sample of 8A. The age of 8B is taken from the time of the chromatogram.

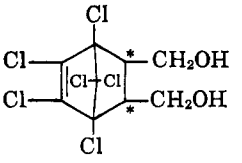
SCHEME I



I
Thiodan
(2-isomers)



II
Thiodan ether



III
Thiodan alcohol

Gas chromatography was known to be suitable for the separation of the two Thiodan isomers[4] and a modification of this method can be employed to distinguish Thiodan alcohol (III) (1,4,5,6,7,7-hexachlorobicyclo[2,2,1]hept-5-ene-2,3-dimethanol) from the two Thiodan isomers (see Scheme I, asterisks show positions of C^{14}). Table I gives the data obtained by g.l.c. analysis on two different occasions of a number of nonradioactive technical samples, and radioactive samples of Thiodan. Nonradioactive samples contained scarcely any Thiodan ether, even after prolonged storage. The radioactive samples accumulated Thiodan ether[5] with increasing age. When access to moisture was permitted, either type of sample decomposed to Thiodan alcohol.

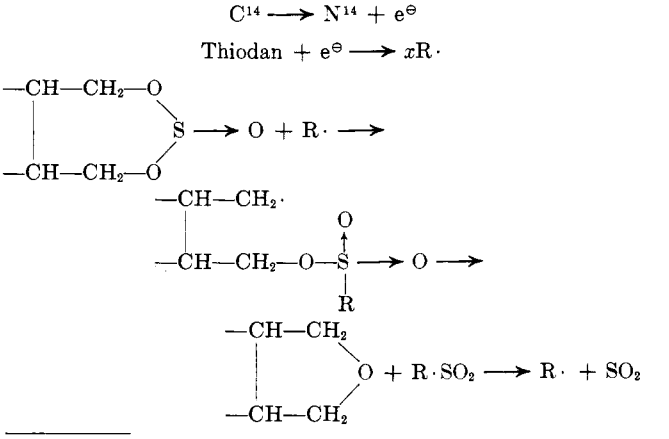
Infrared spectral analysis indicated that the ratio of higher melting to lower melting Thiodan isomers in the radioactive samples had increased from the ratio that was present shortly after preparation. Absorption bands which we usually used to determine the Thiodan isomer ratio are the bands at 1245 and 1266 $cm.^{-1}$, but these could not be used because Thiodan ether absorbs at 1250 $cm.^{-1}$. However, the Thiodan isomer ratio was determined by using the absorptions at 840 and 862 $cm.^{-1}$.

Crystallization of the 0.95-μc./mg. sample of radio-Thiodan from hexane gave mostly higher melting Thiodan isomer in the first crop and largely lower melting Thiodan isomer in the succeeding crops; but, all of the fractions contained Thiodan ether, and it was not possible to remove this contaminant by subsequent recrystallizations.

Column chromatography on Florisil[6] had been used previously to separate the two Thiodan isomers. With hexane and ethyl ether as the solvents, the lower melting isomer is eluted first from the column. The same adsorbent and solvent system was used to separate the higher melting radiotagged Thiodan isomer from Thiodan ether. Although a gas chromatogram showed only a single peak for the purified material, the infrared spectrum showed a weak band at 810 $cm.^{-1}$. Since none of the other infrared bands characteristic for Thiodan ether were apparent, this extraneous band was attributed to a small amount of an unidentified impurity.

Thiodan ether could not be removed by similar column chromatography from a fraction containing largely lower melting radio labeled Thiodan isomer, although some concentration of the Thiodan ether in the earlier fractions was observed.

The radiolysis probably occurs in the manner shown in the equations. β-Rays from the radioactive C^{14} generate free radials which attack the sulfur atoms and



(4) G. Zweig and T. E. Archer, *J. Agr. Food Chem.*, **8**, 190 (1960).

(5) The radioactive Thiodan ether would be 4,5,6,7,8,8-hexachloro-1,3,3a,4,7,7a-hexahydro-4,7-methanoisobenzofurane-3a,7a-C^{14} or Thiodan ether-3a,7a-C^{14}.

(6) Floridin Company, Tallahasse, Fla.

cause one of the C–O bonds to break. The resultant radical is in a favorable position to form Thiodan ether with expulsion of another radical which decomposes to sulfur dioxide and the original radical.

A similar mechanism could result if the radical attacked an oxygen atom.

Except upon the rare occasions when two radicals combine, other collisions of a radical with a Thiodan molecule can result in a chlorine radical, a hydrogen radical, or a radical in which the odd electron is attached to a carbon in the Thiodan molecule. The radicals should, therefore, have high efficiency in the production of Thiodan ether, for other types of radical decompositions would not readily occur, although radical transfers may be frequent, and radical rearrangements can occur.

The $G(-M)$ values were calculated for each sample, when this was possible, and are shown in Table I. Although most of the values are not far apart, the values for sample 8A are considerably larger than the others. This result may be due to the fact that β-rays and volatile free radicals can escape less easily from a large compact mass of matter than from smaller pieces. Samples 6A, 7, and 8A were solid lumps of 2.3, 14, and 31 g., respectively; samples 6B and 8B were loose crystals, 0.6 and 0.13 g., respectively.

Experimental

Recrystallization of Radio-Thiodan.—A 30-g. sample of radio-Thiodan, 0.95 μc./mg., 119 weeks after preparation, consisted of 23% Thiodan ether, 53% lower melting Thiodan isomer, 21% higher melting Thiodan isomer, and 3% Thiodan alcohol. The sample was recrystallized from 150 ml. of hexane. Infrared spectra showed that the first fraction was mostly higher melting Thiodan isomer with some Thiodan ether present and the three subsequent fractions were largely lower melting Thiodan isomer with diminishing amounts of Thiodan ether. Recrystallization of the third fraction from hexane gave as the first crop 1.7 g. with 11% Thiodan ether, 86% lower melting Thiodan isomer, and 3% higher melting Thiodan isomer as shown by gas phase chromatography.

Column Chromatography of Radio-Thiodan.—A 140-g. portion of Florisil[6] activated for 2 hr. at 300° was packed in a chromatographic column, 75 × 2.5 cm. After 500 ml. of hexane had been allowed to pass through the column, 2.0 g. of a fraction of radio-Thiodan from the preceding fractional crystallizations was applied in ethyl ether solution. The chromatogram was developed with hexane containing increasing per cents of ethyl ether.

The second radioactive fraction from the column chromatogram of the higher melting Thiodan isomer showed one peak in the gas phase chromatogram; but the infrared spectrum showed an extraneous weak band at 810 cm.$^{-1}$.

Similar column chromatography of samples of lower melting radio-Thiodan isomer gave, at best, a greater concentration of Thiodan ether in the earlier fractions than in the later ones.

Infrared Spectra.—Infrared spectra were determined with a Baird Model 4-55 apparatus. Samples for qualitative examination were best determined in a potassium bromide pellet, but frequently a film on a sodium chloride flat was used. Quantitative determinations were run in carbon disulfide solution in a 0.5-mm. cell.

The following characteristic bands were used: higher melting Thiodan isomer, 1245 and 840; lower melting Thiodan isomer, 1266 and 862; Thiodan ether, 649 (other bands at 1212, 1053, and 810); Thiodan alcohol, 3280 cm.$^{-1}$. Other bands were used to confirm the presence of the various compounds.

Gas Chromatography.—F & M Model 202 instrument was used with 10 ft. of 0.2-in. o.d. stainless steel tubing packed with 60–80-mesh Chromasorb W containing 20% Dow 11 silicone. The column temperature was 250° with a helium flow of 100 ml. per minute. Samples were injected in chloroform solution. Elution times were as follows: Thiodan ether, 9; lower melting Thiodan isomer, 21; higher melting Thiodan isomer, 32 min. Thiodan alcohol gave two or three unresolved peaks at *ca.* 15.5, 18–20, and 26 min. Peak areas were corrected for thermal response by multiplying with the following factors: Thiodan ether, 1.48; lower melting Thiodan isomer, 1.72; higher melting Thiodan isomer, 1.77.

Acknowledgment.—The authors wish to thank Mr. Arthur Weed and Mr. John Zarembo for doing the gas phase chromatographic work and Mr. Herman Adelman for the determination and interpretation of the infrared spectra. The mechanism for the formation of Thiodan ether evolved as a result of discussions with Professor R. H. Herber of Rutgers University.

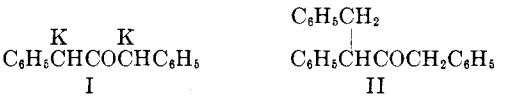
Formation and Benzylation of the Dianion of *sym*-Diphenylurea by Potassium Amide in Liquid Ammonia. Results with Related Compounds

DAVID R. BRYANT,[1a] STEWART D. WORK,[1b] AND CHARLES R. HAUSER

Department of Chemistry, Duke University, Durham, North Carolina

Received June 24, 1963

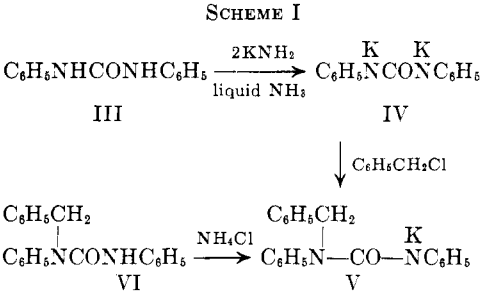
Dibenzyl ketone previously has been converted by two molecular equivalents of potassium amide in liquid ammonia to its dipotassio salt I, which was alkylated in this medium with a molecular equivalent of benzyl chloride to form the monobenzyl derivative (II) in 82% yield.[2] The monopotassio salt of dibenzyl ketone not only underwent benzylation much more slowly under similar conditions, but the dibenzyl derivative as well as II was obtained.[2]



I II

In the present investigation *sym*-diphenylurea (III), which may be regarded as a dinitrogen analog of dibenzyl ketone, likewise was converted to its dipotassio salt IV, which was benzylated to give the monobenzyl derivative (VI) in 75% yield (Scheme I). Benzylation

SCHEME I



of the monopotassio salt of III under similar conditions afforded VI in only 2% yield.

Structure VI was supported by analysis and by its infrared spectrum which exhibited a band at 2.96 μ, in-

(1) (a) National Science Foundation Predoctoral Fellow, 1958–1961; (b) National Science Foundation Cooperative Graduate Fellow, 1959–1962.

(2) C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **81**, 1154 (1959).