in detail,[20] except that the benzene solvent was replaced with 1:1 benzene–ether.[21] The crude hydroxy ester (1.9 g) was dehydrated with 2.2 g of phosphorus oxychloride in 10 g of pyridine, also following the published procedure.[20] Isolation of the product by continuous extraction yielded 670 mg of unsaturated esters which yielded three bands in gas chromatography (20 ft × ³/₈ in. column, 10% NPGS at 138°, helium flow rate 180 cc/min) with respective retention times of 36, 61.7, and 65.5 min. The first band represents the ring-unsaturated isomers, while the latter two bands are the α,β-unsaturated isomers [λ_{max} 220 mμ (ϵ 12,000)]. The nmr spectra[13] of the compounds collected in these two bands are those expected for the structures, and the mass spectra (cf. Table I) show that the band of 61.7-min retention time is isomer 5, while the compound from the band of longer retention time is isomer 6. Further, the mass spectrum of isomer 5 is identical with that of the compound from the 70-min band in Figure 5.

Methyl trans-3-Ethyl-4-methylcyclopentylideneacetates 3 and 4.—The entire sample (650 mg) of gas chromatographed trans ketone 15 was subjected to the Reformatsky reaction and dehydrated as described for the cis isomer. The unsaturated esters (700 mg) were gas chromatographed under the same conditions specified for the isomer above, and gave bands of retention times 29, 53.5, and 57.5 min. The components in the band

of shortest retention time are the ring-unsaturated isomers, while the bands of longer retention time are due to the α,β-unsaturated isomers [λ_{max} 220 mμ (ϵ 13,500)]. The nmr spectra[13] are those expected for the structures, and the mass spectra (cf. Table I) show that the component of the 53.5-min band is isomer 3, while the other compound is isomer 4. Further, the spectra demonstrate that these isomers are identical with the unsaturated esters from degradation which are responsible for the 61.5- and 66-min bands in Figure 5.

Hydrogenation of unsaturated esters 5 and 6, using 10% palladium-on-charcoal catalyst and 95% ethanol as solvent, yielded saturated ester whose gas chromatography (10 ft × ³/₈ in. column, 20% silicone SE-30 at 156°, helium flow rate 150 cc/min) showed two bands of retention time 24.5 and 28.7 min. A following chromatography of fraction III-2-A gave a retention time of 24.5 min. Chromatography on NPGS also gave the same retention times for fraction III-2-A and the band of shorter retention time. Since this band is much the smaller of the two it is assigned the trans geometry of structure 22. Full mass spectra and nmr spectra were recorded.[13]

Hydrogenation of unsaturated esters 3 and 4, as described for the isomers, yielded saturated ester which gave only one band in gas chromatography (10 ft × ³/₈ in. 20% silicone column at 152°, helium flow rate 150 cc/min, retention time 30 min; 20 ft × ³/₈ in. 10% NPGS column at 137°, helium flow rate 180 cc/min, retention time 32 min). Following chromatography of fraction III-2-A showed the same retention times on both columns. Further, mass spectra were the same. Full mass spectra and nmr spectra were recorded.[13]

(20) K. L. Rinehart, Jr., and E. G. Perkins, "Organic Syntheses," Coll. Vol. 4, John Wiley and Sons, Inc., New York, N. Y., 1963, p 444.

(21) J. Cason and R. J. Fessenden, J. Org. Chem., 22, 1326 (1957).

Pseudo-Halogens. VII. Scope and Mechanism of Addition of N,N-Dichlorourethan to Monoolefinic Compounds[1,2]

Thomas A. Foglia and Daniel Swern

Fels Research Institute and Department of Chemistry, Temple University, Philadelphia, Pennsylvania 19122
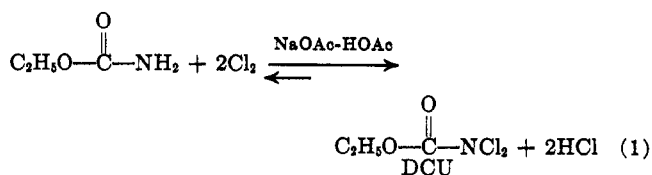
N,N-Dichlorourethan (DCU), a stable, distillable, but reactive pseudo-halogen has been prepared in excellent yield by an improved procedure from chlorine and urethan in buffered aqueous acid solution. DCU adds almost quantitatively to the double bonds of styrene and trans-stilbene to yield β-chloro-N-chlorocarbamates which are reduced with aqueous sodium bisulfite to β-chlorocarbamates. With straight-chain terminal olefins (C_8, C_{10}, C_{12}, C_{18}) and 2-methyl-1-pentene, yields of β-chlorocarbamates are about 60%. Nonterminal olefins with allylic hydrogens give 30–40% yields of β-chlorocarbamates, the predominant reaction involving allylic attack. Norbornene yields 3-chloronortricyclene by homoallylic attack; reaction of norbornene with DCU is a convenient route to this three-ring compound. Reaction of DCU with olefins is a free-radical chain reaction proceeding in an anti-Markovnikov manner as shown by physical and chemical proof. Mechanisms are proposed for the various reactions.

Considerable attention is being given in our laboratory to the preparation and reactivity of pseudo-halogens containing nitrogen. The major objectives of the program are (a) to develop single-step and, hopefully, stereospecific syntheses of compounds containing the carbon–nitrogen bond directly from unsaturated systems, and (b) to study the scope and mechanisms of these double-bond addition reactions. In previous papers we have reported our results with iodine isocyanate[3] and with nitrosyl acylates.[4]

In this paper we are reporting (a) an improved high-yield preparation of N,N-dichlorourethan (DCU), a

stable, distillable yet highly reactive pseudo-halogen, and (b) the scope, limitations, and mechanism of its addition to monoolefinic compounds.

Preparation of DCU.—DCU was first prepared by Datta and Gupta[5] and subsequently by Houben[6] and by Chabrier,[7] but explicit details concerning yields, methods of isolation, and purity and physical characteristics of product were not reported. We have improved Chabrier's[7] procedure and can obtain DCU of analytical purity in excellent yield (80%) by reaction of the calculated quantity of chlorine with urethan in buffered aqueous solution (eq 1). Neutralization of

$$C_2H_5O{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}NH_2 + 2Cl_2 \underset{\longleftarrow}{\overset{NaOAc\text{-}HOAc}{\longrightarrow}}$$

$$C_2H_5O{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}NCl_2 + 2HCl \quad (1)$$
$$\text{DCU}$$

(5) R. L. Datta and S. D. Gupta, J. Am. Chem. Soc., 37, 569 (1915).

(6) J. Houben, J. Prakt. Chem., 105, 7 (1922).

(7) P. Charbrier, French Patent 56,285 (1952).
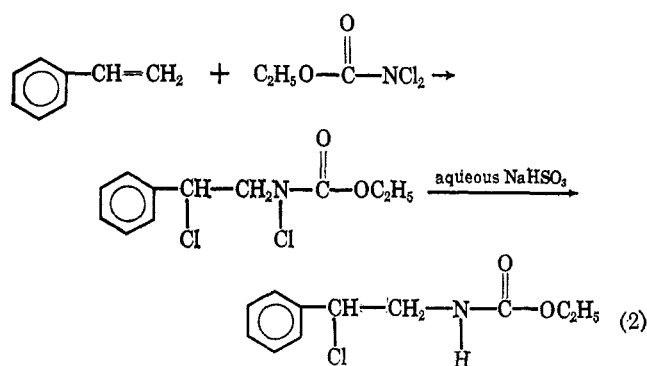
TABLE I

β-CHLOROCARBAMATES BY ADDITION OF DCU TO OLEFINS

Olefin	Method[a]	β-Chlorocarbamate	Yield, %[b]	C, % Calcd	C, % Found	H, % Calcd	H, % Found	N, % Calcd	N, % Found	Cl, % Calcd	Cl, % Found
$C_6H_5CH=CH_2$	A	$C_6H_5CHClCH_2$ │ $NHCO_2Et$	80	58.0	58.1	6.20	6.12	6.15	6.02	15.6	15.4
trans-$C_6H_5CH=CHC_6H_5$	A	$C_6H_5CH—CHC_6H_5$[c] │ │ Cl $NHCO_2C_2H_5$	65	67.2	67.2	5.97	5.99	4.67	4.65	11.7	11.6
(cyclohexene)	B	(cyclohexane-Cl-NHCO₂Et)	30	...	...	...	...	...	...	...	...
$CH_3(CH_2)_3CH=CH_2$	B	$CH_3(CH_2)_3CH—CH_2$ │ │ Cl $NHCO_2Et$	65	52.0	52.1	8.74	8.68	6.74	6.69	17.1	16.8
$CH_3(CH_2)_7CH=CH_2$	B	$CH_3(CH_2)_7CH—CH_2$ │ │ Cl $NHCO_2Et$	65	59.2	59.1	9.93	9.78	5.31	5.33	13.4	13.4
$CH_3(CH_2)_9CH=CH_2$	B	$CH_3(CH_2)_9CH—CH_2$ │ │ Cl $NHCO_2Et$	61	61.7	61.6	10.4	10.2	4.80	4.95	12.2	12.1
$CH_3(CH_2)_{15}CH=CH_2$	B	$CH_3(CH_2)_{15}CH—CH_2$ │ │ Cl $NHCO_2Et$	53	67.1	66.7	11.3	10.9	3.73	3.75	9.43	10.0
$CH_3(CH_2)_2—C=CH_2$ │ CH_3	A	$CH_3(CH_2)_2—CCH_3—CH_2$ │ │ Cl $NHCO_2Et$	60	52.0	52.4	8.74	8.67	6.74	6.87	17.1	17.0
trans-$CH_3CH_2CH=CHCH_2CH_3$	B	$CH_3CH_2CH—CHCH_2CH_3$[c] │ │ Cl $NHCO_2Et$	40	52.0	51.9	8.74	8.87	6.74	6.65	17.1	17.2
$CH_2=CH—C(\!=\!O)—OCH_3$[d]	B	$CH_2—CHCl—C(\!=\!O)—OCH_3$ │ $NHCO_2Et$	25	40.1	40.2	5.77	5.67	6.68	6.49	16.9	17.2

[a] Method A, addition of DCU to olefin at low temperature.   Method B, addition of olefin to DCU at refluxing benzene temperature.   [b] Yields are based on analytically pure products.   [c] Mixture of *erythro* and *threo* isomers.   [d] Inhibited by 15 ppm of the dimethyl ether of hydroquinone.

the hydrochloric acid as it is formed shifts the equilibrium far to the right.   DCU is insoluble in the aqueous system and it precipitates as a dense, golden yellow oil having a sharp odor.   Samples of distilled, analytically pure DCU have been stored at room temperature in the dark for several weeks with only slight loss (about 5%) of positive chlorine.   Redistillation provides pure DCU with little or no loss.

Addition of DCU to Monoolefinic Compounds.— The only previous work in this area is that of Chabrier[8] who added DCU to styrene and to two ring-substituted styrenes.   Specific experimental details were not given but high yields of adducts were reported.   Chabrier concluded that the addition reaction proceeded in an anti-Markovnikov manner although his method of proof was not rigorous.   (As we will describe below, his conclusion is correct.)   The initial adduct is an N-chloro derivative; the chlorine attached to nitrogen still has positive halogen character that can be determined iodometrically.   Washing the adduct with aqueous sodium bisulfite reduces it to the β-chlorocarbamate (eq 2).
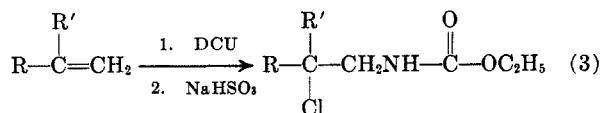
We have studied the addition of DCU to styrene, trans-stilbene, cyclohexene, four straight-chain terminal olefins (C_6, C_{10}, C_{12}, C_{18}), one branched-chain terminal olefin (2-methyl-1-pentene), trans-3-hexene, methyl

(8) P. Chabrier, *Ann. Chim.*, **17**, 353 (1942).

acrylate, and norbornene (Table I).   Disappearance of olefinic compound was followed by glpc, except in the case of trans-stilbene where the consumption of positive halogen was followed iodometrically.   Two addition procedures were employed, the choice depending on the reactivity of the unsaturated compound (see the Experimental Section).

Addition of DCU to styrene, trans-stilbene, and the five terminal olefins is a rapid reaction, complete within 1 hr.   Yields of isolated, analytically pure β-chlorocarbamates are in the range of 60–80%. trans-Stilbene yields an approximately equimolar mixture of the *erythro* and *threo* products.   Styrene and the terminal olefins add DCU in anti-Markovnikov fashion (see structure proof below; eq 3).

$$R\text{—}\underset{\underset{R'}{|}}{C}\text{=}CH_2 \xrightarrow[\text{2. NaHSO}_3]{\text{1. DCU}} R\text{—}\underset{\underset{Cl}{|}}{\overset{\overset{R'}{|}}{C}}\text{—}CH_2NH\text{—}\overset{\overset{O}{\|}}{C}\text{—}OC_2H_5 \quad (3)$$

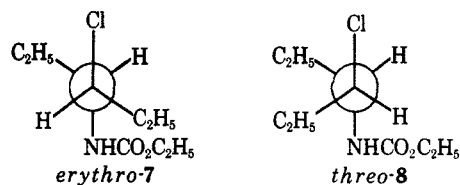when R = C_6H_5, n-C_4, -C_8, -C_{10}, and -C_{16}, R' = H; when R = n-C_3, R' = CH_3

The yield of isolable, analytically pure β-chlorocarbamate decreases with increase in the number of allylic hydrogens in the olefinic compound. In all addition reactions, except to stilbene and styrene, urethan is a by-product, its quantity increasing with the number of allylic hydrogens available.

Addition of DCU to cyclohexene proceeded readily but the glpc trace of the crude reaction mixture showed numerous peaks, the major one corresponding to 37% conversion of cyclohexene to the trans-β-chlorocarbamate (1). A peak was also obtained with a retention time very close to that of the main product, corresponding to 6% of the cyclohexene used. From the retention time, it was assumed to be the cis-β-chlorocarbamate (2). The next major peak (28% of cyclohexene) corresponded to the allylic chlorination product, 3-chlorocyclohexene (3). Two minor products also identified were the nonallylic chlorination products, 1-chlorocyclohexene (4, 5%) and 4-chlorocyclohexene (5, 4%). Thus, 80% of the cyclohexene was accounted for.
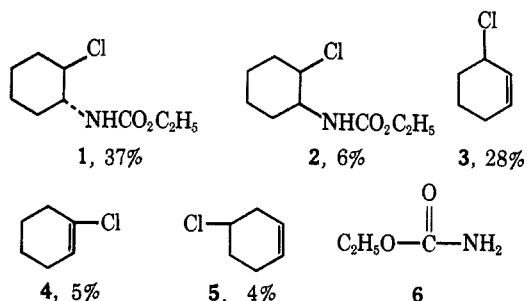

Urethan (6) was isolated by water washing of the crude reaction mixture followed by evaporation of the water. Compound 1 was isolated in pure form in 30% yield (based on cyclohexene) by recrystallization of the mixed reaction products. It was characterized by the identity of its melting point (96–97°) and infrared spectrum with that of the known compound.[9] Its infrared and nmr spectra are essentially identical with those of the trans-β-iodocarbamate prepared from cyclohexene and iodine isocyanate followed by reaction with ethanol.[10]

Addition of DCU to trans-3-hexene gave a 40% yield of β-chlorocarbamates, readily isolated in analytical purity by vacuum distillation. The analytically pure product showed only two sharp peaks of almost equal area (40:60) by glpc, the retention times of which were 1 min apart at 175°. The infrared spectrum and elemental analysis were consistent with the proposed β-chlorocarbamate structure, and the glpc result suggests that the product is an approximately equimolar mixture of the erythro and threo isomers (7 and 8).

(9) W. Lwowski and T. Mattingly, Jr., J. Am. Chem. Soc., **87**, 1947 (1965).

(10) A. Hassner and C. Heathcock, Tetrahedron, **20**, 1037 (1964).

erythro-7   *threo*-8

Methyl acrylate used for reaction with DCU was inhibited with the dimethyl ether of hydroquinone and it reached very slowly (72 hr). The yield of analytically pure adduct (9) was only 25%.


9   10
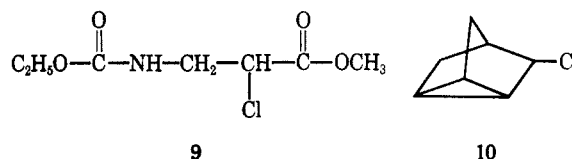
Reaction of DCU with norbornene gave an interesting result. The product isolated in 30% yield by vacuum distillation had an elemental analysis corresponding to the empirical formula C_7H_9Cl and showed no carbonyl absorption in the infrared; it was obviously not the expected β-chlorocarbamate. Its infrared spectrum, with a major peak at 813 cm^{-1} (12.3 μ), was identical in every respect with that reported by Roberts and Bennett[11a] for 3-chloronortricyclene (10). Its nmr spectrum was consistent with the proposed tricyclic structure.[12] A reexamination of the crude norbornene reaction product by glpc showed that it consisted of 45% of 3-chloronortricyclene. Approximately 39% of the crude reaction products (three peaks) had long, almost identical retention times. Although these products were not positively identified, their infrared and nmr spectra were consistent with those of chlorocarbamates of norbornene.

The preparation of 3-chloronortricyclene in 30% yield from norbornene and DCU is a convenient route for obtaining this tricyclic system.

As will be discussed in another report,[13] β-chlorocarbamates are readily converted to aziridines and 5-substituted 2-oxazolidones in good yield.

Proof of Structure of Addition Products.—Addition of DCU to styrene could yield 11, the anti-Markovnikov
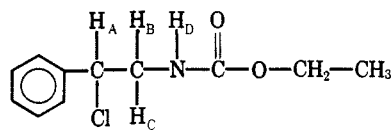
11

product, or its isomer (12). Solvolysis of the adduct with aqueous alcoholic silver nitrate solution resulted in immediate and quantitative precipitation of silver chloride, strongly suggesting that the chlorine is benzylic, as shown in 11. Confirmation of the structural assignment was obtained from study of the nmr spectra of 11 (Figure 1) and of its solvolysis product (13, Figure 2). The nmr spectra are consistent with struc-

(11) (a) J. D. Roberts and W. Bennett, J. Am. Chem. Soc., **76**, 4623 (1954); (b) J. D. Roberts, E. R. Trumbull, Jr., W. Bennett, and R. Armstrong, ibid., **72**, 3116 (1950); (c) G. T. Youngblood, V. D. Trivette, Jr., and P. Wilder, Jr., J. Org. Chem., **23**, 684 (1958).

(12) R. S. Neale and E. B. Whipple, J. Am. Chem. Soc., **86**, 3130 (1964).

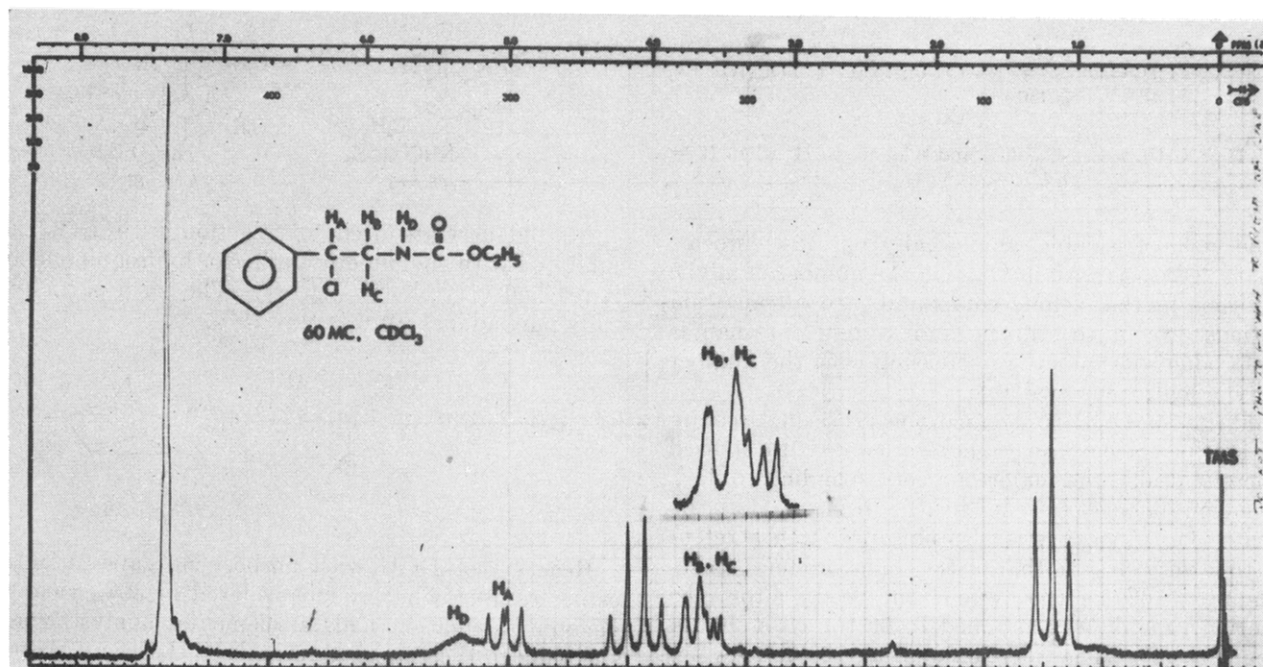(13) T. A. Foglia and Daniel Swern, submitted for publication.

Figure 1.—Nmr spectrum of ethyl (N-2-chloro-2-phenylethyl)carbamate (11) (prepared from styrene and DCU).
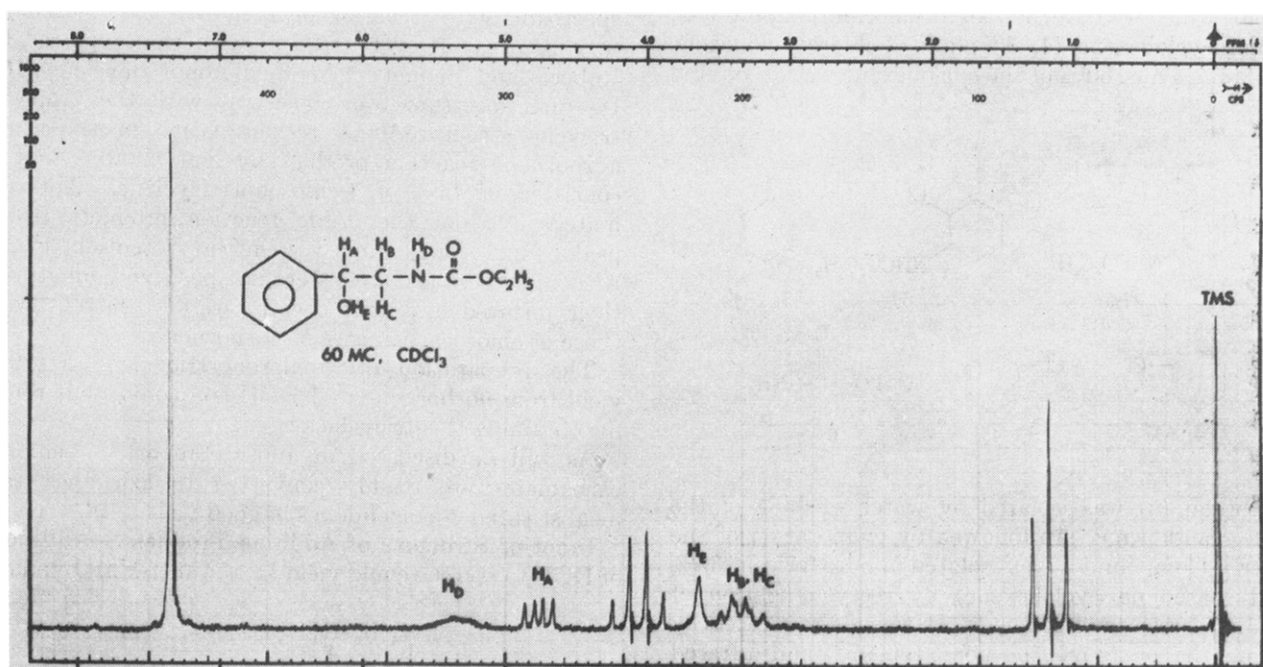
Figure 2.—Nmr spectrum of ethyl (N-2-hydroxy-2-phenylethyl)carbamate (13).

12

tures 11 and 13, the anti-Markovnikov products, and not with their isomers.

In Figure 1, the aromatic protons (5 H by integration) appear as a single peak at 7.4 ppm (TMS = 0).

13
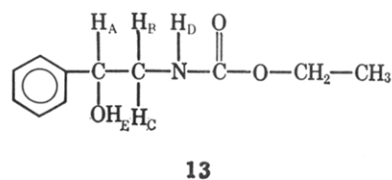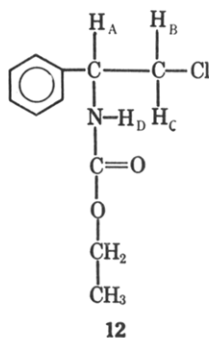
The benzylic proton, H_A (1 H), appears at 5.05 ppm as a quartet of peaks of equal intensity owing to splitting by the nonequivalent protons H_B and H_C.[14] H_B and H_C (2 H) appear as a complex multiplet centered at 3.7 ppm. The multiplet results from splitting of H_B and H_C by each other and by H_A and H_D. H_D (1 H), the proton on nitrogen, gives a typically broad peak at

(14) J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall Co., Inc., New York, N. Y., 1965, pp 119, 120.

Figure 3.—Nmr spectrum of ethyl (N-2-hydroxy-2-phenylethyl)carbamate after treatment with D_2O.

5.3 ppm, partially fused into the quartet of the benzylic proton. The sum of the peak areas of H_A and H_D equals that for two protons. The ethyl group shows the 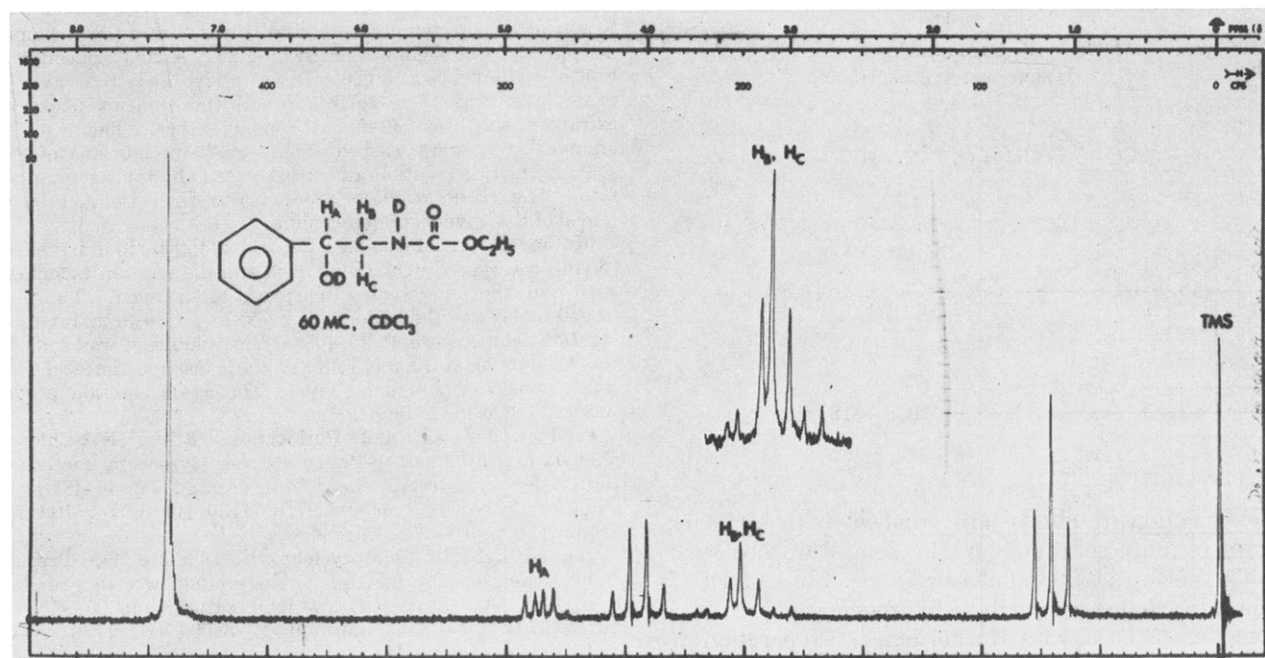typical quartet of the methylene group (2 H) centered at 4.1 ppm and the triplet of the methyl group (3 H) centered at 1.2 ppm.

The isomer of **11**, with the chlorine atom and carbamate group reversed (**12**), would give an nmr spectrum in which the splitting patterns of both the single benzylic proton H_A and of H_B and H_C would be complex multiplets. Finally, solvolysis of **12** with aqueous alcoholic silver nitrate would be expected to be slow.

The nmr spectrum of the solvolysis product (**13**, Figure 2) is also consistent with the proposed structure on the basis of the same first-order analysis just described. The N–H proton, H_D (1 H), however, is now clearly and completely visible at 5.3 ppm because the H_A (1 H) quartet has moved upfield to 4.75 ppm. The hydroxyl proton, H_E (1 H), is seen at 3.65 ppm. Treatment of the alcohol (**13**) with D_2O exchanges H_D and H_E by deuterium. As shown in Figure 3, the quartet of H_A and the multiplet of H_B and H_C, partially buried in Figure 2, are now clearly defined.

Addition of DCU to terminal olefins also yields the anti-Markovnikov adducts (**14**). Their structure was proven by pyrolysis of the adducts to 5-alkyl-2-oxazolidones in good yield, rather than to the 4-alkyl isomers.[13]
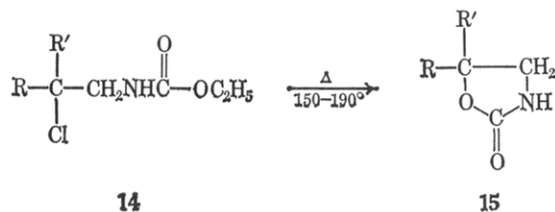
This was established by independent synthesis of **15** (as well as of its isomer in one case). Further proof that the adducts are β-chlorocarbamates is demonstrated by their facile conversion in high yields to aziridines on reaction with base.[13]

Mechanism of Reaction of DCU with Olefins.—
The reaction has numerous characteristics of a free-radical chain reaction: (a) an induction period is observed followed by a rapid exothermic reaction; (b) light causes a rate enhancement and free-radical inhibitors, such as oxygen and ethers of quinones, slow it down; (c) double-bond addition proceeds in anti-Markovnikov fashion and is nonstereospecific; (d) yields of double-bond adducts decrease as the number of allylic hydrogen atoms increases; (e) the yield of urethan increases with the number of allylic hydrogen atoms; and (g) reaction of DCU with norbornene proceeds by homoallylic attack and yields 3-chloronortricyclene and urethan. Reaction sequences which account for these facts are listed in Scheme I. No urethan is produced in reac-

SCHEME I
ADDITION OF DCU TO DOUBLE BONDS
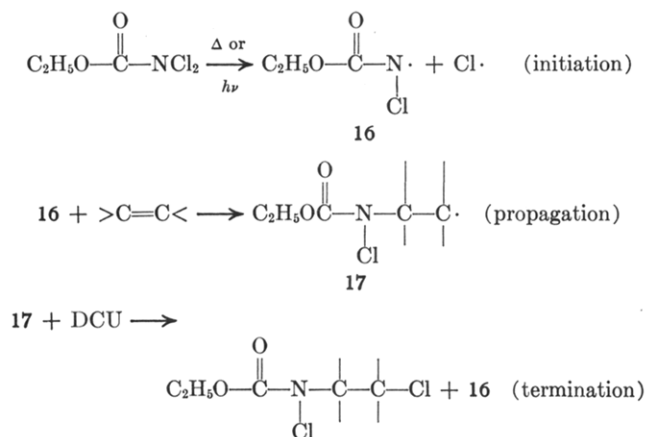
tions of DCU with styrene and stilbene, as no allylic hydrogen atoms are available. The nonstereospecific nature of the products from cyclohexene, *trans*-stilbene, and *trans*-3-hexene results from free rotation of the intermediate radical before termination (Scheme II). Urethan is formed from N-chlorourethan when the

SCHEME II

REACTION OF DCU WITH OLEFINS CONTAINING ALLYLIC
HYDROGEN ATOMS

$$16 + \overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-\overset{}{C}=\overset{}{C}- \longrightarrow C_2H_5O\overset{\overset{\displaystyle O}{\|}}{C}-N-H + -\overset{}{C}-\overset{}{C}=\overset{}{C}-$$

$$\underset{\underset{\displaystyle Cl}{|}}{} \qquad 18$$

$$18 + DCU \longrightarrow -\overset{}{\underset{\underset{\displaystyle Cl}{|}}{C}}-\overset{}{C}=\overset{}{C}- + 16 \text{ (etc.)}$$

$$Cl\cdot + -\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}-\overset{}{C}=\overset{}{C}- \longrightarrow HCl + 18 \text{ (etc.)}$$
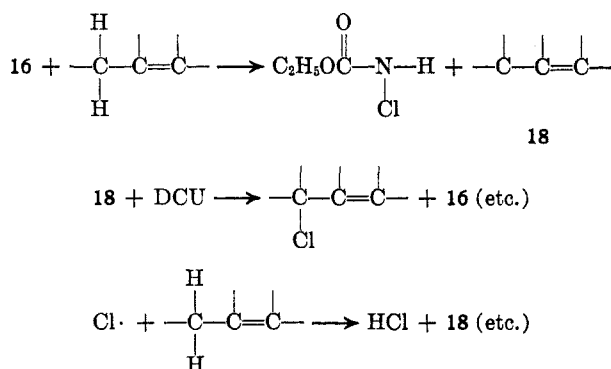
crude reaction products are washed with aqueous
sodium bisulfite solution. Acidic fumes are observed
leaving the top of the condenser in reactions of DCU
with olefins that contain allylic hydrogen atoms.

**Reaction of DCU with Norbornene. Preparation of
3-Chloronortricyclene.**—The formation of 3-chloro-
nortricyclene by homoallylic reaction of radicals with
norbornene can be rationalized by the scheme of
Tobler, Battin, and Foster.[15]

Experimental Section

Materials and Equipment.—Urethan was reagent grade ob-
tained from Fisher Scientific Co. Chlorine gas, reagent grade,
was obtained from a cylinder. The olefins used were chroma-
tographically pure. The infrared spectra were obtained on a
Perkin-Elmer Infracord, Model 137. The nmr spectra were
obtained on a Varian A-60 spectrometer using TMS as internal
standard. Gas chromatography was carried out on a Wilkens
Aerograph Autoprep, Model A-700, employing the following
columns (10 ft × 0.25 in.) as needed: A, 10% butanediol succi-
nate on 60 mesh Anakrom ABS; B, 10% SE-30 on 60 mesh
Anakrom ABS; C, 15% Apiezon-L on 60 mesh Anakrom ABS;
D, 20% SE-30 on Firebrick. Refractive indices were taken
on a Bausch and Lomb refractometer. Molecular weights
were determined on a Mechrolab osmometer, Model 301 A.
Melting and boiling points are uncorrected. Mircoanalyses
were performed by Micro-Analysis Inc., Wilmington, Del.

Preparation of N,N-Dichlorourethan (DCU).—A solution of
urethan (100 g, 1.125 moles), sodium acetate (210 g, 2.56 moles),
and glacial acetic acid (21 g, 0.35 mole) in water (400 ml) was
prepared in a 2-l. flask equipped with a stirrer, thermometer,
and gas inlet tube. Chlorine gas (172 g, 2.40 moles) was con-
densed from the cylinder and allowed to distill slowly into the
stirred solution over a period of 6 hr at room temperature.
When the chlorine addition was complete, the reaction mixture
was allowed to separate into two phases and the lower organic
phase was drawn off and washed with two 100-ml portions of
20% sodium chloride solution. The crude reaction product, a
golden yellow oil with a sharp odor, was then placed in a rotary
evaporator to remove the last traces of water. The oil was then
distilled through a Vigreux column (18 × 0.75 in.). The main
fraction was collected at 74–76° (15 mm). It weighed 143 g
(80% yield), n^{26}D 1.4582. Iodometric analysis indicated a
purity greater than 99.5%. The infrared spectrum shows
$\nu_{max}^{CCl_4}$ at 2980 (CH), 1750 (C=O), 1715, 1370 (ester), 1230,
1100, 1000, and 900 cm^{-1}.

Addition of DCU to Olefins. Method A.—A solution of the
olefin (0.050 mole) in benzene (25 ml) was placed in a 100-ml
flask. The solution was purged with and kept under an at-
mosphere of nitrogen. DCU (8.0 g, 0.05 mole) was then added
dropwise at a rate to maintain the reaction temperature at 5–10°.
After the addition was complete the reaction mixture was allowed

to warm to room temperature, and it was stirred until complete
disappearance of olefin was noted by glpc. A 20% aqueous solu-
tion of sodium bisulfite (50 ml) was added at 5–10°. The or-
ganic layer was then separated and the aqueous phase was
extracted with two 20-ml portions of ether. The combined
organic layers were washed with two 25-ml portions of 20%
sodium chloride solution and dried over anhydrous sodium sul-
fate. The crude reaction product was then isolated by re-
moval of the solvents under vacuum.

Method B.—A solution of DCU (8.0 g, 0.050 mole) in benzene
(25 ml) was placed in a 100-ml flask and the solution was purged
with and kept under an atmosphere of nitrogen. The olefin
(0.050 mole) was then added dropwise at a rate to maintain the
reaction temperature at 35–40°. When addition was complete
the reaction mixture was refluxed until disappearance of olefin
was complete as noted by glpc. The crude reaction product
was isolated as in method A.

**Product Isolation and Purification. Ethyl (N-2-Chloro-2-
phenylethyl)carbamate.**—Prepared from styrene by method A,
the product was recrystallized from hexane: mp 46–48° (yield
80%); infrared $\nu_{max}^{CCl_4}$ 3400 (NH), 1730 (C=O), 1510 cm^{-1}
(amide II); mol wt 223 (calcd 228).

trans-**Ethyl (N-2-Chlorocyclohexyl)carbamate (1).**—Prepared
from cyclohexene by method B, the product was recrystallized
from 10% Et$_2$O–hexane at low temperature: mp 96–97° (lit.[9]
mp 96–97°); yield 30%; infrared $\nu_{max}^{CCl_4}$ 3400 (NH), 1730 (C=O),
and 1510 cm^{-1} (amide II).

Compounds **3, 4,** and **5** were identified by comparison of their
glpc retention times with those of authentic samples using column
C (20 ft × 0.25 in.) at 100° and column D at 170°, and also by
adding known quantities of the reference compounds to the re-
action mixture and observing the increase in peak areas.

Ethyl (N-2-Chloro-*n*-hexyl)carbamate.—Prepared from 1-
hexene by method B, the product was distilled under vacuum:
bp 91–93° (0.15 mm); yield 64%; n^{26}D 1.4542; infrared ν_{max}^{neat}
3340 (NH), 1720 (C=O), 1520 (amide II), and 780 cm^{-1} (CCl).

Ethyl (N-1,2-Diethyl-2-chloroethyl)carbamate.—Prepared
from *trans*-3-hexene by method B, the product was distilled
under vacuum: bp 74–75° (0.25 mm); yield 40%; n^{26}D 1.4540;
infrared ν_{max}^{neat} 3300 (NH), 1710 (C=O), 1520 (amide II), and
780 cm^{-1} (CCl). Glpc analysis of this product on columns B
and C at 175° indicated a 60:40 mixture of *erythro* and *threo*
isomers.

Ethyl (N-2-Chloro-2-methylpentyl)carbamate.—Prepared from
2-methyl 1-pentene by method A, the product was distilled under
vacuum: bp 65–66° (0.04 mm); yield 60%; n^{25}D 1.4558; in-
frared ν_{max}^{neat} 3350 (NH), 1740 (C=O), 1520 (amide II), and 780
cm^{-1} (CCl).

Ethyl (N-2-Chloro-*n*-decyl)carbamate.—Prepared from 1-de-
cene by method B, the product was recrystallized from petroleum
ether (bp 30–60°) at low temperature: mp 34–35°; yield 65%;
infrared $\nu_{max}^{CCl_4}$ 3400 (NH), 1740 (C=O), and 1510 cm^{-1} (amide
II).

Ethyl (N-2-Chloro-*n*-dodecyl)carbamate.—Prepared from 1-
dodecene by method B, the product was recrystallized from
hexane at low temperature: mp 44–45°; yield 59%; infrared $\nu_{max}^{CCl_4}$
3450 (NH), 1730 (C=O), and 1520 cm^{-1} (amide II).

Ethyl (N-2-Chloro-*n*-octadecyl)carbamate.—Prepared from
1-octadecene by method B, the product was recrystallized from
hexane at low temperature: mp 53–54°; yield 63%; infrared
$\nu_{max}^{CCl_4}$ 3440 (NH), 1725 (C=O), and 1520 cm^{-1} (amide II).

Ethyl (N-2-Chloro-1,2-diphenylethyl)carbamate.—Prepared
from *trans*-stilbene by method A, the product was recrystallized
from 25% benzene–hexane: mp 82–115°; yield 65%; the prod-
uct is a mixture of *erythro* and *threo* isomers; infrared $\nu_{max}^{CCl_4}$
3450 (NH), 1740 (C=O), 1510 (amide II), 1240, and 1060 cm^{-1}.

Methyl β-(N-carboethoxyamino)-α-chloropropionate.—Pre-
pared from methyl acrylate by method B, the product was dis-
tilled under vacuum: bp 99–100° (0.15 mm); yield 25%;
n^{26}D 1.4588; infrared ν_{max}^{neat} 3350 (NH), 1750, 1720 (C=O), 1520
(amide II), and 780 cm^{-1} (CCl).

3-Chloronortricyclene.—Prepared from norbornene by method
A, the product was distilled under vacuum: bp 61–62° (4 mm),
yield 31%; n^{26}D 1.4948 [lit.[11b] bp 60.4–61.0° (32 mm), n^{25}D
1.4947–1.4948]. The analytical sample was obtained by pre-
parative glpc at 175° using a 10 ft × ³/₈ in. column packed with
15% Apiezon-L on Anakrom ABS; infrared ν_{max}^{neat} 2950, 1305,
1295, 960, 815, and 770 cm^{-1}.

Anal. Calcd for C$_7$H$_9$Cl: C, 65.38; H, 7.05; Cl, 27.57.
Found: C, 65.55; H, 7.01; Cl, 27.47.

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Quantitative glpc study of the crude reaction product was conducted at 185° using column D. 3-Chloronortricyclene (45%) had a retention time of about 2 min and the β-chlorocarbamates (39%) had retention times of 16–19 min. The compounds were isolated by preparative glpc at 185° using a column 10 ft × ³/₈ in. packed with 20% Carbowax on 60 mesh Anakrom ABS.

Preparation of Ethyl (N-2-Hydroxy-2-phenylethyl)carbamate.—A solution of ethyl (N-2-chloro-2-phenylethyl)carbamate (1.14 g, 0.005 mole) in 50% ethanol (40 ml) in a 100-ml flask was treated with a solution of silver nitrate (1.70 g, 0.010 mole) in 50% ethanol (20 ml), added in one portion. An immediate precipitate of silver chloride formed; the reaction mixture was stirred for 30 min. The silver chloride was separated by filtration (0.70 g, calcd 0.72 g). The filtrate was evaporated to dryness on a rotary evaporator and the residue was extracted with three 30-ml portions of ether. The ether extracts were dried over anhydrous sodium sulfate and the solvent was removed under vacuum. The residue was then taken up in 20% Et₂O-hexane solution (25 ml) and the solution was cooled in an ice bath. Colorless crystals separated which were collected and dried: mp 86–87° (lit.[8] mp 85°); yield 57%; infrared $\nu_{max}^{CHCl_3}$ 3500 (OH), 3450 (NH), 1700 (C=O), 1510 (amide II), 1230, and 700 cm⁻¹.

Stereochemistry of the Most Active Racemate of Norbormide. A Selective Rat Toxicant

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The stereochemistry of the most active of the eight possible racemates of the selective rat toxicant norbormide has been determined by X-ray single-crystal analysis of the *p*-bromobenzyl derivative. The conventional *R* index is 12.6% for the 2547 independent observed reflexions.

Norbormide is the common name for the mixture of stereoisomers of 5-(α-hydroxy-α-2-pyridylbenzyl)-7-(α-2-pyridylbenzylidene)-5-norbornene-2,3-dicarboximide (C₃₃H₂₅N₃O₃). It was shown to be a highly selective rat toxicant and a considerable difference in toxicity exists among the different isomers.[1] The eight possible racemates have been isolated and studied chemically by Mohrbacher, *et al.*[2] A three-dimensional, X-ray, single-crystal analysis was undertaken in order to determine in detail the stereochemistry of the most active of the racemates.

Experimental Section

Single crystals of the *p*-bromobenzyl derivative (C₄₀H₃₀N₃O₃-Br) suitable for X-ray analysis were kindly provided by McNeil Laboratories Inc. They are triclinic with the following unit cell dimensions (precession photographs, Cu Kα radiation): *a* = 14.50 ± 0.07 A, *b* = 11.69 + 0.06 A, *c* = 10.46 ± 0.06 A, α = 103.07 ± 0.10°, β = 110.91 ± 0.10°, γ = 78.61 ± 0.10°.

Weissenberg photographs were taken for layers 0–8 about the *a* axis and 0–4 about the *b* axis. (Crystal size was 0.40 × 0.18 × 0.15 mm.³) The intensities were estimated visually and corrected for the Lorentz and polarization factors. No absorption correction was applied.

There are two molecules per unit cell. The racemic nature of the compound indicates that the space group is P̄1. A statistical analysis of the distribution of intensities[3] also conforms with this space group.

The position of the bromine atom of the asymmetric unit was easily derived from a three-dimensional Patterson series calculated with coefficients sharpened to correspond to those from point atoms at rest.[4] As there is only one bromine atom in the large molecule, the heavy atom phased electron density series contained much spurious information. The carbon atoms of the *p*-bromobenzyl group could, however, be identified with certainty and were included in the next round of structure factors calculation. The situation in the second electron density series was much clearer and new parts of the molecule could be located. After four rounds of Fourier refinement the whole molecular skeleton had been derived.

At this stage it was obvious that the X-ray analysis fully confirmed the formula (I) of Mohrbacher, *et al.*,[2] for norbormide. The oxygen atoms and the imide nitrogen atom of the molecule were therefore easily identified. These positions were also confirmed from the peak heights in the electron density series. The remaining two nitrogen atoms were identified as follows. The molecular parameters were refined by block diagonal least-

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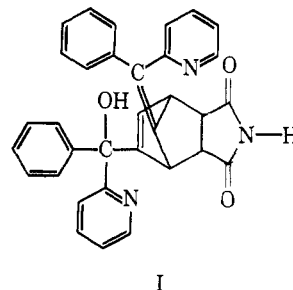
squares treatment[5] assigning carbon atom form factor values to all still unidentified heavier atoms. Isotropic factors were refined for all atoms except the bromine atom which was given anisotropic temperature factors. After a few rounds the temperature factors of two atoms had dropped to values about 1.5 A² lower than those of the neighboring atoms. This indicates that these atoms represent the two pyridyl nitrogens and they were given nitrogen form factor values in the following structure factors calculations. In the next rounds of refinement the temperature factors of these atoms increased to normal values. The final refinement was performed using anisotropic temperature factors for the heavier atoms. All hydrogens except that of the hydroxyl group were included at their expected positions and with isotropic temperature factors corresponding to those of the parent atoms. These parameters were not varied. The progress of the refinement was checked at various stages by difference series calculations. One of these contained a peak (0.6 e A⁻³) at a possible position for the hydroxyl hydrogen, which was also included in the structure factors calculation. The refinement was terminated when the *R* value for the 2547 observed independent reflexions was 12.6%. The maximum and mean values of the ratios between the shifts and the standard deviations were then 0.40 and 0.06, respectively, for positional and 0.33 and 0.09, respectively, for vibrational parameters.

The calculations were performed on a Datasaab D21 computer using the integrated program system of Abrahamsson, *et al.*[6]

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