Preparation and Insecticidal Evaluation of Alcohol and Amine Adducts of Kepone

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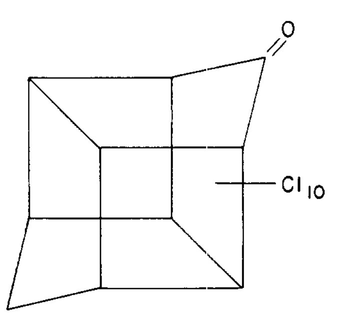
A series of adducts was prepared from Kepone with various alcohols and amines. The insecticidal activity spectrum of the alcohol adducts is similar to that of Kepone, which functions primarily by stomach action. The amine adducts show a different toxicity pattern, and are concluded to function primarily by contact action. Both types of adducts are more toxic than Kepone to some species.

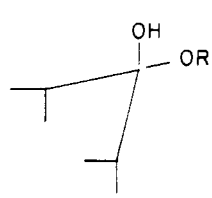
THE insecticide-fungicide Kepone (I) [decachloro-octahydro-1,3,4-metheno-2*H*-cyclobuta (*cd*) pentalen-2-one, or decachloropentacyclo-$(5.3.0.0^{2,6}.0^{4,10},0^{5,9})$ decan-3-one] has a reactive ketonic group which is generally known to form adducts with alcohols and with amines (*3*). Except for three of the alcohol adducts (*2*), none of these compounds has been characterized in detail. The former is presumed to have the hemiketal structure (II) (*2*); the latter is similarly constituted (III). This paper reports the preparation and insecticidal evaluation of both types of compounds as part of a study of Kepone analogs and derivatives (*1*).

This general preparative procedure was employed with 54 primary, secondary, and tertiary aliphatic and cycloaliphatic alcohols with varied substituents, and with 16 ethylene oxide condensates derived from various alcohols, phenols, and amines. Primary and secondary alcohols gave adducts, but tertiary alcohols did not, probably because the keto group in Kepone is sterically hindered by the surrounding chlorine atoms. High-boiling alcohols were applied in slight excess, using chloroform, toluene, hexane, or a similar inert solvent as reaction medium. Acetone is not a satisfactory solvent, since it reacts with Kepone (*1*). The presence of unreacted Kepone was easily established from the infrared spectrum of the reaction mixture; reaction was completed when necessary by further heating with an additional portion of the alcohol.



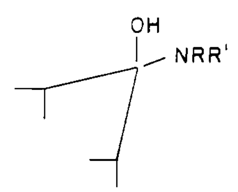
I

Kepone



II

Alcohol adduct (Hemiketal)



III

Amine adduct

Preparation of Test Compounds

Kepone–*n*-Butyl Hemiketal. Kepone hydrate, purified by recrystallization from methanol (18 grams, 0.032 mole), and 1-butanol (15 grams, 0.2 mole) were refluxed for 1 hour, after which water and excess butanol were removed by distillation. Residual butanol was then completely removed in vacuo. The crude product, obtained in quantitative yield, was recrystallized from 30 to 60° petroleum ether [m.p. (uncorr.) 162–65° C.].

The infrared spectrum showed hydroxyl stretching at 2.78 microns and carbon-hydrogen stretching at 3.35 and 3.46 microns. The absence of Kepone hydrate is shown by the lack of absorption at 6.1 microns (water) and at 2.8 to 3.1 microns (hydroxyl).

Kepone–*n*-Hexylamine Adduct. Purified Kepone hydrate (530 grams, 0.95 mole), *n*-hexylamine (120 grams, 1.19 mole), and hexane (1 liter) were refluxed for 30 minutes, then distilled to remove the solvent and water. Residual solvent and amine were removed in vacuo. Since the infrared spectrum revealed the presence of some unreacted Kepone, more amine (25 grams) was added, the mixture was heated for 1 hour, and the excess amine was then removed in vacuo.

The spectrum now showed complete reaction. Recrystallization from petroleum ether gave a product melting at 57–59° C. The compound shows characteristic nitrogen-hydrogen stretching at 2.96 microns in its infrared spectrum.

This type of procedure was employed for preparing the adducts from ammonia and from 57 amines, including aliphatic and aromatic primary, secondary, and tertiary types. Tertiary amines (R_3N) did not give adducts, possibly for steric reasons or because the carbonyl group of Kepone is insufficiently electron-deficient. A tertiary amine adduct would, of course, differ from the others, since there is no hydrogen on the nitrogen atom and a tertiary alcohol would not be generated by adduct formation.

Many of the alcohol and amine adducts have excellent solubility in aromatic solvents such as xylene, and yield 40% solutions which show no separation on standing 24 hours at −18° C. Kepone hydrates, on the other hand, are considerably less soluble.

Biological Evaluation

The test procedures employed are described in detail elsewhere (*1*). The test compounds were evaluated on an equal weight basis, which means that the actual Kepone content varies with the compound tested. Kepone was used as the di- to trihydrate. Kepone is inactive on mites and pea aphids, even at heavy dosages. The LC_{50} values on Mexican bean beetle larvae and southern armyworm larvae are 0.05 and 0.007%, respectively, expressed as weight per cent toxicant in the spray. The dosages used to obtain the test data on those insects in Tables I and II were sufficiently low to reveal possible greater toxicity in the compounds being compared with Kepone.

Insecticidal screening test data on representative types of Kepone-alcohol adducts in comparison with Kepone are given in Table I. It is concluded that these compounds have the same general

Table I. Insecticidal Evaluation of Kepone-Alcohol Adducts

Alcohol	Screening Data, % Kill[a] Mites[b] (0.0625)	Pea aphids (0.0625)	Mexican bean beetle larvae (0.0313)	Southern armyworm larvae (0.0078)
1-Butanol	14	0	100	80
1-Octadecanol	11	0	60	80
Mixed primary amyl	4	0	60	80
Ethylene oxide condensate[c]	10	0	100	60
Kepone	0	0	30	50

[a] At weight % toxicant in spray indicated parenthetically.
[b] Mites. *Tetranychus telarius* (Linneaus).
Pea aphids. *Macrosiphum pisi* (Harris).
Mexican bean beetle larvae. *Epilachna varivestis* Mulsant.
Southern armyworm larvae. *Prodenia eridania* (Cramer).
[c] Nonylphenol plus 4 moles ethylene oxide.

Table II. Insecticidal Evaluation of Kepone-Amine Adducts

Amine	Screening Data, % Kill[a] Mites (0.0625)	Pea aphids (0.0625)	Mexican bean beetle larvae (0.0313)	Southern armyworm larvae (0.0078)
Ammonia	10	60	0	100
n-Hexyl	12	100	0	100
n-Decyl	38	100	0	80
n-Dodecyl	25	100	0	100
n-Tetradecyl	68	100	20	80
n-Hexadecyl	55	100	0	83
n-Octadecyl	22	91	0	100
tert-Nonyl	9	100	0	67
tert-C 12-14	4	100	0	60
tert-C 18-21	38	100	0	100
Cyclohexylamine	7	100	0	80
Di-(*n*-butyl)	5	100	0	100
2-Ethylhexyl	16	100	0	100
Diethylenetriamine	8	100	0	60
Triethylenetetramine	7	100	0	100
Piperidine	19	100	0	100
Furfurylamine	15	100	0	100
Aniline	14	100	0	100
Kepone	0	0	30	50

[a] At weight % toxicant in spray indicated parenthetically.

type of activity spectrum as Kepone itself, with little or no activity on mites and aphids and fair to high toxicity against Mexican bean beetle larvae and southern armyworm larvae. The adducts appear to be considerably more toxic than Kepone itself on the last two species. These materials therefore resemble Kepone in functioning primarily as stomach insecticides.

The ammonia and amine adducts (Table II), on the other hand, show different behavior, except for activity on mites, which remains poor. Kepone is inactive on aphids and active on bean beetle larvae, but the ammonia and amine adducts behave oppositely. It, therefore, appears that adducting with amines has modified the activity from that of a stomach insecticide toward that of a contact toxicant, since aphids are sucking insects, while bean beetle larvae feed by chewing. (Southern armyworm larvae, although chewing insects, are relatively easy to kill, and are therefore highly susceptible to both types of adducts and to Kepone itself.) The ammonia adduct has activity resembling that of the amine compounds, showing that the presence of an organic moiety on the amino group is not essential. The modified activity of the ammonia and amine adducts may therefore simply result from neutralization of the acidic carbonyl group in Kepone. Kepone is effective on plum curculio [*Conotrachelus nenuphar* (Herbst)], which is a chewing insect. Several of the amine adducts are considerably more effective, however, since they gave good to excellent kills at dosages at which Kepone is relatively ineffective. They also gave complete control of mosquito larvae at 0.0625 p.p.m.; Kepone is nearly ineffective in this case. On the other hand, the ammonia and amine adducts are totally ineffective on adult houseflies when a liquid sugar bait is used, whereas Kepone gives complete kill.

Since Kepone has fair to good fungicidal activity on 20 plant diseases, some of the alcohol and amine adducts of Kepone were tested comparatively. A laboratory spore germination test on *Monolinia (Sclerotinia) fructicola* gave complete inhibition at 10 p.p.m. with the adducts of 1-butanol, nonylphenol plus 4 moles of ethylene oxide, and *n*-dodecylamine; Kepone is ineffective at this dosage. On *Stemphylium sarcinaeforme* (Cav.) at 10 p.p.m., Kepone and the two alcohol adducts are ineffective, but the *n*-dodecylamine adduct showed 90% inhibition of germination.

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