Alkyl and Aryl Neoalkanamides: Highly Effective Insect Repellents

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ABSTRACT Alkyl and aryl neoalkanamides with a total carbon number between 11 and 14, or within a molecular weight range between 185 and 227, were highly effective repellents of male German cockroaches, *Blattella germanica* (L.). Comparison with known repellents showed that members of this unique family of secondary amides are among the most effective and long-lasting repellents of cockroaches examined to date. In assays with females and nymphs of the German cockroach, male American cockroaches, *Periplaneta americana* (L.), and carpenter ant workers, *Camponotus pennsylvanicus* (De Geer) methyl neodecanamide, propyl neodecanamide, and methyl neotridecanamide were found highly repellent. Because of their broad spectrum of activity, longevity, and safety, these compounds, along with several other members of this family, have important applications as repellents of nuisance pests and of arthropods of public health importance.

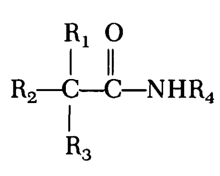
KEY WORDS Insecta, repellent, cockroach, alkyl neoalkanamides

HEAVY RELIANCE ON INSECTICIDES for the control of household pests has generally precluded studies of alternative methods. However, recent concern with human and environmental safety and prevalence of resistance to insecticides have prompted interest in noninsecticidal manipulation of pest populations. Physical modification of the indoor environment usually enhances the effects of other controls against cockroaches (see Schal & Hamilton 1990). Physical changes can reduce areas that otherwise would require insecticide treatment by changing available resources and insect movement and dispersion patterns, which may increase contact with residual insecticides. Repellents alter existing structures to reduce these resources.

It is important to distinguish between repellents lacking insecticidal activity and insecticides or their formulations with repellent properties. The literature on repellents of cockroaches is replete with studies on repellency of insecticides, which usually conclude that the efficacy of insecticides is inversely related to their repellency (Ebeling et al. 1966, 1967) and that repellency adversely affects insecticide efficacy (Bennett & Wright 1971, Rust 1986, Schal & Hamilton 1990). Because noninsecticidal repellents cause directed movement away from the treated surface, they have important uses in protecting merchandise in transport and storage (e.g., returnable bottles), sensitive equipment such as computers, and in the case of broad-spectrum repellents, protecting humans, livestock, and pets. For such applications, repellents must have low mammalian toxicity and relatively long residual activity.

Arthropod repellents have been studied for many years, usually on pathogen-transmitting arthropods of medical and veterinary importance. The more effective compounds are regarded to be *N,N*-diethyl-*m*-toluamide (DEET), fencholic acid (Bodenstein & Fales 1976), and 2-hydroxyethyl-*n*-octyl sulfide (MGK 874) (Goodhue 1960, Burden & Eastin 1960). Others include sulfonamides (McGovern et al. 1974a, McGovern et al. 1975), carboxamides (McGovern & Burden 1985), *N,N*-diethylcyclohexaneacetamide and *N,N*-diethylcyclohexanepropanamide (Hagenbuch et al. 1987), and heterocyclic amides (McGovern et al. 1974b). Derivatives of cyanoacetic acid have also been reported as effective cockroach repellents (Schwartz et al. 1970). Other reports of cockroach repellents have included such diverse natural materials as cucumber peelings and bay leaves (Scriven & Meloan 1984a), cedar wood (Appel & Mack 1989) and various terpenoids and essential oils including cineole and spearmint oil (Inazuka 1982b).

Alkyl and aryl neoalkanamides are new, unique secondary amides, made from commercially available highly branched neo acids. Structures are defined as



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where R_1, R_2, and R_3 are alkyl substituents consisting of a total of either three carbon atoms (pivalic or neopentanoic acid), 5C (neoheptanoic acid), 7C (neononanoic acid), 8C (neodecanoic acid), 9C (neoundecanoic acid), or 11C (neotridecanoic acid). R_4 is alkyl or aryl. *Neo* designates a structure in which the α-carbon atom is connected to four other carbon atoms. Alkyl secondary amides made from C_7, C_9, C_{10}, C_{11}, or C_{13} neoacids are unique as all the homologs are in liquid physical state and, in general, have a mild, pleasant odor. Generally, the analogous straight-chain secondary amides are solid and have only faint odors. The pivalamides (C_5) are isomerically pure and they have a high degree of structural symmetry and are solid. Because of their unique physical properties and long lasting substantiveness and economy and the relationship to tertiary amide repellents, these secondary neoamides were evaluated for repellency. We also examined structure–activity relationships within this group of compounds.

Materials and Methods

Insects. German, *Blattella germanica* (L.), and American, *Periplaneta americana* (L.), cockroaches were from established colonies maintained at 27°C in a 12:12 (L:D) photoperiod and fed commercial dog food. Carpenter ant workers, *Camponotus pennsylvanicus* (De Geer), were collected from a log that contained a queen-right colony. Ants were kept in the same conditions as the cockroaches and were fed a mixture of ground dog food and yeast with water and sugar-water available ad libitum.

Bioassay. Forty-eight hours before initiation of an assay, 50 male German cockroaches were allowed to acclimate to the plastic test cages (51 by 28 by 20 cm) with food and water available in the center. A thin film of teflon emulsion (Fluon AD-1, Northern Products, Woonsocket, R.I.) on the sides of the cages restricted the insects to the floor of the cage. For some assays we used 50 nymphal German cockroaches, 20 male American cockroaches, or 50 carpenter ant workers.

A modification of the method of Goodhue & Tissol (1952) was used to evaluate the repellency of compounds over time. Before application of a chemical to an 8-oz (237 ml) unwaxed ice cream carton (Dixie No. 2188), two 1.5-cm holes were cut on opposite sides of the lip of the cup. Two milliliters of a 1% solution (wt/vol) of experimental compound in acetone was applied to the entire inside surface (188 cm^2) of the cup to achieve a deposition of 0.106 mg/cm^2. Control cups were treated with acetone only. The cups were allowed to dry in a fume hood for 1 h, and a control and a treated cup were inverted into each of the test cages. Food and water were provided in the center of each cage, outside of the cups. The number of insects that rested on the inner walls of each cup was recorded in the middle of the photophase daily for 25 d or until equal numbers were found in treated and untreated cups. After each count the insects were disturbed and the positions of the treated and control cups were reversed. Thus, each day the distribution of cockroaches may be considered independent of previous days.

Repellency was defined as the percentage of insects that avoided the treated surface and was calculated as

$$\%\ repellency = 100 - \frac{100 \times (N_t)}{(N_t + N_c)}$$

where N_t is the number of insects on the treated surface and N_c is the number on the acetone-treated control surface. To evaluate the repellency of compounds we used the number of days of complete (100%) repellency and a maximum likelihood probit analysis of time–repellency (SAS Institute 1985) from which a measure was calculated of the number of days of 90% repellency (RT_{90} – 10% of the insects on the treated surface, 90% on the control surface). Values were considered to be significantly different if the 95% FL did not overlap. Each evaluation of repellents included methyl neodecanamide as a standard.

Synthetic Procedures. The neoacid starting materials are manufactured by reacting petroleum-derived olefins with carbon monoxide under catalytic conditions (Fefer 1978). The secondary amides are synthesized either by reacting the neo acid chloride with the respective amine or by direct condensation of the respective amine with the neo acid. The reaction with neoalkanoyl chloride involved the slow addition of acid chloride via a dropping funnel to the amine. The exothermic reaction required cooling either with an ice bath or with circulating cooling to avoid discoloration. The reaction did not require a solvent although diethyl ether or methylene chloride were used in several cases. The amine was used in 10% excess to assure complete reaction of the more expensive acid chloride which is also more difficult to remove. Generated hydrogen chloride was consumed by adding molar equivalents of triethyl amine to form the amine salt which was removed by filtration. The amide product was purified by distillation or by acid and base washing followed by water washing. Three of the homologues (n-octyl-, coco-, and tallow-) were made by direct condensation of amine with free acid. Reaction conditions required 240°C for 7 h conducted under nitrogen or vacuum to avoid discoloration. Methyl neodecanamide was made by both the acid chloride and condensation methods. Purity for each chemical was 95.9% minimum; impurities consisted of 3.0% maximum free acid, 0.1% maximum free amine, and 1.0% maximum mois-

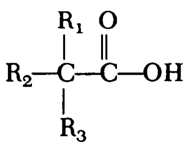
Table 1. Physical properties of alkyl and aryl neoalkanamides

Alkyl amine	C_5	C_7	C_9	C_{10}	C_{11}	C_{13}
Methyl	sd, mp 89–90°C	bp 195°C/760 mm	bp 120°C/30 mm	bp 235°C/760 mm	bp 145°C/1.0 mm	bp 123–127°C/0.5–0.8 mm
Ethyl	sd, mp 45–48°C	lq	bp 199°C/3.0 mm	bp 105–106°C/0.8 mm	bp 110°C/1.2 mm	lq
n-Propyl	—	bp 87°C/1.4 mm	bp 100°C/1.5 mm	bp 117°C/1.5 mm	lq, semi sd, bp 113°C/0.8 mm	bp 122°C/1.0 mm
Iso-propyl	—	—	—	bp 110°C/1.0 mm	—	—
n-Butyl	—	—	bp 105°C/1.0 mm	bp 120°C/0.2 mm	—	—
Iso-butyl	—	—	—	bp 105°C/1.0 mm	—	—
t-Butyl	sd, mp 118°C	—	—	bp 75°C/0.5 mm	—	bp 85–100°C/0.5 mm
n-Hexyl	lq, bp 95°C/0.5 mm	bp 112°C/1.0 mm	—	bp 145°C/2.0 mm	—	—
Phenyl	sd, mp 132–134°C	sd, mp 64–65°C	—	bp 140°C/0.1 mm	—	—
n-Octyl	—	—	—	lq	—	—
Coco	—	—	—	lq	—	—
Tallow	—	—	—	lq, semi sd	—	—

Solids (sd) are indicated by the melting point (mp) and liquids (lq) by their boiling points (bp) in °C.

ture. Physical properties of the various neoalkanamides are shown in Table 1.

The neoacids used in this study included pivalic (C_5), neoheptanoic (C_7), neononanoic (C_9), neodecanoic (C_{10}), neoundecanoic (C_{10} to C_{12}), and neotridecanoic (C_{12} to C_{14}) acids. Except for pivalic acid, the neoacids are all complex mixtures of isomers. An example of the isomer distribution is neodecanoic acid, which is >95% C_{10} neoacid (the remainder is C_9 and C_{11} neoacids) with the structure



where $R_1 + R_2 + R_3 = 8$ carbon atoms, having a relative isomeric abundance of

$$R_1 \text{ and } R_2 = CH_3;\ R_3 = C_6H_{13} \ldots\ldots 31\%$$

$$R_1 = CH_3;\ R_2 > CH_3;\ R_3 < C_6H_{13} \ldots\ldots 67\%$$

$$R_1 \text{ and } R_2 > CH_3;\ R_3 < C_5H_{11} \ldots\ldots 2\%$$

Results

Structure–Repellency Relationship. Thirty-three different alkyl and aryl neoalkanamides were synthesized and evaluated for repellency to cockroaches. These included structures in which the neoacid carbon number ranged from 5 to 13 and the alkyl amine group ranged from methyl to tallow (C_{18}), and included all the propyl and butyl isomers. The alkyl neoalkanamide structures ranged from 6 to 28 carbons. The phenyl ring was the only aryl group examined.

Repellency to *B. germanica* males is summarized in Table 2 by the number of days of 90% repellency obtained from probit analyses. Methyl neodecanamide was used as a reference standard in each test and an index of repellency was calculated by dividing the RT_{90} of test compounds by that for methyl neodecanamide. Fig. 1 plots this repellency index against alkyl length and the number of carbons in the neoacid group; methyl neodecanamide is assigned a value of unity.

Effective cockroach repellency was generally observed when the neoalkanamide molecular carbon number was within the range of 10–15. Structures with <10 carbons or >15 carbons were ineffective (Table 2; Fig. 1). The most effective repellents of the family were within the molecular carbon number range of 11 (M_r 185) to 14 (M_r 227) and included methyl neodecanamide (11 carbons), the 12-carbon compounds methyl undecanamide and ethyl neodecanamide, the 13-carbon compounds n-hexyl neoheptanamide, phenyl neoheptanamide, the two isomers of propyl neodecanamide and ethyl undecanamide and the 14-carbon compounds *n*-butyl neodecanamide, iso-butyl neodecanamide, and methyl neotridecanamide. All of these materials except for phenyl neoheptanamide were in the liquid physical state (Table 1).

Interestingly, *t*-butyl neodecanamide showed low repellent activity, whereas the *n*-butyl and isobutyl isomers were very active. Similarly, phenyl pivalamide exhibited much lower repellency than compounds of equal carbon number such as methyl neodecanamide (Table 2; Fig. 1).

Table 2. Contact repellency of alkyl and aryl neoalkanamides to *B. germanica* males

Alkyl amine	Days 90% repelled (95% FL)					
	C_5	C_7	C_9	C_{10}[a]	C_{11}	C_{13}
Methyl	0 (0 –0.5)	0.1 (0 – 1.0)	3.8 (1.5– 5.2)	9.9 (6.9–12.1)	14.3 (11.1–17.5)	>25 nf
Ethyl	0 nf	1.6 (0.2– 3.0)	4.8 (0.6– 6.9)	15.2 (9.4–19.4)	10.2 (7.7–12.2)	2.3 (0 –5.4)
n-Propyl	—	5.5 (2.1– 8.1)	4.5 (1.6– 6.8)	19.8 (17.9–22.0)	6.0 (2.5– 8.6)	0.7 (0 –6.8)
Iso-propyl	—	—	—	10.4 (7.8–12.1)	—	—
n-Butyl	—	—	10.8 (6.6–14.3)	18.4 (14.7–20.2)	—	—
Iso-butyl	—	—	—	32.5 (26.6–51.5)	—	—
t-Butyl	0 nf	—	—	1.4 (0.1– 3.0)	—	2.6 (0.5–4.4)
n-Hexyl	5.0 (2.2–7.1)	18.8 (17.9–19.7)	—	1.3 (0.1– 2.9)	—	—
Phenyl	1.6 (0 –5.9)	24.8 (14.2–∞)	—	1.1 (0.1– 2.5)	—	—
n-Octyl	—	—	—	1.0 (0 – 2.6)	—	—
Coco	—	—	—	0.1 (0 – 1.2)	—	—
Tallow	—	—	—	0.2 (0 – 1.3)	—	—

Days of 90% repellency determined by probit analysis ± 95% FL. Where the RT_{90} value is 0, probit analysis was not possible (nf, no fit) and the compound was clearly not repellent. Where the RT_{90} value is >25, probit analysis was not possible (nf, no fit) because 100% repellency extended past day 25. —, not available.

[a] Values represent the means of 35 different assays.

Tertiary dialkyl amides in this family showed relatively low repellent activity on *B. germanica* males even though they were in the preferred 11–14 carbon number range (Table 3). A related amide, *N*-(1,1-dimethyl-1-1-hydroxyethyl)-2,2-diethylbutanamide, also exhibited no repellent activity (RT_{90} = 0, 95% FL = 0–0.5 d).

Dose–Response Relationships and Other Insects. Repellency of methyl neodecanamide was independent of male density when tested on three different densities of male German cockroaches (Table 4). Three of the compounds (methyl neodecanamide, propyl neodecanamide, and methyl neotridecanamide) were tested at reduced application rates to determine the smallest dosage needed for repellency. For all three compounds, complete repellency for more than 1 d was observed at only 0.025 mg/cm^2 on a paper cup. Methyl neodecanamide, at 0.0125 mg/cm^2, exhibited >95% repellency after 24 h (Table 5).

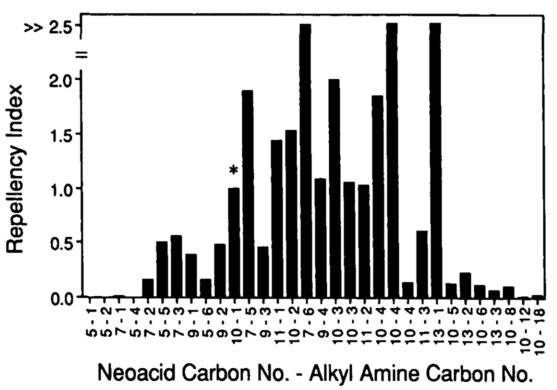


Fig. 1. Repellency of various alkyl neoalkanamides to male German cockroaches. Time of 90% repellency for each compound, from probit analysis, was divided by the time of 90% repellency for methyl neodecanamide, the standard reference compound was assigned a value of 1 and was denoted by *. Compounds are arranged from left to right in increasing total carbon number.

The same three compounds were also tested for repellency to other insect species. They showed excellent repellency with the American cockroach, carpenter ants, and German cockroach females and nymphs (Table 6).

Comparison with Other Repellents. The repellent activity of alkyl neoalkanamides was compared with previously reported repellents which included commercially available compounds, essential oils, terpenoids, and various experimental materials reported as highly effective. The neoalkanamides in the 11–14 carbon range appeared to be superior repellents to most other compounds against *B. germanica* males under our test conditions (Table 7).

Discussion

This study has clearly documented that the alkyl neoalkanamides within the range of 11–14 total carbons are highly effective repellents of cockroaches and carpenter ants. The German cockroach appears the most difficult species to repel (see also McGovern et al. 1974b, Bodenstein & Fales 1976), and male German cockroaches were repelled less than either conspecific females or nymphs, suggesting that studies of mixed sex and age populations may confound the results. From our structure-activity data we

Table 3. Contact repellency of tertiary dialkyl neoalkanamides to *B. germanica* males

Dialkyl neoalkanamide	Days 90% repelled (95% FL)
N,N-dimethyl neodecanamide	4.4 (1.8–6.4)
N,N-diethyl neodecanamide	0.8 (0 –2.7)

Days of 90% repellency determined by probit analysis ± 95% FL.

Table 4. Effect of density on contact repellency of methyl neodecanamide to *B. germanica* males

Density (males)	Days 90% repelled (95% FL)
100	6.0 (2.8– 8.5)
50	8.5 (2.8–12.5)
24	7.0 (1.3–10.9)

Days of 90% repellency determined by probit analysis ± 95% FL.

conclude that, with few exceptions, molecular size is the most important determinant of repellency within this family of compounds.

Test Methodologies. The literature on cockroach repellents is extensive, but difficult to interpret and integrate because test methodologies, dosages per unit area, species and sexes used and standard references, if used, are seldom comparable. Repellency assays currently in use include choice boxes (Ebeling et al. 1966), arena tests with either multiple chemicals tested simultaneously (Inazuka 1982a, Zungoli et al. 1988, Prakash et al. 1990) or two inverted cartons (one treated, one not), which serve as shelters (Goodhue & Tissol 1952) and the slanting card method (Goodhue 1960). Schneider & Bennett (1985) compared various harborage choice methods and the slanting card and concluded that the latter method was best for simple screening of insecticidal repellents. The Goodhue & Tissol (1952) method, which we used in the current investigation, is similar in principle and symmetry to the slanting card method. However, evaluations of methods for screening noninsecticidal repellents of cockroaches are lacking, as are effective methods to distinguish between vapor or olfactory repellency and long-lasting contact repellency.

We used the time that 90% of the insects were repelled, derived from probit analysis, as a comparative measure of repellency. Dethier (1956) argued against such measures because they represent the tail of a normal distribution and are therefore subject to great variability. Instead, he suggested using repellency of 50% of the population as a more effective measure of intrinsic repellency of compounds. In preliminary tests, we found that to use the 50% measure and simultaneously to maintain a reasonable schedule of replicated tests, the dosages would have to be reduced, resulting in greater variability in the results. Indeed, 50% values may be obtained for some compounds from probit analysis, but for many compounds these extrapolated values exceed the longevity of the insects. The dosage per unit area that we used (0.106 mg/cm^2) was comparable to or lower than dosages used by others in similar assays (0.122 and 0.133 in Bodenstein & Fales 1976, 0.087–0.218 in Goodhue 1960, 1.064 in Burden & Eastin 1960, 0.45 mg/cm^2 in Hagenbuch et al. 1987).

Cockroach Repellents. Most studies of cockroach repellents are either methodological reports or screening of unrelated candidate materials (Bodenstein & Fales 1976, Goodhue 1960, Hagenbuch et al. 1987). Therefore, with few exceptions (e.g., McGovern et al. 1974a, 1975) generalizations about structure–activity relationships and mode of action of repellents cannot be deduced at this time. Even for mosquitoes, where a great deal of information on volatile repellents is available (Daykin et al. 1965, Garson & Winnike 1968, Wright 1975), most researchers conclude that little can be deduced of the relationship between structure and activity. Recently, even the validity of the various proposed mechanisms of action has been questioned (Davis 1985). Wright (1975) concluded that effective mosquito repellents have a molecular weight of between 150 and 250 but may be in any class of organic compounds.

For comparative studies with the neoalkanamides, we attempted to obtain and evaluate all of the commercial or other available materials reported to be highly effective against arthropods. Many tertiary amides, including *N,N*-diethyl toluamide and *N,N*-diethyl nonanamide, have been reported to be highly effective repellents of cockroaches (see "Introduction"). Similarly, the diols Rutgers 612 (2-ethyl-1,3-hexanediol) and 2-(*n*-butyl)-2-ethyl-1,3-propanediol, as well as dimethyl phthalate, Tabutrex (dibutyl succinate), 1-(butylsulfonyl)-piperidine and sev-

Table 5. Effect of concentration on contact repellency of three neoalkanamides to *B. germanica* males

Solution concn,[a] %	Application, mg/cm^2	Days 90% repelled (95% FL)		
		Methyl neodecanamide	Propyl neodecanamide	Methyl neotridecanamide
1.0	0.106	10.0 (7.2–12.0)	19.8 (17.9–22.0)	>25 nf
0.5	0.053	7.9 (4.2–13.3)	9.9 (7.7–11.8)	25.7 (21.6–30.0)
0.25	0.025	5.4 (1.2– 5.6)	2.9 (0.8– 4.8)	4.9 (2.2– 6.8)
0.125	0.0125	1.1 (0 – 2.8)	—	—
0.062	0.0062	0.0 nf	—	—

Days of 90% repellency determined by probit analysis ± 95% FL. Where the RT_{90} value is 0, probit analysis was not possible (nf, no fit) and the compound was clearly not repellent. Where the RT_{90} value is >25, probit analysis was not possible (nf, no fit) because 100% repellency extended past day 25. —, not available.

[a] Percentage of active ingredient in 2-ml acetone solution applied to the inside surface of an 8 oz. paper cup.

Table 6. Contact repellency of three neoalkanamides to cockroaches and ants

	Days 90% repelled (95% FL)		
	Methyl neodecanamide	Propyl neodecanamide	Methyl neotridecanamide
German cockroach			
Males	10.0 (7.2–12.0)	19.8 (17.9–22.0)	>25 nf
Females	>25 nf	>25 nf	>25 nf
Nymphs	27.4 (22.9–52.6)	29.5 (23.7–72.3)	>25 nf
American cockroach			
Males	>25 nf	14.5 (12.7–15.7)	>25 nf
Carpenter ants	13.4 (0 –19.0)	>25 nf	>25 nf

Days of 90% repellency determined by probit analysis ± 95% FL. Where the RT_{90} value is >25, probit analysis was not possible (nf, no fit) because 100% repellency extended past day 25.

eral commercial insect repellents such as the MGK compounds (Table 7) have been reported as effective mosquito or cockroach repellents (Goodhue 1960, Burden & Eastin 1960, Bodenstein & Fales 1976). However, all are inferior to methyl neodecanamide and related alkyl neoalkanamides tested herein.

Hagenbuch et al. (1987) reported that two experimental compounds, *N,N*-diethylcyclohexaneacetamide and *N,N*-diethyl-3-cyclohexanepropanamide, were more effective than a standard reference, fencholic acid, in repelling mixed groups of male and female German cockroaches. Both compounds were less effective against the American cockroach. We compared these and several other experimental USDA compounds with the alkyl neoalkanamides (Tables 2, 7). Under identical test conditions, several members of the alkyl neoalkanamide family were superior to these compounds as well as to fencholic acid.

N,N-diethylphenylacetamide (DEPA) has been reinvestigated as a repellent of various arthropods, including cockroaches (Prakash et al. 1990, Rao & Rao 1991). It was concluded that, at a concentration of 0.5 mg/cm^2, it exhibited residual repellency for 3 wk against the German cockroach (Prakash et al. 1990). However, at 0.1 mg/cm^2 DEPA repelled only 67% of the cockroaches 1 d after treatment. In our assays, using 0.106 mg/cm^2, DEPA was significantly inferior to several alkyl neoalkanamides (Tables 2 and 7).

Pyrethrins, in combination with synergists such as piperonyl butoxide (PBO), are effective repellents against mosquitoes (Wright & Burton 1969). Synthetic analogs such as permethrin are effective repellents and toxicants against ticks (Schreck et al. 1986). However, both pyrethrins and PBO appear to be ineffective long-term repellents of German cockroaches (Table 7).

Mint oils (*Mentha arvensis* and *M. spicata*) were shown to be the most effective repellents from among 86 essential oils tested on German cockroaches in no-choice tests (Inazuka 1982a, b). The constituents (–)-limonene, (–)-menthone, (–)-menthol and (–)-carvone were the most effective repellents, whereas their (+)-enantiomers and racemic compounds were less effective (Inazuka 1982b). Interestingly, (+)-limonene exhibited the same high degree of repellency as dimethyl phthalate against the *Aedes aegypti* mosquito (Hwang et al. 1985), whereas effective mosquito repellents such as oils of citronella, lavender, rosemary, and pennyroyal had marginal or no effectiveness against cockroaches (Inazuka 1982a). However, in our assays, both enantiomers of limonene and all other terpenoids we tested were ineffective repellents of male German cockroaches. Cineole has been shown to be an effective repellent of American cockroaches in choice tests lasting only 8 h (Scriven & Meloan 1984b), but our data do not indicate prolonged repellency of this terpenoid against the German cockroach. Long-term choice box assays have shown that cedar-wood flake boards were relatively repellent to German cockroaches, but were ineffective against the American and smokybrown cockroaches (Appel & Mack 1989). In our assays, cedar wood oil was ineffective, corroborating the comparatively low repellency (<63%) of cedar boards, but also suggesting that other constituents in cedar wood may be repellent, and that cedar wood varieties must be considered in such tests. The importance of using comparable test methodologies and standard references is again highlighted.

Triterpenoids isolated from seeds of the neem tree have been reported to be toxic, to inhibit feeding and growth, and to be repellent to various insects including cockroaches (Adler & Uebel 1985). In our tests, however, neither a 1% solution of neem oil nor 2 ml of Margosan-O, a commercial formulation of neem seed extract, exhibited any appreciable repellency of *B. germanica* males (Table 7).

Substantivity. Repellent activity is related to the intrinsic repellency of the compound, or its ability to stimulate the insect, and its persistence on various substrates. The repellent activity of "6-2-2", a mixture of dimethyl phthalate, indalone and ethylhexanediol (Rutgers 612), is superior to that of its components because of improved persistence, not greater intrinsic repellency (Kellogg et al. 1968). Indeed, these authors concluded that "molecule for molecule,

Table 7. Contact repellency of previously reported insect repellents to German cockroach males: days of 90% repellency determined by probit analysis ± 95% FL

Compound	Days 90% of males repelled (95% FL)
A. Commercial repellents	
N,N-diethyltoluamide (DEET)	5.4 (3.7– 6.6)
2-Hydroxyethyl-*n*-octyl sulfide (MGK 874)	5.9 (3.4– 7.5)
N-Octyl bicycloheptene dicarboximide (MGK 264)	10.1 (0 –28.1)
Synergistic blend: 66% MGK 264 + 33% MGK 874	6.5 (3.9– 8.5)
Hexahydrodibenzofura carboxaldehyde (MGK 11)	1.1 (0 – 3.1)
Di-*n*-propyl isocinchomerate (MGK 326)	0.5 (0 – 2.4)
2-Ethyl-1,3-hexanediol (Rutgers 612)	6.6 (5.0– 7.9)
2-(*n*-butyl)-2-ethyl-1,3-propanediol	8.1 (5.5– 9.9)
Dimethyl phthalate	0 nf
Dibutyl succinate (Tabutrex)	5.3 (2.8– 6.9)
Piperonyl butoxide	3.8 (1.5– 5.8)
Pyrethin (0.1%)	0 nf
B. Essential oils	
Mentha arvensis (Chinese cormint)	2.1 (0.7– 3.4)
M. piperita (U.S. midwest peppermint)	4.4 (1.3– 6.4)
M. spicata (U.S. farwest American spearmint)	5.4 (3.3– 6.9)
M. cardiaca (U.S. farwest scotch spearmint)	0.1 (0 – 1.6)
Lemongrass East Indian oil	5.1 (2.4– 7.3)
Lemon oil California	0 nf
Citronella oil java	3.2 (0.9– 5.3)
Cedarwood oil, eastern (*Juniperus virginia* L.)	0 nf
Pine oil	0.5 (0 – 1.1)
C. Terpenoids	
(–)-Limonene	0 (0 – 0.5)
(+)-Limonene	0 (0 – 1.3)
(–)-Carvone	0.5 (0 – 1.5)
Cineole (eucalyptol)	0 nf
Linalool	0.6 (0 – 1.4)
Gum camphor	0 nf
Citronellal	0 (0 – 0.5)
Apha terpineol	0.8 (0 – 2.6)
Fencholic acid (3-isopropyl-1-methylcyclopentanecarboxylic acid)	8.8 (7.2–10.1)
Neem oil	0 (0 – 0.6)
2-MI margosan (neem seed extract)	0 (0 – 1.9)
D. Experimental repellents	
N,N-Diethylcyclohexaneacetamide	5.9 (4.3– 7.1)
1,2,3,6-Tetrahydro-1-(2-methyl-1-oxopentyl) piperidine	3.1 (1.5– 4.4)
4-Methyl-1-(3-methyl-1-oxo-2-butenyl) piperidine	3.4 (1.9– 4.9)
2-Ethyl-1-(2-methyl-1-oxo-2-butenyl) piperidine	3.4 (1.1– 4.8)
N,N-Diethyl-3-cyclohexanepropanamide	11.9 (9.1–13.9)
N,N-Diethyl nonanamide	11.8 (9.1–13.5)
N,N-Diethylphenylacetamide	3.6 (1.5– 5.6)

Where the RT_{90} value is 0, probit analysis was not possible (nf, no fit) and the compound was clearly not repellent.

the commonly used [mosquito] repellents are about equally effective, and that any difference in their performance in the field is likely to depend on their persistency when applied to the person." This would argue against the practice of using short-term studies for testing repellents of cockroaches. The alkyl neoalkanamides are, as a class, especially persistent. Evaporation rate studies from filter paper indicated that methyl neodecanamide had an evaporation half-life of 7 d compared with 3–4 d for DEET (R.J.S., unpublished data). This may contribute to its superiority as a cockroach repellent. The availability within the alkyl neoalkanamide class of a wide range of molecular weights may prove useful in obtaining mixtures with high initial, possibly vapor, repellency, as well as persistent repellency.

Repellents and Cockroach Control. In suppressing indoor cockroach populations, the insecticide-treated area should be minimized and the efficacy of the insecticide maximized with proper sanitation, structural modification, the use of pheromones and other attractants to increase exposure of the insect to insecticides, and application of repellents to adjoining areas (Schal & Hamilton 1990). Repellents may be effective in two main approaches. First, they may be applied in difficult-to-reach hidden places such as electrical and plumbing systems, which may serve as runways for cockroaches and facilitate their dispersal between apartments (Runstrom & Bennett 1984, 1990). Here, repellents are usually applied along with residual insecticides, or insecticidal formulations which are repellent, such as sorptive dusts, are applied for preventive control (Rust 1986). On exposed surfaces, repellency clearly interferes with the efficacy of insecticides, and therefore insecticides and repellents are incompatible on the same surface. Here, effective noninsecticidal repellents may be used to "corral" cockroaches onto insecticide-treated surfaces. This second approach is based on nontoxic, relatively substantive and nonodorous repellents that, in some cases, may be applied to surfaces through cleaning solutions. Other uses include treatment of soft drink and beer containers (Mallis et al. 1961), packaging materials, sensitive areas such as hospital facilities, computers and electronic equipment, as constituents of perfumes, suntan lotions, cosmetic creams, and other preparations which are applied directly to the human skin for protection against body lice, mosquitoes, biting flies, chiggers, ticks, and fleas. The alkyl neoalkanamides fit these criteria. Safety investigations to date indicate that alkyl neoalkanamides are a safe and mild class of chemicals. These investigations will be published separately. Saturated aliphatic amides are a broad chemical class that includes surfactant chemicals that have a record of long, safe consumer use.

Alkyl neoalkanamides with a molecular weight range of 185–227 consisting of 11–14 carbon atoms show commercial potential as a new class of safe and effective insect repellents. This is based on their longer lasting cockroach and ant repellency, safety, and aesthetics. In addition, this chemical class is chemically stable and relatively economical.

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