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Extended summaries 9th International Congress of Pesticide Chemistry

The following are Extended Summaries based on material from poster presentations at the 9th International Congress of Pesticide Chemistry, organised by the International Union of Pure and Applied Chemistry (IUPAC) and held in London, UK, 2–7 August 1998. They are entirely the responsibility of the authors and do not necessarily reflect the views of the Editorial Board of Pesticide Science.

New fluoro intermediates for herbicidal sulfonylureas

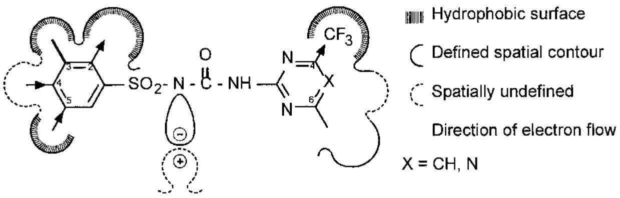
Gerhard Hamprecht,* Horst Mayer, Karl-Otto Westphalen and Helmut Walter
BASF Aktiengesellschaft D-67056 Ludwigshafen, Germany

Abstract: New pyrimidine and triazine intermediates for herbicidal sulfonylureas are prepared as follows: 2,4-dichloro-6-methylpyrimidine is converted via a halogenation, halogen exchange and substitution sequence to 2-amino-4-trifluoromethyl-6-trifluoromethoxypyrimidine. New fluoromethyl-triazines are available starting from guanidine, trichloroacetonitrile and difluoroacetic anhydride, or alternatively from thiocarbamoyl guanidine and chlorodifluoroacetic ester ring closure. To obtain new *o*-fluoroalkyl-benzenesulfonamide precursors, *o*-chlorobenzaldehyde was fluorinated with sulfur tetrafluoride, or a bromobenzene derivative was subjected to a substitution reaction with sodium pentafluoropropionate. Sulfonylureas derived from trifluoromethylpyrimidines with an *m*-methylthio substituent are selective post-emergence herbicides in cotton, presumably due to sulfone metabolization. Selectivity in wheat is obtained by combining 4-methoxy-6-trifluoromethylpyrimidine with a lipophilic difluoromethylbenzenesulfonamide moiety. Also in the difluoromethyl-triazine series, the combination with the difluoromethyl-benzenesulfonamide moiety is a good choice for wheat selectivity. Chlorodifluoromethyl- and trifluoromethyltriazines, however, combine better with an aromatic ester for best activity and selectivity in wheat. Selected compounds are undergoing broad field tests in wheat.

Keywords: side-chain-fluorinated pyrimidines; triazines; benzenesulfonamides; SAR of herbicidal sulfonylureas

1 INTRODUCTION

Due to their low use rates and low mammalian toxicity sulfonylureas have emerged as commercially important innovative herbicides. Acetolactate binding site models[1] showed small substituents in the 4,6-positions of the pyrimidine and triazine moieties, preferentially methyl, methoxy and chlorine, to be the best choice for herbicidal activity, with metsulfuron-methyl[2] and chlorimuron-ethyl[3] selected for wheat and soybean selectivity. In the case of primisulfuron-methyl[4,] a pseudohalide like the difluoromethoxy group contributes significantly to corn selectivity. We have recently shown that chlorodifluoromethoxy and trifluoromethoxy groups point in the same direction,[5] revealing the importance of an alternative hydrophobic surface in the heterocyclic moiety.



We then became interested in the influence of fluorinated methyl groups on structure/activity relationships. In addition, *O*-demethylation of methoxypyrimidines – being the predominant pathway for metabolism[6] – should be enhanced by an electron-withdrawing trifluoromethyl group, thus providing an opportunity for crop selectivity.

2 MATERIALS AND METHODS

2.1 Synthesis

2.1.1 2-Amino-4-trifluoromethyl-6-trifluoromethoxypyrimidine

2,4-Dichloro-6-methylpyrimidine (Fig 1; **A**) is converted by a sequence of chlorination and substitution steps to 2-chloro-4-trichloromethyl-6-trichloromethoxypyrimidine (**B**) in a 73% overall yield, which is the starting material for the final fluorination to **C**. Leaving-group ability of the trifluoromethoxy group is shown in the side reaction of **C** with ammonia, even at −75 °C, resulting in 21% of the 4-amino displacement product **E**, while formation of **D** (48% yield) is still preferred (Fig 1).

2.1.2 4-Substituted-2-amino-6-trifluoromethylpyrimidines

Condensation of guanidine hydrochloride with ethyl 4,4,4-trifluoroacetoacetate[7] and chlorination with phosphorus oxychloride[8] resulted in 2-amino-4-chloro-6-trifluoromethylpyrimidine (**G**), which, upon reaction with nucleophiles, gave high yields of the

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* Correspondence to: Gerhard Hamprecht, BASF Aktiengesellschaft, D-67056 Ludwig shafen, Germany

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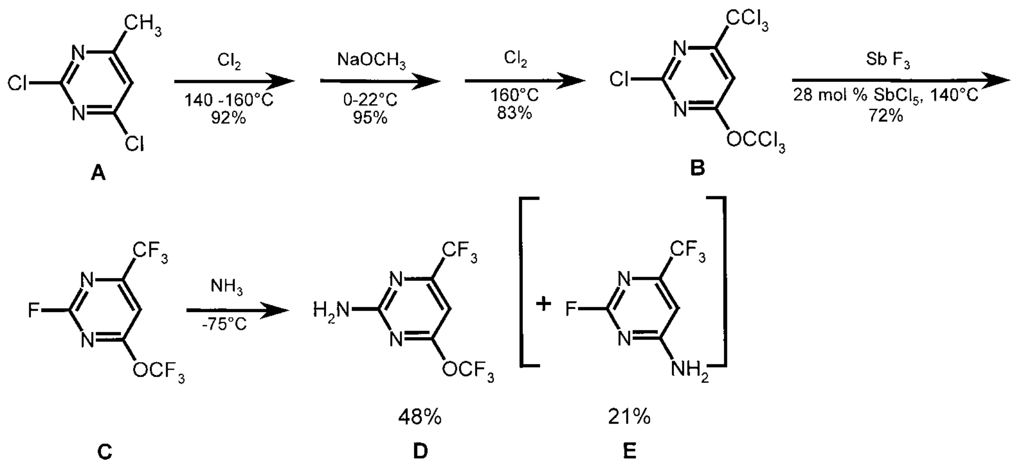

Figure 1. Synthesis route to 2-amino-4-trifluoromethyl-6-trifluoromethoxypyrimidine.

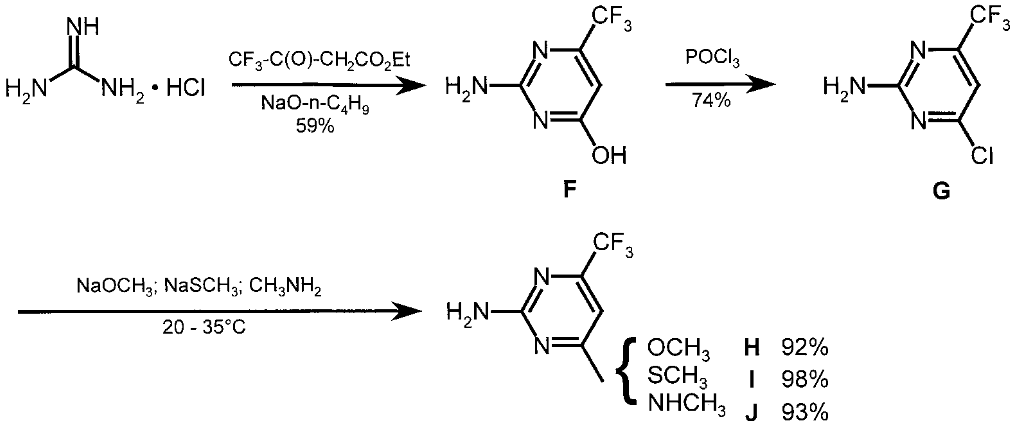

Figure 2. Synthetic routes to 4-substituted-2-amino-6-trifluoromethylpyrimidines.

corresponding 4-methoxy-, 4-methylthio- and 4-methylaminopyrimidines (**H**–**J**),[8] (Fig 2).

2.1.3 *2-Amino-4-difluoromethyl-6-methoxytriazine*

Likewise, the trichloromethyl group in triazine **K**, introduced by condensation of guanidine with trichloroacetonitrile and subsequent difluoroacetic anhydride ring closure, serves as an excellent leaving group for the synthesis of 2-amino-4-difluoromethyl-6-methoxytriazine (Fig 3; **L**)

2.1.4 *2-Amino-4-chlorodifluoromethyl-6-methoxytriazine*

The 4-chlorodifluoromethyltriazines **M** and **N** are accessible from cyanoguanidine by reaction with hydrogen sulfide, methylation, methyl chlorodifluoroacetate ring closure and subsequent methanolysis (Fig 4).

2.1.5 *o-Fluoroalkyl-benzenesulfonamides*

Key steps for the synthesis of new *o*-fluoroalkylbenzene sulfonamides[9] are (a) the conversion of an aromatic aldehyde function with sulfur tetrafluoride, or (f) bromine substitution by sodium pentafluoropropionate. Standard procedures (b–d)[10] allow introduction of the sulfonamide moiety in place of the remaining aromatic halide (Fig 5).

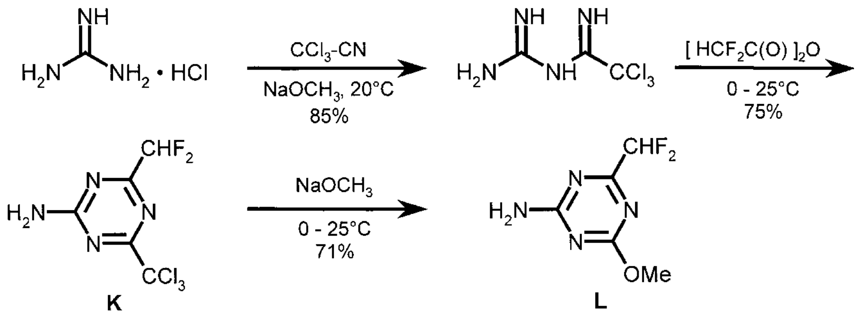

Figure 3. Synthetic route to 2-amino-4-difluoromethyl-6-methoxytriazine.

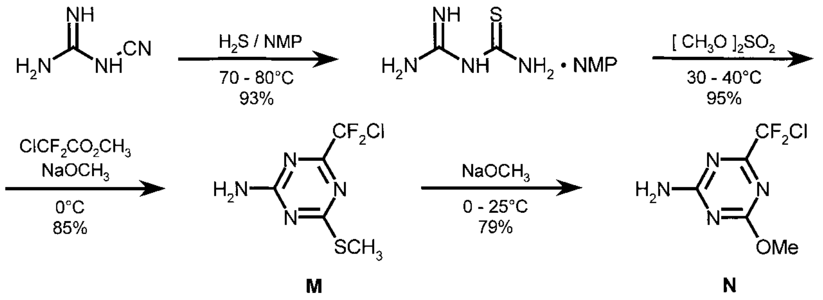

Figure 4. Synthetic route to 2-amino-4-chlorodifluoromethyl-6-methoxytriazine.

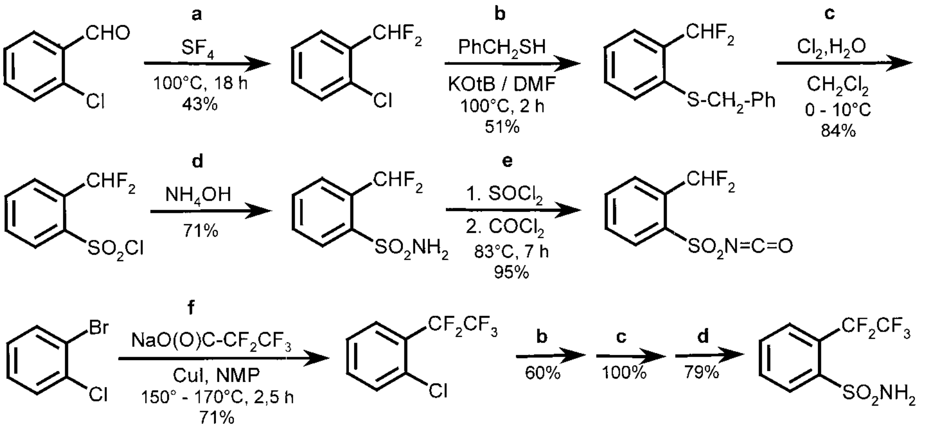

Figure 5. Synthetic routes to *o*-fluoroalkyl-benzenesulfonamides.

2.2 Biological tests

2.2.1 Greenhouse experiments

All the data were taken from screening-type trials in the greenhouse. For post-emergence tests, plants were cultivated in plastic pots of 8.6 cm diameter containing loamy sand with about 1.2% humus as the substrate. The test plants were sown, grown in the test pots to a height of 4–12 cm and then treated with the test compound in a spray chamber at a rate of 15.6 g ha^{-1}. The number of replicates was one and, for comparison, four untreated control pots were included in each test. After the application, the plants were kept for 18–20 days at 18–27 °C, during which period the plants were maintained and their reaction to the individual treatments was assessed and recorded.

The assessments of injury to the plants were on a scale from 0 to 100 in comparison to the untreated controls, 0 denoting no damage and 100 denoting complete destruction of at least the visible plant parts.

2.2.2 Test species

The following plant species were used: *Gossypium hirsutum* L (Goshi), *Abutilon theophrasti* (L) Medic (Abuth) *Amaranthus retroflexus* L (Amare), *Chenopodium album* L (Cheal), *Chrysanthemum coronarium* L (Cimco), *Echinochloa crus-galli* Beauv (ECHGG), *Lamium amplexicaule* L (Lamam), *Matricaria inodora* L (Mamn), *Polygonum persicaria* L, *Setaria faberi* Herrm (Setfa), *Sinapis alba* L (Sinal), *Solanum nigrum* L (Solni), *Stellaria media* Vill (Steme) and *Triticum aestivum*. L (Trzaw).

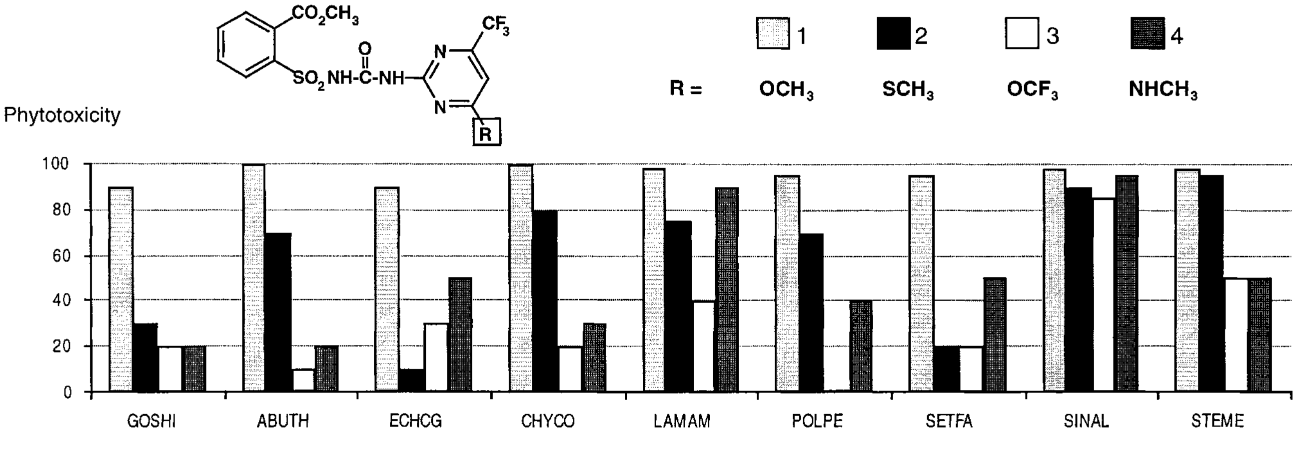

Figure 6. Metabolism-oriented design: reactive pyrimidine substituents.

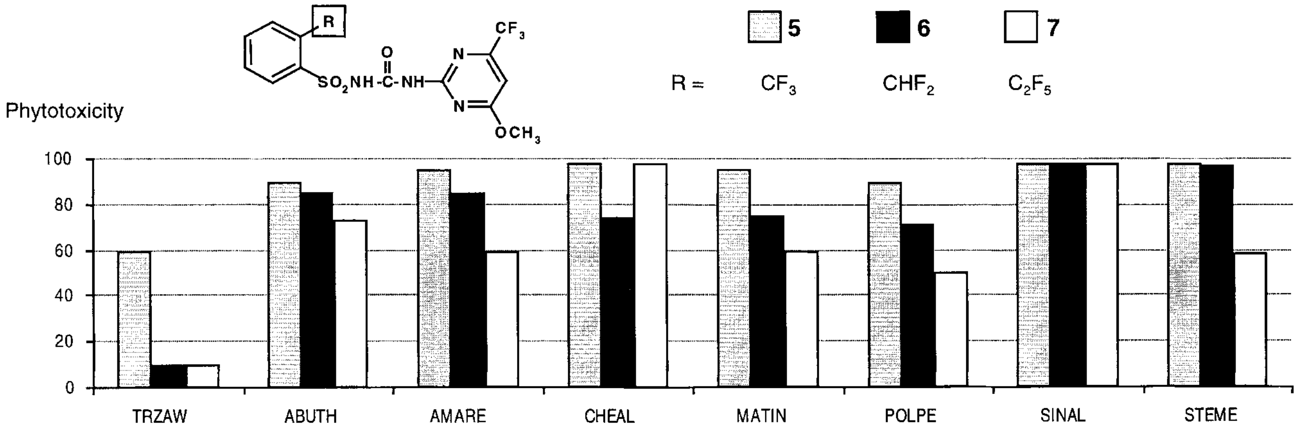

Figure 7. Introduction of fluorinated side-chains into the benzenesulfonamide moiety.

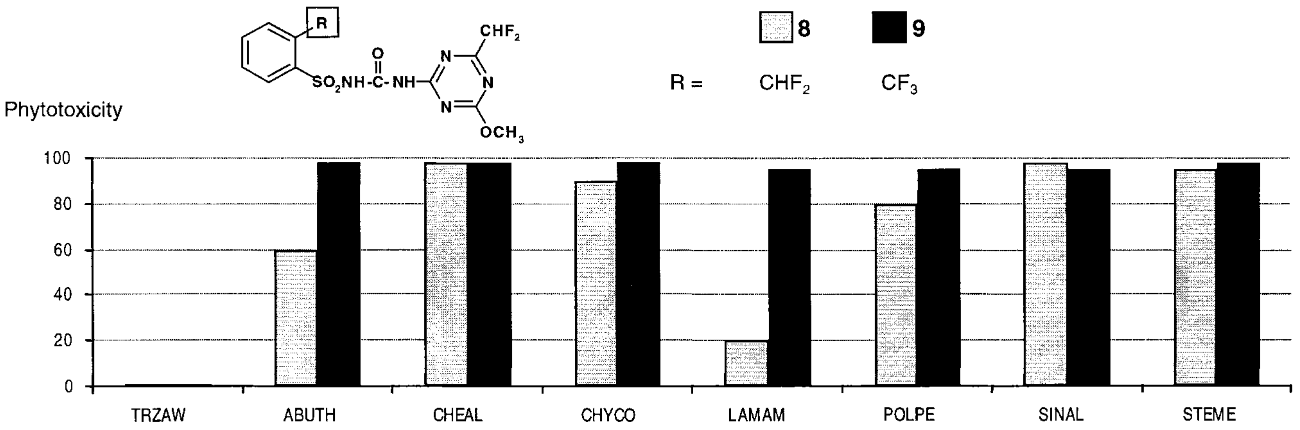

Figure 8. Combining fluorinated benzenesulfonamides with difluoromethyltriazines.

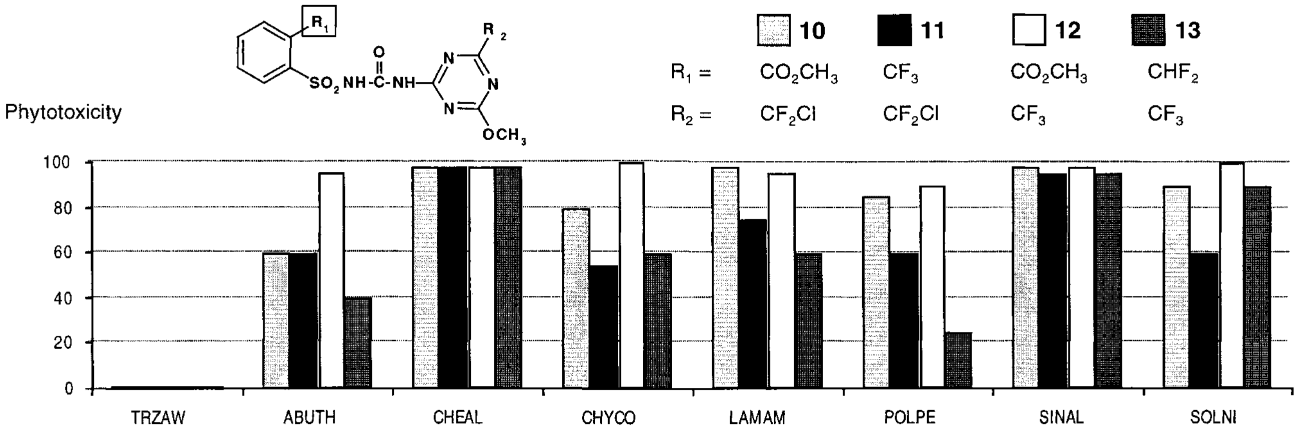

Figure 9. Influence of new triazine substituents: CClF$_2$/CF$_3$.

3 RESULTS AND DISCUSSION

3.1 Structure - activity relationships (SAR)

3.1.1 Metabolism-oriented design: Reactive trifluoromethyl-pyrimidines (Fig 6)

Reactive trifluoromethylpyrimidine substituents change the herbicidal activity of the sulfonylureas in question. Compound **1** with methoxy has high activity on broad-leaved weeds and grasses, whereas the methylthio derivative **2** loses grass activity but gains crop tolerance in cotton – presumably by faster metabolization to a sulfone intermediate. Trifluoromethoxy **3** and methylamino **4** reduce activity notably, because they are too lipophilic or hydrophilic respectively.

3.1.2 INTRODUCTION of fluorinated side chains into the benzenesulfonamide moiety (Fig 7)

2-Trifluoromethylbenzenesulfonamide is the most active side chain, whereas difluoromethyl is weaker but has additional wheat tolerance. Pentafluoroethyl reduces activity notably.

3.1.3 Combining fluorinated benzenesulfonamide with difluoromethyltriazine (Fig 8)

After variation of the heterocyclic moiety from trifluoromethylpyrimidine to difluoromethyltriazine, trifluoromethyl as side chain on the benzenesulfonamide again leads to more active compounds than difluoromethyl. Both show good wheat selectivity.

3.1.4 Influence of new triazine substituents: $CClF_2$ vs CF_3 (Fig 9)

However, chlorodifluoromethyl- and trifluoromethyltriazine are different, in that each combines better with an aromatic ester than with the fluorinated side chain. Selectivity in wheat is common to all.

4 CONCLUSION

Side-chain-fluorinated pyrimidines, triazines and benzenesulfonamides are ideal building blocks for the research chemist. They offer chemical and biological flexibility for new sulfonylureas as post-emergence herbicides. Selectivity in wheat and cotton is observed, best herbicidal activity being obtained up to the three- to four-leaf stage of the weeds. Selected compounds are undergoing broad field tests in wheat.

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Semiochemical modulation of oviposition behaviour in the gregarious desert locust *Schistocerca gregaria*

Baldwyn Torto,* Yousif OH Assad, Peter GN Njagi and Ahmed Hassanali

International Centre of Insect Physiology and Ecology, PO Box 30772, Nairobi, Kenya

Abstract: Bioassays have shown that sand freshly contaminated by ovipositing females of the gregarious desert locust *Schistocerca gregaria* (Forskal) is more effective in inducing further oviposition from conspecifics than contaminated sand stored for three or six months, which contrasts with results obtained previously with *Locusta migratoria* (Reiche & Farmaire). The activity of contaminated sand correlated with the levels of three unsaturated aliphatic ketones, (*Z*)-6-octen-2-one, (*E,E*)-3,5-octadien-2-one and its geometric isomer (*E,Z*)-3,5-octadien-2-one present in the volatile emissions from the sand.

Keywords: *Schistocerca gregaria*; (*Z*)-6-octen-2-one; (*E,E*)-3,5-octadien-2-one; (*E,Z*)-3,5-octadien-2-one; oviposition; seimiochemical; locust

Gregarious females of the desert locust *Schistocerca gregaria* (Forskal) and *Locusta migratoria* (Reiche & Farmaire) produce pheromones during oviposition which attract conspecifics to lay their eggpods at common sites.[1–4] In *L migratoria*, repeated layings by females increase the preference of the sand for further oviposition.[3,4] Of the two locust species, pheromone identification has been carried out for *S gregaria* in recent work from our laboratory. Two aromatic compounds, acetophenone and veratrole were identified from the volatiles emitted by the froth plug of the eggpod as oviposition pheromone components.[5,6] In the present study, the oviposition response of females of *S gregaria* to sand in which conspecifics had laid previously, but without the froth or eggs, was compared to that of clean sand. On average, about 75% of the eggpods deposited by females were laid into moist sand contaminated by conspecifics compared to 25% into clean moist sand. However, much of the activity of contaminated sand was lost after long storage at room temperature, dropping to 56% after three months, with a total loss of activity after six months. These results contrast with those obtained previously for *L migratoria* for which the activity of contaminated sand can last for as long as six months.[4] Gas chromatographic-electroantennographic detection (GC-EAD) analysis revealed the presence of three candidate oviposition pheromone components in the volatiles of freshly contaminated sand. These were identified by GC-MS as (*Z*)-6-octen-2-one, (*E,E*)-3,5-

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* Correspondence to: Baldwyn Torto, International Centre of Insect Physiology and Ecology, PO Box 30772, Nairobi, Kenya
E-mail: btorto@icipe.org

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