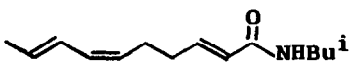
Tetrahedron Letters,Vol.29,No.32,pp 3949-3950,1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

A GENERAL AND HIGHLY STEREOSELECTIVE APPROACH TO UNSATURATED ISOBUTYLAMIDES VIA ARSONIUM SALT. NEW SYNTHESIS OF PELLITORINE†

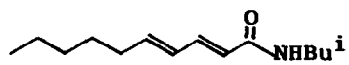
Lilan Shi*, Jianhua Yang, Xueqing Wen, Yao-Zeng Huang
Shanghai Institute of Organic Chemistry, Academia Sinica,
345 Lingling Lu, Shanghai, China

Abstract: The highly stereoselective synthesis of conjugated unsaturated isobutylamides in good yields via the arsonium salt is described, and the new synthesis of pellitorine is also reported.

Lipid amides which have general type of (2E)- and (2E,4E)-unsaturated isobutylamides occur widely in higher plants. Such amides are comparatively unstable and difficult to access, occurring only in small amount in plants.[1] The most representative compounds are spilanthol **1** and pellitorine **2** which are naturally occurring insecticides isolated from Spilanthes Oleranceae[2] and Anacyclus Pyrethrum roots[3], respectively. Several groups have reported successful syntheses

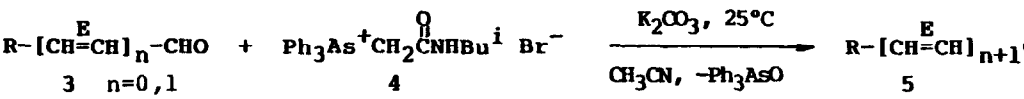


1



2

of unsaturated isobutylamides.[1,4] Recently, Crombie et al. reported a hydrozirconation method.[5] The interesting insecticidal activity of such lipid amides stimulated us to develop a more convenient and versatile synthetic method for lipid isobutylamides. Here we report a general and highly stereoselective synthesis of both (2E)- and (2E,4E)-unsaturated isobutylamides by means of the arsonium salt **4**, starting from readily available aldehydes **3**. The approach is outlined below and the results are summarized in Table.



N-(Isobutyl)aminocarbonylmethyltriphenylarsonium bromide (**4**), mp 174-5°C, prepared in 96% yield by the procedure described previously(CH_3CN as solvent)[6] was reacted with aldehydes **3** at rt in the presence of K_2CO_3 in two solvent systems: A, CH_3CN (trace H_2O); B, CH_3CN (trace $HCONH_2$). For aliphatic aldehydes and benzaldehydes, the solvent A gave the α,β-unsaturated carboxamides **5** in excellent yields (entry 1-5). However for α,β-unsaturated aldehydes and benzaldehydes with electron releasing group where the solvent A was unsatisfactory,[7] the solvent B was quite effective (entry 6-8). The difference in reactivity could be attributed to the stronger basicity of potassium carbonate in $HCONH_2$ than in H_2O.

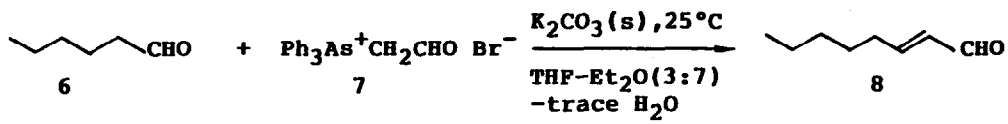
In order to test utilization of the present methodology, we have synthesized an insecticide pellitorine **2** although many reports for its synthesis have appeared in the literatures.[1a,5] Formylolefination of **6** with the reagent **7** was

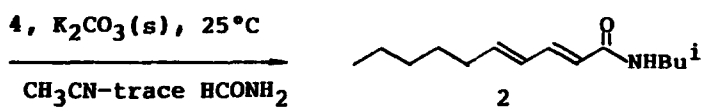
Table Conversion of Aldehyde 3 to (2E)-, and (2E,4E)-Isobutylamide 5[a)]

Entry	Aldehyde 3	Solvent[b)]	Reaction Time(h)	Product 5[c)]	Yield (%)[d)]
1	C_6H_5CHO	A	19	C_6H_5-CH=CH-$CONHBu^i$	96
2	p-Cl-C_6H_4CHO	A	12	p-Cl-C_6H_4-CH=CH-$CONHBu^i$	95
3	p-O_2N-C_6H_4CHO	A	7	p-O_2N-C_6H_4-CH=CH-$CONHBu^i$	99
4	$CH_3(CH_2)_4CHO$	A	12	$CH_3(CH_2)_4$-CH=CH-$CONHBu^i$	95
5	$CH_3(CH_2)_8CHO$	A	11	$CH_3(CH_2)_8$-CH=CH-$CONHBu^i$	97
6	p-CH_3O-C_6H_4CHO	A	21	p-CH_3O-C_6H_4-CH=CH-$CONHBu^i$	60
		B	24		92
7	C_6H_5-CH=CH-CHO	A	21	C_6H_5-CH=CH-CH=CH-$CONHBu^i$	61
		B	17		93
8	CH_3-CH=CH-CHO	A	15	CH_3-CH=CH-CH=CH-$CONHBu^i$	57
		B	18		78

a) All reactions were run at 25°C. b) Solvent A: CH_3CN-H_2O (200:1); Solvent B: CH_3CN-$HCONH_2$ (100 :1). c) All compounds were characterized by ^1H NMR, IR, MS, and elemental analysis. No Z stereoisomer was found in all cases. d) Isolated yields after flash column chromatography.

achieved according to our procedure,[6a)] affording the α,β-unsaturated aldehyde **8** in 81% yield(>97% pure by GC). Compound **8** was reacted with the reagent **4** in the solvent B to give pellitorine **2** in 79% yield. The ^1H NMR analysis of our synthetic **2** failed to detect any Z double bond isomer.





Our synthetic method reported here is a highly stereoselective and versatile route to a wide range of lipid isobutylamides.

Acknowledgement. We are grateful for partial financial support from National Natural Science Foundation of China.

References and notes

† This is paper 64 in the series on the application of organic compounds substituted with elements of groups 15 and 16 in organic synthesis.
(1) (a) R.Bloch, D. Hassan-Gonzales, Tetrahedron, **42**, 4975(1986). (b) L. Crombie, D. Fisher, Tetrahedron Lett., **26**, 2477(1985).
(2) M. Jacobson, Chem. and Ind., 50(1957).
(3) L. Crombie, J. Chem. Soc., 999(1955).
(4) L. Crombie, R, Denman, Tetrahedron Lett., 25, 4267(1984). R. J. Blade, J. E. Robinson, ibid, **27**, 3209(1986).
(5) L. Crombie, A. J. W. Hobbs, M. K. Horsham, Tetrahedron Lett., **28**, 4875 (1987). L. Crombie, M. A. Horsham, R. J. Blade, ibid, **28**, 4879(1987).
(6) (a) Y. Z. Huang, L. L. Shi, J. H. Yang, Tetrahedron Lett., **26**, 6447(1985). (b) Y. Z. Huang, L. L. Shi, J. H. Yang, J. T. Zhang, ibid, **28**, 2159(1987).
(7) Starting aldehydes **3** were partly recovered.

(Received in Japan 25 January 1988)