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SYNTHESIS OF 3,11-DIMETHYL-2-NONACOSANONE,
A SEX PHEROMONE OF THE GERMAN COCKROACH,
BLATTELLA GERMANICA[1]

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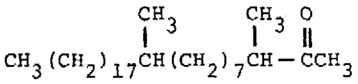
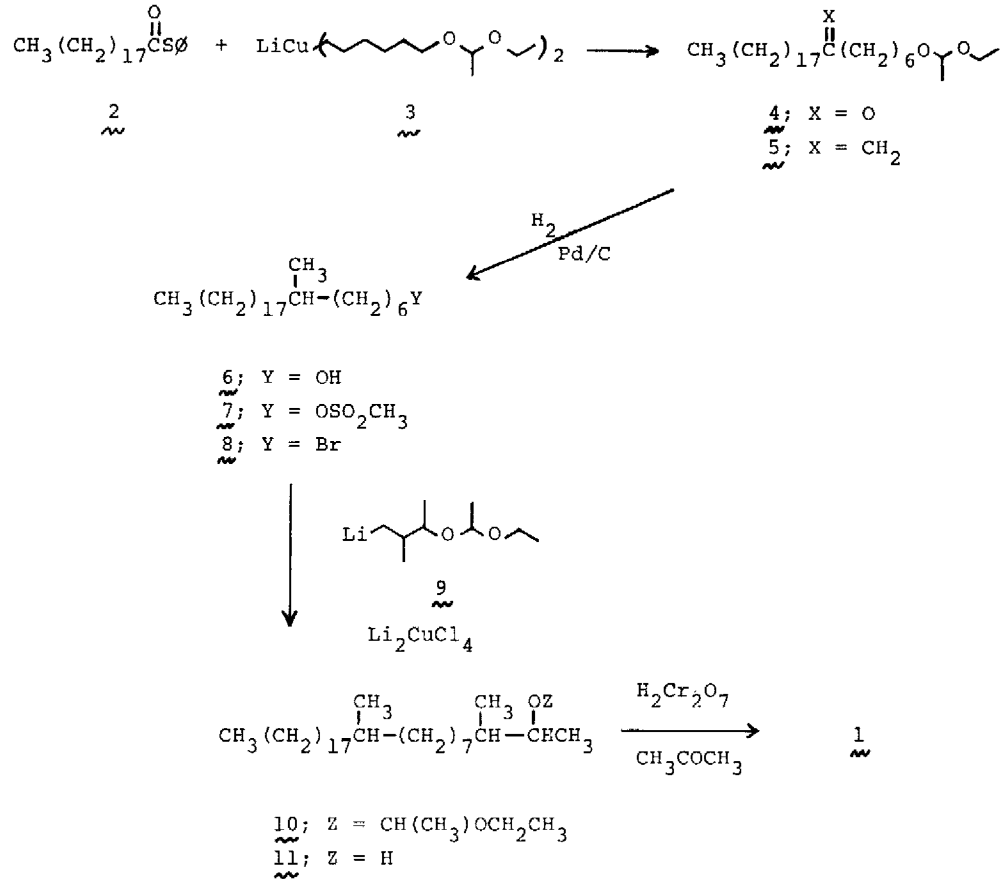
Nishida, Fukami and Ishii recently reported[2a] the isolation of two compounds from virgin females of the German cockroach, Blattella germanica (L.), which independently elicit a wing-raising response in males. These investigators characterized one of the two pheromones as 3,11-dimethyl-2-nonacosanone (1) from spectral data[2a] and comparison with a synthetic sample.[2b] We communicate here an alternative preparation of methyl ketone 1.[3]



$$CH_3(CH_2)_{17}\overset{CH_3}{\overset{|}{C}H}(CH_2)_7\overset{CH_3}{\overset{|}{C}H}-\overset{O}{\overset{\|}{C}}CH_3$$

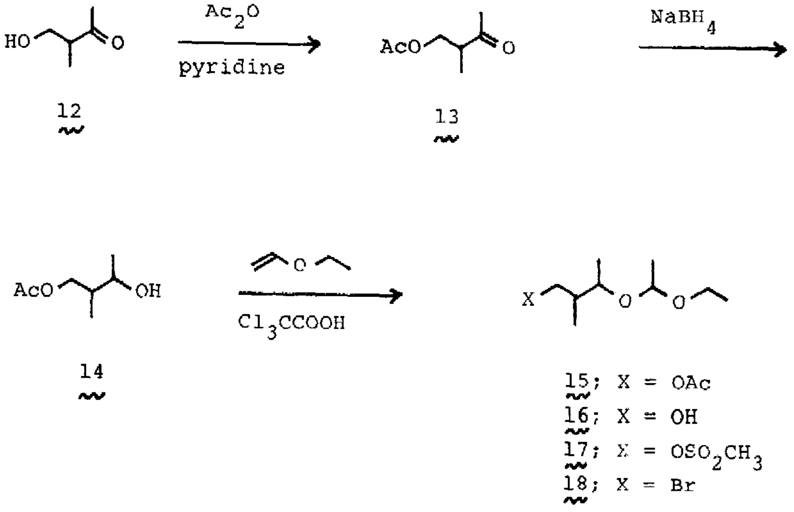
1

Treatment of S-phenyl nonadecanethioate (2, mp 43-44°; prepared from nonadecanoyl chloride and benzenethiol) in ether at -40° for 1 hr with one equiv of lithium di-6-[(1-ethoxy)ethoxy]hexylcuprate (3), obtained from the ethoxyethyl ether of 6-chlorohexanol, gave the ketoacetal 4 in 75% yield, mp 47.5-48.0°.[4,5] Reaction of 4 with triphenylphosphonium methylide in tetrahydrofuran at 25° (20 hr) produced the methylene acetal 5 in 84% yield.[5] Hydrogenation of 5 in hexane over 5% palladium on charcoal followed by hydrolysis in aqueous-tetrahydrofuran with a catalytic amount of p-toluenesulfonic acid gave the saturated alcohol 6 (mp 48°) in an overall yield of 83% from 5. Conversion of 6 to the corresponding bromide in an 87% yield was achieved by



reaction of 6 with mesyl chloride and triethylamine in dichloromethane at 0°[6] for 1 hr to give the mesylate 7 which on treatment with four equiv of lithium bromide in acetone at 40° for 16 hr produced bromide 8. Copper-catalyzed (Li_2CuCl_4) coupling[7] of 8 with 3-[(1-ethoxy)ethoxy]-2-methylbutyllithium (9) in tetrahydrofuran at -20° gave the acetal 10, and hydrolysis of the latter in aqueous-tetrahydrofuran at 65° for 1 hr with a catalytic amount of trichloroacetic acid, followed by oxidation of the resultant alcohol 11 (mp 30-31°) with Jones reagent in acetone at 10° gave the pheromone 1 as a diastereomeric mixture (mp 31.5-33.5°)[8] in 74% yield after preparative tlc.

The lithioacetal 9 was prepared as follows. Acetylation of 4-hydroxy-3-methyl-2-butanone (12) with acetic anhydride-pyridine in ether, followed by reduction of the ketoacetate 13 with sodium borohydride in methanol at 0°, and trichloroacetic acid catalyzed ether formation from the alcohol 14 and ethyl vinyl ether gave the acetoxy acetal 15 in 60% yield after distillation (bp 70-72° at 0.7 mm). Potassium carbonate treatment of 15 in methanol produced alcohol 16 in 93% yield. This alcohol reacted with mesyl chloride and



12

13

14

15; X = OAc
16; X = OH
17; X = OSO_2CH_3
18; X = Br

triethylamine in dichloromethane[6] at 0° to give mesylate 17, which was converted to the corresponding bromide (18) by the action of excess lithium bromide in dimethylformamide in a yield of 35%.[9] Bromoacetal 18 was smoothly converted to the lithio reagent 9 with three equiv of lithium-1% sodium in diethyl ether at 0° in 75% yield.[10]

References

(1) Contribution No. 44 from the Research Laboratory of Zoecon Corporation.

(2) (a) R. Nishida, H. Fukami, and S. Ishii, *Experientia*, 30, 978, (1974);
(b) R. Nishida, H. Fukami, and S. Ishii, *Appl. Ent. Zool.*, 10, 10 (1975).

(3) For other syntheses of pheromone 1, see A. W. Burgstahler, L. O. Weigel, W. J. Bell, and M. K. Rust, *J. Org. Chem.*, 40, 3456 (1975); M. Schwarz, J. E. Oliver, and P. E. Sonnet, *J. Org. Chem.*, 40, 2410 (1975).

(4) R. J. Anderson, C. A. Henrick, and L. D. Rosenblum, *J. Amer. Chem. Soc.*, 96, 3654 (1974).

(5) Yield after column chromatographic purification.

(6) R. K. Crossland and K. L. Servis, J. Org. Chem., **35**, 3195 (1970).

(7) R. J. Anderson and C. A. Henrick, J. Amer. Chem. Soc., **97**, 4327 (1975).

(8) This synthetic sample gave a wing-raising response in the males of the German cockroach comparable to that previously reported for other samples.[2b,3] The natural product is reported to have a melting point of 45-46° whereas previous synthetic samples (mixtures of diastereoisomers of **1**) are reported to have *ca.* mp 28-31°.[2b,3]

(9) Yield after retreatment of the crude bromo derivative with ethyl vinyl ether and subsequent column chromatography. An analytically pure sample of **18** was obtained by a subsequent evaporative distillation from potassium carbonate.

(10) Satisfactory nmr, ir, and mass spectra and elemental analyses were obtained for all new compounds.