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EASY ENTRY TO THE TRICYCLO(7,3,1,0^{1-6})TRIDECANE SYSTEM

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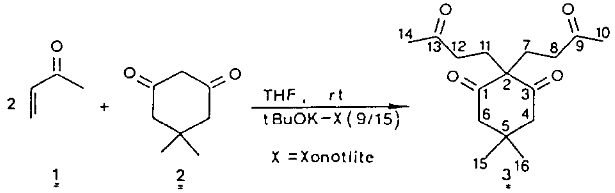
Abstract : Michael addition of two equivalents of methylvinylketone to dimedone, followed by acid-catalyzed cyclization give in 64% overall yield a strained tricyclic molecule with a spiro ring junction.

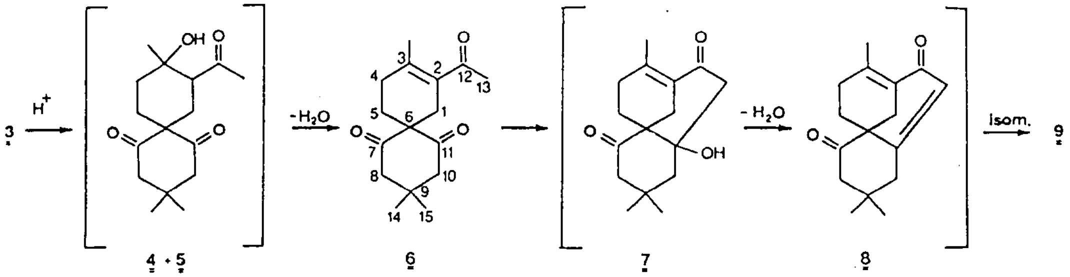
AVAILABILITY of a potent novel catalyst made by impregnation of xonotlite[1] with t-butoxide, active in the Michael[2] and Knoevenagel[3] condensations, let us to combine a Michael addition and a Robinson annulation[4-5]. In this manner, starting from a cyclohexane-1,3-dione, entry is gained in two high-yield steps into the hitherto unfamiliar tricyclo(7,3,1,0^{1-6})tridecane system, present nevertheless in a number of natural products with an interesting pharmacology[6].

Addition of two equivalents of methylvinylketone 1 to 5,5-dimethyl-cyclohexane-1,3-dione (dimedone 2) gave tetraketone 3[7] in 80% isolated yield :

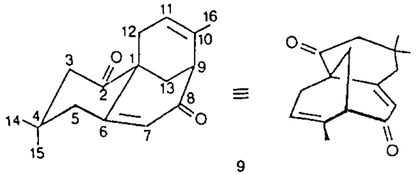


When p-toluenesulfonic acid (2.9mmol) was added to a refluxing solution of 3 (5mmol in 25ml) in the presence of a Dean-Stark water trap, Robinson annulation was induced. And this annulation was regiospecific : preference for six-membered ring formation, versus four- or five-membered rings, saw to it (Scheme).

SCHEME



The mixture of diastereomers 4 and 5 was neither isolated nor separated, but we did isolate bicycle 6, their dehydratation product[8]. When placed under the (acidic) reaction conditions, 6 underwent a second annulation. Regiospecificity of the second cyclization, i.e. non-intervention of the ring carbonyls as donors, can be ascribed to the decreased electrophilicity of the α,β-unsatured carbonyl. Presumably through tertiary alcohol 7 whose dehydratation would give the Bredt rule marginal $(S=7)^{9-10}$ bridgehead olefin 8, the final racemic product 9^{11} was formed in 79% isolated yield from 3.



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Molecule 9^{11} has five of the six trigonal carbons accumulated in the bicyclo(3,3,1) moiety. Its cmr and pmr spectra[11] are fully characteristic for such a structure.

Acknowledgments :

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7. mp : 105-106°C; ms : 280(M^+), 210; pmr ($CDCl_3$) : δ 0.85 (s,6H,15+16); 1.83 (t,4H,7+11, 7.5Hz); 1.95 (s,6H,10+14); 2.19 (t,4H,8+12,7.5Hz); 2.48 (s,4H,4+6); cmr ($CDCl_3$, ppm) 27.1 (t,7+11); 28.2 (q,15+16); 29.5 (q,10+14); 30.2 (s,5); 37.7 (t,8+12); 50.8 (t,4+6); 66.2 (s,2); 206.5 (s,9+13); 208.8 (s,1+3).
8. mp : 92°C; ms : 262 (M^+), 244, 220, 202; pmr ($CDCl_3$) : δ 0.90 (s,3H,15/16); 1.13(s,3H,16/15); 1.85 (m,3H,14); 2.01 (t,2H,5,6.3Hz); 2.13 (m,2H,4); 2.33 (s,3H,13); 2.48 (AB,2H,8+10,13.9Hz); 2.65 (m,2H,1); 2.84 (AB,2H,8+10,13.9Hz); cmr ($CDCl_3$, ppm) : 21.2 (q); 27.3 (q); 27.9 (t); 29.8 (q); 29.8 (t); 30.0 (q); 30.6 (t); 30.9 (s); 50.8 (t,8+10); 64.6 (s,6); 131.4 (s,2); 137.9 (s,3); 203.1 (s,12); 207.5 (s,7+11).
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11. mp : 117-118°C; ms : 244 (M^+); ir (CCl_4, cm^{-1}) 1715 (CO-2); 1680 (CO-8); 1615 (C=C 6-7); cmr ($CDCl_3$, ppm) : 21.5 (q,14); 25.7 (q,15); 30.6 (q,16); 30.8 (t,13); 33.3 (s,4); 33.5 (t,12); 45.7 (t,3); 48.6 (s,1); 48.9 (d,9); 51.6 (t,5); 119.3 (d,11); 124.7 (d,7); 132.8 (s,10); 161.1 (s,6); 198.4 (s,2); 210.9 (s,8); pmr : ($CDCl_3$, assignments from double resonance experiments; only the absolute sign of coupling constants was determined; nevertheless the geminal ${}^2J$'s are stated with the correct negative sign; a total of 17 different coupling constants were measured, and they are all nicely consonant with structure 9) : δ 0.79 (CH_3-14, ${}^4J_{3a}$=0.96Hz, ${}^4J_{5a}$=0.85Hz); 1.12 (CH_3-15); 1.68 (CH_3-16, ${}^4J_9$=0.40Hz, ${}^4J_{11}$=1.53Hz, ${}^5J_{12}$=2.27Hz, ${}^5J_{12'}$=1.70Hz); 2.00 (H-13s, ${}^3J_9$=2.79Hz, ${}^4J_{12e}$=1.66Hz); ∿2.2 (H-13a, ${}^2J_{13s}$=-13.22Hz); ∿2.2 (H-12, ${}^3J_{11}$=4.67Hz); ∿2.2 (H-12', ${}^3J_{11}$=2.67Hz); ∿2.2 (H-5e); ∿2.2 (H-3e); 2.55 (H-3a, ${}^2J_{3e}$=-14.35Hz); 2.66 (H-5a, ${}^2J_{5e}$=-14.76Hz); 2.79 (H-9, ${}^4J_7$= 0.93Hz); 5.34 (H-11, ${}^4J_9$=0.61Hz); 5.75 (H-7, ${}^4J_{5e}$=0.50Hz, ${}^4J_{5a}$=2.14Hz); elemental analysis (high-resolution ms) : obs = 244.146490; calc($C_{16}H_{20}O_2$) = 244.146320.

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