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INTRAMOLECULAR [2+2] CYCLOADDITIONS OF KETENES AND VINYLKETENES TO OLEFINS -III. THE SYNTHESIS OF ANGULAR ANNULATED TRIQUINANE DERIVATIVES

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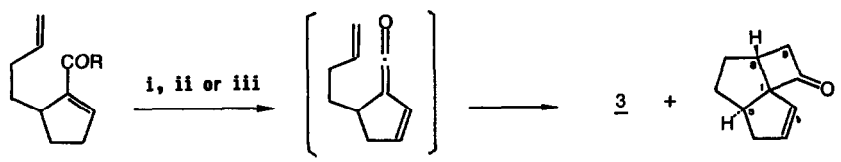
Summary: Intramolecular [2+2] cycloaddition of vinylketene 2 or ketene 6 to an olefin yielded the angular annulated triquinane precursors 4 or 7. The rate enhancement by DMAP in this process was demonstrated.

The intramolecular [2+2] cycloaddition of ketenes to unactivated olefins is a powerful tool for the stereospecific construction of bicyclic[1,2] and tricyclic cyclobutanones[3]. This approach is very versatile since cyclobutanones allow numerous selective transformations including ring expansion to cyclopentanones[4].

In this paper we report our approach to angular annelated triquinanes[5] using the intramolecular [2+2] cycloaddition of vinylketene 2 or ketene 6. The former has the advantage that a synthetically useful olefinic functionality is incorporated in the molecule. Finding suitable experimental conditions proved to be crucial for the success of the cycloaddition reaction, using acid chloride 1[6] as ketene precursor.



1 R = Cl
3 R = OMe

2

3 + 4

i : Et_3N, 130°C, toluene, 40 min.[b], then MeOH; 42% 3[a] and 21% 4[a].

ii : Et_3N, 0.2 eq. DMAP, 130°C, toluene, 40 min.[b]; 68% 4[a].

iii : iPr_2NEt, 0.03 eq. DMAP, 108°C, toluene, 16 hrs.; 78% 4[a].

a) All numbers refer to isolated yields. b) Reaction carried out in a pressure bottle.

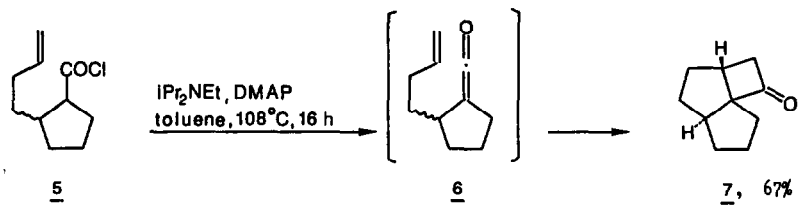
scheme 1

When 1 was treated under conditions i, (i.e. 130°C for 40 minutes followed by quenching with MeOH) we isolated the α,β-unsaturated ester 3 besides a small amount of cycloadduct 4. It is likely that 3 originates from the acid chloride 1 rather than the vinylketene 2. The latter would produce, upon MeOH quench, at least partially deconjugated product[9] which actually was not detected.

Presumably, during the generation of vinylketene 2 the formation of an acyl-ammonium complex is the most difficult step, due to steric hindrance.

By use of a catalytic amount of 4-dimethylaminopyridine (DMAP) under otherwise similar conditions (conditions ii) the amount of the acylammonium complex should be increased. Indeed a beneficial effect upon rate and yield of the reaction was observed. The yield of 4[10] could even be improved at somewhat lower temperature using the less volatile diisopropylethylamine (conditions iii). To our best knowledge this is the first DMAP catalysis demonstrated in ketene cycloadditions.

Similarly the saturated angular annulated cyclobutanone 7 was obtained. Treatment of acid chloride 5 (3:1 mixture of epimers) gave the cycloadduct 7 in 67% isolated yield under these optimized reaction conditions.



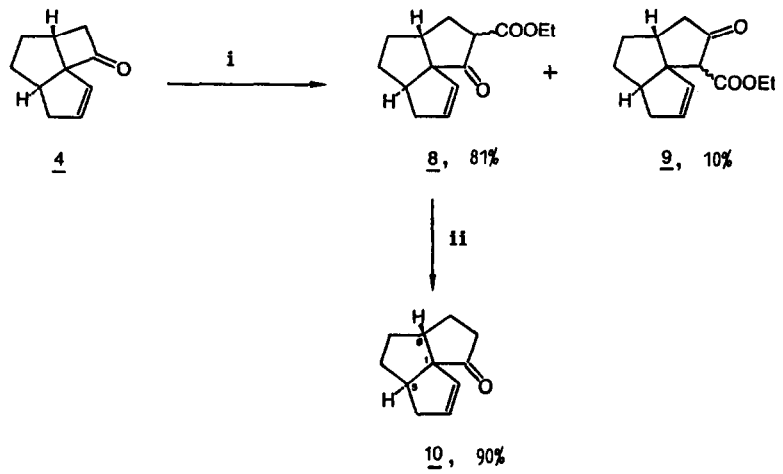
5 6 7, 67%

scheme 2

Previous studies of intramolecular ketene cycloadditions in our laboratory have shown a remarkable difference in the behaviour of ketenes vs. vinylketenes[1]. Ketene 6 undergoes cycloaddition almost as readily as vinylketene 2. This can be explained by the conformational rigidity imposed by the annulated ring system.

The angular annulated triquinane ring system was finally obtained through the following sequence: Treatment of 4 with ethyl diazoacetate in the presence of $BF_3 \cdot OEt_2$[11] gave a 8:1 mixture of the isomeric ketoesters 8 and 9, which could be separated on silicagel.

Decarboxylation of 8 produced the angular annulated triquinane 10[10] in 90% yield.



4 8, 81% 9, 10%

10, 90%

i. $N_2CHCOOEt$, $BF_3 \cdot OEt_2$, ether, -30°C → RT.
ii. 4N HCl, AcOH, reflux.

scheme 3

The above mentioned methodology opens an elegant and straightforward approach to natural occuring angular annulated triquinanes like isocumene, silphinene and pentalene[5].

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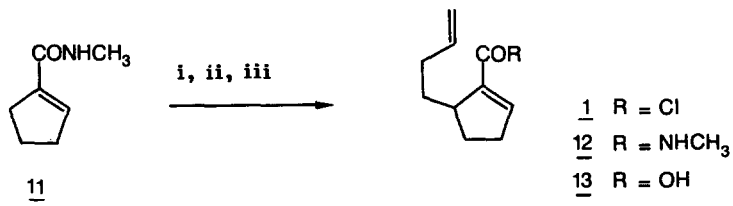
6. 1 was obtained in a 3-step procedure from 11:



11

i. s-BuLi, TMED, THF, -100°C; Br〰 ; 17% of 12[7].
ii. NaOH, $HOCH_2CH_2OH$, 180°C, 18 h; 72% of 13.
iii. 1-Chloro-N,N,2-trimethylpropenylamine[8]; quantitative.

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9. L. Lombardo, Tetrahedron Lett. 26, 381 (1985).
10. All compounds reported herein exhibited NMR, IR and MS spectra in full accord with the assigned structure. Satisfactory combustion analysis were obtained on all compounds.
4: ^{13}C-NMR ($CDCl_3$, 75.4 MHz): δ 212.9 (C=O); 134.1 (C-2); 128.2 (C-2); 88.9 (C-1); 48.4 (C-5); 47.8 (C-9); 38.9 (C-4); 37.2 (C-8); 32.4, 31.9 (C-6, C-7).
10: ^{13}C-NMR ($CDCl_3$, 75.4 MHz): δ 226.6 (C=O); 133.8 (C-1); 130.9 (C-3); 75.1 (C-1); 48.4, 47.8 (C-5, C-8); 40.6, 38.5 (C-4, C-10); 34.0, 32.2 (C-6, C-7); 24.7 (C-9).
11. For ring expansion of cyclobutanones with ethyldiazoacetate see J.R. Stille, R.H. Grubbs, J. Am. Chem. Soc. 108, 855 (1986) and references cited therein.

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