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Photoselective Bond Cleavage of Tricyclo[5.3.1.$0^{1,7}$]Undecane Derivatives. A Facile Entry to Carbocyclic Taxane [A,B] Ring System

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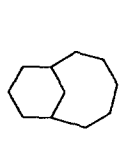
Abstract: The selective control cyclopropyl bond cleavage of tricyclo[5.3.1.$0^{1,7}$]undecan-2-one by photochemical electron transfer produces a new approach to the construction of the carbon skeleton of the [A,B] ring system of the carbocyclic frame of taxane.

The bicyclo[5.3.1]undecane ring system **1** is the carbon skeleton of the [A,B] ring system of the carbocyclic frame of taxol, which is a very promising antitumour drug, in use for the treatment of breast, head, neck and ovarian cancers[1].



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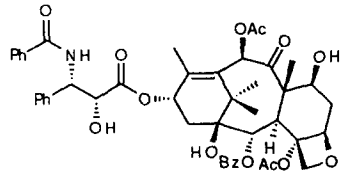

Taxol

Cyclopropylcarbinyl rearrangement of bicyclic systems have been studied intensively[2] and more recently tricyclic systems have been studied. The selective central cyclopropyl bond cleavage in tricyclo[5.3.1.$0^{1,7}$]undeca-2,4-dien-10-one by lead tetraacetate provided an approach to the construction of the carbocyclic frame [A,B] ring of taxol[3]. This carbocyclic frame [A,B] ring of taxol was obtained also by treatment of the tricyclo[5.3.1.$0^{1,7}$]undecanol system in acidic conditions[4]. We would like to report here that bicyclo[5.3.1]undecane ring systems can be obtained by cleavage of the central cyclopropyl bond of tricyclo[5.3.1.$0^{1,7}$]undecanones under photoelectron transfer conditions[5], depending on the position of the carbonyl group. The study was achieved on ketones **2** and **6**. These ketones were respectively obtained from enones **1**[6] and **3**[7]. The tricyclic ketone **2** was obtained in one step by treatment of enone **1** with trimethylsulfoxonium iodide in DMSO[8], and ketone **6** was synthetized in three steps from the bicyclo[5.3.0]undec-1(7)-en-2-one **3**. After reduction of the enone **3** by $NaBH_4$ in the presence of $CeCl_3$, the allylic alcohol was cyclopropanated by using CH_2I_2 in the presence of $ZnEt_2$[9]. The tricyclo[5.3.1.$0^{1,7}$]undecanol **5** was isolated and treated with PDC to produce the desired ketone **6**.

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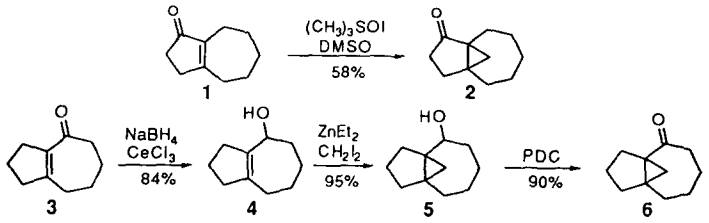
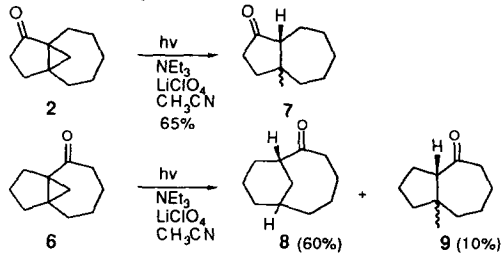


Irradiation of **2** (0.01 mole) in acetonitrile at 254 nm in the presence of Et_3N (10 eq) and $LiClO_4$ (1 eq) for 2 h led to the bicyclic ketone **7** with a yield of 65%. No trace of the ring expanded product was detected. On the contrary, the irradiation of the tricyclic ketone **6** under the same conditions led to the ring expanded product **8** (60%)[10] and to the 7-methylbicyclo[5.3.0]alkanone **9** (10%)[10] as the minor product.



We have shown that the bicyclo[5.3.1]undecane ring system, that constitutes the [A,B] ring of taxane, can be easily obtained from the tricyclo[5.3.1.$0^{1,7}$]undecan-2-one **6**. These results are in agreement with the previous results we obtained in the bicyclo[n.1.0]alkanone series, in which the cleavage of the C-C bond of the cycloprane unit depends on the value of n[5].

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10- **Compound 8** is constituted by one isomer. The relative stereochemistry between H-1 and H-7 could not be established by NOE experiments. IR (film): 1720 cm^{-1}; ^1H NMR ($CDCl_3$, 300MHz) δ: 0.9–2.5 (m, 16H); 1.7 (m, 1H, C<u>H</u>-CH_2), 2.3 (m, 1H, C<u>H</u>-CO); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 16.5 (t), 23.9 (t), 24.2 (t), 28.6 (t), 29.2 (t), 30.9 (t), 31.4 (t), 32.8 (d), 41.2 (t), 45.7 (d), 217.5 (s), MS (EI, 70 eV): *m/z* 166 (40), 148 (20), 122 (25), 111 (30), 97 (90).81 (100), 67 (80). **Compound 9** is constituted by two inseparable isomers in a ratio 2 to 1 determined by ^1H NMR spectra. For both isomers: IR (film): 1720 cm^{-1}; MS (EI, 70 eV): *m/z* 166 (23), 151 (30), 122 (25), 111 (30), 97 (90).81 (100), 67 (80). ^1H NMR ($CDCl_3$, 300MHz) δ: 0.9–2.9 (m, 14H), [Minor isomer: 1.05 (s, 3H, CH_3); Major isomer: 1.10 (s, 3H, CH_3)], 2.6 (m, 1H, C<u>H</u>-CO); Major isomer ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 22.9 (t), 23.5 (t), 23.7 (t), 26.2 (t), 27.5 (q), 38.2 (t), 42.6 (t), 42.8 (d), 43.9 (s), 59.9 (d), 213.6 (s). Minor isomer ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 19.8 (t), 20.7 (t), 23.8 (t), 24.6 (t), 25.8 (q), 43.6 (t), 43.9 (s), 44.0 (t), 44.5 (t), 59.4 (d), 213.4 (s).

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