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Base Catalyzed Pentacyclo[4.3.0.0^{2,4}.0^{3,8}.0^{5,7}]nonan-9-one (Norsnoutanone) → Tricyclo[3.2.1.0^{2,7}]octaneTransformation: A Higher Order Fragmentation?

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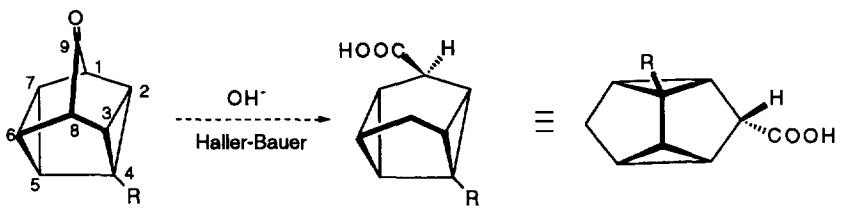
Abstract: 4-Substituted pentacyclo[4.3.0.0^{2,4}.0^{3,8}.0^{5,7}]nonan-9-ones undergo base catalysed, novel, higher order fragmentation reaction to furnish functionalized tricyclo[3.2.1.0^{2,7}]octene derivatives.

In connection with an on ongoing research program, we needed access to a difunctionalized tetracyclo[3.3.0.^{1,5}0^{2,8}.0^{4,6}]octane ring system **1**. While several methods are available in the literature for the synthesis of this homoquadricyclane system,[1] these were not considered well suited for the generation of the desired substitution pattern, e.g. **1**. We, therefore, sought to prepare **1** through a base catalyzed Haller-Bauer type cleavage[2] in a 4-substituted pentacyclo[4.3.0.0^{2,4}.0^{3,8}.0^{5,7}]nonan-9-one (norsnoutanone) **2** derivatives.[3] The pentacyclic precursor **2** in turn could be prepared through the Ag(I) catalyzed rearrangement of the readily available homocubane derivatives.[4] In this context, while attempting the base catalysed Haller-Bauer cleavage on several derivatives of **2** (R=EWG), we have encountered an interesting fragmentation process leading to the formation of tricyclo[3.2.1.0^{2,7}]octane ring system and wish to record here this novel observation.



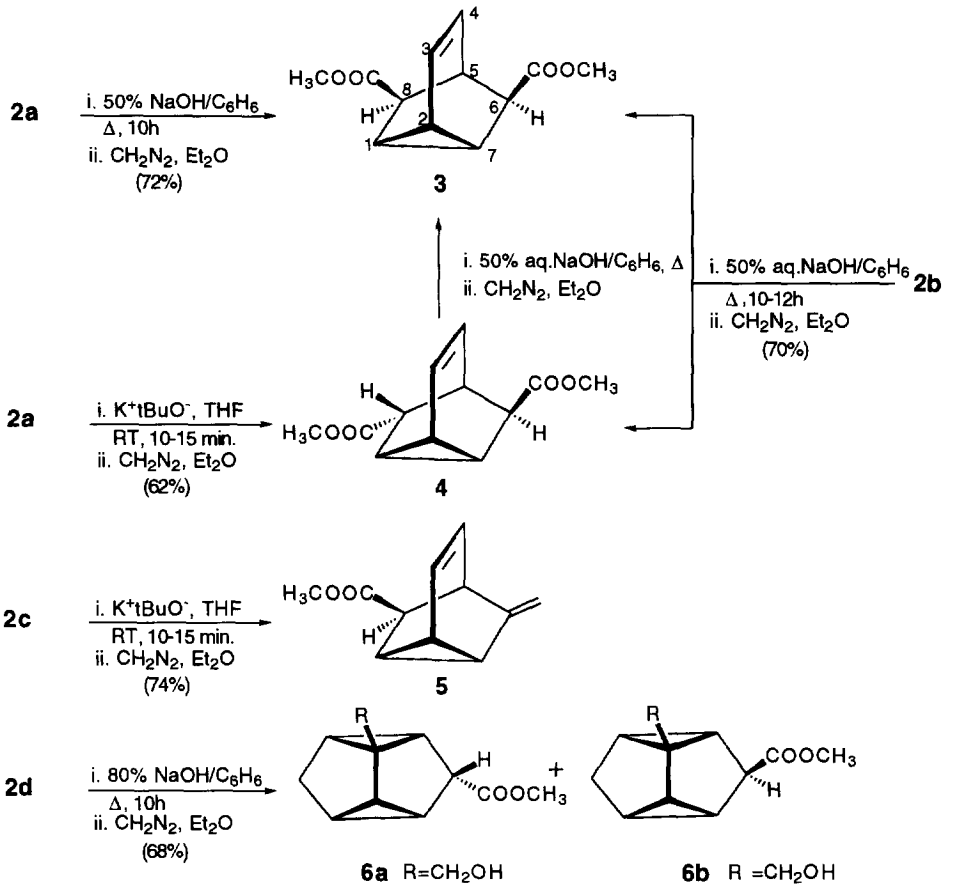
2a R=COOCH$_3$
2b R=CN
2c R=CH$_2$Cl
2d R=CH$_2$OH

1

Refluxing the pentacyclic keto-ester **2** in aq.alkali and diazomethane esterification of the product led to the isolation of tricyclic diester **3**[5] along with traces of epimeric diester **4**.[5] Structure of **3** followed from its 8 line ^{13}C NMR spectrum (Cs-symmetry) with diagnostic resonances due to olefinic, cyclopropyl and ester moieties.[5] These structural features were further confirmed through the analysis of the ^{1}H NMR spectrum. In particular, the stereochemistry was revealed through the

exceptional shielding of the methine proton attached to the ester group in **4** (δ 2.35) compared to **3** (δ 2.92) due to the transannular double bond . Also, the methine proton attached to the ester group in **3** appears as a doublet (J=5Hz), characterstic of this tricyclic system, due to coupling with the bridgehead proton; thus confirming the stereo -disposition of the ester groups[6]. However, when the Haller-Bauer cleavage on **2a** was carried out in potassium ter-butoxide in moist THF for a short duration, only the diastereomeric diester **4** was realized. The structure of **4** and its relationship with **3** was established through its complete epimerization to the thermodynamically more stable **3** on refluxing with 50% sodium hydroxide.

Scheme 1

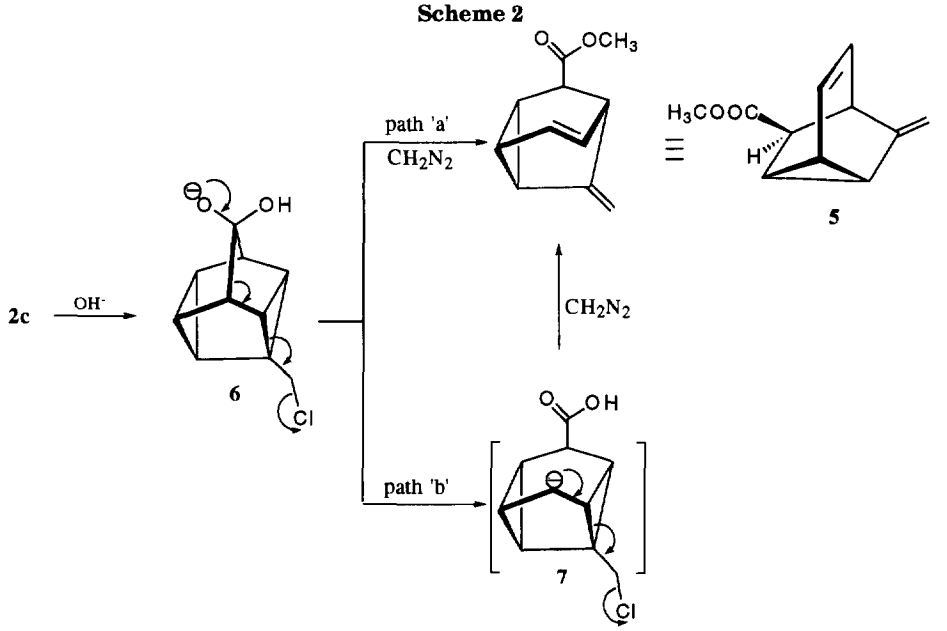


The pentacyclic ketonitrile **2b** on subjecting to Haller-Bauer cleavage in refluxing aq.alkali followed by diazomethane esterification also furnished a mixture of tricyclic diesters **3** and **4**, resulting from the hydrolysis of the nitrile moiety as well as epimerization during the reaction conditions. In a response similar to **2a** and **2b**, the 4-chloromethyl derivative **2c** on treatment with potassium ter-butoxide in moist THF and esterfication furnished a single tricyclic di-olefinic ester **5**[5] (74%). The stereostructure of **5** followed from the comparison of the spectral data (presence of *exo*-methylene

group: δ 4.87, 1H, s and 4.72, 1H, s and a disubstituted double bond: δ 6.00, 1H, m & 5.83, 1H, s) with **3** and **4**. However, the 4-hydroxymethyl derivative **2d**, lacking a nucleofugal group, on base catalyzed Haller-Bauer cleavage and esterification furnished the 1,3-disubstituted tetracyclo[3.3.0.^{1,5}.0^{2,8}.0^{4,6}]-octane derivatives, **6a**[5] and **6b**,[5] in almost equal amounts and their structures were gleaned from an incisive scrutiny of their spectral data, Scheme 1. It is worth mentioning that in the case of **3-6**, the ester moiety undergoes predictable epimerization to the more stable configuration during the base catalyzed reaction.

Formation of tricyclics **3-5** from the pentacyclic precursors **2a-c** under Haller-Bauer conditions involves a fragmentation sequence in which two C-C bond scissions occur, in a single pot reaction, as shown in Scheme 2 for **2c**, with the carbomethoxy, cyano and the chloromethyl groups at C_4 serving as acceptor/nucleofugal groups. The tetrahedral intermediate **6** formed through the addition of hydroxide ion from the *syn*-face of **2c**, is perfectly poised, with *anti*-periplanar arrangement of the electrofugal and nucleofugal groups at the termini and the intervening C-C bonds, for a higher order fragmentation process. Whether **6** transforms synchronously to **5** (path 'a') or through the intermediacy of **7** (path 'b',tandem Haller-Bauer-Grob fragmentation), is not established with certainty but we have been unable to encounter products corresponding to the tetracyclo-[3.3.0.^{1,5}0^{2,8}.0^{4,6}]octane ring system **1** expected through the interventionist protonation of **7**. In the case of **2d**, which lacks the acceptor/nucleofugal group, products **6a,b** derived from the protonation of intermediate like **7**, are only encountered.

Scheme 2



While the literature records many examples of Grob and related fragmentations,[7] examples of higher order fragmentation are extremely rare[8]and we are not aware of any that involve scission of two contiguous C-C bonds. The rigid, well-defined geometry of the groups and bonds, present in the

two contiguous C-C bonds. The rigid, well-defined geometry of the groups and bonds, present in the pentacyclic frame **2**, is primarily responsible for the facile fragmentation observed here and presage further possibilities for accessing still higher order fragmentation processes of synthetic value,in chosen, suitably crafted polycyclic systems.

Acknowledgement: One of us (CRK) wishes to thank UGC for the award of a Research Fellowship.

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2. For examples of base catalyzed Haller-Bauer type cleavage of non-enolizable ketones, see, Gassman, P.G.; Lumb, J.T.; Zalar, F.V. *J. Am. Chem. Soc.* **1967**, *89*, 946; Mehta, G.; Praveen, M. *J. Chem. Soc. Chem. Commun.* **1993**, 1573.
3. Haller-Bauer cleavage of parent pentacyclo[4.3.0.$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]nonan-9-one (norsnoutanone) has been reported but it furnishes bicyclo[3.2.1]octa-2,6-diene derivative *via* the involvement of a bishomocyclopentadienyl anion intermediate. Dauben, W.G.; Twieg, R.J. *Tetrahedron Lett.*, **1974**, 531. However, in the substituted derivatives **2a-c**, the electron withdrawing substituent suppresses this pathway and only fragmentation products are obtained.
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5. All new compounds reported here gave satisfactory spectral (IR, ^{1}H and ^{13}C NMR) data and elemental analyses. Selected data for the key compounds is given here. **3**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.16 (1H, m), 5.59 (1H, m), 3.60 (6H, s), 3.35 (1H, m), 2.92 (2H, d, J=5Hz), 1.91-1.80 (3H, m). ^{13}C NMR (50.0 MHz, $CDCl_3$): δ 172.3, 126.9, 122.2, 51.4(2C), 44.0(2C), 37.1 , 17.6(2C), 14.9. **4**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.14 (1H, m), 5.85 (1H, m), 3.65 (3H, s), 3.58 (3H, s), 3.21 (1H, m), 3.13 (1H, m), 2.35 (1H, m), 1.92 (2H, m), 1.75 (1H, m). ^{13}C NMR (50.0 MHz, $CDCl_3$): δ 174.7, 172.5, 125.8, 125.6, 51.8, 51.3, 46.1, 42.3, 38.4, 18.7, 17.0, 16.8. **5**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.00 (1H, m), 5.83 (1H, m), 4.87 (1H, s), 4.72 (1H, s), 3.62 (3H, s), 3.24 (1H, m), 2.91 (1H, m), 1.99-2.11 (3H, m). ^{13}C NMR (50.0 MHz, $CDCl_3$): δ 172.5, 148.6, 125.4, 124.8, 102.5, 51.4, 43.7, 42.9, 22.7, 20.9, 20.8. **6a/6b**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.87 (2H, s), 3.70 (3H, s), 3.17 (1H, m), 1.90-1.57 (5H, m). ^{13}C NMR (50.0 MHz, $CDCl_3$): δ 174.9, 64.1, 51.6, 43.6, 39.3, 30.9, 30.5, 26.9, 26.3, 25.2, 24.3. **6a/6b**: ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.15 (1H, m), 3.71 (3H, s), 3.61 (1H, s), 2.76 (1H, s), 1.98-1.78 (3H, m), 1.71-1.46 (2H, m). ^{13}C NMR (50.0 MHz, $CDCl_3$): δ 175.9, 64.1, 51.9, 41.2, 39.5, 32.1, 30.0(2C), 25.0, 24.2, 23.4.
6. For the characterization of tricyclo[3.2.1.$0^{2,7}$]octene derivatives, see: Huebner, C.F.; Donoghue, E.; Dorfman, L.; Stuber, F..A.; Danieli, N.; Wenkert, E. *Tetrahedron Lett.*, **1966**, 1185.
7. Grob, C.A.; Schiess, P.W. *Angew. Chem. Int. Engl.* **1967**, *6*, 1.
8. For an example of decarboxylative higher order fragmentation, see: Sternbach, D.; Shibuya, M.; Jaisli, F.; Bonetti, M.; Eschenmoser, A. *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 634.

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