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On the purported synthesis of a bicyclo[2.2.1]heptene diester by reaction of diazomethane with dimethyl 1,3-cyclohexadiene-1,4-dicarboxylate

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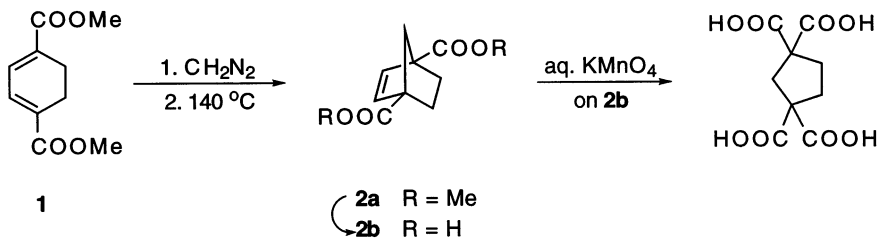
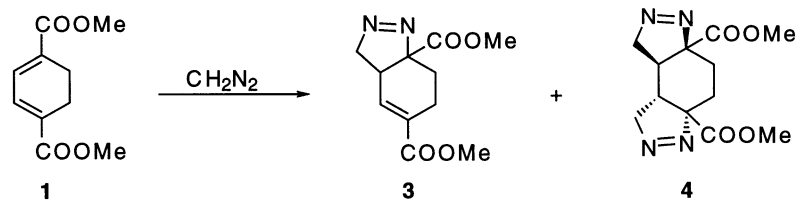
Abstract—Addition of diazomethane to dimethyl 1,3-cyclohexadiene-1,4-dicarboxylate, followed by thermolysis at 140°C, had been reported to yield a bicyclo[2.2.1]heptene diester. This report is not correct. The products are now shown to be a diene diester, a cyclopropane and an *exo*-methylene diester.

In a search for synthesis of bridgehead-functionalized bicyclo[2.2.1]heptenes, we noted in Beilstein reference to a citation describing the formation of diester **2a** by reaction of diazomethane with cyclohexadiene diester **1** followed by thermolysis at 140°C.[1] The cited authors reported that diester **2a** gave the correct C, H analysis and was converted by acid hydrolysis to diacid **2b**, mp 255°C. This on $KMnO_4$ oxidation yielded a substance, mp 188°C, regarded as cyclopentane-1,1,3,3-tetracarboxylic acid on the basis of an undepressed mixed melting point with a 'genuine sample' (Scheme 1).

Because the claimed transformation of **1** to **2a** seemed unusual, we repeated the published procedure several times. For example, reaction of 10 mmol of **1** (Aldrich) with 15–20 mmol of CH_2N_2 (from *N*-nitrosomethylurea and 50% aq. KOH; **CAUTION**: CH_2N_2 is toxic and potentially explosive) in 150 mL of ether at 0°C for 48 hours, followed by partial removal of solvent in an argon stream at 0°C, then in vacuo, gave a yellow oil, separable by silica gel chromatography (hexane:ethyl acetate = 10:1) into one major and one minor component. On the basis of the characteristic ABX system in



Scheme 1.



Scheme 2.

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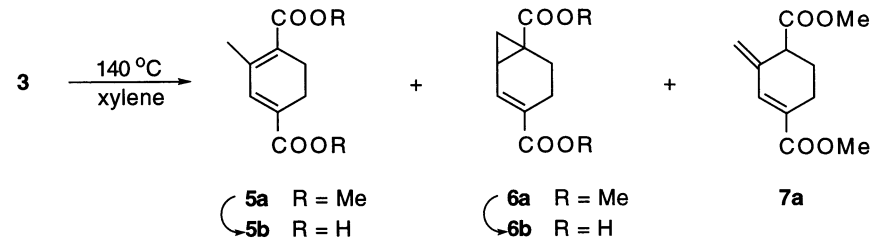
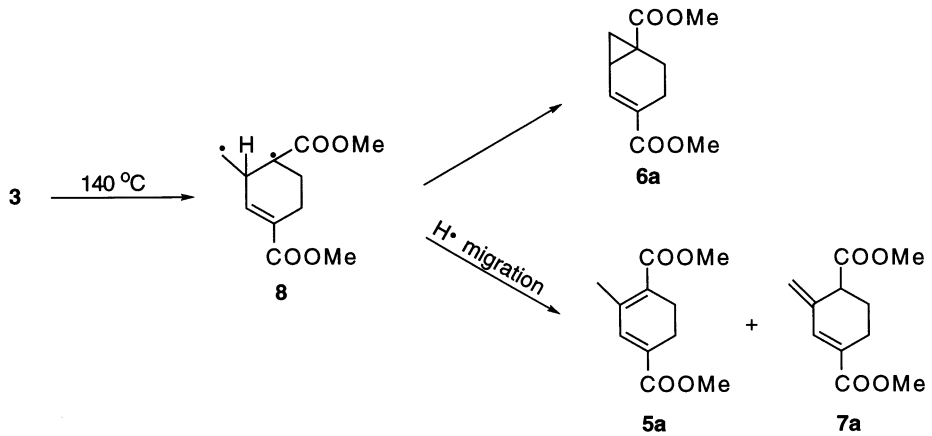


Scheme 3.



Scheme 4.

the ^{1}H NMR and its mass spectrum[2] the major product (52% yield) was identified as the typical pyrazoline **3**,[3] and the minor product (11% yield) was a diadduct **4**[4] (Scheme 2). The proportion of **4** decreased as reaction time was shortened or the mole ratio of CH_2N_2 was decreased.

When purified **3** was held at 140°C in xylene for 2–6 hours, followed by chromatography as above, three fractions were isolated (Scheme 3). Fraction 1 (56% yield) was found to be the new diene diester **5a** on the basis of its ^{1}H and ^{13}C NMR spectra,[5] mass spectrum and its UV absorption spectrum ($\lambda_{max}^{MeOH}=309$ nm, $\varepsilon=6.8\times10^4$), very similar to that of starting diene **1** ($\lambda_{max}^{MeOH}=306$ nm, $\varepsilon=4.8\times10^4$). Fraction 2 (28% yield) was shown to be the cyclopropane diester **6a**, by NMR, MS and its UV absorption ($\lambda_{max}^{MeOH}=242$ nm, $\varepsilon=3.0\times10^4$).[6] Fraction 3 (13% yield) was an inseparable 2:1 mixture of **6a** and *exo*-methylene diester **7a**, in which the structure of **7a** was readily identified by its ^{1}H NMR,[7] which contained two one-proton singlets at δ 5.39 and 5.25, characteristic of the methylene group.

Hydrolysis of diester **5a** gave the corresponding diacid **5b**,[8] which melted with decomposition at ca. 257–258°C. Hydrolysis of **6a** gave diacid **6b**,[9] likewise melting with decomposition at 257–258°C. These values approximate the 255°C reported by the original authors for the alleged bicyclo[2.2.1]heptene diacid **2b**. At this point each of the acids **5b** and **6b** was subjected to $KMnO_4$ oxidation as originally described. From the ^{1}H NMR of the total crude oxidation products it was clear that each had given a complex mixture, and the virtual absence of alicyclic CH_2 signals confirmed that neither the claimed cyclopentane-1,1,3,3-tetracarboxylic acid nor any corresponding bis-decarboxylation product, cyclopentane-1,3-dicarboxylic acid,[10] had been produced.

We conclude that the bicyclo[2.2.1]heptene structures claimed by the original authors are incorrect, and that the reaction of diazomethane with diene diester **1** proceeds along more conventional pathways.[11,12] Thus, an initial 1,3-dipolar addition to **1** yields pyrazoline **3**, which on thermolysis decomposes by homolytic extrusion of N_2 to yield the diradical **8** (Scheme 4). Radical coupling yields cyclopropane **6a**, whereas competing 1,2-H• migration yields either **5a** or **7a**. Although a vinylcyclopropane rearrangement of **6a** could theoretically yield a bicyclo[2.2.1]heptene structure, such a rearrangement was not obtained at 140°C for 2–48 hours under our conditions.

References

1. Guha, P. C.; Hazra, G. D. *J. Indian Inst. Sci.* **1939**, *22A*, 263; *Chem. Abstr.* **1940**, *34*, 2822;[4] *Beilstein* **1971**, *9*, III, 4044b.
2. Compound **3**: light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): 2.18 (m, 1H), 2.35–2.43 (m, 2H), 2.54 (m, 1H), 3.12 (m, 1H), 3.74 (s, 3H), 3.77 (s, 3H), 4.57, 4.76 (ABX, 2H, $J_{AB}=17.5$ Hz, $J_{AX}=4.4$ Hz, $J_{BX}=8.9$ Hz), 6.76 (m, 1H) ppm. ^{13}C NMR (100 MHz, CD_3OD): 19.36 (t), 25.69 (t), 35.19 (d), 50.97 (q), 52.05 (q), 81.58 (t), 94.17 (s), 130.19 (s), 136.87 (d), 166.70 (s), 169.80 (s) ppm. MS (API-ES): m/z, 261 (M^++23).

3. (a) Pelletier, S. W.; Djarmati, Z.; Lajsic, S. D.; Micovic, I. V.; Yang, D. T. C. *Tetrahedron* **1975**, *31*, 1659; (b) Tuloup, R.; Danion-Bougot, R.; Danion, D. *Can. J. Chem.* **1989**, *67*, 1125.
4. Compound **4**: light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): 1.54 (m, 2H), 2.27 (m, 2H), 2.56 (m, 2H), 3.79 (s, 6H), 4.43, 4.89 (ABX, 4H $J_{AB}=18.8$, $J_{AX}=9.6$, $J_{BX}=6.0$ Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 23.03 (t), 32.25 (d), 53.22 (q), 84.20 (t), 95.01 (s), 171.02 (s) ppm. MS (API-ES): m/z, 303 (M^++23). The assumed *trans*-stereochemistry pictured has not been proven.
5. Compound **5a**: colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 2.22 (m, 3H), 2.46–2.54 (m, 4H), 3.79 (s, 3H), 3.81 (s, 3H), 6.96 (t, 1H, $J=1.4$ Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 20.11 (q), 21.67 (t), 24.13 (t), 51.45 (q), 51.91 (q), 126.76 (s), 131.77 (s), 138.45 (d), 140.92 (s), 167.08 (s), 168.20 (s) ppm. MS (API-ES): m/z, 233 (M^++23).
6. Compound **6a**: colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 1.33 (t, 1H, $J=4.8$ Hz), 1.67 (dd, 1H, $J=9.3$, 4.3 Hz), 1.93 (m, 1H), 1.96–2.02 (m, 2H), 2.27 (m, 1H), 2.68 (m, 1H), 3.72 (s, 3H), 3.74 (s, 3H), 7.28 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 18.96 (t), 19.55 (t), 20.08 (t), 21.48 (d), 28.29 (s), 51.62 (q), 52.08 (q), 126.98 (s), 139.26 (d), 167.01 (s), 174.61 (s) ppm. MS (API-ES): m/z, 233 (M^++23). The observed UV absorption of **6a** is in good agreement with the electronic spectra reported for related cyclopropylacrylic esters by: Jorgenson, M. J.; Leung, T. *J. Am. Chem. Soc.* **1968**, *90*, 3769.
7. Compound **7a**: colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 1.83 (m, 1H), 1.99 (m, 1H), 2.42 (m, 2H), 3.40 (m, 1H), 3.73 (s, 3H), 3.77 (s, 3H), 5.25 (s, 1H), 5.39 (s, 1H), 7.23 (s, 1H) ppm. MS (API-ES): m/z, 233 (M^++23).
8. Compound **5b**: white solid. ^{1}H NMR (400 MHz, CD_3OD): 2.20 (m, 3H), 2.41–2.44 (m, 2H), 2.49–2.52 (m, 2H), 6.98 (m, 1H) ppm. MS (API-ES): m/z, 181 (M^+–1).
9. Compound **6b**: white solid. ^{1}H NMR (400 MHz, CD_3OD): 1.40 (t, 1H, $J=4.6$ Hz), 1.64 (dd, 1H, $J=9.2$, 4.2 Hz), 1.86–2.03 (m, 3H), 2.23 (m, 1H), 7.31 (m, 1H) ppm. MS (API-ES): m/z, 181 (M^+–1)
10. *cis*-Cyclopentane-1,3-dicarboxylic acid, mp 120–121°C, was prepared for reference by Dr. Jiong Lan following the procedure of: Hronowski, L. J. J.; Szarek, W. A. *Can. J. Chem.* **1988**, *66*, 61.
11. For example, see: Barrero, A. F.; Manzaneda, E. A.; Manzaneda, R. A. *Bull. Soc. Chim. Fr.* **1989**, 859.
12. For example, see: Van Auken, T. V.; Rinehart, Jr., K. L. *J. Am. Chem. Soc.* **1962**, *84*, 3736 and references cited therein.