ISSN 1070-4280 Russian Journal of Organic Chemistry, 2006, Vol. 42, No. 2, pp. 288–289. © Pleiades Publishing, Inc. 2006.
Original Russian Text © F.A. Gimalova, V.A. Egorov, N.K. Selezneva, M.S. Miftakhov, 2006, published in Zhurnal Organicheskoi Khimii, 2006, Vol. 42, no. 2, pp. 303–304.

SHORT COMMUNICATIONS

# Synthesis of 2-(3-Bromo-1,1-dimethyl-2-methoxypropyl)-2,4,5-trichlorocyclopent-4-ene-1,3-dione

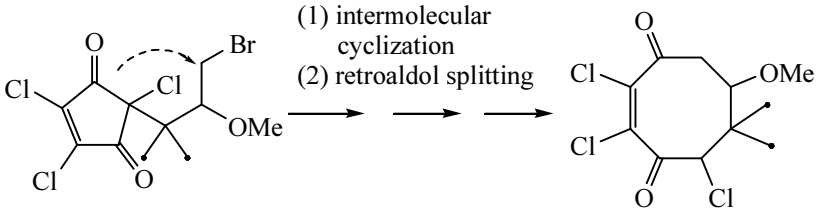
**F.A. Gimalova, V.A. Egorov, N.K. Selezneva, and M.S. Miftakhov**

*Institute of Organic Chemistry, Ufa Scientific Centre, Russian Academy of Sciences, Ufa, 450054 Russia*
*e-mail: bioreg@anrb.ru*

Received April 26, 2005

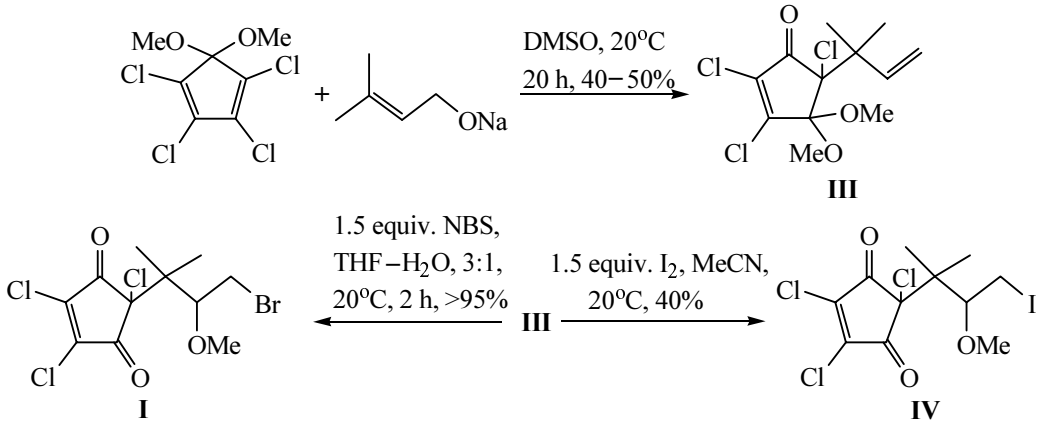
**DOI:** 10.1134/S1070428002120230

*gem*-Dimethyl group is foung in the structures of numerous naturally occurring compounds, in particular, it is present in the eight-membered B ring if taxol [1]. We formerly demonstrated the fundamental possibility of a promoted by $SmI_2$ intramolecular cyclization of the 5-allenyl-4,4-dimethoxy-2,3,5-trichlorocyclopent-2-en-1-one into a functionalized *Z,E*-cyclooctadiene [2]. In extension of this research we report here on a chemorational version of preparation of the chlorocyclopentenone block **I** which contains a corresponding functionalized side substituent and is fit for subsequent bringing into the intramolecular cyclization leading to the equivalents of the B ring in taxoids **II** along the pathway given further.




**I** **II**

First using the previously developed procedure [3] we synthesized from the sodium derivative of 3-methyl-2-buten-1-ol (prenol) and 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene new trichlorocyclopentenone (**III**) with a *gem*-dimethyl group. Alkene **III** was brought into the bromohydroxylation reaction with NBS in aqueous THF affording compound **I** in a quantitative yield. The iodo derivative **IV** related to methoxybromide **I** was obtained in a moderate yield in the course of deprotecting ketal **III** with $I_2$ in MeCN. This reaction type we previously con-




**III** **I** **IV**

sidered [4] by an example of reaction between 5-allyl-4,4-dimethoxy-2,3,5-trichlorocyclopentenone and $I_2$.

It should be noted in conclusion that both compounds obtained, **I** and **IV**, may be good initial substances for the planned synthesis of structure **II**.

**2-(3-Bromo-1,1-dimethyl-2-methoxypropyl)-2,4,5-trichlorocyclopent-4-ene-1,3-dione (I).** To a solution of 0.15 g (0.47 mmol) of compound **III** in 30 ml of a mixture THF–$H_2O$, 3:1, was added at stirring 0.14 g (0.82 mmol) of NBS, the reaction mixture was stirred at room temperature for 3–4 h (TLC monitoring). The THF was evaporated, the reaction products were extracted into $CHCl_3$ (3 × 20 ml). The combined extract was washed with a NaCl solution, dried with $MgSO_4$, and evaporated. We obtained 0.18 g (>98%) of compound **I** that crystallized on standing in a refrigerator and melted at room temperature. A sample for analysis was purified by column chromatography on $SiO_2$. IR spectrum, $cm^{-1}$: 696, 736, 880, 936, 980, 1048, 1088, 1208, 1376, 1464, 1592, 1616 (C=C), 1736, 1760, 1776 (C=O). $^1H$ NMR spectrum, δ, ppm: 1.26 s and 1.39 s (3H each, $CH_3$), 3.24 s (3H, $OCH_3$), 3.44–3.64 m (3H, $CH_2Br$, OCH). $^{13}C$ NMR spectrum, δ, ppm: 16.95 and 21.98 ($CH_3$), 29.58 ($CH_2Br$), 49.44 ($\underline{CMe_2}$), 58.45 ($OCH_3$), 67.34 ($C^2$), 86.07 (OCH), 146.08 ($C^5$), 150.29 ($C^4$), 184.23 and 186.71 ($C^1$, $C^3$). Found, %: C 35.32; H 3.30. $C_{11}H_{12}BrCl_3O_3$. Calculated, %: C 34.91; H 3.20.

**4,4-Dimethoxy-5-(1,1-dimethyl-2-propen-1-yl)-2,3,5-trichlorocyclopent-2-en-1-one (III).** To a stirred solution of 3.0 g (11.36 mmol) of 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene in 4 ml of anhydrous DMSO under an argon atmosphere was added dropwise 8 ml of a solution of a sodium derivative of prenol in DMSO prepared from 0.39 g (17.1 mmol) of Na and 3 ml of prenol. The reaction mixture was stirred at 20°C for 10 h and quenched by addition of an equal volune of cold water. The reaction products were extracted into $CHCl_3$ (3 × 20 ml), the combined extracts were washed with a saturated water solution of NaCl, dried with $MgSO_4$, evaporated, and the residue was purified by vacuum distillation. We obtained 1.5 g (42%) of oily compound **III**, bp 90–95°C (1 mm Hg). IR spectrum, $cm^{-1}$: 736, 856, 912, 1072, 1088, 1096, 1152, 1216, 1384, 1608 (C=C), 1748 (C=O). $^1H$ NMR spectrum, δ, ppm: 1.21 s and 1.29 s (3H each, $CH_3$), 3.39 s and 3.54 s (3H each, $OCH_3$), 4.99 d [1H, $=CH_2$ ($H^A$), $J$ 17.46 Hz] and 5.05 d [1H, $=CH_2$ ($H^B$), $J$ 10.82 Hz], 6.04 d.d (1H, =CH, $J$ 10.82 and 17.46 Hz). $^{13}C$ NMR spectrum, δ, ppm: 24.43 and 25.18 ($CH_3$), 45.03 ($\underline{CMe_2}$), 52.96 and 53.27 ($OCH_3$), 85.81 ($C^5$), 103.14 ($C^4$), 113.34 ($=CH_2$), 134.31 ($C^2$), 142.77 (=CH), 156.78 ($C^3$), 188.99 ($C^1$).

**2-(3-Iodo-1,1-dimethyl-2-methoxypropyl)-2,4,5-trichlorocyclopent-4-ene-1,3-dione (IV).** To a solution of 0.15 g (0.47 mmol) of compound **III** in 10 ml of acetonitrile was added at stirring 0.61 g (2.39 mmol) of $I_2$ and 0.51 g (4.79 mmol) of $NaHCO_3$. The reaction mixture was stirred in the darkness at room temperature till complete disappearance of the initial compound (~3 h, TLC monitoring). Then 10 ml of $CHCl_3$ was added to the reaction mixture, it was treated with 10% solution of $Na_2S_2O_3$, the organic layer was separated, the products were extracted from the water layer with 10 ml of $CHCl_3$, the combined extracts were washed with a saturated water solution of NaCl, dried with $MgSO_4$, evaporated, and the residue was subjected to column chromatography on $SiO_2$ to yield 0.08 g (~40%) of compound **IV**. IR spectrum, $cm^{-1}$: 740, 1100, 1210, 1580, 1620 (C=C), 1730, 1780 (C=O). $^1H$ NMR spectrum, δ, ppm: 1.29 s and 1.42 s (3H each, $CH_3$), 3.26 s (3H, $OCH_3$); 3.04 d.d (1H, $J$ 4.7 and 11.7 Hz) and 3.36 m (1H, $CH_2I$); 3.67 m (1H, OCH). $^{13}C$ NMR spectrum, δ, ppm: 0.43 ($CH_2I$), 16.87 and 22.35 ($2CH_3$), 50.28 ($\underline{CM\varepsilon_2}$), 58.37 ($OCH_3$), 67.44 ($C^2$), 86.13 (OCH), 146.32 ($C^5$), 150.22 ($C^4$), 184.39 and 186.73 ($C^1$, $C^3$).

IR spectra were recorded on spectrophotometers UR-20 and Specord-80 from thin film or mull in mineral oil. $^1H$ and $^{13}C$ NMR spectra were registered on a spectrometer Bruker AM-300 at 300.13 and 75.47 MHz respectively, internal reference TMS.

## REFERENCES

1. Nicolaou, K.C., Dai, W.-M., and Guy, R.K., *Angew. Chem., Int. Ed.,* 1994, vol. 33, p. 15.
2. Ivanova, N.A., Shainurova, A.M., Spirikhin, L.V., and Miftakhov, M.S., *Izv. Akad. Nauk, Ser. Khim*., 1998, p. 2552.
3. Akhmetvaleev, R.R., Akbutina, F.A., Ivanova, N.A., and Miftakhov, M.S., *Izv. Akad. Nauk, Ser. Khim*., 2001, p. 1417.
4. Vostrikov, N.S., Vasikov, V.Z., Spirikhin, L.V., and Miftakhov, M.S., *Zh. Org. Khim*., 2001, vol. 37, p. 1403.