Vicinal Bromopropargoxylation of Cyclic Olefins and Cobaloxime-Mediated Heteroannulation to Functionalized 3-Methyleneoxacyclopentanes

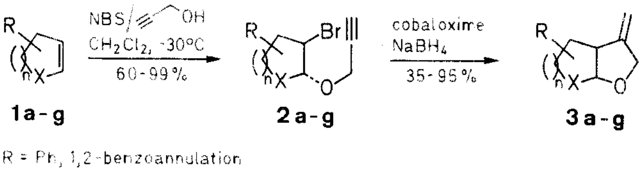
Klaus Last, H. M. R. Hoffmann*

Department of Organic Chemistry, University of Hannover, Schneiderberg 1 B, D-3000 Hannover, Federal Republic of Germany

The reaction of *N*-bromosuccinimide (NBS) and 2-propynol with cyclic olefins **1**, including heteroaromatic benzofuran and *N*-protected indole, gave *β*-bromo-*α*-propargyl ethers **2**. The adducts **2**, some of which were quite sensitive, were cyclized with cobaloxime/sodium borohydride to give functionalized 3-methyleneoxacyclopentanes **3**. The reaction sequence amounts to a simple two-step heteroannulation procedure.

Our interest in the synthesis of aflatoxins[1] and related benzoannulated heterodiquinanes such as physovenine[2,3] and physostigmine[2-4] led us to explore free radical promoted cyclizations. Background investigations have shown that the tributyltin hydride method[5-9] was not always efficient, but has drawbacks[1] for obtaining this class of polyfunctionalized compounds. We therefore tried the potentially simpler, cobaloxime-catalyzed cyclization.[10-15] Our plan was to heteroannulate cyclic 5-membered olefins and, for comparison, also 6-membered olefins, by the shortest possible route. As it turned out, the two-step sequence (Scheme **A**) proved to be simple and efficient.

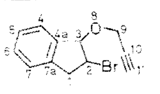
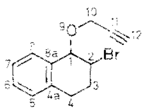
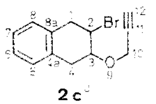
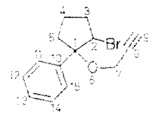
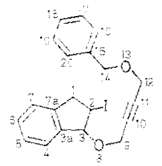
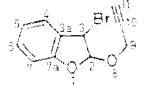
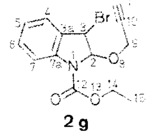
Given suitable conditions, a variety of carbon–carbon double bonds were found to enter into vicinal bromopropargoxylation.[9,10] For instance, reaction of indene (**1a**) with *N*-bromosuccinimide (NBS) (2 equiv) and an excess of propargyl alcohol gave adduct **2a** in 99% yield (Table 1). Purification of the product was unneccessary for the subsequent cyclization. Cyclohexene derivatives (cf. **2b**, **2c**) were also obtained in good yields. Bromopropargoxylation of benzofuran (**1f**) was more difficult, giving 3-bromobenzofuran via electrophilic substitution at the electron rich C-3 carbon. However, when the heteroaromatic compound was added slowly to a solution of NBS in propargyl alcohol, initially at −40 °C, the mixture was warmed up and worked up under controlled conditions, we were able to isolate adduct **2f** in 65% yield. Even the protected indole adduct **2g** was obtained (80%). In this instance, it was *essential* to use silica gel (0.5 equiv) for the reaction: In the absence of silica gel, adduct **2g** decomposed. Most other additions were not improved in the presence of silica gel.[16] It is advisable to work up the reaction mixture rapidly once it has reached room temperature or below. The mother liquor must be washed with ice-cold alkali to neutrality, and the excess of the propargyl alcohol should be removed at 0.1 Torr without external heating.



Scheme **A**

All additions were regioselective in that the electrophilic bromine attacked the double bond to give the more stable carbocation, which was trapped by the 2-propynoxy group preferentially from the side opposite to bromine. The formation of adduct **2g** from indole **1g** is an infrequent case of electrophilic *addition*, rather than normal substitution, at the enamine-like C^2–C^3 double bond of this heteroaromatic compound. One should bear in mind that 2-propynol is advantageous in the bromoalkyloxylation step.[9,10] NBS and 2-propenol (i.e. allyl alcohol) do not add satisfactorily to olefins. As is well known, formation of epibromohydrin and other products compete in this case.

Table 1. β-Bromo-α-propargyl Ethers **2a**–**g** Prepared

Product[a]	Yield (%)	bp (°C)/ mbar	Molecular Formula[b]	IR (film/KBr) ν cm^{-1})	^{1}H-NMR (CDCl$_3$/TMS) δ, J(Hz)	^{13}C-NMR (CDCl$_3$/TMS), δ	MS (70 eV) m/z (%)
 **2a**	99	140/ 0.013	$C_{12}H_{11}BrO$ (251.1)	3295 (vs), 2120 (w), 1706 (m), 1045 (s), 820 (w), 750 (s), 735 (s), 640 (m)	2.53 (t, 1H, ^4J = 2.5, H-11); 3.18 (dd, 1H, ^3J = 4.5, ^2J = 17, H-1); 3.76 (dd, 1H, ^3J = 6.5, ^2J = 17, H-1); 4.39 (d, 2H, ^4J = 2.5, H-9); 4.53 (m, 1H, ^3J = 3.5, H-2); 5.28 (d, 1H, ^3J = 3.5, H-3); 7.28 (m, 2H, H-5, H-6); 7.39 (m, 2H, H-4, H-7)	41.59 (t, C-1); 51.13 (d, C-2); 57.15 (t, C-9); 75.12 (d, C-11); 79.68 (s, C-10); 89.01 (d, C-3); 124.75 (d, C-5); 124.90 (d, C-6); 127.23 (d, C-7); 129.20 (d, C-4); 139.51 (s, C-7a); 140.60 (s, C-4a)	250/252 (7), 212 (38), 171 (48), 141 (94), 132 (65), 115 (100), 103 (49), 77 (36)
 **2b**	85	102/ 0.013	$C_{13}H_{13}BrO$ (265.2)	3200 (s), 2930 (w), 2120 (w), 1492 (w), 1215 (w), 1045 (vs), 1025 (m), 772 (m), 750 (m), 640 (m)	2.13 (m, 1H, H-3); 2.47 (m, 1H, H-3); 2.56 (t, 1H, ^4J = 2.5, H-12); 2.80 (t, 1H, H-4); 3.02 (m, 1H, H-4); 4.33 (t, 2H, ^4J = 2.5, 2 × H-10); 4.64 (m, 1H, H-2); 4.78 (d, 1H, ^3J = 4, H-1); 7.13 (dd, 1H, ^4J = 3, H-5); 7.24 (m, 2H, H-6, H-7); 7.35 (dd, 1H, ^4J = 3, H-8)	25.54 (t, C-3); 26.75 (t, C-4); 49.76 (d, C-2); 58.93 (t, C-10); 75.17 (d, C-12); 78.35 (d, C-1); 79.85 (s, C-11); 126.17 (d, C-5); 128.45 (d, C-7); 128.88 (d, C-6); 130.68 (d, C-8); 132.26 (s, C-8a); 135.83 (s, C-4a)	264/266 (9), 185 (14), 158 (20), 147 (19), 119 (25), 91 (25), 77 (5)
 **2c**[c]	61	–	$C_{13}H_{13}BrO$ (265.2)	3280 (s), 3029 (w), 2928 (m), 2893 (m), 2125 (w), 1428 (m), 1250 (m), 1078 (vs), 1040 (m), 848 (m), 680 (s), 620 (m)	2.46 (t, 1H, ^3J = 2.5, H-12); 2.90 (dd, 1H, ^2J = 17, ^3J = 5, H-1); 3.19 (dd, 1H, ^2J = 17, ^3J = 6, H-1); 3.40 (dd, 1H, ^2J = 17, ^3J = 5, H-4); 3.60 (dd, 1H, ^2J = 17, ^3J = 5, H-4); 4.08 (q, 1H, H-2); 4.31 (dd, 2H, ^5J = 1, ^4J = 2.5, H-10); 4.42 (q, 1H, H-3); 7.10 (m, 4H, H-5, 6, 7, 8)	32.76 (t, C-1); 36.64 (t, C-4); 49.88 (d, C-2); 57.10 (t, C-10); 74.69 (d, C-12); 76.91 (s, C-3); 79.74 (s, C-11); 126.32 (d, C-7); 126.57 (d, C-6); 128.37 (d, C-5); 129.01 (d, C-8); 132.52 (s, C-8a); 132.89 (s, C-5a)	264/266 (5); 253 (5), 187 (9), 134 (14), 133 (14), 132 (100), 91 (25), 77 (9)
 **2d**	60		$C_{14}H_{15}BrO$ (279.2)	3315 (s), 3065 (w), 3005 (m), 2970 (m), 2440 (m), 2860 (m), 2120 (w), 1495 (w), 1455 (m), 1445 (m)	2.15 (m, 4H, H-3, H-4); 2.45 (t, 1H, ^4J = 2.5, H-9); 2.63 (m, 2H, H-5); 4.20 (dd, 2H, ^4J = 2.5, H-7); 4.47 (t, 1H, ^3J = 3, H-2); 7.33 (m, 3H, H_{arom}); 7.58 (m, 2H, H_{arom})	29.54 (t, C-4); 30.90 (t, C-3, C-5); 55.30 (t, C-7); 73.00 (s, C-1); 74.00 (d, C-2); 83.33 (d, C-9); 80.08 (s, C-8); 126.21 (d, C-13); 128.39 (d, C-11, C-15); 131.48 (d, C-12, C-14); 135.10 (s, C-10)	278/280 (6), 200 (21), 198 (35), 187 (24), 168 (40), 142 (100), 128 (65), 117 (76), 115 (52), 91 (47), 77 (75)
 **2e**[d]	90	oil	$C_{20}H_{19}IO_2$ (418.3)	3065 (w), 3030 (m), 2860 (m), 1610 (w), 1455 (m), 1350 (m), 1120 (s), 1070 (s), 750 (s), 700 (s)	3.29 (dd, 1H, ^3J = 4.5, H-1); 3.75 (dd, 1H, ^3J = 6.5, H-1); 4.26 (t, 2H, ^4J = 2, H-14); 4.46 (q, 2H, ^4J = 2.4, H-12); 4.53 (p, 1H, ^3J = 3.6, ^5J = 1, H-2); 4.64 (s, 2H, H-9); 5.38 (d, 1H, ^3J = 3.6, H-3); 7.29 (m, 3H, H-5, 6, 7); 7.35 (m, 5H, H-16, 17, 18, 19, 20); 7.47 (m, 1H, H-4)	25.97 (d, C-2); 43.58 (t, C-1); 57.48 (t, C-9); 57.51 (t, C-12); 71.71 (t, C-14); 82.81 (s, C-10); 83.14 (s, C-11); 90.71 (d, C-3); 125.38 (d, C-5); 124.32 (d, C-20); 124.73 (d, C-16); 127.20 (d, C-18); 127.85 (d, C-4); 128.04 (d, C-7); 128.30 (d, C-17); 128.43 (d, C-19); 129.23 (d, C-6); 137.43 (s, C-3a); 139.88 (s, C-7a); 141.80 (s, C-15)	418 (1), 391 (3), 204 (6), 181 (16), 133 (10), 117 (26), 91 (100), 77 (8)
 **2f**	65	oil	$C_{11}H_9BrO_2$ (253.1)	3310 (s), 2115 (w), 1617 (w), 1605 (m), 1471 (m), 1480 (m), 1090 (vs), 640 (s)	2.52 (t, 1H, ^4J = 2.5, H-11); 4.39 (d, 2H, ^4J = 2.5, H-9); 5.28 (s, 1H, H-3); 5.98 (s, 1H, H-2); 7.13 (m, 4H, H-4, 5, 6, 7)	48.9 (d, C-3); 55.7 (t, C-9); 75.8 (d, C-11); 78.0 (s, C-10); 110.0 (d, C-2); 111.0 (d, C-4); 122.4 (d, C-7); 126.0 (d, C-6); 126.4 (d, C-3a); 131.0 (d, C-5); 158.3 (s, C-7a)	254/252 (8), 208 (25), 173 (59), 145 (100), 115 (78), 77 (95)
 **2g**	80	oil	$C_{14}H_{14}BrNO_3$ (324.2)	3310 (s), 2110 (w), 1725 (vs), 1095 (vs), 635 (m)	1.42 (t, 3H, ^3J = 9, CH$_3$); 2.45 (t, 1H, ^4J = 2.5, H-11); 4.35 (d, 2H, ^4J = 2.5, H-9); 4.37 (q, 2H, ^3J = 9, H-14); 5.20 (s, 1H, H-3); 5.97 (s, 1H, H-2); 7.08 (t, 1H, ^3J = 8, H-5); 7.36 (m, 3H, H-4, 6, 7)	–	325/323 (16), 244 (100), 216 (43), 189 (22), 172 (37), 160 (35), 144 (64), 132 (68), 117 (67), 77 (28)

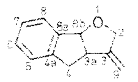
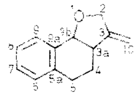
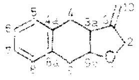
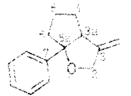
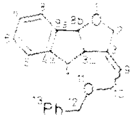
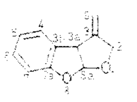
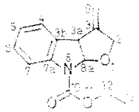
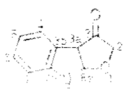
[a] Et$_2$O/petroleum ether mixture in the following proportions were used to separate and purify the products by chromatography: **2a**, **g** = 1 : 4; **2b** = 1 : 1; **2c**, **e**, **f** = 1 : 10; **2d** = 1 : 100.

[b] The calculated and observed values for M$^+$ in HRMS were within the range of ±0.0001.

[c] Prepared from 1,4,5,8-tetrahydronaphthalene and NBS (2 equiv). Apparently, 1 equiv of NBS is required to aromatize one six-membered ring of the cyclic olefin precursor.

[d] N-iodosuccinimide is used, instead of NBS, and monobenzylated 2-butyn-1,4-diol.

Table 2. Compounds **3a**–**g** and **4** Prepared

Product[a]	Yield (%)	mp (°C) or bp (°C)/mbar	Molecular Formula[b]	IR (film/KBr) ν(cm^{-1})	^{1}H-NMR (CDCl$_3$/TMS) δ, J(Hz)	^{13}C-NMR (CDCl$_3$/TMS) δ	MS (70 eV) m/z (%)
 **3a**	95	125/0.013	$C_{12}H_{12}O$ (172.2)	2930 (m), 1475 (m), 1458 (m), 1435 (m), 1060 (vs), 890 (m), 740 (m)	2.96 (dd, 1H, ^2J = 16, ^3J = 2.2, H-4); 3.27 (dd, 1H, ^2J = 16, ^3J = 8, H-4); 3.43 (m, 1H, H-3a); 4.18 (dd, 1H, ^2J = 13, ^4J = 1, H-2); 4.38 (dd, 1H, ^2J = 13, ^4J = 2, H-2); 4.95 (q, 1H, H-9); 5.05 (q, 1H, H-9); 5.61 (d, 1H, ^3J = 7, H-8b); 7.19 (m, 3H, H-5, 7, 8); 7.42 (m, 1H, H-6)	38.3 (t, C-4); 46.3 (d, C-3a); 71.0 (t, C-2); 88.0 (d, C-8b); 104.9 (t, C-9); 124.9 (d, C-5); 125.2 (d, C-6); 127.0 (d, C-7); 128.7 (d, C-8); 141.7 (s, C-4a); 142.8 (s, C-8a); 153.6 (s, C-3)	172 (21), 143 (34), 128 (50), 116 (100), 77 (7)
 **3b**	62	72	$C_{13}H_{14}O$ (186.3)	2930 (m), 2865 (m), 1475 (m), 1450 (s), 1065 (vs), 892 (m)	1.83 (m, 2H, H-4); 2.80 (m, 2H, H-5); 2.98 (m, 1H, H-3a); 4.43 (m, 2H, H-2); 4.64 (m, 1H, H-9b); 4.88 (d, 1H, H-10); 5.04 (dq, 1H, H-10); 7.17 (m, 3H, H-6, 8, 9); 7.41 (m, 1H, H-7)	–	186 (32), 168 (29), 158 (23), 146 (19), 130 (100), 116 (43), 91 (31), 77 (12)
 **3c**	80	–[d]	$C_{13}H_{14}O$ (186.3)	3000 (w), 2930 (s), 2860 (m), 1490 (w), 1455 (m), 1065 (s), 890 (m)	2.70 (m, 2H, H-4); 2.87 (m, 1H, H-3a); 3.00 (m, 2H, H-9); 4.23 (m, 2H, H-2); 4.51 (m, 1H, H-9a); 5.01 (q, 1H, H-10); 5.05 (q, 1H, H-10); 7.20 (m, 4H, H-5, 6, 7, 8)	–	186 (75), 168 (19), 142 (34), 129 (56), 104 (100), 91 (14), 77 (9)
 **3d**	35	oil	$C_{14}H_{16}O$ (200.3)	3070 (w), 3015 (m), 2960 (s), 2870 (m), 1480 (m), 1445 (s), 1370 (m), 1070 (vs), 1045 (vs), 960 (m), 890 (m)	2.24 (m, 2H, H-5); 2.80 (m, 1H, H-3a); 3.00 (t, 2H, H-4); 3.24 (t, 2H, H-6); 4.25 (q, 2H, H-2); 5.57 (q, 1H, H-7); 5.96 (q, 1H, H-7); 7.18 (m, 5H, H$_{arom}$)	22.35 (d, C-3a); 50.58 (t, C-6); 67.25 (t, C-2); 73.50 (s, C-6a); 116.20 (t, C-7); 126.50 (d, C$_{arom}$); 126.87 (d, C$_{arom}$); 126.90 (d, C$_{arom}$); 128.30 (d, C$_{arom}$); 128.32 (d, C$_{arom}$); 139.01 (s, C$_{arom}$); 141.19 (s, C-3)	200 (35), 170 (16), 157 (21), 140 (19), 128 (17), 115 (5), 105 (100), 77 (23)
 **3e**	35	oil	$C_{20}H_{20}O_2$ (292.4)	3030 (w), 2930 (m), 2850 (m), 1455 (m), 1095 (s), 1065 (s), 940 (m), 750 (s), 700 (s)	2.96 (dd, 1H, ^2J = 17, H-4); 3.29 (dd, 1H, ^2J = 17, H-4); 3.54 (m, 1H, H-3a); 3.90 (m, 1H, H-12); 4.14 (m, 2H, H-10, H-12); 4.45 (dd, 2H, H-2, H-10); 4.53 (dd, 1H, H-2); 5.60 (m, 1H, H-9); 5.61 (d, 1H, ^3J = 7, H-8b); 7.30 (m, 9H, H-5, 6, 7, 9, Ph)	38.6 (t, C-4); 45.0 (d, C-3a); 68.0 (t, C-12); 69.8 (t, C-2); 72.0 (t, C-10); 88.0 (d, C-8b); 117.0 (d, C-9); 124.5–129.0 (d, 9 × C$_{arom}$); 138.3 (s, C-13); 141.6 (s, C-4a); 142.9 (s, C-8a); 148.2 (s, C-3)	292 (5), 183 (82), 154 (40), 116 (100), 91 (64), 77 (10)
 **3f**	85	131	$C_{11}H_{10}O_2$ (174.2)	3100 (w), 1680 (m), 1485 (m), 1470 (m), 968 (s)	4.31 (d, 1H, ^3J = 5.5, H-3a); 4.36 (dd, 2H, H-2); 5.02 (q, 1H, H-9); 5.27 (q, 1H, H-9); 6.34 (d, 1H, ^3J = 5.5, H-8a); 6.88 (q, 2H, H-5, 6); 7.18 (m, 2H, H-4, 7)	51.4 (d, C-3a); 70.4 (t, C-2); 106.1 (t, C-9); 109.6 (d, C-8a); 111.4 (d, C-6); 121.1 (d, C-7); 124.2 (d, C-4); 126.8 (s, C-3b); 129.0 (d, C-5); 148.0 (s, C-7a); 158.6 (s, C-3)	174 (74), 150 (70), 145 (100), 133 (72), 117 (70), 103 (30), 91 (30), 78 (24)
 **3g**	90	88	$C_{14}H_{15}NO_3$ (245.3)	1723 (vs), 1601 (m), 1050 (s), 905 (m)	1.48 (t, 3H, ^3J = 7, H-13); 4.30 (m, 5H, H-3a, 2, 12); 5.05 (q, 1H, H-9); 5.35 (q, 1H, H-9); 6.28 (d, 1H, ^3J = 6, H-8a); 7.8–7.0 (m, 4H, H-4, 5, 6, 7)	14.8 (q, C-13); 50.0 (d, C-3a); 62.0 (t, C-12); 70.0 (t, C-2); 93.2 (d, C-8a); 106.6 (t, C-9); 114.8 (d, C-6); 123.2 (d, C-5); 124.1 (d, C-7); 128.6 (d, C-4), 129.0 (s, C-7a); 129.5 (s, C-3b); 141.5 (s, C-3); 148.5 (s, C-10)	245 (100), 172 (36), 144 (61), 130 (30), 117 (41), 89 (19), 77 (15)
 **4**[c]	95	89	$C_{10}H_8O_3$ (176.2)	2940 (vs), 2870 (m), 1725 (vs), 1465 (s), 1160 (s)	4.03 (d, 1H, ^3J = 6, H-3a); 4.10 (d, 2H, 2 × H-2); 6.61 (d, 1H, ^3J = 6, H-8a); 6.91 (m, 2H, H-5, H-6); 7.27 (m, 2H, H-4, H-7)	52.70 (d, C-3a); 68.91 (t, C-2); 109.90 (d, C-8a); 110.07 (d, C-6); 121.04 (s, C-3b); 122.04 (d, C-7); 124.70 (d, C-4); 130.07 (d, C-5); 147.97 (s, C-7a); 208.45 (s, C-3)	176 (75), 161 (100), 147 (18), 133 (53), 115 (24), 105 (27), 91 (26), 78 (20), 77 (31)

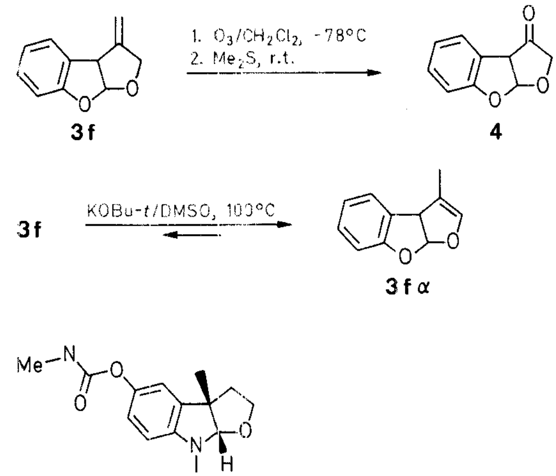
[a] Et$_2$O/petroleum ether in the following proportions were used to separate and purify the products by chromatography: **3a, b, d** = 1 : 100; **3c, e** = 1 : 10; **3f, 4** = 1 : 5; **3g** = 1 : 4.

[b] The calculated and observed values for M$^+$ in HRMS were within the range of ±0.0001.

[c] Conventional ozonolysis (anhydrous MeOH, −70 °C) until the solution was just light blue; reductive work-up (Me$_2$S).

[d] The mp was not determined due to decomposition of the crystalline compound.

After the reactive precursors **2a**–**2g** had been dissolved in ethanol under argon, solid sodium borohydride (1.1 equiv) was added rapidly together with 10 N sodium hydroxide (1 equiv) and catalytic cobaloxime (ca. $^1/_5$ of 0.05 equiv at a time). Cyclization proceeded smoothly in 5-*exo-dig* fashion, and in each instance the newly formed five-membered ring was fused *cis* to the pre-existing five-membered ring (cf. also **3a, 3d, 3e, 3f, 3g**) and also six-membered ring (cf. **3b, 3c**). Oxygen-sensitive acetal **3f** and also *O,N*-acetal **3g** were separated and purified on neutral alumina (activity III) (Table 2). All other acetals could be obtained by chromatography on silica gel. Ozonolysis of **3f** by *equimolecular* amounts of ozone gave ketone **4**, without cleavage of the acetalic C–H bond (Scheme **B**). Exomethylene derivative **3f** was isomerized to **3fα** (**3f**: **fα** = 1:1), which is a model for aflatoxin B_1. Oxazadiquinane **3g** contains the tricyclic skeleton of physovenine (**5**), an indole alkaloid isolated from Calabar beans.[2]



Scheme **B**

In conclusion, a range of 1-bromo-2-propargyloxy adducts of cyclic olefins are readily available by reaction of NBS in the presence of an excess of propargyl alcohol. Benzylic bromides **2f, 2g** and also homobenzylic bromides such as **2a**–**2e** have been found to be suitable precursors for cobaloxime/tetrahydroborate-induced cyclizations. In particular, the doubly homobenzylic radical arising from **2a** cyclizes in high yield. The heteroannulated ring systems are useful in natural products synthesis, as illustrated in Scheme **B**. Being cyclic allylic ethers, they can also be oxidized to α-methylene-γ-butyrolactones, a widespread class of biologically active compounds.[18]

All NMR spectra were recorded using a Bruker 200 MHz spectrometer. Petroleum ether used refers to boiling range 40–65°C.

Vicinal Bromopropargoxylation of Cyclic Olefins. 2-Bromo-1-(2-propynyloxy)indane (2a):

Anhydrous NBS (7.12 g, 40 mmol) is added quickly to distilled 2-propynol (20 mL, 0.34 mol) precooled to 0°C under inert gas (N_2 or Ar). The mixture is cooled to –30°C and during 2 h indene (**1a**; 2.38 g, 20 mmol) in CH_2Cl_2 (10 mL) is added dropwise. The resulting suspension is stirred for 1 h at –30°C, allowed to reach +15°C overnight, and extracted with ice-cold 1 N NaOH (25 mL). The aqueous phase is extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic phase is washed with ice-cold 1 N NaOH (2 × 10 mL) and dried ($MgSO_4$). After removal of the solvent and Kugelrohr distillation, the bromoether **2a** is obtained as a colorless oil; yield: 5 g (99%) (smaller samples are purified by chromatography). The compound can be stored at –20°C. At r.t., it decomposes, changing its color from yellow to dark red and, eventually, black.

The same procedure is used for **2b, 2c** and **2e**. Bromoether **2d** is obtained after 0.5 h at –45°C and then allowing the reaction mixture to reach ca. 0°C within 5 min. After neutralization with ice-cold sat. $NaHCO_3$, the solvent is removed in the cold (waterbath temperature ca. 15–20°C), giving a light yellow, very reactive oil, which is chromatographed (neutral Al_2O_3, activity III, Et_2O/light petroleum, 1:100). The resulting oil (2.95 g, 60%) must be used quickly in the cyclization step (Table 1).

3-Bromo-2-(2-propynyloxy)-*N*-ethoxycarbonylindole (2g):

A two-neck flask, previously dried with a hair-dryer, is charged with NBS (290 mg, 16 mmol), redistilled 2-propynol (15 mL, 270 mmol) and silica gel (40 µm mesh, 0.15 g). The apparatus is flushed with Ar and cooled to –40°C to –50°C (MeOH, solid CO_2, Dewar vessel). *N*-Ethoxycarbonylindole (**1g**; 238 mg, 15 mmol) in CH_2Cl_2 (5 mL) is added to the magnetically stirred mixture at 1 drop/10 sec, giving a yellow solution. After 2 h the cooling mixture is replenished with solid CO_2. The reaction solution is well stirred, allowed to reach r.t. overnight and checked for complete reaction (TLC monitoring). After neutralization (ph 7–8) with aq. $NaHCO_3$, the mixture is extracted with CH_2Cl_2 (3 × 10 mL). The organic phase is dried (Na_2SO_4), the solvent and excess of 2-propynol are removed *in vacuo* (1 Torr) without warming to give a yellow oil, which decomposes on warming, taking on a dark green coloration. It is purified on neutral Al_2O_3 (activity III, Et_2O/light petroleum, 1:4); yield: 387 mg (80%).

Compound **2f** is prepared and purified analogously (Et_2O/light petroleum, 1:10), however, without silica gel which shows no improvement.

Cyclization of β-Bromoethers to Fused 3-Methyleneoxacyclopentanes. 8-Ethoxycarbonyl-3-methylene-2,3,3a,8a-tetrahydrofuro[2,3-*b*]indole (3g); Typical Procedure:

To a solution of β-bromoether **2g** (323 mg, 1 mmol) in 95% EtOH (10 mL) is added solid $NaBH_4$ (40 mg, 1.1 mmol) and 10N NaOH (0.01 mL, 1 mmol). The solution is flushed with Ar, and several portions of finely powdered cobaloxime[19] (22 mg, 0.05 mmol) are added during 1 h at 50°C (oil bath temperature 65°C). The solution turns dark and after each addition of cobaloxime, a gas is liberated. After stirring for a further 1 h, no more gas is evolved. The EtOH is removed on a rotary evaporator, and after addition of brine (10 mL) the product is extracted with Et_2O (3 × 10 mL). The organic phase is washed with H_2O (5 mL), brine (5 mL), and dried (Na_2SO_4). On removal of solvent red brown crystals are precipitated. Recrystallization from EtOH affords **3g** as a colorless solid; yield: 220 mg (90%); mp 88°C (Table 2).

We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for support of our work.

Received: 9 February 1989; revised: 28 June 1989

(1) Wolff, S., Hoffmann, H.M.R. *Synthesis* **1988**, 760.
(2) Robinson, B. *The Alkaloids*, Vol. 10, Manske, R.F.H. (ed.), **1968**, Academic Press, New York, 1968, p. 383.
(3) Shishido, K., Shitara, E., Komatsu, H., Hiroya, K., Fukumoto, K., Kametani, T. *J. Org. Chem.* **1986**, *51*, 3007.
(4) Wijnberg, J., Speckamp, W.N. *Tetrahedron* **1978**, *34*, 2399.
(5) Curran, D.P. *Synthesis* **1988**, 417, 489.
(6) Neumann, W.P. *Synthesis* **1987**, 665.
(7) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541.
(8) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*, Pergamon Press, Oxford, 1986.

(9) Dulcere, J.P., Rodriguez, J., Santelli, M., Zahra, J.P. *Tetrahedron Lett.* **1987**, *28*, 2009.

(10) Okabe, M., Tada, M. *J. Org. Chem.* **1982**, *47*, 5382.
Okabe, M., Abe, M., Tada, M. *J. Org. Chem.* **1982**, *47*, 1775.

(11) Torii, S., Inokuchi, T., Yukawa, T. *J. Org. Chem.* **1985**, *50*, 5875.

(12) Bhandal, H., Pattenden, G., Russell, J.J. *Tetrahedron Lett.* **1986**, *27*, 2299.
Begley, M.J., Ladlow, M., Pattenden, G. *J. Chem. Soc. Perkin Trans 1* **1988**, 1095.

(13) Baldwin, J.E., Li, C.-S. *J. Chem. Soc., Chem. Commun.* **1987**, 166.

(14) Schrauzer, G.N. *Angew. Chem.* **1976**, *88*, 465; *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 417.

(15) Reviews: Scheffold, R., Rytz, G., Walder, L. in: *Modern Synthetic Methods*, Vol. 3, Scheffold, R. (ed.), Diesterweg/Salle Sauerlander, Frankfurt, 1983, p. 355.
Scheffold, R. *Chimia* **1985**, *39*, 203.
Scheffold, R. *Nachr. Chem. Tech. Lab.* **1988**, *36*, 261.

(17) cf. also Smith, K. *Bull. Soc. Chim. Fr.* **1989**, 272.

(18) Hoffmann, H.M.R., Rabe, J. *Angew. Chem.* **1985**, *97*, 96; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 94.

(19) Schrauzer, G.N. *Inorg. Synth.* **1968**, *11*, 61.

6 7

(17) cf. also Smith, K. *Bull. Soc. Chim. Fr.* **989**, 272.

(18) Hoffmann, H.M.R., Rabe, J. *Angew. Chem.* **1985**, *97*, 96; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 94.

(19) Schrauzer, G.N. *Inorg. Synth.* **1968**, *11*, 61.