1.45 (br, 2 H); ^{13}C NMR, see Table I; mass spectrum, *m/e* 233 (M; 232 for *un*labeled compound), B 187 (M - COOH).

1-(Hydroxymethyl)diamantane-*15*-^{13}C (3) was synthesized by reacting **2** (0.380 g) with lithium aluminum hydride in a manner previously described[18] to give a quantitative yield of product which was chromatographed (F-20 Alcoa alumina, *n*-pentane) to give 0.137 g (38%) of **3**: mp 206-209 °C (sealed); IR 3400, 1210; ^1H NMR δ ($CDCl_3$) 3.17 (d, 2 H, J = 136 Hz; s for *un*labeled compound), 2.85 (s, 1 H), 2.12 (br, 2 H), 1.90 (br, 2 H), 1.5-1.2 (br, 13 H), 0.92 (br, 2 H); ^{13}C NMR, see Table I; mass spectrum, *m/e* 219 (M; 218 for *un*labeled compound), B 188 (M - CH_2O).

Acknowledgment. The authors are indebted to the Robert A. Welch Foundation (Grant No. B-325) and to North Texas State University Faculty Research for financial support of this research.

(18) J. L. Marshall, S. A. Conn, and M. Barfield, *Org. Magn. Reson.*, **9**, 404 (1977).
(19) M. Barfield, J. L. Marshall, and E. D. Canada, Jr., *J. Am. Chem. Soc.*, **102**, 7 (1980).

An Approach to the Synthesis of *dl*-Furopelargones[1]

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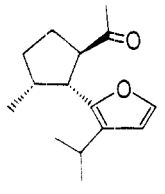
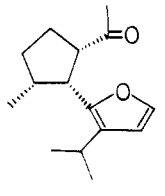
Furopelargones A (**1**) and B (**2**),[2,3] ketonic constituents

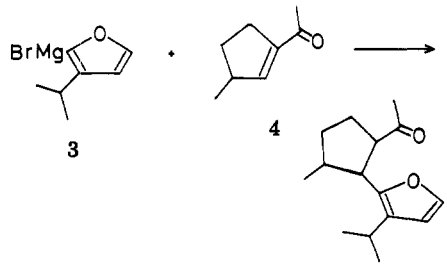


1



2

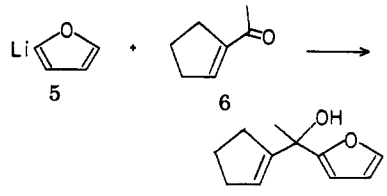
of Geranium Bourbon Oil, have been synthesized by Büchi and Wüest[4] through several steps from citral. A survey of the structures reveals that the furan ring moiety of these compounds may be introduced by the Michael addition of 3-isopropyl-2-furylmagnesium bromide (**3**) to the conjugated system of 1-acetyl-3-methylcyclopentene (**4**).[5] As



3 **4**

a part of our work on the synthetic approach to the carbon skeleton of natural products by means of Michael addition,[5,6] we carried out the reaction of the Grignard reagent **3** with the α,β-unsaturated ketone **4** in the presence of copper(I) chloride (CuCl) in order to prepare furopelargones. This paper deals with the isolation and structural identification of the diastereomeric mixture obtained in this reaction. The stereochemistry of these isomers has been confirmed principally on the basis of IR and NMR spectral data.

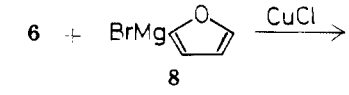
The use of 2-lithiofuran (**5**)[7] in the appropriate Michael



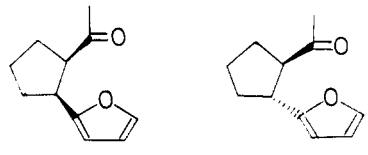
5 **6** **7**

addition was abandoned, since the preliminary experiment has shown that the reaction of **5** with 1-acetylcyclopentene (**6**)[5] proceeds only in the mode of 1,2-addition to give 1-(1-cyclopentenyl)-1-(2-furyl)ethanol (**7**), either in the presence or in the absence of CuCl.

To the contrary, the reaction of 2-furylmagnesium bromide (**8**)[8,9] with the ketone **6** afforded a mixture (isomer



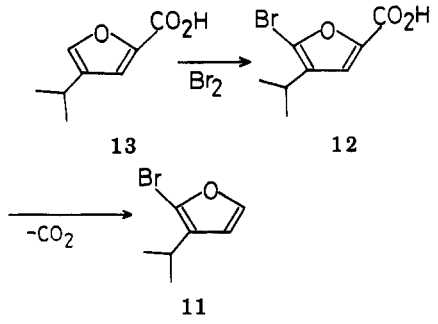
8



9 **10**

ratio ca. 1:1) of *cis*- and *trans*-*dl*-2-(2-acetylcyclopentyl)-furans (**9** and **10**), although the yield was as low as 15% as a result of the formation of an intractable material. The structural assignment of **9** and **10** is based on the chemical shift of the acetyl methyl protons, which are thought to be affected by the shielding effect of furan ring current more in the cis isomer (δ 1.70) than in the trans isomer (δ 2.04). The same effect has been observed in the chemical shift of the acetyl methyl protons of furopelargones A and B.[2]

The starting material of the present synthesis, 2-bromo-3-isopropylfuran (**11**) was prepared in a 48% yield



13 **12** **11**

by the pyrolysis of 4-isopropyl-5-bromofuran-2-carboxylic

(1) Presented in part at the 9th Symposium on Heterocyclic Chemistry, Fukuoka, Oct 1976.
(2) G. Lukas, J. C. N. Ma, J. A. McCloskey, and R. E. Wolff, *Tetrahedron*, **20**, 1789 (1964).
(3) M. Romanůk, V. Herout, F. Sorm, Y. R. Naves, P. Tullen, R. B. Bates, and C. W. Sigel, *Collect. Czech. Chem. Commun.*, **29**, 1048 (1964).
(4) G. Büchi and H. Wüest, *J. Am. Chem. Soc.*, **87**, 1589 (1965).
(5) A. Takeda, K. Shinhama, and S. Tsuboi, *Bull. Chem. Soc. Jpn.*, **50**, 1831 (1977). The ester was hydrolyzed with ethanolic KOH and then converted to the corresponding chloride by the action of $SOCl_2$.
(6) A. Takeda, T. Sakai, S. Shinohara, and S. Tsuboi, *Bull. Chem. Soc. Jpn.*, **50**, 1133 (1977).
(7) V. Ramanathan and R. Levine, *J. Org. Chem.*, **27**, 1216 (1962).
(8) A. F. Shepard, N. R. Winslow, and J. R. Johnson, *J. Am. Chem. Soc.*, **52**, 2083 (1930).
(9) H. Gilman, J. M. Peterson, and F. Schulze, *Recl. Trav. Chim. Pays-Bas*, **47**, 19 (1928).

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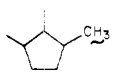
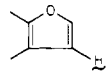
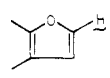
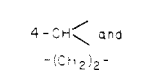
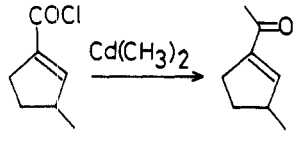
Table I. ^{1}H NMR Chemical Shifts (CCl_4, δ) of Furopelargone A (1) and its Diastereomers

						
1	0.67[a] (0.70)[b] (d, J = 7 Hz, 3 H)	1.13[a] (1.14)[b,c] (d, J = 7 Hz, 6 H)	1.98 (1.98)[b] (s, 3 H)	6.17[a] (6.17)[b] (d, J = 2 Hz, 1 H)	7.17[a] (7.17)[b] (d, J = 2 Hz, 1 H)	1.4-3.7[a] (m, 8 H)
2[b]	0.73 (d, J = 7 Hz, 3 H)	1.16 (d, J = 7 Hz, 6 H)	1.77 (d, 3 H)	6.20 (d, J = 2 Hz, 1 H)	7.23 (d, J = 2 Hz, 1 H)	
15	0.92 (d, J = 6 Hz, 3 H)	1.11 (d, J = 7 Hz, 6 H)	1.89 (s, 3 H)	6.10 (d, J = 2 Hz, 1 H)	7.11 (d, J = 2 Hz, 1 H)	1.5-3.5 (m, 8 H)
16	0.91 (d, J = 6 Hz, 3 H)	1.17 (d, J = 7 Hz, 6 H)	1.54 (s, 3 H)	6.14 (d, J = 2 Hz, 1 H)	7.12 (d, J = 2 Hz, 1 H)	1.5-3.2 (m, 8 H)

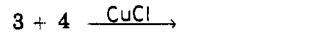
[a] Values are chemical shifts measured by us. Samples were prepared by following the procedure reported by Büchi and Wüest; see ref 4. [b] Values reported by Lukas et al; see ref 2. [c] J = 11 Hz.

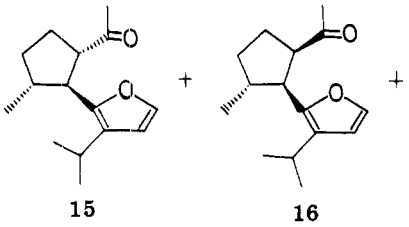
acid (12), readily derived from 4-isopropyl-2-furancarboxylic acid (13). The ketone 4 was prepared in 46%



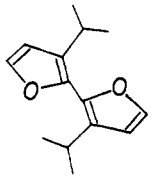
14 4

yield by the reaction of 3-methyl-1-cyclopentenecarbonyl chloride (14) with dimethylcadmium(II). The Grignard reagent 3 was derived from the bromofuran 11 by the method of Gilman, using magnesium–copper alloy. The Michael addition of 3 to ketone 4 in the presence of copper(I) chloride gave a mixture of the two diastereomers 15 and 16 (isomer ratio ca. 1:1) in 25% yield, together with





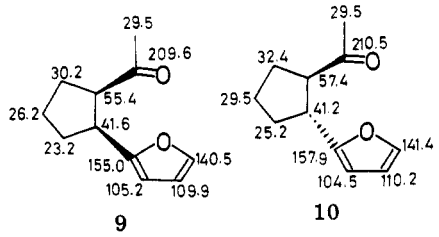
15 16



17

3,3′-diisopropyl-2,2′-bifuran (17) as a byproduct. ^{1}H NMR data of 15 and 16 are summarized in Table I, in which those of furopelargone A (1)[4] and furopelargone B (2)[2] are also included. The acetyl methyl protons of the epimer in which the furan ring and the acetyl group are arranged in a cis configuration are considered to be affected more by the shielding effect of the furan ring than those of the other isomer, for the same reason mentioned in the case of 9 and 10. Accordingly, the isomer in which the signals of acetyl methyl protons appear at higher field (δ 1.54) has been assigned to 16, and the other isomer to 15. The geometry of the furan ring and the methyl group attached to the cyclopentane ring, in 15 as well as in 16, also can be reasonably assigned as trans, because the signals due to the ring methyl protons in both epimers were observed at lower fields (δ 0.92 and 0.91) as compared with furopelargone A. The stereochemical relationship between the methyl and the furan groups in the final products as shown is quite consistent with the consideration that the approach of the incoming Grignard reagent to the ketone 4 should be from the least hindered face of the β-enone carbon, which clearly will be trans to the methyl group.

Chart I. ^{13}C NMR Chemical Shifts of Epimers 9 and 10



9 10

The IR spectra of 15 and 16 were identical with those of 1 and 2 for the most part, and the mass spectra also showed similar patterns. The ^{13}C NMR spectra of 9, 10, 1, 15, and 16 have been tentatively assigned[10] and summarized in Chart I and Table II. The higher field shift of the signal of the carbon atom jointed to the acetyl group in the compound 9 seems to be due to a larger steric hindrance[11] present in the cis form as compared with 10. The analogous shift of carbon signal was observed between the compound 16 and the trans epimers such as 1 and 15. The chemical shift of the methyl carbon attached to the cyclopentane ring of 1 is also exhibited at higher field as compared with those of 15 and 16.

Experimental Section

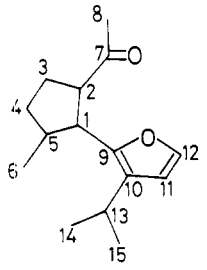
The melting points and boiling points are uncorrected. Elemental analyses were carried out by Mr. Eiichiro Amano of our laboratory. Analytical determinations by GLC were performed on a Hitachi Model K-53 gas chromatograph fitted with 10% Apiezon L Grease on Chromosorb W (3 mm o.d. × 1 m). Mass spectra were obtained with a Hitachi Model RMS-4 mass spectrometer. ^{1}H NMR spectra (60 MHz) were recorded with a Hitachi Model R-24 apparatus. ^{13}C NMR spectra were obtained with a JEOL LTD. JNM-FX100 apparatus.

Ethyl 3-methyl-1-cyclopentenecarboxylate and 1-cyclopentenyl methyl ketone (6) were prepared by the method described in the previous paper.[5] The authentic sample of furopelargone A (1) was synthesized from citral by following a procedure reported by Büchi and Wüest.[4]

(10) Off-resonance decoupling technique was used to assure the assignment. The data of simple homologues reported in the literature were instructive in making the assignment of ^{13}C chemical shifts of cyclopentane and furan rings. (a) T. F. Page, Jr., T. Alger, and D. M. Grant, J. Am. Chem. Soc., 87, 5333 (1965). (b) M. Christl, H. J. Reich, and J. D. Roberts, J. Am. Chem. Soc., 93, 3463 (1971).

(11) D. M. Grant, B. V. Cheney, J. Am. Chem. Soc., 89, 5315 (1967).

Table II. ^{13}C NMR Chemical Shifts (δ) of Furopelargones



	1	15	16
1	42.1	47.9	47.8
2	55.6	56.7	55.4
3	34.2	33.6	33.8
4	28.0	27.1	26.5
5	39.2	41.0	38.7
6	16.3	18.2	18.6
7	210.1	210.2	210.2
8	29.3	29.7	29.6
9	149.0	148.5	147.6
10	127.1	128.1	128.3
11	108.6	108.8	108.9
12	140.2	140.8	141.1
13	24.3[a]	24.4[a]	24.5[a]
14	23.9[a]	24.0[a]	23.9[a]
15	24.1[a]	24.2[a]	24.3[a]

[a] May be interchanged in assignment.

Magnesium–Copper Alloy.[9] A mixture of powdered magnesium (1.8 g) and copper (0.2 g) was heated to red hot for 20 min under a N_2 atmosphere in a glass test tube (15 mm o.d. × 150 mm). After being allowed to come to room temperature, it was crushed in a mortar.

1-(1-Cyclopentenyl)-1-(2-furyl)ethanol (7). Procedure A. According to the procedure of Ramanathan et al.,[7] a mixture of butyllithium (12.2 mmol) and 0.83 g (12.2 mmol) of furan in 10 mL of ether was heated at reflux for 4 h. A solution of 1.34 g (12.2 mmol) of **6** in 1 mL of ether was added to the mixture in the course of 10 min at 0 °C. After being stirred for 11.5 h at room temperature, it was poured into saturated aqueous ammonium chloride solution. The organic layer was extracted with ether. The solvent was removed under vacuum, and the residue was distilled to give 1.14 g (52%) of **7**: bp 94–97 °C (7 mm); IR (neat) 3420, 1160, 1011, 813, 735 cm^{-1}; ^1H NMR (CCl_4) δ 1.56 (s, 3 H, CH_3), 1.6–2.6 (m, 6 H, $(CH_2)_3$), 2.68 (s, 1 H, OH), 5.51 (m, 1 H, cyclopentene =CH—), 6.0–6.3 (m, 2 H, β-protons of furan), 7.22 (apparent s, 1 H, α-proton of furan); mass spectrum (70 eV), m/e (relative intensity) 160 (100, M – H_2O). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.88; H, 7.96.

Procedure B. The reaction gave 1.03 g (47%) of the alcohol **7** when 100 mg of CuCl was added before the addition of the ketone **6**.

***cis*- and *trans*-2-(2-Acetylcyclopentyl)furans (9 and 10).** A mixture of 710 mg (containing 26.4 mmol of Mg) of magnesium–copper (90:10) alloy and 240 mg of iodine was heated at 50 °C under a N_2 atmosphere for 1 h. After it was cooled, a solution of 2-bromofuran (2.58 g, 17.6 mmol) in 5 mL of tetrahydrofuran (THF) was slowly added to the mixture in the course of 20 min. The mixture was stirred for 3 h at room temperature. After the formation of 2-furylmagnesium bromide (**8**) was demonstrated by Michler's ketone,[12] 100 mg of CuCl was added to the mixture. A solution of **6** (1.21 g, 11 mmol) in 3 mL of THF was then added in the course of 5 min. The mixture was stirred for 20 h at room temperature and then neutralized with saturated aqueous ammonium chloride solution. The organic layer was extracted with ether, and the combined ether solutions were washed, dried over $MgSO_4$, and evaporated. The residue was distilled to give 296 mg (15%) of the mixture of **9** and **10** (1:1 by ^1H NMR), bp 100–150 °C (bath temperature (3 mm)). Analytical samples of **9** and **10** were obtained by preparative TLC (silica gel, 19:1 hexane–ether, two developments).

(12) H. Gilman and F. Schulze, *J. Am. Chem. Soc.*, **47**, 2002 (1925).

9: R_f 0.2; IR (neat) 1705, 1590, 1501, 1358, 1170, 1010, 802, 731 cm^{-1}; ^1H NMR (CCl_4) δ 1.2–2.3 (m, 6 H, $(CH_2)_3$), 1.70 (s, 3 H, $COCH_3$), 2.8–3.7 (m, 2 H, methine protons of cyclopentane), 5.90 (d, J = 3.5 Hz, 1 H, C_3-H of furan), 6.17 (q, J = 2 and 3.5 Hz, 1 H, C_4-H of furan), 7.20 (d, J = 2 Hz, 1 H, C_5-H of furan); mass spectrum (70 eV), m/e (relative intensity) 178 (38, M^+), 163 (22, M – CH_3), 135 (100, M – $COCH_3$). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.25; H, 7.81.

10: R_f 0.3; IR (neat) 1705, 1592, 1500, 1356, 1169, 1010, 801, 732 cm^{-1}; ^1H NMR (CCl_4) δ 1.2–2.4 (m, 6 H, $(CH_2)_3$), 2.04 (s, 3 H, $COCH_3$), 2.7–3.6 (m, 2 H, methine protons of cyclopentane), 5.91 (d, J = 3 Hz, 1 H, C_3-H of furan), 6.15 (q, J = 2 and 3 Hz, C_4-H of furan), 7.22 (d, J = 2 Hz, 1 H, C_5-H of furan); mass spectrum (70 eV), m/e (relative intensity) 178 (26, M^+), 163 (22, M – CH_3), 135 (100, M – $COCH_3$). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.16; H, 7.78.

4-Isopropyl-2-furancarboxylic acid (13) was prepared from 4-isopropyl-2-furancarbaldehyde[13,14] in 85% yield by adaptation of the method described in the literature:[9,13,15] mp 75–76 °C (lit.[14] mp 76–77 °C); IR (Nujol) 3500–2200 (OH), 1680 (C=O), 1600, 1511, 1423, 1294, 1204, 945 cm^{-1}; ^1H NMR (CCl_4) δ 1.25 (d, J = 6 Hz, 6 H, $CH(CH_3)_2$), 2.82 (m, 1 H, $CH(CH_3)_2$), 7.16 (s, 1 H, β-H of furan), 7.32 (s, 1 H, α-H of furan).

5-Bromo-4-isopropyl-2-furancarboxylic Acid (12). Bromine (48 g, 0.30 mol) was added dropwise with stirring to 35 g (0.23 mol) of **13** in the course of 2 h at 80 °C. Stirring was continued for an additional 4 h. After being cooled, the mixture was poured into water and the organic layer was extracted with ether. The ethereal extract was washed with saturated aqueous sodium chloride solution and dried over $MgSO_4$. Removal of the solvent under vacuum gave 40.7 g (76%) of oil, which was used without further purification: IR (neat) 3600–2300 (OH), 1690 (C=O), 1600, 1500, 1293, 1207, 1028, 764 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 (d, J = 7 Hz, 6 H, $CH(CH_3)_2$), 2.83 (m, 1 H, –CH(), 7.20 (s, 1 H, furan ring =CH—), 10.59 (br s, 1 H, CO_2H). ^1H NMR spectral data of the crude product were identical with those of the literature.[16]

2-Bromo-3-isopropylfuran (11). This compound was prepared by the procedure of Shepard et al.[8] A mixture of 7 g of copper powder, 47 mL of quinoline, and 10 g (0.043 mol) of the acid **12** was heated in a 200-mL Claisen flask at 230 °C for 20 min. After the first crop of furan **11** was collected, being accompanied by a portion of quinoline, additional portions of the acid **12** (37.9 g, 0.139 mol), copper powder (20 g), and quinoline (50 mL) were added in the course of 1.5 h, and the heating was continued for further 2 h. Distillation of the combined distillate gave 18.6 g (48%) of **11**, which was dried over CaO and stored in a refrigerator: bp 95–97 °C (87 mm); IR (neat) 1590, 1575, 1158, 1058, 1005, 887, 730 cm^{-1}; ^1H NMR (CCl_4) δ 1.15 (d, J = 6 Hz, 6 H, $CH(CH_3)_2$), 2.78 (m, 1H, –CH(), 6.21 (d, J = 2 Hz, 1 H, β-H of furan), 7.27 (d, J = 2 Hz, 1 H, α-H of furan). Anal. Calcd for C_7H_9BrO: C, 44.47; H, 4.80. Found: C, 44.21; H, 4.77.

1-Acetyl-3-methylcyclopentene (4) was prepared by the reaction of dimethylcadmium(II) with the acid chloride **14**,[5] by the procedure described in the literature:[17] yield 46%; bp 42–43 °C (5 mm) [lit.[17] bp 70–75 °C (13 mm)].

Diastereomers (15 and 16) of Furopelargone A. A mixture of 0.6 g of magnesium–copper alloy (22 mmol of Mg) and 0.3 g of iodine was heated at 50 °C under a N_2 atmosphere for 2 h. After it was cooled, a solution of the bromofuran **11** (1.17 g, 6.2 mmol) in 3 mL of THF was slowly added to the mixture in the course of 15 min. To the mixture, which was stirred for 1 h further at room temperature was added 30 mg of CuCl. The stirring was continued for an additional 2 h. A solution of **4** (270 mg, 2.2 mmol) in 1 mL of THF was added with caution to the resultant mixture in the course of 10 min. The mixture was further stirred for 11 h at room temperature and then was neutralized with cold, dilute

(13) H. Gilman and N. O. Calloway, *J. Am. Chem. Soc.*, **55**, 4197 (1933).
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HCl. The organic layer was extracted with ether. The combined ether solutions were washed with saturated aqueous sodium chloride solution, dried over $MgSO_4$, and concentrated. Distillation of the residue gave 208 mg of a clean oil, bp 150–180 °C (bath temperature) (0.5 mm). GLC analysis showed that it consisted of 61 parts of a mixture of epimers **15** and **16** (25% yield from the bromide **11**) and 31 parts of the bifuran **17** (10% yield from the bromide **11**). The ^1H NMR spectrum indicates that the ratio of epimers **15** and **16** is nearly 1:1, by comparison of the signals due to acetyl methyl protons. Two purifications by TLC (silica gel, 19:1 hexane–ether) gave analytical samples of **15** and **16**.

Epimer 15: R_f 0.3; IR (neat) 2950, 1710, 1510, 1363, 1163, 1070, 736, 702 cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity) 234 (14, M^+), 219 (3, M – CH_3), 191 (16, M – $COCH_3$), 43 (100, $COCH_3$). Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.92; H, 9.58.

Epimer 16: R_f 0.2; IR (neat) 2960, 1710, 1510, 1363, 1163, 1068, 748, 717 cm^{-1}; mass spectrum (70 eV), *m/e* (relative intensity) 234 (16, M^+), 219 (4, M – CH_3), 191 (15, M – $COCH_3$), 43 (100, $COCH_3$). Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.78; H, 9.42.

3,3′-Diisopropyl-2,2′-bifuran (17): R_f 0.8; IR (neat) 2930, 1460, 1380, 1166, 1060, 889, 732 cm^{-1}; ^1H NMR (CCl_4) δ 1.18 (d, *J* = 7 Hz, 12 H, 2 $CH(CH_3)_2$), 3.28 (m, 2 H, 2 $CH(CH_3)_2$), 6.28 (d, *J* = 2 Hz, 2 H, 2β-H of furan), 7.23 (d, *J* = 2 Hz, 2 H, 2α-H of furan); mass spectrum (70 eV), *m/e* (relative intensity) 218 (39, M^+), 203 (50, M – CH_3), 175 (14, M – $CH(CH_3)_2$), 18 (100). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.30; H, 8.35.

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Registry No. (±)-1, 73803-38-0; (±)-4, 73770-50-0; 6, 16112-10-0; (±)-7, 73770-51-1; (±)-9, 73770-52-2; (±)-10, 73770-53-3; 11, 73770-54-4; 12, 53875-11-9; 13, 38071-68-0; (±)-14, 73770-55-5; (±)-15, 73803-39-1; (±)-16, 73803-40-4; 17, 73770-56-6; furan, 110-00-9; 2-bromofuran, 584-12-3; 4-isopropyl-2-furancarbaldehyde, 16015-07-9.

Thermal Rearrangement of 6-(Benzylamino)uracils to 5-Benzyl-6-aminouracils

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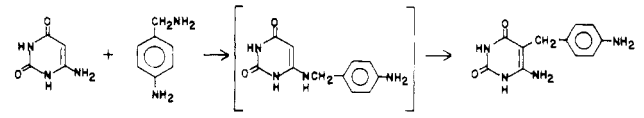
As part of our continuing interest in the chemistry of pyrimidines that are inhibitors of DNA polymerases[1,2] we have uncovered several rearrangements of N^6-substituted 6-aminouracils.[3,4] A recent attempt to prepare 6-(*p*-aminobenzylamino)uracil (1) as an inhibitor of *Bacillus subtilis* DNA polymerase III by the reaction between 6-aminouracil and *p*-aminobenzylamine led, unexpectedly, to the isolation of a compound which was isomeric with 1.[1] We report here the proof of the structure of this product and of others obtained by thermal rearrangement of 6-(benzylamino)uracils as 5-benzyl-6-aminouracils and propose a mechanism for this reaction. 5-Benzylpyrimidines and related compounds, e.g., trimethoprim, are of considerable interest as antibacterial and chemotherapeutic agents because of their ability to inhibit, selectively, dihydrofolate reductases.[5] Although many analogues bearing amino and oxo substituents in the pyrimidine ring have been synthesized,[6] 5-benzyl-6-aminouracils have not been reported. We also postulate a reason for the absence of these compounds from the literature.



2

The product of the reaction between 6-aminouracil and *p*-aminobenzylamine in boiling water had an elemental composition corresponding to an isomer of 1. Its proton NMR spectrum in dimethyl-d_6 sulfoxide showed downfield resonances typical of uracil N–H protons[7] and resonances corresponding to the benzyl group. However, the 5-H resonance was absent, and two broad resonances suggestive of amino groups were present. Reaction of this compound with acetic anhydride produced a monoacetyl derivative, **3**. On the basis of these data, two possible structures were postulated, 5-(*p*-aminobenzyl)-6-aminouracil (**2**) and the isomeric 5-[*p*-(aminomethyl)phenyl]-6-aminouracil. The two possibilities were distinguished by comparison of the proton NMR spectra of **2** and its acetyl derivative, **3**, with those of several model compounds. Phenyl proton resonances of *p*-aminobenzylacetamide (δ 6.91, 6.49) were closer to those of **2** (δ 6.87, 6.42) than to those of *p*-acetamidobenzylamine (δ 7.20, 7.49), suggesting that **2** possessed the aminophenyl rather than the (aminomethyl)phenyl structure. Further, the acetyl derivative (**3**) showed phenyl proton resonances at δ 7.10 and 7.40 similar to those of *p*-acetamidobenzylamine (see above) and *p*-acetamidobenzylacetamide (δ 7.17, 7.55); the acetamido NH and Me resonances of **3** (δ 9.74 and 2.00, respectively) were also commensurate with those derived from an aromatic amino group (δ 9.85, 2.02) rather than from an aminomethyl group (δ 8.20, 1.85).

The product **2** was postulated to result from a thermal rearrangement of 1, the expected product of the reaction. Indeed, when 1 [prepared by hydrolysis of 6-(*p*-acetamidobenzylamino)uracil[1]] was heated at reflux in *N,N*-dimethylaniline, an 80% yield of a compound identical with **2** was obtained. Examination of the thermal lability of other 6-(benzylamino)uracils has now shown that his rearrangement is characteristic of such compounds.

Several 6-(benzylamino)uracils were recovered unchanged after reflux in *N,N*-dimethylaniline (bp 194 °C). However, the use of biphenyl (bp 256 °C) as solvent afforded good yields of compounds whose proton NMR spectra suggested that they were 5-benzyl-6-aminouracils. Table I lists the products obtained from the thermal rearrangement of 6-(benzylamino)uracils. Several generalizations can be made about the rearrangement. First, only compounds with electron-releasing groups in the phenyl ring undergo rearrangement in boiling biphenyl; 6-(benzylamino)uracil and 6-(*p*-nitrobenzylamino)uracil were recovered unchanged under these conditions. Second, increasing the reaction temperature by the use of *n*-decylbenzene (bp 300 °C) as solvent led to decomposition of 6-(benzylamino)uracil but to a 20% yield of 3-methyl-5-benzyl-6-aminouracil from the 3-methyl starting com-

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