Flavonoids. 41 [1]. Stereospecific Synthesis of 2,3-Dihydro-*c*-3-substituted-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-ones

Tamás Patonay* [2], Erzsébet Patonay-Péli, György Litkei,
László Szilágyi, Gyula Batta and Zoltán Dinya

Department of Organic Chemistry, Kossuth Lajos University,
H-4010 Debrecen 10, P.O.B. 20, Hungary

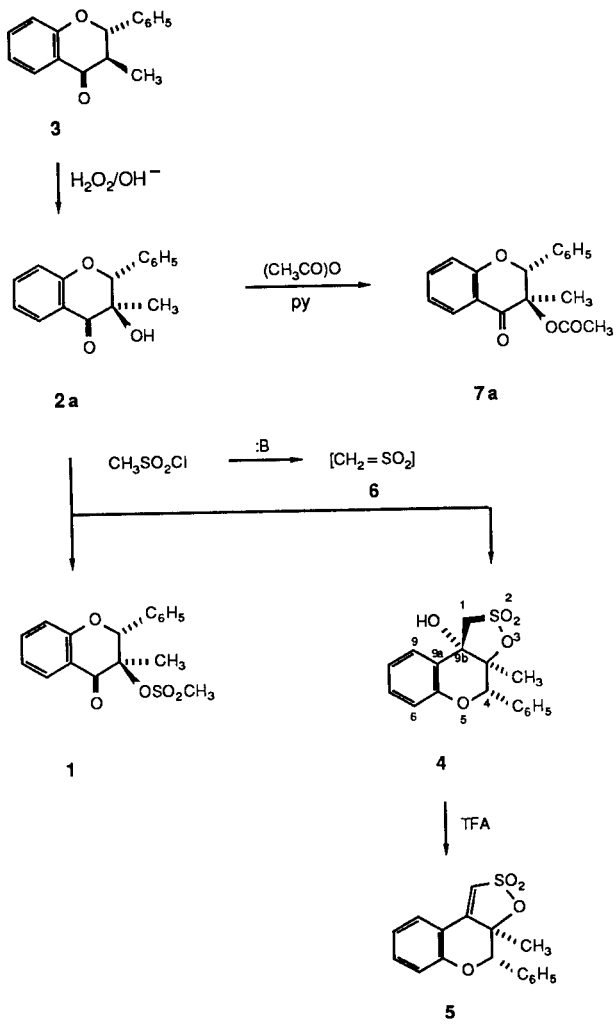
Received April 10, 1987

The synthesis of 2,3-dihydro-*t*-3-mesyloxy-*c*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**1**) is described. The reaction of mesylate **1** with various nucleophiles, first of all *O*- and *N*-nucleophiles, yields the corresponding 2,3-dihydro-*c*-3-substituted-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-ones **2b**, **7b**, **9**, **10**, **12**, **14** and **18**. Azide **14** is a useful intermediate for the synthesis of flavonoids **15-17**.

J. Heterocyclic Chem., **25**, 343 (1988).

As a part of our program to investigate the applicability of the nucleophilic displacement reaction for the synthesis of 3-substituted-flavonoids and the mechanism of the substitution reaction [1a,3], we wished to extend our studies to the reactivity of the tertiary substrates. 2,3-Dihydro-*t*-3-mesyloxy-*c*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**1**) was chosen as model compound. The starting material 2,3-dihydro-*t*-3-hydroxy-*c*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**2a**) was synthesized by means of Algar-Flynn-Oyamada oxidation of 2,3-*trans*-2,3-dihydro-3-methyl-2-phenyl-4*H*-1-benzopyran-4-one (**3**). This procedure was found to give better yields than the earlier reported oxidation of 2'-hydroxy-α-methylchalcone [4]. Reaction of **2a** with mesyl chloride and pyridine resulted in the formation of the mixture of mesylate **1** and the unexpected **4**. The structure of sultone **4** was established on the basis of spectral evidence and its acid-catalyzed dehydration into **5** (Scheme 1). No isomerisation between **1** and **4** was observed even under forced conditions. As mesylates are known to form by addition of alcohols to the reactive intermediate, thioformaldehyde dioxide (**6**) [5] thus sultone can be supposed to be produced in an unusual cycloaddition reaction.

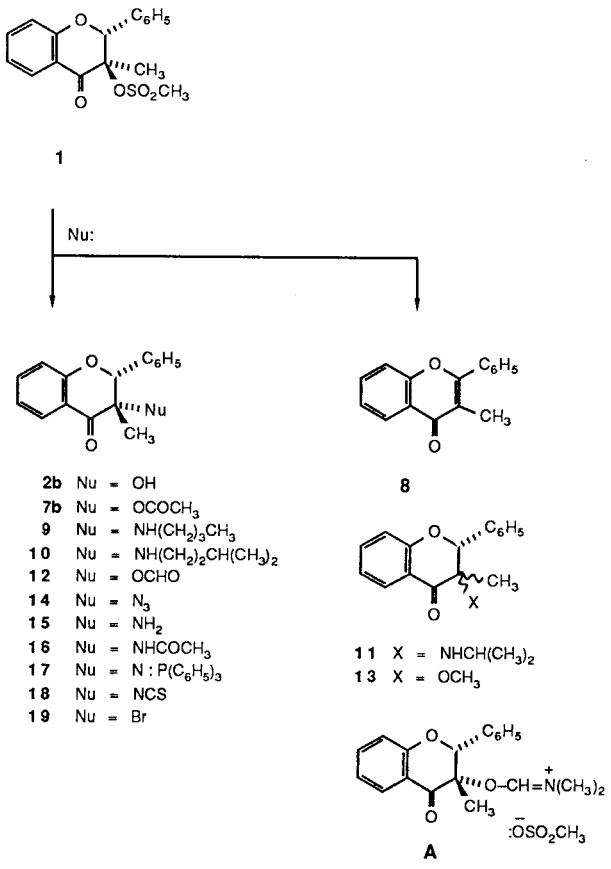
Scheme 1



The reaction of **1** with potassium acetate in hot dimethyl sulfoxide (DMSO) afforded *c*-3-acetoxy-2,3-dihydro-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**7b**), 2,3-dihydro-*c*-3-hydroxy-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**2b**) and 3-methyl-2-phenyl-4*H*-1-benzopyran-4-one (**8**). Similar treatment of **1** with butylamine or isopentylamine in hot *N*,*N*-dimethylformamide (DMF) led to the formation of *c*-3-butylamino-2,3-dihydro-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**9**) and 2,3-dihydro-*c*-3-isopentylamino-*t*-3-methyl-4*H*-1-benzopyran-4-one (**10**), respectively, besides **2b** and **8** (Scheme 2).

The stereochemistry of the products of the substitution reaction was determined by comparison with the known epimer (in case of **2a-2b** and **7a-7b**) and nuclear Overhauser effect (nOe) measurements. Reactions require forced conditions because of the steric hindrance at the tertiary centre. When **1** was treated with butylamine at room temperature the reaction-time was extremely long though the yield of **9** was better and no formation of **2b** was observed.

Scheme 2



The importance of the steric factors is indicated by the lack of any substitution in the reaction of **1** with more crowded amines. Thus, treatment of **1** with isopropylamine (a primary amine carrying an α-branch) yielded only **2b** and **8**, substitution product **11** could not be detected. When **1** was reacted with piperidine only extensive degradation was observed.

Experiments were performed to determine the origin of **2b** as its stereochemistry excluded the simple hydrolysis of the sulfonate function. Furthermore, **2b** was obtained from **1** in hot DMF in the presence of either water, methanol or isopropylamine and even in pure, dry DMF in a sealed tube. From this latter reaction mixture 2,3-dihydro-*c*-3-formyloxy-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**12**) was also isolated, in addition to **2b** and **8**. Therefore, an attack of the solvent must be proposed at elevated temperature to afford a reactive intermediate **A** which transforms into formate **12** and then by hydrolysis into alcohol **2b**.

Attempted methanolysis of **1** in refluxing methanol failed as the bulk of the starting material remained unchanged after 60 hours and only small amount (*ca.* 5%) of a new product was formed. This component was isolated by tlc and its ms spectra (molecular peak at m/e = 268, loss of a methyl and methoxy groups at 253 and 237, retro-Diels-Alder fragment [6] at 148) agrees with the presumed 2,3-dihydro-3-methoxy-3-methyl-2-phenyl-4*H*-1-benzopyran-4-one (**13**) structure.

Reaction of **1** with sodium azide gave *c*-3-azido-2,3-dihydro-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**14**) in high yield. Selective reduction of **14** under controlled conditions [7] provided *c*-3-amino-2,3-dihydro-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**15**), whereas the Staudinger reaction [8] of **14** yielded the expected iminophosphorane **17** (Scheme 2). The attempted cycloaddition reaction of **14** and diethyl acetylendicarboxylate [9], probably because of steric hindrance, failed just like the planned transformations of **17** into other nitrogen-containing derivatives though iminophosphoranes, are considered as utilizable intermediates [8,10].

Surprisingly, mesylate **1** showed low sensitivity toward *S*-nucleophiles contrary to the observed high reactivity of 2,3-*trans*-2,3-dihydro-3-mesyloxy-2-phenyl-4*H*-1-benzopyran-4-ones [1a,3c] and other α-ketomesylates [11]. Mesylate **1** reacted with potassium thiocyanate only in the presence of a phase-transfer-catalyst and gave a small amount of 2,3-dihydro-*c*-3-isothiocyanato-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**18**) in addition to **8** as the major product. It is noteworthy that a similar reaction of α-ketomesylates and α-haloketones was reported to give exclusively α-thiocyanatoketones [3b,12]. Our efforts to synthesize **18** from **17** in refluxing carbon disulfide [8] was unsuccessful. Reaction of **1** with potassium thiolacetate resulted in extensive degradation and no product could be isolated.

Treatment of **1** with tetrabutylammonium bromide in hot DMF furnished solely **8** and only traces of **2b** could be detected by tlc. *c*-3-Bromo-2,3-dihydro-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**19**) can be proposed as the primary product which readily transforms into **8** in a secondary elimination process.

These experiments reveal that the reaction of mesylate **1** with nucleophiles (especially with *O*- and *N*-nucleophiles) offers a convenient synthetic method for the preparation of 2,3-dihydro-*c*-3-substituted-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-ones not available by other procedures.

The observed inversion during the displacement reaction, the importance of the steric factors, the lack of any rearrangement and the fact that α-ketocarbonium ions have been reported to form under acidic conditions [13], all these arguments are consistent only with a sterically hindered, energetically unfavourable S_N2-type substitution reaction. At the same time, the clear differences in the reactivity and selectivity of **1** and 2,3-*trans*-2,3-dihydro-3-mesyloxy-2-phenyl-4*H*-1-benzopyran-4-ones [1a,3] toward

various nucleophiles indicate functioning of a quite different and more complex mechanism in the reactions of these latter substrates.

EXPERIMENTAL

Melting points were determined on a Kofler apparatus and are uncorrected. The ir spectra were recorded with a Perkin-Elmer 283 instrument in potassium bromide discs. The pmr (200 MHz) and proton decoupled cmr (50.3 MHz) spectra obtained on Bruker WP 200 SY spectrometer in deuteriochloroform solutions unless otherwise stated. Tetramethylsilane was used as internal standard and chemical shifts are quoted in parts per million. The mass spectra were recorded with a VG 7035 gc-ms system, electron impact at 70 eV unless otherwise specified. Kieselgel 40 or 60 (Merck, 0.063-0.2 mm) was used for column chromatography.

2,3-Dihydro-*t*-3-hydroxy-*c*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**2a**).

A suspension of **3** [4] (5.8 g, 24.34 mmoles) in ethanol (60 ml) and 50% aqueous sodium hydroxide solution (15 ml) was stirred at room temperature and 30% aqueous hydrogen peroxide was added over a period of 180 minutes. After 24 hours the mixture was acidified with hydrochloric acid and diluted with water (*ca.* 800 ml).

The precipitate was filtered off and crystallized from petroleum ether to give 3.15 g (51%) of **2a**, mp 108-109°, lit [4] mp 107-107.5°; ir: 3470 (OH), 2980, 2870 (CH_3), 1690 (C=O), 1305, 1230 (flavanone skeleton); pmr: 7.72 (dd, 1H, H-5), 5.12 (s, 1H, H-2), 3.65 (s, 1H, OH) 1.13 (s, 3H, CH_3); ms: 254 ($M^{+\cdot}$, 2), 211 (100), 183 (10), 181 (5), 165 (5.5), 133 (100), 121 (36), 105 (13), 91 (30), 77 (22).

2,3-Dihydro-*t*-3-mesyloxy-*c*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**1**) and *c*-9b-Hydroxy-*c*-3a-methyl-*r*-4-phenyl-1,3a,4,9b-tetrahydro[1,2]-oxathiolo[5,4-*c*][1]benzopyran 2,2-Dioxide (**4**).

To a cooled (0°) solution of **2a** (13.0 g, 51.12 mmoles) in pyridine (140 ml) was added mesyl chloride (9.7 ml, 0.128 mole) and allowed to stand at room temperature for 9 days. The mixture was poured into crushed ice, the precipitated solid was collected, washed with water and separated by fractional crystallization from petroleum ether to yield **1** (6.07 g, 36%) as the more soluble component, mp 110-112°; ir: 2937 (CH_3), 1695 (C=O), 1355, 1166 (SO_2), 1304, 1236 (flavanone skeleton); pmr: 7.59 (dd, 1H, H-5), 5.75 (s, 1H, H-2), 3.07 (s, 3H, CH_3SO_2), 1.39 (s, 3H, CH_3); cmr (DMSO-d_6): 183.76 (C-4), 159.91 (C-8a), 137.30 (C-7), 133.03 (C-1'), 122.78 (C-6), 118.61 (C-4a), 118.02 (C-8), 88.21 (C-3), 82.83 (C-2), 41.26 (CH_3SO_2) 17.06 (CH_3); not assigned signals: 128.89, 128.07, 127.88, 127.49; ms: 332 ($M^{+\cdot}$, 2), 253 (100), 238 (12.5), 237 (12.5), 236 (20), 235 (43), 223 (15), 212 (6), 181 (10), 161 (33.5), 147 (35.5), 133 (66), 121 (41), 120 (11), 116 (28), 105 (35), 91 (15), 77 (57).

Anal. Calcd. for $C_{17}H_{16}O_5S$: C, 61.43; H, 4.85; S. 9.65. Found: C, 61.99; H, 4.72; S, 9.64.

The less soluble product was identified as **4** (3.07 g, 18%), mp 183-186 dec; ir: 3498 (OH), 2958, 2890 (CH_3), 1358, 1171 (SO_2), 1239, 1050 (flavan skeleton), 1189 (C-OH); pmr (DMSO-d_6): 7.59 (dd, 1H, H-9), 6.99 (dd, 1H, H-6), 6.69 (s, 1H, OH deuterium oxide exchangable), 5.75 (s, 1H, H-4), 4.58 (d, 1H, H-1 endo, J_{AB} = 14.5 Hz), 4.20 (d, 1H, H-1 exo, J_{AB} = 14.5 Hz), 1.24 (s, 3H, CH_3), nOe: irradiation of OH, H-9 (12%), H-1 exo (3.2%), CH_3 (6.8%), irradiation of H-4: Ar-H (17.7%), H-1 endo (10.6%), irradiation of CH_3, Ar-H (11%), OH (13%); cmr (DMSO-d_6): [14] 152.15 (C-5a), 134.72 (C-1'), 129.92 (C-7), 125.26 (C-9a), 122.15 (C-8), 116.70 (C-6), 90.06 (C-3a), 78.39 (C-4), 77.38 (C-9b), 58.71 (C-1), 13.08 (CH_3); not assigned signals: 128.54, 128.36, 128.02, 127.78; ms: 332 ($M^{+\cdot}$, 5), 237 (100), 225 (12), 199 (10), 178 (3), 162 (5), 147 (7), 134 (25), 121 (35), 105 (20), 91 (17.5), 77 (18).

Anal. Calcd. for $C_{17}H_{16}O_5S$: C, 61.43; H, 4.85; S, 9.65. Found: C, 60.93; H, 4.89; S, 9.53.

3a,4-Dihydro-*c*-3a-methyl-*r*-4-phenyl[1,2]oxathiolo[4,5-*c*][1]benzopyran 2,2-Dioxide (**5**).

A solution of **4** (586 mg, 1.76 mmoles) in trifluoroacetic acid (18 ml) was refluxed for 45 minutes, evaporated to dryness and residue was purified by column chromatography (benzene) to afford **5** (174 mg, 31%) as white crystals, mp 198-199°; ir: 1630 (C=C), 1335, 1168, 1152 (SO_2), 1214, 1011 (flavan skeleton); pmr: 6.76 (s, 1H, H-1), 5.32 (s, 1H, H-4), 1.48 (s, 3H, CH_3); ms (30 eV) 314 ($M^{+\cdot}$, 5.5), 250 (100), 249 (15), 235 (8), 207 (90), 178 (44), 173 (13), 149 (41), 145 (20), 134 (10), 115 (16), 105 (25), 97 (23), 83 (25), 77 (24.5).

Anal. Calcd. for $C_{17}H_{14}O_4S$: C, 64.95; H, 4.49; S, 10.20. Found: C, 64.71; H, 4.53; S, 10.17.

c-3-Acetoxy-2,3-dihydro-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**7b**) and 2,3-dihydro-*c*-3-hydroxy-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**2b**).

A mixture of **1** (1g, 3.01 mmoles), anhydrous potassium acetate (0.6 g, 6.11 mmoles) and dry DMSO (20 ml) was heated at 100° for 10 hours then poured into brine, extracted with ethyl acetate and dried (magnesium sulfate). The residue, obtained by evaporation of the solvent, was fractionated by column chromatography (benzene) to yield 52.5 mg (5.3%) of unreacted **1** and 83 mg (9.3%) of **7b**, mp 168-170° (petroleum ether); ir: 1746 (ester C=O), 1696 (ketone C=O), 1310, 1228, 1023 (flavanone skeleton), 1243, 1037 (ester C-O-C); pmr: 7.85 (dd, 1H, H-5), 5.18 (s, 1H, H-2), 1.96 (s, 3H, CH_3COO), 1.45 (s, 3H, CH_3); nOe: irradiation of CH_3, H-2 (14%), irradiation of H-2: Ar-H (15%), CH_3 (3%); cmr: [14] 189.68 (C-4), 169.2 (CH_3CO), 160.06 (C-8a), 135.45 (C-7), 134.62 (C-1'), 121.85 (C-6), 119.92 (C-4a), 117.24 (C-8), 85.95 (C-2), 78.80 (C-3), 20.83 (CH_3CO), 17.12 (CH_3); not assigned signals: 129.14; 128.94, 128.84, 128.42, 128.24, 127.96; ms: 296 ($M^{+\cdot}$, 5), 254 (64), 236 (8), 235 (6), 253 (9), 211 (100), 183 (4.5), 181 (8), 148 (17.5), 147 (13.5), 134 (59), 133 (54), 121 (72), 116 (11), 105 (21), 91 (21), 77 (15).

Anal. Calcd. for $C_{18}H_{16}O_4$: C, 73.57, H, 5.44. Found: C, 73.11; H, 5.05.

Further elution afforded 69 mg (9.0%) of **2b**, mp 144-146 (petroleum ether-ethyl acetate); ir: 3440 (OH), 2973, 2885 (CH_3), 1679 (C=O), 1301, 1230, 1008 (flavanone skeleton), 1145 (C-OH); pmr: 7.90 (dd, 1H, H-5), 5.34 (s, 1H, H-2), 3.07 (s, 1H, OH), 1.51 (s, 3H, CH_3); nOe: irradiation of CH_3, H-2 (9.6%), OH (3.4%); ms: 254 ($M^{+\cdot}$, 9), 235 (4), 211 (87), 183 (7), 181 (4), 165 (4.5), 133 (100), 121 (46), 105 (9), 91 (25), 77 (13).

Anal. Calcd. for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.51; H, 5.40.

Next eluted fraction yielded 115 mg (16%) of 3-methyl-2-phenyl-4*H*-1-benzopyran-4-one (**8**).

t-3-Acetoxy-2,3-dihydro-*c*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**7a**).

A solution of **2a** (0.5 g, 1.97 mmoles) and acetic anhydride (2 ml) in dry pyridine (5 ml) was heated at 100° for 9 hours, poured into water and the precipitate was filtered off to yield **7a** (459 mg, 79%), mp 148-149° (benzene-petroleum ether), lit [4] mp 140-141°; ir: 2988 (CH_3), 1753 (ester C=O), 1702 (ketone C=O), 1296, 1233, 1014 (flavanone skeleton), 1245, 1033 (ester C-O-C); pmr: 8.00 (dd, 1H, H-5), 6.28 (s, 1H, H-2), 2.15 (s, 3H, CH_3CO), 1.35 (s, 3H, CH_3); cmr: 191.04 (C-4), 169.86 (CH_3CO), 160.58 (C-8a), 136.08 (C-7), 134.50 (C-1), 122.36 (C-6), 119.50 (C-4a), 117.93 (C-8), 81.32 (C-3), 80.42 (C-2), 21.04 (CH_3CO), 16.45 (CH_3); not assigned signals: 128.65, 128.28, 128.14, 128.12; ms: 296 ($M^{+\cdot}$, 3), 254 (35), 253 (8), 236 (78), 235 (77.5), 211 (100), 183 (5.5), 181 (11), 148 (7), 147 (16), 134 (50), 133 (68), 121 (63), 120 (3.5), 115 (14), 105 (22), 91 (24.5), 77 (24).

Attempted acid-catalyzed acetylation of **2a** according to lit [4] failed to give **7a**.

3-Methyl-2-phenyl-4*H*-1-benzopyran-4-one (**8**).

A solution of **1** (332 mg, 1 mmole) and tetrabutylammonium bromide (650 mg, 2.02 mmoles) in dry DMF (10 ml) was heated at 100° for 15 hours then poured into brine and extracted with methylene chloride. The dried and concentrated extract was purified by column chromatography (benzene) to afford 153 mg (65%) of **8**, mp 74-75° (petroleum ether), lit [15] 72-74; ir: 1638 (C=O), 1616 (C=C), 1371, 1135 (flavone skeleton);

pmr: 8.28 (dd, 1H, H-5), 2.15 (s, 1H, CH_3) and 15 mg (4.5%) of unreacted **1**.

Only traces of **2b** could be detected by tlc.

Solvolysis of Mesylate **1**. 2,3-Dihydro-*c*-3-hydroxy-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**2b**) and 3-Methyl-2-phenyl-4*H*-1-benzopyran-4-one (**8**).

A solution of **1** (332 mg, 1 mmole) in DMF (10 ml) and water (1 ml) was heated at 100° for 80 hours then poured into water, extracted with methylene chloride. The evaporated extract was fractionated by column chromatography (ethylene dichloride:benzene (3:1, v/v)) to afford 109 mg (43%) of **2b** and 96 mg (41%) of **8**.

The reaction was repeated using a mixture of dry DMF (10 ml) and dry methanol (1 ml) as solvent. After 105 hours the workup gave 82.5 mg (33%) of **2b** and 113 mg (48%) of **8** besides 39 mg (12%) of unreacted starting **1**. No traces of **13** could be detected.

When the reaction was repeated using a mixture of dry DMF (15 ml) and isopropylamine (0.5 ml) the workup after 65 hours afforded 40 mg (16%) of **2b**, 44 mg (17%) of **8** and 24 mg (7.2%) of unchanged **1**. No traces of 2,3-dihydro-3-isopropylamino-3-methyl-2-phenyl-4*H*-1-benzopyran-4-one (**11**) could be isolated.

When a solution of **1** (332 mg, 1 mmole) in dry DMF (10 ml) was heated in a sealed tube at 100° for 80 hours, the workup yielded 71 mg (28%) of **2b**, 117 mg (50%) of **8** and a new product identified as **12** (44 mg, 16%), mp 143-145° (hexane-ethanol); ir: 2922 (CH), 1733 (ester C=O), 1697 (ketone C=O), 1304, 1229, 1011 (flavanone skeletone), 1156 (ester C-O-C); pmr: 7.96 (s, 1H, OCHO), 7.92 (dd, 1H, H-5), 5.23 (s, 1H, H-2), 1.51 (s, 3H, CH_3); nOe: irradiation of CH_3, OCHO (4.4%), H-2 (11.3%), irradiation of H-2, Ar-H (15.8%), CH_3 (3.8%); ms: 282 ($M^{+\cdot}$, 5), 253 (3), 236 (6), 235 (7), 211 (100), 183 (7.5), 181 (6.5), 148 (9), 147 (6.5), 134 (54), 133 (80), 121 (88.5), 115 (21.5), 105 (16.5), 91 (49), 77 (25).

Anal. Calcd. for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.11, H, 5.12.

c-3-Butylamino-2,3-dihydro-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**9**).

A mixture of **1** (332 mg, 1 mmole), butylamine (0.2 ml, 2.02 mmoles) and dry DMF (10 ml) was allowed to stand at room temperature for 50 days, then poured into water and extracted with methylene chloride. The concentrated extract was separated by column chromatography (petroleum ether:ethyl acetate (4:1, v/v)) to afford **9** (183 mg, 59%), mp 114-115° (hexane); ir: 3306 (NH), 2952, 2869 (CH_3), 2921, 1467, 1460 (CH_2), 1675 (C=O), 1323, 1299, 1230, 1008 (flavanone skeleton); pmr: 8.00 (dd, 1H, H-5), 5.12 (s, 1H, H-2), 2.35 (m, 2H, NCH_2), 1.63 (s, 1H, NH), 1.26 (m, 4H, CH_2CH_2), 1.1 (s, 3H, CH_3), 0.79 (t, 3H, CH_2CH_3); nOe: irradiation of CH_3, H-2 (13%).

Anal. Calcd. for $C_{20}H_{23}NO_2$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.33; H, 7.45; N, 4.57.

Further elution afforded 56 mg (17%) of unreacted **1** and 14 mg (5.9%) of **8**.

The reaction was repeated at 100° (reaction time, 18 hours) and the workup afforded 56 mg (18%) of **9**, 64 mg (25%) of **2b**, 8 mg (3.4%) of **8** and 12 mg (3.6%) of unchanged **1**.

2,3-Dihydro-*c*-3-isopentylamino-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**10**).

A solution of **1** (332 mg, 1 mmole) and isopentylamine (0.6 ml, 5.16 mmoles) in dry DMF (10 ml) was heated at 100° for 42 hours and worked up as described for the preparation of **9**. Column chromatography (benzene) yielded **10** (55 mg, 17%), mp 133-136° (hexane); ir: 3305 (NH), 2947 (CH_3), 2920, 2861 (NCH_2), 1674 (C=O), 1298, 1228, 1009 (flavanone skeleton); pmr: 8.00 (dd, 1H, H-5), 5.11 (s, 1H, H-2), 2.40 (m, 2H, NCH_2), 1.62 (br s, 1H, NH), 1.51 (m, 1H, CH), 1.21 (m, 2H, CH_2), 1.11 (s, 3H, CH_3), 0.77 (2d, each of 3H, $CH(CH_3)_2$); ms: 323 ($M^{+\cdot}$, 85), 294 (9), 249 (6.5), 248 (7), 238 (16.5), 218 (20), 209 (12), 203 (100), 181 (16), 161 (19), 160 (39), 147 (66), 146 (67), 144 (28.5), 132 (27.5), 121 (33), 120 (19), 117 (33), 115 (45), 112 (23.5), 105 (16), 103 (17), 92 (48), 91 (51.5), 77 (29), 71 (40).

Anal. Calcd. for $C_{21}H_{25}NO_2$: C, 77.98; H, 7.79; N, 4.33. Found: C, 77.85; H, 7.64; N, 4.43.

Further elution gave 44 mg (17%) of **2b**, 36 mg (15%) of **8** and 29 mg (8.7%) of unchanged **1**.

c-3-Azido-2,3-dihydro-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**14**).

A mixture of **1** (0.5 g, 1.5 mmoles), sodium azide (0.25 g, 3.84 mmoles) and DMF (12.5 ml) was stirred at room temperature for 75 hours then poured into water and extracted with ether. The concentrated extract was crystallized from hexane:ethanol (20:1, v/v) to give 283 mg (67%) of **14**, mp 125-127.5°; ir: 2982, 2879, (CH_3), 2103, 1260 (N_3), 1672 (C=O), 1307, 1229 (flavanone skeleton); pmr: 8.04 (dd, 1H, H-5), 5.10 (s, 1H, H-2), 1.37 (s, 1H, CH_3); nOe: irradiation of CH_3, H-2 (5%).

Anal. Calcd. for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.05. Found: C, 69.28, H, 4.88; N, 14.68.

The mother liquor was fractionated by preparative tlc (Kieselgel 60 F_{254}, benzene:ethyl acetate (4:1, v/v)) to afford 21 mg (5.0%) of **14**, 6 mg (1.7%) of **8** and 5 mg (1.0%) of unreacted **1**.

The pmr investigation of the reaction mixture after workup precluded the presence of the epimeric *t*-3-azido-2,3-dihydro-*c*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one.

c-3-Amino-2,3-dihydro-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**15**) and *c*-3-Acetamido-2,3-dihydro-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**16**).

A mixture of **14** (104 mg, 0.37 mmole), 5% palladium on calcium carbonate (45 mg) and ethanol (20 ml) was hydrogenated at room temperature. Having terminated the reduction (tlc check) the catalyst was filtered off, the filtrate was poured into diluted hydrochloric acid and washed with ether. The acidic fraction was neutralized with ammonium hydroxide, extracted with ether, the extract was dried and evaporated *in vacuo* to give **15** (86 mg, 91%), mp 88-89° (hexane:ethyl acetate (10:1, v/v)); ir (carbon tetrachloride): 3392, 3927 (NH_2), 2980 (CH_3), 1697 (C=O), 1307, 1228 (flavanone skeleton); pmr: 8.02 (dd, 1H, H-5), 5.13 (s, 1H, H-2), 1.78 (br s, 2H, NH_2), 1.21 (s, 3H, CH_3).

Anal. Calcd. for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53. Found: C, 75.70; H, 5.67; N, 5.27.

A solution of **15** (125 mg, 0.49 mmole) and acetic anhydride (1 ml) in dry pyridine (5 ml) was allowed to react at room temperature for 4 days, poured into diluted hydrochloric acid and extracted with ether. The residue obtained by evaporation of the solvent was crystallized from hexane:benzene (10:1, v/v) to yield 81.5 mg (56%) of **16**, mp 90-92°; ir: 3370 (NH), 1691 (C=O), 1668 (amide), 1324, 1300, 1216 (flavanone skeleton); pmr: 8.01 (dd, 1H, H-5), 6.76 (br s, 1H, NH), 6.43 (s, 1H, H-2), 1.92 (s, 3H, CH_3), 1.87 (s, 3H, $NHCOCH_3$).

Anal. Calcd. for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.35; H, 5.71; N, 4.65.

2,3-Dihydro-*t*-3-methyl-*r*-2-phenyl-*c*-3-(triphenylphosphoranediylamino)-4*H*-1-benzopyran-4-one (**17**).

A solution of **14** (283 mg, 1.01 mmoles) and triphenylphosphine (280 mg, 1.07 mmoles) in dry ether (15 ml) was allowed to stand at room temperature until the reaction completed (20 days). The precipitated crystals were collected to afford pure **17** (161 mg, 31%), mp 186-188°; ir: 2966 (CH_3), 1676 (C=O), 1433, 1106 (C-P), 1327 sh, 1317 (N=P), 1299, 1234 (flavanone skeleton); pmr (DMSO-d_6): 5.22 (d, 1H, H-2, $^4J_{P-H}$ = 8.4 Hz), 0.83 (s, 3H, CH_3); cmr (deuteriochloroform-DMSO-d_6): [14] 182.97 (d, C-4, $^3J_{P-C}$ = 3.5 Hz), 160.25 (C-8a), 134.35 (C-7), 133.91 (C-1'), 131.75 (d, C-2'', $^2J_{P-C}$ = 9.9 Hz), 127.68 (d, C-3'', $^3J_{P-C}$ = 11.7 Hz), 120.35 (C-6), 119.74 (C-4a), 116.59 (C-8), 87.14 (d, C-2, $^3J_{P-C}$ = 17.1 Hz), 60.51 (d, C-3, $^2J_{P-C}$ = 2 Hz), 21.03 (d, CH_3, $^3J_{P-C}$ = 4.1 Hz); not assigned signals: 136.67, 131.93, 130.71 (d), 129.05, 127.40, 126.78; ms: 513 ($M^{+\cdot}$, 42), 498 (2), 484 (2), 408 (8), 393 (10), 302 (4), 277 (22), 262 (82), 234 (12), 209 (16), 185 (100), 183 (53), 167 (18), 152 (9), 108 (26), 105 (10.5), 77 (16).

Anal. Calcd. for $C_{34}H_{28}NPO_2$: C, 79.52; H, 5.50; N 2.73. Found: C, 79.89; H, 5.31; N, 2.62.

The filtrate of the reaction mixture was evaporated *in vacuo* and the

residue was crystallized from diisopropyl ether to give further 137 mg (26%) of **17**.

The reaction was repeated starting from 420 mg (1.50 mmoles) of **14** in hot diisopropyl ether (15 ml) (reaction time, 6.5 hours) and 563 mg (73%) of **17** was obtained.

2,3-Dihydro-*c*-3-isothiocyanato-*t*-3-methyl-*r*-2-phenyl-4*H*-1-benzopyran-4-one (**18**) and 3-Methyl-2-phenyl-4*H*-1-benzopyran-4-one (**8**).

A mixture of **1** (582 mg, 1.75 mmoles), potassium thiocyanate (350 mg, 3.60 mmoles), 18-crown-6 (119 mg, 0.45 mmole) and dry acetonitrile (15 ml) was refluxed for 114 hours, the precipitate was filtered off, washed with ether, the combined filtrates were concentrated and separated by column chromatography to furnish 41 mg (7.9%) of **18** as a pale yellow oil: ir (carbon tetrachloride): 2014 s (NCS), 1705 (C=O), 1299, 1225, 1038 (flavanone skeleton); pmr: 8.03 (dd, 1H, H-5), 5.11 (s, 1H, H-2), 1.41 (s, 3H, CH_3), nOe: irradiation of CH_3, H-2 (8.5%); ms: 295 ($M^{+\cdot}$, 33), 238 (25), 236 (17.5), 235 (16.5), 223 (11), 197 (17), 175 (97.5), 161 (17.5), 142 (16), 138 (18), 121 (64), 119 (92), 117 (100), 105 (29.5).

Anal. Calcd. for $C_{17}H_{13}NO_2S$: N, 4.74; S, 10.86. Found: N, 4.83; S, 10.70.

Further elution afforded 348 mg (84%) of **8** and 24 mg (4.1%) of unreacted **1**.

Acknowledgement.

The authors are grateful to Soros Foundation for the financial support.

REFERENCES AND NOTES

[1a] Part **40**: T. Patonay, E. Patonay-Péli and Gy. Litkei, *Tetrahedron*, **43**, 1827 (1987); [b] Presented in part at the IUPAC 6th International Conference on Organic Synthesis, August 10-15, 1986, Moscow, USSR.

[2] To whom correspondence should be addressed.

[3a] T. Patonay, M. Rákosi, Gy. Litkei and R. Bognár, *Ann. Chem.*, 161 (1979); [b] T. Patonay, Gy. Litkei and R. Bognár, *Acta Chim. Acad. Sci. Hung.*, **108**, 135 (1981); [c] T. Patonay, Gy. Litkei and R. Bognár, *Tetrahedron*, **40**, 3425 (1984).

[4] W. P. Cullen, D. M. X. Donnelly, A. K. Keenan, T. P. Lavin, D. P. Melody and E. M. Philbin, *J. Chem. Soc.*, (C), 2848 (1971).

[5a] G. Opitz, *Angew. Chem.*, **79**, 161 (1967); [b] J. F. King and T. W. S. Lee, *J. Am. Chem. Soc.*, **91**, 6524 (1969).

[6] A retro-Diels-Alder process was found to be characteristic or the main fragmentation of all investigated 2,3-dihydro-3-substituted-3-methyl-2-phenyl-4*H*-1-benzopyran-4-ones.

[7] E. J. Corey, K. C. Nicolaou, R. D. Balanson and Y. Machida, *Synthesis*, 590 (1975).

[8] H. Staudinger and J. Meyer, *Helv. Chim. Acta*, **2**, 635 (1919); H. Staudinger and E. Hauser, *Helv. Chim. Acta*, **4**, 861 (1921).

[9a] T. Sheradsky, "The Chemistry of Azido Group", S. Patai, ed, Wiley-Interscience, London-New York-Sydney-Toronto, 1971, p 377; [b] E. P. Kyba, "Azides and Nitrenes", E. F. V. Scriven, ed, Academic Press, London-New York, 1984, p 21 and the references cited therein.

[10a] G. Singh and H. Zimmer, *Organomet. Chem. Rev.*, **2**, 279 (1967); [b] Yu. G. Golobov, I. N. Zhmurova, and L. F. Kasukhin, *Tetrahedron*, **37**, 437 (1981).

[11] S. S. Simons, M. Pons and D. F. Johnson, *J. Org. Chem.*, **45**, 3084 (1980).

[12a] Zh. M. Ivanova, T. V. Kim, I. E. Boldeskul and Y. G. Golobov, *Zh. Obshch. Khim.*, **49**, 1464 (1979); *Chem. Abstr.*, **91**, 157197 (1979); [b] T. Thorstenson and J. Songstad, *Acta Chem. Scand.*, **32A**, 133 (1978).

[13a] J. P. Béqué, M. Charpentier-Morize and C. Pardo, *Tetrahedron Letters*, 4737 (1971); [b] M. Maleki, A. C. Hopkinson and E. Lee-Ruff, *Tetrahedron Letters*, **24**, 4911 (1983); [c] X. Creary, *J. Org. Chem*, **44**, 3938 (1979); [d] X. Creary and C. C. Geiger, *J. Am. Chem. Soc.*, **105**, 7123 (1983).

[14] Assignments were confirmed by J-modulated spin-echo technique. C. Le Cocq and J.-Y. Lallemand, *J. Chem. Soc., Chem. Commun.*, 150 (1981).

[15] A. T. M. Dunne, J. E. Gowan, J. Keane, B. M. O'Kelly, D. O'Sullivan, M. M. Roche, P. M. Ryan and T. S. Wheeler, *J. Chem. Soc.*, 1252 (1950).