peratures, 80–115 °C, 30 ml/min)] showed the hydrolysis products to have VPC retention times identical with those of authentic samples of benzaldehyde and acetone. The later eluting product was isolated from the hydrolysis extracts by preparative VPC on column B (70 °C and 70 ml/min). This compound's ir spectrum correlated exactly with that of an authentic sample of benzaldehyde.

2,3-Dimethylindole (29). The indole was isolated by preparative VPC from an ether solution of the 480 °C pyrolysate of **19d**. The ir spectrum correlated exactly with ir spectrum 911G, Aldrich Library, for 2,3-dimethylindole: ir 3492, 3060, 2940, 2880, 1625, 1550, 1476, 1346, 1310, 1270, 1253, 1010, 932, 730 cm^{-1}; NMR (CCl_4) δ 2.19 (s, 3 H, 3-CH_3), 2.32 (s, 3 H, 2-CH_3), 6.50–6.85 (broad, 1 H, NH), 6.90–7.45 (m, 4 H, phenyl).

3,4-Dihydroisoquinoline (27). This compound was isolated by preparative VPC of the 580 °C pyrolysate of **19a** on column C (100 °C, 100 ml/min); ir 3100, 3040, 2970, 2920, 2878, 1626, 1576, 1484, 1452, 1443, 1426, 1294, 1272, 1204, 1188, 1113, 1051, 1029, 1000, 951, 918, 873, 857, 683 cm^{-1}; NMR (CCl_4) δ 2.67 (t, J = 7.1 Hz, 2 H, NCH_2CH_2), 3.73 (t of d, J = 7.1, 2.1 Hz, 2 H, NCH_2CH_2), 6.95–7.42 (m, 4, aromatic), 8.17 (t, J = 2.1 Hz, 1 H, imino H). The structure proof was confirmed by oxidation at 530 °C over Pd/C in a quartz flow system. Oxidized product spectra correlated exactly with those of authentic isoquinoline.

Isoquinoline (28). The 580 °C pyrolysis of **19a** produces isoquinoline, presumably from oxidation of 3,4-dihydroisoquinoline.[18] This pyrolysis product was isolated by preparative VPC of a concentrated ether solution of the pyrolysate (column C, 100 °C, 100 ml/min): ir 3080, 3002, 2987, 1628, 1589, 1574, 1505, 1382, 1375, 1270, 1247, 1213, 1136, 1033, 1011, 941, 853, 816 cm^{-1}; NMR (CCl_4) δ 6.90–8.2 (m, 6 H), 5.58 (d, 1 H), 6.29 (s, 1 H). The spectral data correlated exactly with the spectra of an authentic sample of isoquinoline.

3,4-Dihydro-3-methylisoquinoline (26). **26** was isolated from a concentrated ether solution of **19c** by preparative VPC on column C (100 °C, 100 ml/min): ir 3078, 3040, 2980, 2943, 2897, 2840, 1670, 1585, 1500, 1468, 1439, 1390, 1368, 1327, 1304, 1227, 1211, 1141, 1130, 1058, 1043, 960, 943, 930, 898, 820, 709 cm^{-1}; NMR (CCl_4) δ 1.31 (d, J = 6.8 Hz, 3 H, $-CH_3$), 2.68 (d, J = 4.0 Hz, 2 H, CH_3CHCH_2-), 3.32–4.90 (m, 1 H, $-CHCH_3$), 6.90–7.40 (m, 4 H, aromatic), 8.18 (d, J = 2.2 Hz, 1 H, imino H); mass spectrum M^+ m/e 145, 144, 130, 117, 103, 90, 76, 77, 51, 27. This dihydroisoquinoline was oxidized in the same manner as described for 3,4-dihydroisoquinoline (**27**). In the course of oxidation, the methyl group was cleaved, and isoquinoline was obtained.

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Registry No.—**19a**, 16205-14-4; **19b**, 51209-52-0; **19c**, 14491-02-2; **19d**, 57573-53-2; **25**, 51209-53-1; **26**, 14123-78-5; **27**, 3230-65-7; **28**, 119-65-3; **29**, 91-55-4.

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A Convenient Two-Step Synthesis of 4-(2-Imidazolyl)phthalazones from *o*-Phthaloyl Dichloride

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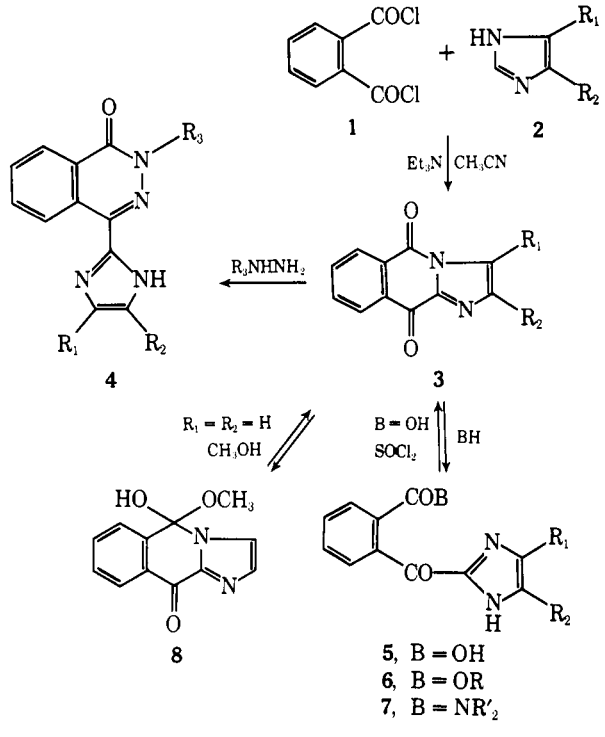
The imidazo[1,2-*b*]isoquinoline-5,10-diones (**3**) derived from the condensation of equimolar amounts of *o*-phthaloyl dichloride (**1**) and an imidazole (**2**) in the presence of 2 molar equiv of Et_3N, react readily with hydrazines R_3NHNH_2 (R_3 = H, alkyl, aryl) to form 4-(2-imidazolyl)phthalazones (**4**), a new class of compounds. The reactions of these carbonyl reagents differ from those of nucleophiles such as hydroxide ion, alcohols, and amines which attack **3** at the lactam carbonyl group and form the carboxylic acid derivatives (**5–7**).

The patent literature[1,2] describes the condensation of equimolar amounts of *o*-phthaloyl dichloride (**1**) and imidazoles or benzimidazoles (**2**) possessing unsubstituted 1 and 2 positions in CH_3CN containing 2 molar equiv of Et_3N to produce imidazo[1,2-*b*]isoquinoline-5,10-diones (**3**), which react with nucleophiles such as hydroxide ion,

Scheme I



alcohols, and amines at the lactam carbonyl group to form the corresponding carboxylic acids (5), esters (6), and amides (7) (Scheme I). We have verified these observations, and have included a few representative examples of structures 3 and 5–7 in the Experimental Section to illustrate their spectral characteristics, which were not described in the Bayer patents. We have also shown structure 3 (R_1 + R_2 = CH=CHCH=CH) to be identical with the CrO_3 oxidation product of α-(2-benzimidazolyl)-o-toluic acid[3] by mixture melting point and spectra.

The reaction products of 3 with carbonyl reagents have not been previously described, and we have discovered a convenient two-step synthesis of the new 4-(2-imidazolyl)phthalazones (4) from 1 as a consequence of this work. Reactive difunctional carbonyl reagents such as hydrazine and its monosubstituted analogues (R_3 = CH_3, C_6H_5) attack both the ketonic and lactam carbonyl groups of 3 to form the new heterocyclic ring in 4 and leave the imidazole moiety as a pendant group. This reaction has some similarities to our recent synthesis of 2-aryl-3,3a-dihydro-8*H*-pyrazolo[5,1-*a*]isoindol-8-ones from 3-phenacylphthalides[4] where hydrazine attacks both a ketonic and a lactone carbonyl group to form a new heterocyclic ring.

A few comments are in order concerning the interconversions of structures 3 and 5–7, which are not evident from the Bayer work. We have found that the carboxylic acid 5 (R_1 = C_6H_5; R_2 = H) is readily cyclized to 3 (R_1 = C_6H_5; R_2 = H) with excess $SOCl_2$. Ring opening of the imidazo[1,2-*b*]isoquinoline-5,10-diones (3) with alcohols does not occur as readily as that of the more strained 2-aryl-8*H*-pyrazolo[5,1-*a*]isoindol-8-ones which we recently described.[4,5] The latter compounds have some structural similarity to 3. Attempts to cleave 3 (R_1 = R_2 = H) with MeOH containing traces of methoxide at 25° produced recovered 3 on evaporation.[5] However, the uv spectrum of 3 in DMF differs from that in MeOH, indicating that the first step in the methanolysis is formation of structure 8. Unless considerable amounts of acid or base are present, 8 reverts to 3. More vigorous conditions, such as refluxing the alcoholic solvent containing 3 and molar amounts of base[2] or mineral acid, are required to convert 3 to 6.

Experimental Section[6]

Imidazo[1,2-*b*]isoquinoline-5,10-dione (3, R_1 = R_2 = H) was prepared from 1 and imidazole according to the literature[1] in 32% yield (0.1 mol scale) after recrystallization (DMF). The crude product is a green powder, but after repeated recrystallization it forms yellow prisms with mp 238–239 °C dec (lit.[1] mp 236 °C); ν_{max} 1720, 1670, and 1580 cm^{-1}; λ_{max} (DMF) 365 nm (ε 2040) and 322 (3980); ^1H NMR (Me_2SO-d_6) δ 8.33–7.85 (m) 5 H and 7.48 ppm (d, J = 2 Hz) 1 H. Anal. Calcd for $C_{11}H_6N_2O_2$: C, 66.66; H, 3.05; N, 14.14. Found: C, 67.42; H, 3.05; N, 14.25.

2(3)-Phenylimidazo[1,2-*b*]isoquinoline-5,10-dione[7] (3, R_1 = C_6H_5; R_2 = H) was prepared similarly from 1 and 4-phenylimidazole (Aldrich) in 32–49% crude yield as a green powder. Recrystallization (DMF) gave pure material as olive-bronze crystals with mp 285–288 °C dec; ν_{max} 1715 and 1670 cm^{-1}; λ_{max} (DMF) 402 nm (ε 2400) and 274 (23 800); ^1H NMR ($CDCl_3$) δ 8.58–8.37 (m) and 8.20–7.88 (m) 4 H, 7.67 (m) 4 H, 7.53 (m) and 7.40 ppm (m) 2 H. Anal. Calcd for $C_{17}H_{10}N_2O_2$: C, 74.44; H, 3.68; N, 10.21. Found: C, 74.19; H, 3.82; N, 10.26.

Benzimidazo[1,2-*b*]isoquinoline-5,12-dione (3, R_1 + R_2 = CH=CHCH=CH) was prepared similarly from 1 and benzimidazole in 64% yield after recrystallization (DMF). The pure material was a yellow, crystalline solid with mp 268–271 °C dec (lit.[1,3] 270, 261–262 °C); ν_{max} 1710 and 1670 cm^{-1}; λ_{max} (DMF) 418 nm (ε 2170) and 283 (20 600); ^1H NMR (CF_3CO_2H) δ 8.33–7.88 (m) 3 H and 7.67–7.45 ppm (m) 5 H. Anal. Calcd for $C_{15}H_8N_2O_2$: C, 72.57; H, 3.25; N, 11.29. Found: C, 72.46; H, 3.37; N, 11.28.

4-(2-Imidazolyl)phthalazone (4, R_1 = R_2 = R_3 = H). A mixture of 3 (R_1 = R_2 = H) (10.0 g, 50.5 mmol), EtOH (100 ml), and hydrazine hydrate (5.0 g, 0.10 mol) was stirred at reflux for 3 h and cooled to 0 °C, and the crystalline product was filtered. Recrystallization (DMF) gave an 87% yield of colorless, crystalline phthalazone with mp >300 °C; ν_{max} 3420 and 1650 cm^{-1}; λ_{max} (CF_3CO_2H) 310 nm (ε 6700), 300 (9600), and 292 nm (10 200); ^1H NMR (CF_3CO_2H) δ 8.77–8.00 (m) 4 H (C_6H_4) and 8.03 ppm (s) 2 H (CH=CH). Anal. Calcd for $C_{11}H_8N_4O$: C, 62.25; H, 3.80; *m/e* 212.0698. Found: C, 62.20; H, 3.70; *m/e* 212.0695.

2-Methyl-4-(2-imidazolyl)phthalazone (4, R_1 = R_2 = H; R_3 = CH_3) was prepared similarly from 3 (R_1 = R_2 = H) and methylhydrazine in 55% yield after recrystallization (CH_3CN). It formed colorless crystals with mp 241–242 °C; ν_{max} 1660 cm^{-1}; λ_{max} (CF_3CO_2H) 313 nm (ε 10 400) and 302 (12 000); ^1H NMR (CF_3CO_2H) δ 8.65–7.90 (m) 4 H (C_6H_4), 7.57 (s) 2 H (CH=CH), and 4.07 ppm (s) 3 H (NCH_3). Anal. Calcd for $C_{12}H_{10}N_4O$: C, 63.70; H, 4.46; *m/e* 226.0854. Found: C, 63.72; H, 4.28; *m/e* 226.0814.

2-Phenyl-4-(2-imidazolyl)phthalazone (4, R_1 = R_2 = H; R_3 = C_6H_5) was prepared similarly in aqueous HOAc from 3 (R_1 = R_2 = H) and phenylhydrazine in 60% yield after recrystallization (50% DMF). It formed orange crystals with mp 210–211 °C; ν_{max} 3340, 3210, and 1700 cm^{-1}; λ_{max} (DMF) 443 nm (ε 1910) and 284 (3250); ^1H NMR (CF_3CO_2H) δ 8.58–7.58 (m) 4 H (C_6H_4), 7.43 (s) 2 H (CH=CH), and 7.22 ppm (s) 5 H (C_6H_5). Anal. Calcd for $C_{17}H_{12}N_4O \cdot H_2O$: C, 66.65; H, 4.61; N, 18.29. Found: C, 67.37; H, 4.84; N, 18.65.

2-Methyl-4-(4-phenyl-2-imidazolyl)phthalazone (4, R_1 = C_6H_5, R_2 = H, R_3 = CH_3) was prepared similarly from 3 (R_1 = C_6H_5, R_2 = H) and methylhydrazine in 45% yield after recrystallization (80% DMF). It formed yellow crystals with mp 307 °C dec; ν_{max} 3400, 3250, and 1630 cm^{-1}; λ_{max} (DMF) 413 nm (ε 2380) and 339 (12 000); ^1H NMR (Me_2SO-d_6) δ 12.82 (broad) 1 H (NH), 9.75–7.25 (m) 10 H (aromatic), and 3.83 ppm (s) 3 H (NCH_3). Anal. Calcd for $C_{18}H_{14}N_4O$: C, 71.51; H, 4.67; N, 18.53. Found: C, 71.52; H, 4.54; N, 18.98.

4-(2-Benzimidazolyl)phthalazone (4, R_1 + R_2 = CH=CHCH=CH; R_3 = H) was prepared similarly from 3 (R_1 + R_2 = CH=CHCH=CH) and hydrazine hydrate in 87% yield after recrystallization (75% DMF). It formed colorless crystals with mp >315 °C; ν_{max} 3220 and 1660 cm^{-1}; λ_{max} (DMF) 324 nm (ε 18 000) and 281 (14 100); ^1H NMR (CF_3CO_2H) δ 8.33–8.12 (m) 1 H and 7.73–7.17 (m) 7 H. Anal. Calcd for $C_{15}H_{10}N_4O$: C, 68.69; H, 3.84; N, 21.37. Found: C, 68.79; H, 3.87; N, 21.12.

2-Methyl-4-(2-benzimidazolyl)phthalazone (4, R_1 + R_2 = CH=CHCH=CH; R_3 = CH_3) was prepared similarly from 3 (R_1 + R_2 = CH=CHCH=CH) and methylhydrazine in 81% yield after recrystallization (45% DMF). It formed yellow crystals with mp 253–255 °C; ν_{max} 3290 and 1630 cm^{-1}; λ_{max} (DMF) 401 nm (ε 830), 332 (17 700), and 281 (14 100); ^1H NMR (CF_3CO_2H) δ 8.30–8.10 (m) 1 H, 7.72–7.22 (m) 7 H, and 3.67 ppm (s) 3 H (NCH_3). Anal. Calcd for $C_{16}H_{12}N_4O$: C, 69.55; H, 4.38. Found: C, 69.39; H, 4.32.

2-(2-Carboxybenzoyl)imidazole (5, $R_1 = R_2 = H$). A mixture of 3 ($R_1 = R_2 = H$) (5.77 g, 29 mmol), H_2O (30 ml), MeOH (30 ml), and NaOH (2.0 g, 50 mmol) was stirred at 25 °C for 2 h. Neutralization of the resulting solution (pH 7) gave a colorless precipitate which was recrystallized (210 ml of MeOH) to give 4.31 g (20 mmol, 69%) of product as colorless needles with mp 228–229 °C dec (lit.[2] 200 °C); ν_{max} (Nujol) 3290 and 1670 cm^{-1}; λ_{max} (MeOH) 287 nm (ϵ 13 300); ^1H NMR (Me_2SO-d_6) δ 12.17 (broad) 2 H (CO_2H, NH), 8.03–7.80 (m) and 7.67–7.53 (m) 4 H (C_6H_4), and 7.27 ppm (s) 2 H (CH=CH). Anal. Calcd for $C_{11}H_8N_2O_3$: C, 61.11; H, 3.73; N, 12.96. Found: C, 61.17; H, 3.75; N, 13.23.

2-(2-Carboxybenzoyl)-4-phenylimidazole[7] (5, $R_1 = C_6H_5$, $R_2 = H$) was prepared similarly from 3 ($R_1 = C_6H_5$; $R_2 = H$) in 82% yield after recrystallization from a mixture of MeOH (20 ml), Me_2SO (10 ml), and H_2O (2 ml). The product was a colorless solid with mp 280 °C dec; ν_{max} (Nujol) 3350 and 1670 cm^{-1}; λ_{max} (MeOH) 323 nm (ϵ 16 300) and 250 (12 700); ^1H NMR (Me_2SO-d_6) δ 8.00–7.58 (m) 7 H and 7.47–7.17 ppm (m) 3 H. Anal. Calcd for $C_{17}H_{12}N_2O_3$: C, 69.85; H, 4.14; N, 9.59. Found: C, 69.54; H, 4.23; N, 9.32.

2-(2-Carboxybenzoyl)benzimidazole (5, $R_1 + R_2 = CH{=}CHCH{=}CH$) was prepared similarly from 3 ($R_1 + R_2 = CH{=}CHCH{=}CH$) in 92% yield after recrystallization (67% MeOH). The product was a colorless solid with mp 270–271 °C (lit.[2] 250 °C); ν_{max} 3380, 3320, and 1680 cm^{-1}; λ_{max} (MeOH) 310 nm (ϵ 15 300) and 240 (10 200); ^1H NMR (Me_2SO-d_6) δ 13.40 (broad) 2 H (CO_2H, NH) and 8.12–7.17 ppm (m) 8 H (aromatic). Anal. Calcd for $C_{15}H_{10}N_2O_3$: C, 67.66; H, 3.79; N, 10.52. Found: C, 66.86; H, 3.70; N, 10.23.

Cyclization of 2-(2-Carboxybenzoyl)-4-phenylimidazole. A mixture of 5 ($R_1 = C_6H_5$; $R_2 = H$) (1.0 g, 3.43 mmol) and $SOCl_2$ (20 ml) was warmed on a steam bath for 5 min, then evaporated to leave 0.8151 g (2.98 mmol, 87%) of 2(3)-phenylimidazo[1,2-*b*]isoquinoline-5,10-dione (3, $R_1 = C_6H_5$; $R_2 = H$) as a yellow solid, mp 288–290.5 °C. Recrystallized material (DMF) was identical spectrally with material prepared from 1 and 2 ($R_1 = C_6H_5$; $R_2 = H$) above.

Treatment of 3 ($R_1 = R_2 = H$) with MeOH. A mixture of 3 ($R_1 = R_2 = H$) (1.0 g, 5.05 mmol), MeOH (20 ml), and a small chip of sodium was stirred at 25 °C for 1.5 h. The yellow color faded and the dione went into solution, but isolation by evaporation gave only starting material. Comparison of the uv spectra of 3 ($R_1 = R_2 = H$) in DMF [λ_{max} 365 nm (ϵ 2040) and 322 (3980)], where no reaction can occur, and in MeOH [λ_{max} 290 nm (ϵ 14 200)] with an authentic sample of ester 6 ($R_1 = R_2 = H$; $R = C_2H_5$) [λ_{max} (EtOH) 290 nm (ϵ 13 100)] suggests the presence of species 8 in methanol solutions of 3; 8 reverts to 3 on isolation.

2-(2-Carboethoxybenzoyl)imidazole (6, $R_1 = R_2 = H$; $R = C_2H_5$) was prepared by stirring a mixture of 3 ($R_1 = R_2 = H$) (5.77 g, 29.0 mmol), EtOH (50 ml), and H_2SO_4 (2 ml) at reflux for 2 h, during which time the solid dissolved. The mixture was diluted (H_2O) and neutralized (pH 7) to give 8 as a colorless precipitate, yield 4.97 g (20.4 mmol, 70%) after recrystallization (160 ml of 25% EtOH). Pure 6 had mp 156–158 °C (lit.[2] 170 °C); ν_{max} 1700, 1600, and 1270 cm^{-1}; λ_{max} (EtOH) 290 nm (ϵ 13 100) and 214 (13 800); ^1H NMR ($CDCl_3$) δ 11.67 (broad) 1 H (NH), 8.42–7.77 (m) 4 H (C_6H_4), 7.18 (s) 2 H (CH=CH), 4.12 (q, J = 7 Hz) 2 H (OCH_2), and 1.07 ppm (t, J = 7 Hz) 3 H (CH_3). Anal. Calcd for $C_{13}H_{12}N_2O_3$: C, 63.92; H, 4.95; N, 11.47. Found: C, 63.81; H, 4.80; N, 11.84.

2-(2-Carbamoylbenzoyl)imidazole (7, $R_1 = R_2 = R' = H$). A mixture of 3 ($R_1 = R_2 = H$) (5.77 g, 29 mmol) and liquid NH_3 (100 ml) was stirred at −33 °C for 1 h. The solid dissolved to form a colorless solution, evaporation of which gave the crude amide. Recrystallization from a mixture of MeOH (90 ml), Me_2SO (70 ml), and H_2O (150 ml) gave 4.59 g (21.4 mmol, 74%) of colorless, crystalline product with mp 193–194 °C dec; ν_{max} (Nujol) 3290 and 1675 cm^{-1}; λ_{max} (MeOH) 275 nm (ϵ 1265); ^1H NMR (Me_2SO-d_6) δ 12.22 (broad) 1 H (NH), 9.13 and 7.12 (broad) 2 H (NH_2), 7.82–7.42 (m) 4 H (C_6H_4), and 6.92 ppm (s) 2 H (CH=CH). Anal. Calcd for $C_{11}H_9N_3O_2$: C, 61.39; H, 4.22. Found: C, 61.11; H, 4.28.

Registry No.—1, 88-95-9; 2 ($R_1 = C_6H_5$; $R_2 = H$), 670-95-1; 2 ($R_1 + R_2 = CH{=}CHCH{=}CH$), 51-17-2; 3 ($R_1 = R_2 = H$), 36142-27-5; 3 ($R_1 = C_6H_5$; $R_2 = H$), 57594-19-1; 3 ($R_1 + R_2 = CH{=}CHCH{=}CH$), 6659-72-9; 4 ($R_1 = R_2 = R_3 = H$), 57594-20-4; 4 ($R_1 = R_2 = H$; $R_3 = CH_3$), 57594-21-5; 4 ($R_1 = R_2 = H$; $R_3 = C_6H_5$), 57594-22-6; 4 ($R_1 = C_6H_5$; $R_2 = H$; $R_3 = CH_3$), 57594-23-7; 4 ($R_1 + R_2 = CH{=}CHCH{=}CH$; $R_3 = H$), 57594-24-8; 4 ($R_1 + R_2 = CH{=}CHCH{=}CH$; $R_3 = CH_3$), 57594-25-9; 5 ($R_1 = R_2 = H$), 41200-40-2; 5 ($R_1 = C_6H_5$; $R_2 = H$), 57594-26-0; 5 ($R_1 + R_2 = CH{=}CHCH{=}CH$), 41200-57-1; 6 ($R_1 = R_2 = H$; $R_2 = C_2H_5$), 41200-53-7; 7 ($R_1 = R_2 = R' = H$), 57594-27-1; 8, 57594-28-2; methylhydrazine, 60-34-4; phenylhydrazine, 100-63-0; hydrazine hydrate, 10217-52-4.

References and Notes

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(2) E. Regel, K. Lürssen, and K. Büchel, West German Patent 2 145 456 (1973) to Bayer A.G.
(3) M. F. Sartori, A. Oken, and H. E. Schroeder, *J. Org. Chem.*, **31**, 1498 (1966).
(4) E. W. Bousquet, M. D. Moran, A. L. Johnson, J. Harmon, and J. W. Summers, *J. Org. Chem.*, **40**, 2208 (1975).
(5) This chemistry should be compared with that of 3-aryl-5-pyrazolylbenzoic acids: A. L. Johnson and P. B. Sweetser, *J. Org. Chem.*, **41**, 110 (1976).
(6) Melting points are uncorrected, and were determined in a Mel-Temp capillary apparatus; ir spectra were determined in KBr on a Perkin-Elmer 621 instrument; uv spectra were determined on a Cary Model 14 instrument; NMR spectra were determined vs. internal Me_4Si on a Varian Associates A-60 instrument; mass spectra were determined by direct injection into a Consolidated CEC-110 instrument.
(7) These compounds are not described in ref 1 and 2.

The Mechanism of Bromination of 4(3*H*)-Quinazolinone, Its 3-Methyl and Its 1,3-Dimethyl Derivatives in Aqueous Acidic Solutions

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The kinetics of bromination of 4(3*H*)-quinazolinone, 3-methyl-4-quinazolinone, and 1,4-dihydro-1,3-dimethyl-4-oxoquinazolinium perchlorate have been measured in dilute aqueous acid media. The kinetic order of the reactions, the acidity dependence of the rates, the inverse dependence of the rates on bromide ion, and the relative reactivities of the substrates are all consistent with a mechanism in which the rate-determining step is attack by molecular bromine upon the covalent hydrate (or pseudobase) of the substrates.

Relatively little has been done on the mechanistics aspects of quinazoline chemistry, although many derivatives have been prepared for potential medicinal purposes.[1] It is known,[2] however, that several simple quinazolines show appreciable covalent hydration,[2,3] particularly in their protonated forms. In aqueous solution 2(1*H*)-quinazolinone[4] exists to the extent of 25% as the covalent hydrate formed by addition of water across the C_4–N_3 double bond,[5] but there is no direct evidence for the covalent hydration of 4(3*H*)-quinazoline (1, R = H). However, it is interesting to