

Aliphatic diazo compounds. IX. The base-induced dimerization of α -diazo ketones^{1,2}

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Treatment of 2-diazoacetophenone (**1**) with potassium *t*-butoxide in *t*-butyl alcohol gives a colorless dimer, which is shown to be 5-benzoyl-2-phenacyltetrazole (**4**) by its independent synthesis by phenacylation of 5-benzoyltetrazole. The latter reaction also gives 5-benzoyl-1-phenacyltetrazole (**3**), which is distinguished from **4** by its reduction to di(2-hydroxy-2-phenylethyl)amine and by its cyclization on treatment with ammonium acetate. The assignment of the structure of the colorless dimer of **1** permits the postulation of related pathways for its formation and that of the red-brown dimer obtained on treatment of **1** with potassium hydroxide in dimethyl sulfoxide. 2-Phenacyltetrazole (**22**) and benzoic acid are formed in addition to **4** on treatment of **1** with potassium *t*-butoxide in *t*-butyl alcohol; these are considered to arise via cleavage of **4**, since prolonged treatment of **4** and **3** with potassium *t*-butoxide in *t*-butyl alcohol gives **22** and 1-phenacyltetrazole (**24**), respectively. Compounds **22** and **24** have been prepared independently by phenacylation of tetrazole.

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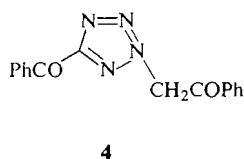
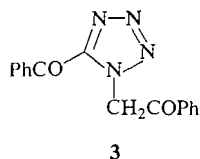
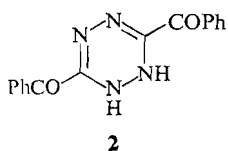
α -Diazo ketones have been observed to give two types of dimer on reaction with bases. Treatment of 2-diazoacetophenone (**1**) with potassium hydroxide in dimethyl sulfoxide gives a red-brown dimer that has been shown to be 3,6-dibenzoyl-1,2(4)-dihydro-tetrazine (**2**) by independent synthesis (**3**). Treatment of 2-diazoacetophenone with potassium *t*-butoxide in *t*-butyl alcohol gives a colorless dimer that was previously considered to be 5-benzoyl-1-phenacyltetrazole (**3**) (**2**), but is now shown to be 5-benzoyl-2-phenacyltetrazole (**4**). Both types of dimer have also been obtained from the α -diazo ketones **5** and **6** under various basic conditions (**3**, **4**).

RCOCHN_2

1, R = Ph

5, R = 2,4,6-(CH₃)₃C₆H₂

6, R = (CH₃)₃C



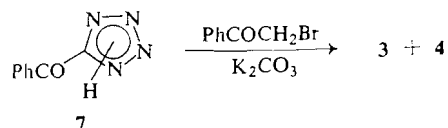
The colorless dimer, m.p. 114–114.5°, was obtained in 69% yield by reaction of 2-diazoacetophenone (**1**) with 1.2 molar equivalents of

¹For Part VIII, see reference 1.

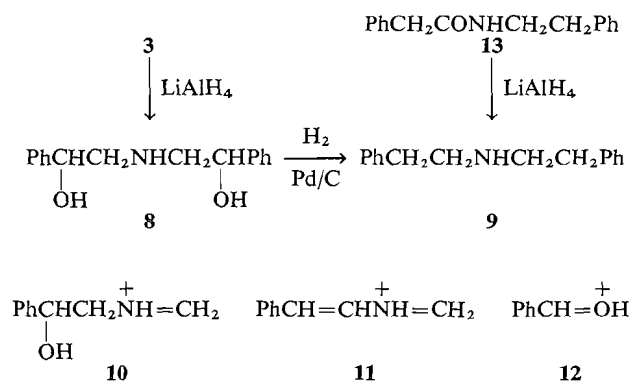
²Part of this work has been reported in a preliminary communication (**2**).

potassium *t*-butoxide in dilute solution in *t*-butyl alcohol at room temperature. Its infrared spectrum, which included bands at 5.85 and 5.95 μ , suggested that it contained two carbonyl groups; the absence of a band in the 2.75–3.2 μ region further indicated that the dimer possessed no N—H bond. These conclusions and the earlier observation of the formation of 5-benzoyltetrazole (**7**) in the reaction of **1** with methanolic sodium methoxide (**1**) led to the formulation of the dimer as either **3** or **4**. These structures were in accord with its proton magnetic resonance (p.m.r.) spectrum, which showed a two-proton singlet at δ 6.31 and a ten-proton multiplet at δ 7.5–8.5, assignable to the methylene and aromatic protons, respectively. Its formulation as a C-benzoyl nitrogen heterocycle was also in accord with the presence of a strong band at 10.82 μ in its infrared spectrum (**5**).

This structural assignment was confirmed by the independent synthesis of **3** and **4** by treatment of **7** with phenacyl bromide and potassium carbonate in acetone. The major product (65% yield) from this reaction was a compound shown



to be identical with the colorless dimer of **1**. A second, isomeric product, m.p. 126–127°, was obtained in 14% yield; its infrared spectrum, which included bands at 5.85, 5.97, and 10.80 μ ,



and its p.m.r. spectrum, with signals at δ 6.33 (2H, s) and 7.5–8.6 (10H, m), were very similar to the spectra of the major product. These compounds were clearly the two possible *N*-phenacylation products derivable from **7**; the unusually short wavelength (5.85 μ) of the carbonyl-stretching band attributable to the phenacyl carbonyl group can be interpreted in terms of the strong electron-withdrawing effect of the tetrazole ring.

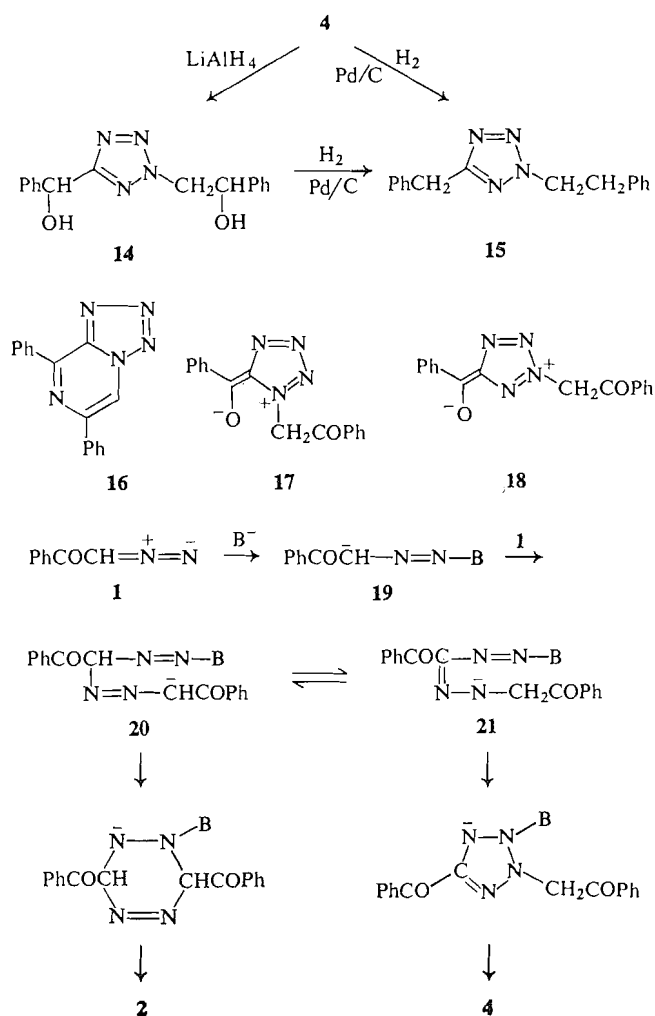
It remained to assign individual structures to the two phenacylation products. The isomer, m.p. 126–127°, was shown to have structure **3** in the following way [cf. (6)]. Reduction with lithium aluminium hydride gave a compound, $\text{C}_{16}\text{H}_{19}\text{NO}_2$, which was shown to be di(2-hydroxy-2-phenylethyl)amine (**8**) by its spectral properties and its conversion on catalytic hydrogenolysis to di(2-phenylethyl)amine (**9**). The amine **8** showed bands at 2.77 and 3.0 μ in its infrared spectrum, but no band in the carbonyl-stretching region. Its p.m.r. spectrum showed a two-proton multiplet at δ 4.75 and a ten-proton signal at δ 7.36, assigned to the methine and aromatic protons, respectively. The remaining protons gave rise to a seven-proton multiplet at δ 2.75–3.0 that was replaced by a four-proton doublet (J 6 Hz) at δ 2.82, assigned to the methylene protons, after treatment of the sample with deuterium oxide. The mass spectrum of the product showed no molecular ion peak, but exhibited a fragmentation pattern in accord with the structural assignment [cf. (7)], with peaks at m/e 150, 132 (base peak), and 107, attributable, respectively, to the ions **10**, **11**, and **12**; a metastable peak at 116.1 corroborated the formation of **11** from **10** (calcd. 116.2). The structure of the hydrogenolysis product **9** was established by

direct comparison of it and its hydrochloride with authentic samples prepared via reduction of *N*-(2-phenylethyl)phenylacetamide (**13**) with lithium aluminium hydride.

The formation of **8** on reductive cleavage of the tetrazole, m.p. 126–127°, establishes that this tetrazole has structure **3** rather than **4**, and leads to the assignment of the latter structure to the dimer, m.p. 114–114.5°, of 2-diazoacetophenone. Reduction of **4** with lithium aluminium hydride failed to cleave the tetrazole ring; the product obtained was the diol **14**.³ This was converted by hydrogenolysis to 2-benzyl-5-(2-phenylethyl)-tetrazole (**15**), which was also obtained directly from **4** by hydrogenolysis under analogous conditions. The tetrazole ring of **15** was also resistant to cleavage by lithium aluminium hydride.

The individual assignments of structure **3** and **4** were confirmed by treatment of **3** with ammonium acetate in boiling acetic acid. There was thus obtained a product, $\text{C}_{16}\text{H}_{11}\text{N}_5$, in 78% yield, that is assigned structure **16**. Its infrared spectrum showed no bands in the N—H or C=O stretching regions, and its p.m.r. spectrum, which was confined to the δ 7.5–9.1 region, included a three-proton signal at δ 8.9–9.1 consisting of a singlet superimposed on a multiplet. Subjection of **4** to similar conditions failed to effect any analogous reaction. The difference between the ultraviolet spectra of **3** and **4** could also be interpreted in terms of these structural assignments. The spectrum of compound **3** showed a maximum at 252 m μ (ϵ 19 500) with a shoulder at 272 m μ (ϵ 15 500), while that of **4** showed a simple max-

³Although both diastereomers of the diols **14** and **8** are very probably formed during the reduction of **4** and **3**, respectively, the sharp-melting product isolated in each case may well have been a single diastereomer.

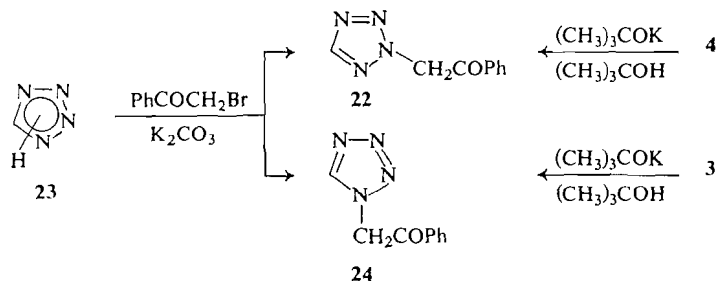


imum at 250 μ (ϵ 24 600). These spectra represent the superimposition of bands due to the $\text{C}_6\text{H}_5\text{COCH}_2\text{X}$ system [cf. acetophenone, $\lambda_{\text{max}}(\text{EtOH})$ 243 μ (ϵ 12 600) (8)] and the *C*-benzoyltetrazole system [cf. 5-benzoyltetrazole, $\lambda_{\text{max}}(\text{EtOH})$ 261 μ (ϵ 12 600) (9)]. The presence of the long wavelength shoulder in the case of **3**, but not of **4**, is compatible with the circumstance that the *C*-benzoyltetrazole system of the former is linearly conjugated, while that of the latter is cross-conjugated (cf. reduced charge separation in **17** vs. **18**).⁴

⁴A misinterpretation of the relationship between the ultraviolet spectra of **3** and **4** originally led to erroneous individual structural assignments (2).

The establishment of **4** as the structure of the dimer of 2-diazoacetophenone (**1**) formed on its treatment with potassium *t*-butoxide in *t*-butyl alcohol⁵ reveals that it has a close relationship to the dimer **2** formed on treatment with potassium

⁵It is appropriate here to clarify several confusing aspects of the literature. In the paper by Yates and Farnum (2) there is a typographical error on p. 24, where 5-benzoyl-1-phenacylpyrazole(VII) should have read 5-benzoyl-1-phenacyltetrazole(VII). In the paper by Yates, Meresz, and Morrison (3) there is a typographical error in the first sentence, where 5-benzoyl-2-phenacyltetrazole(I) should have read 5-benzoyl-1-phenacyltetrazole(I). In a recent review (10) it is erroneously stated that Yates and Farnum (2) observed the formation of both **3** and **4** from **1** on treatment with potassium *t*-butoxide in *t*-butyl alcohol.

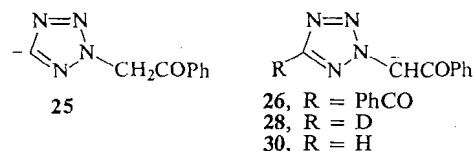


hydroxide in dimethyl sulfoxide. The formation of both can readily be rationalized in terms of the intermediacy of an anion of type **19**, formed via terminal attack (11) of base (B^-) on **1**. Addition of **19** to a second molecule of **1** could give **20** and **21**, which could serve as the source of **2** and **4**, respectively.⁶ The manner in which the nature of the basic reagent controls the type of dimer found has not been established.

As previously mentioned, the yield of **4** on treatment of **1** with potassium *t*-butoxide in *t*-butyl alcohol is 69%; the remainder of the starting material is accounted for by two other products, benzoic acid and a compound, $\text{C}_9\text{H}_8\text{N}_4\text{O}$. The spectra of the latter suggested that it was 2-phenacyltetrazole (**22**), and this was established by its independent synthesis by phenacylation of tetrazole (**23**) and by cleavage of **4** with potassium *t*-butoxide in *t*-butyl alcohol. The major product in the phenacylation of **23** was 1-phenacyltetrazole (**24**), which was also obtained by the cleavage of **3** with potassium *t*-butoxide in *t*-butyl alcohol.

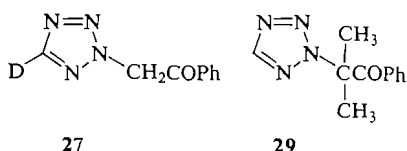
The cleavage of **4** with base was also carried out by treating it with potassium *t*-butoxide in commercial "anhydrous" ether. The solution momentarily assumed a red coloration, which changed to pale yellow with concomitant formation of a precipitate. Work-up with aqueous ammonium chloride gave **22** and benzoic acid. The possibility that reaction occurred by attack of *t*-butoxide ion at the 5-benzoyl group to give *t*-butyl benzoate and the anion **25**, was excluded by the demonstration that *t*-butyl benzoate was neither a reaction product nor was it converted in major extent to benzoic acid under the conditions of the reaction. It seemed probable that

the cleavage of **4** had occurred as a result of the adventitious presence of water, and that the cleavage involved formation of the anion **25** by attack of hydroxide ion at the 5-benzoyl group and was of a type recently investigated by Gassman and co-workers (13). This view was corroborated by the observation that treatment of **4** with potassium *t*-butoxide in ether that had been distilled from lithium aluminium hydride immediately prior to use led to a red coloration that persisted in the anhydrous medium. Work-up



with deuterium chloride in acetic acid-*d* led to the recovery of **4** with partial deuteration of the methylene group, indicating the formation of the anion **26** in the basic medium; no 2-phenacyltetrazole (**22**) was formed. When the anhydrous ether was treated with deuterium oxide (1.67 moles per mole of **4**) before use, the red coloration again rapidly gave way to a yellow coloration, and after work-up with aqueous ammonium chloride the deuterated cleavage product **27** was obtained. It seems likely that **27** is first formed in the reaction mixture by transfer of deuterium to the anion **25** from benzoic acid-*d* formed simultaneously in the cleavage reaction; subsequent reaction with *t*-butoxide ion could give the anion **28**, from which **27** would be regenerated in the aqueous work-up. Further, when **4** was cleaved with potassium *t*-butoxide in commercial "anhydrous" ether and the solid obtained from the reaction mixture was treated with methyl iodide, only the side-chain methylation product **29** was isolated, suggesting that the anion **25** is converted by reaction with benzoic acid to **22** which then reacts

⁶A related route involving initial proton abstraction (12) rather than terminal attack also leads to an anion that could serve as an intermediate in the formation of both **2** and **4**.



with *t*-butoxide ion to give the anion **30**. The isolation of the dimethylated product is ascribed to the presence of excess potassium *t*-butoxide in the solid product subjected to methylation.

The demonstration that the presence of water is required for the cleavage of **4** by potassium *t*-butoxide in ether suggests that the cleavage of both **3** and **4** with potassium *t*-butoxide in *t*-butyl alcohol may also have involved the intervention of adventitious water.

Experimental

Melting points, which were determined with a Thomas Hoover "Uni-melt" capillary melting point apparatus, are uncorrected. Solutions in organic solvents were dried over anhydrous magnesium sulfate. Unless otherwise stated, infrared spectra were recorded in solution in dichloromethane, ultraviolet spectra in 95% ethanol, and proton magnetic resonance (p.m.r.) spectra at 100 MHz in deuteriochloroform with tetramethylsilane as internal reference.

Reaction of 2-Diazoacetophenone (**1**) with Potassium *t*-Butoxide in *t*-Butyl Alcohol: Formation of 5-Benzoyl-2-phenacyltetrazole (**4**) and 2-Phenacyltetrazole (**22**)

2-Diazoacetophenone (1.00 g) was added to a solution of potassium *t*-butoxide (0.92 g) in *t*-butyl alcohol (55 ml) and the mixture was swirled to dissolve the diazo ketone. The solution immediately became red and after standing for 30 min at room temperature was poured into cold, dilute hydrochloric acid. The mixture was extracted with several portions of dichloromethane, and the extract was dried and stripped of solvent. The resulting solid was dissolved in benzene and chromatographed on a Florisil column (100 g, packed in benzene). Elution with dichloromethane - benzene (1:1) gave 2-phenacyltetrazole (**22**) (0.15 g, 23%), m.p. 104-104.5° after recrystallization from benzene - hexane (*vide infra*).

Elution of the column with 2% methanol - dichloromethane yielded 5-benzoyl-2-phenacyltetrazole (**4**) (0.69 g, 69%), m.p. 114-114.5° after recrystallization from 95% ethanol; λ_{\max} 5.85, 5.95, 6.23, 6.30, 10.82 μ ; λ_{\max} 250 m μ (log ϵ 4.39); δ 6.31 (2H, s), δ 7.5-8.5 (10H, m).

Anal. Calcd. for $C_{16}H_{12}N_4O_2$: C, 65.75; H, 4.14; N, 19.17. Found: C, 65.58; H, 4.25; N, 18.80.

Elution of the column with 10% methanol - dichloromethane gave benzoic acid (0.17 g).

Phenacylation of 5-Benzoyltetrazole (**7**): Formation of 5-Benzoyl-1-phenacyltetrazole (**3**) and 5-Benzoyl-2-phenacyltetrazole (**4**)

5-Benzoyltetrazole¹ (0.87 g) was dissolved in dry acetone (20 ml) and potassium carbonate (0.35 g) was

added. The mixture was swirled and warmed until most of the base had dissolved, and phenacyl bromide (1.00 g) was added. The reaction mixture was boiled gently under reflux for 30 min, diluted to the cloud point with water, and chilled to 0°. The crystalline deposit was recrystallized from 95% ethanol to give **4** (0.70 g, 47%), m.p. 113.5-114°, undepressed on admixture with the 5-benzoyl-2-phenacyltetrazole (**4**) obtained above; the infrared spectra of the two samples were identical.

The original filtrate was combined with the recrystallization mother liquors, diluted with water, and extracted with dichloromethane. The extract was dried and evaporated, and the residue (0.64 g) was chromatographed on a Florisil column packed in benzene. Elution of a pale yellow band with dichloromethane - benzene (1:1) afforded colorless needles of 5-benzoyl-1-phenacyltetrazole (**3**) (0.20 g, 14%), m.p. 126-127° after recrystallization from 95% ethanol; λ_{\max} 5.85, 5.97, 6.23, 6.30, 10.80 μ ; λ_{\max} 252 m μ (log ϵ 4.29), 272 m μ (sh, log ϵ 4.19); δ 6.33 (2H, s), 7.5-8.6 (10H, m).

Anal. Calcd. for $C_{16}H_{12}N_4O_2$: C, 65.75; H, 4.14; N, 19.17. Found: C, 65.69; H, 4.23; N, 19.39.

Elution with 5% methanol - dichloromethane gave a further quantity of tetrazole **4** (0.25 g; total yield 65%).

Reduction of **3** with Lithium Aluminium Hydride:

Formation of Di(2-hydroxy-2-phenylethyl)amine (**8**)

A solution of the tetrazole **3** (0.151 g) in tetrahydrofuran (15 ml) was added dropwise to a suspension of lithium aluminium hydride (0.240 g) in boiling tetrahydrofuran (20 ml) under reflux. The solution was boiled under reflux for 18 h, and the excess of the hydride was decomposed by the cautious addition of 0.2 N hydrochloric acid. The mixture was added to concentrated aqueous sodium hydroxide and extracted with ether. The extract was dried and stripped of solvent to give crude **8** in quantitative yield. Recrystallization from benzene afforded plates (0.075 g, 54%), m.p. 115-117°; λ_{\max} 2.77, 3.0, 6.68 μ ; δ 2.75-3.0 (7H, m) [2.82 (4H, d, *J* 6 Hz) after treatment with D_2O], 4.75 (2H, m; t, *J* 6 Hz, after treatment with D_2O), 7.36 (10H, m).

Anal. Calcd. for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.77; H, 7.46; N, 5.54.

Hydrogenolysis of **8**: Formation of Di(2-phenylethyl)amine (**9**)

The amine **8** (0.245 g) in acetic acid (10 ml) was added to a stirred suspension of 10% palladium on charcoal (0.065 g) in acetic acid (10 ml) containing a catalytic amount of dilute hydrochloric acid. The solution was maintained at 80° under hydrogen for 12 h. After cooling, the hydrogen uptake was 45 ml at 27° and 753 mm (96% of the volume of hydrogen required for complete hydrogenolysis). The catalyst was removed by filtration, and the filtrate was cautiously added to cold, concentrated aqueous sodium hydroxide. The mixture was extracted with several portions of chloroform. The extract was dried and stripped of solvent to give di(2-phenylethyl)amine (**9**) (0.170 g, 79%); λ_{\max} ($CHCl_3$) 3.13, 6.26, 6.76 μ . This was shown by infrared spectral comparison to be identical with an authentic sample (*vide infra*).

The amine (**9**) was dissolved in ether containing a little chloroform, and hydrogen chloride was bubbled through the solution. The solid deposited was recrystallized from

ethanol-ether to give di(2-phenylethyl)amine hydrochloride, m.p. 265–266° [lit. (14) m.p. 267–268°], undepressed on admixture with an authentic sample (*vide infra*); its infrared spectrum was identical with that of the authentic sample.

Reduction of N-(2-Phenylethyl)phenylacetamide (13) with Lithium Aluminium Hydride: Formation of Di(2-phenylethyl)amine (9)

Phenylacetyl chloride (15.4 ml) was added dropwise to a solution of 2-phenylethylamine (24.2 ml) in benzene (40 ml). After standing for 1 h the reaction mixture was partitioned between dichloromethane and water. The organic layer was dried and stripped of solvent to give *N*-(2-phenylethyl)phenylacetamide (13) (16.5 g), m.p. 93.5–94° after recrystallization from benzene-ligroin [lit. (15) m.p. 94–95°]; λ_{\max} 3.02, 6.04, 6.66 μ ; δ 2.72 (2H, t), 3.3–3.7 (4H, s superimposed on m), 5.5 (1H, br s), 7.0–7.5 (10H, m).

A solution of 13 (0.98 g) in 1,2-dimethoxyethane (20 ml) was added dropwise to a suspension of lithium aluminium hydride (0.30 g) in boiling 1,2-dimethoxyethane (25 ml), and the mixture was boiled under reflux for 50 h. The excess of hydride was decomposed by the successive addition of anhydrous magnesium sulfate, Celite, and aqueous 1,2-dimethoxyethane. The solution was filtered, dried, and stripped of solvent to give 9 as an oil. This was converted to its hydrochloride as described above; m.p. 266–267°; λ_{\max} 3.70, 3.95, 4.15, 6.3 μ ; δ (CF₃CO₂H) 3.05 (4H, t, *J* 7 Hz), 3.3–3.7 (4H, m), 7.1–7.5 (10H, m).

Reduction of 4 with Lithium Aluminium Hydride: Formation of 14

A solution of the tetrazole 4 (0.28 g) in anhydrous ether (250 ml) was slowly added to a suspension of lithium aluminium hydride (0.64 g) in ether (30 ml). The mixture was boiled under reflux for 4 h and then cooled to room temperature. Celite and anhydrous magnesium sulfate were added, followed by moist ether. The mixture was filtered, and the filtrate was dried and stripped of solvent to give an oily residue; crystallization at 0° from benzene-ligroin gave 14 (0.16 g, 57%), which was recrystallized from benzene; m.p. 108–109.5°; λ_{\max} 2.85, 2.95, 6.23, 6.71 μ ; δ 3.50 (1H, br s; absent after D₂O treatment), 3.78 (1H, br s; absent after D₂O treatment), 4.6–4.9 (2H, m), 5.3 (1H, m), 6.14 (1H, d, *J* 4 Hz; s after treatment with D₂O), 7.4 (10H, m).

Anal. Calcd. for C₁₆H₁₆N₄O₂: C, 64.85; H, 5.44; N, 18.91. Found: C, 65.04; H, 5.67; N, 18.79.

Hydrogenolysis of 14: Formation of 5-Benzyl-2-(2-phenylethyl)-tetrazole (15)

A solution of the diol 14 (0.100 g) in acetic acid (3 ml) was added to a stirred suspension of 10% palladium on charcoal (0.015 g) in acetic acid (10 ml) under hydrogen. The mixture was stirred for 20 h at room temperature, and hydrogen (6.1 ml at 27° and 754 mm, ca. 0.8 molar equiv.) was absorbed; it was then heated to 80–90° and maintained at this temperature for a further 7 h. The total hydrogen consumption was 19.1 ml at 27° and 745 mm (ca. 2.25 molar equiv.). The mixture was filtered, and the solvent was removed from the filtrate by freeze-drying to yield 15 (0.090 g, 100%) as an oil, b.p. 150–152° (0.02 mm); λ_{\max} (CCl₄) 6.23, 6.73 μ ; δ 3.30 (2H, t,

J 8 Hz), 4.16 (2H, s), 4.82 (2H, t, *J* 8 Hz), 7.0–7.5 (10H, m).

Anal. Calcd. for C₁₆H₁₆N₄: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.45; H, 6.38; N, 21.35.

The tetrazole 4 was also converted directly to 15 under analogous conditions.

Reaction of 3 with Ammonium Acetate in Acetic Acid: Formation of 16

A solution of 3 (0.145 g) in acetic acid (15 ml) containing ammonium acetate (0.200 g) was boiled under reflux for 19 h. The solvent was removed by freeze-drying, the residue was dissolved in chloroform, and the solution was washed with aqueous sodium bicarbonate. The organic layer was dried and stripped of solvent to give 16, (0.105 g, 78%), m.p. 160.5–161° after recrystallization from ethanol; λ_{\max} 6.24, 6.33, 6.84 μ ; δ 7.5–7.8 (6H, m), 8–8.3 (2H, m), 8.9–9.1 (3H, s superimposed on m).

Anal. Calcd. for C₁₆H₁₁N₅: C, 70.31; H, 4.06; N, 25.63. Found: C, 70.47; H, 4.35; N, 25.58.

Similar treatment of 4 failed to give an analogous product; thin layer chromatography of the crude reaction product showed that it consisted mainly of starting material.

Phenacylation of Tetrazole (23): Formation of 2-Phenacyltetrazole (22) and 1-Phenacyltetrazole (24)

A solution of tetrazole (23) (0.35 g) and phenacyl bromide (1.00 g) in hot acetone (50 ml) was treated with potassium carbonate (0.70 g), and the mixture was boiled gently under reflux for 30 min. The reaction mixture was poured into water, and the oil which separated was extracted with dichloromethane. The extract was dried and stripped of solvent to yield an oil, which crystallized from benzene to give 1-phenacyltetrazole (24) (0.53 g, 56%) as needles, m.p. 100–104°. Several recrystallizations of the crude product from benzene afforded pure material, m.p. 110.5–111.5°; λ_{\max} 5.86, 6.26, 6.34, 8.51, 9.09 μ ; δ 6.01 (2H, s), 7.5–8.2 (5H, m), 8.94 (1H, s).

Anal. Calcd. for C₉H₈N₄O: C, 57.44; H, 4.29; N, 29.77. Found: C, 57.56; H, 4.33; N, 29.94.

The semi-solid residue obtained upon evaporation of the mother liquors, after several recrystallizations from aqueous methanol with treatment with Norit, afforded faintly yellow needles of 2-phenacyltetrazole (22) (0.050 g, 5%), m.p. 104–104.5°, undepressed on admixture with material obtained from the reaction of 2-diazoacetophenone (1) and of 5-benzoyl-2-phenacyltetrazole (4) with potassium *t*-butoxide in *t*-butyl alcohol; the infrared spectra of these samples were identical.

*Cleavage of 4 with Potassium *t*-Butoxide in *t*-Butyl Alcohol: Formation of 22*

A solution of 5-benzoyl-2-phenacyltetrazole (4) (0.69 g) in hot *t*-butyl alcohol (5 ml) was poured into a solution of potassium *t*-butoxide prepared from potassium (0.29 g) and *t*-butyl alcohol (25 ml). The reaction mixture, which immediately became red, was stirred at room temperature for 84 h, during which time the intensity of the red color diminished. The resulting orange solution was added to an excess of 10% aqueous sodium bicarbonate, and the mixture was extracted with dichloromethane. The crude product obtained by drying and stripping the extract of solvent was chromatographed on

a Florisil column (100 g, packed in benzene). 2-Phenacyltetrazole (**22**) (0.29 g, 70% based on unrecovered starting material) was eluted with dichloromethane - benzene (1:1) and after recrystallization from benzene - hexane had m.p. 104-104.5°; λ_{\max} 5.85, 6.26, 6.32, 8.37, 8.42, 8.92 μ ; δ 6.18 (2H, s), 7.5-8.2 (5H, m), 8.69 (1H, s).

Anal. Calcd. for $C_9H_8N_4O$: C, 57.44; H, 4.29; N, 29.77. Found: C, 57.76; H, 4.41; N, 29.87.

Starting material (**4**) (0.035 g) was isolated on elution of the column with 5% methanol - dichloromethane. Benzoic acid (0.091 g) was isolated from the sodium bicarbonate extract.

Cleavage of **3** with Potassium *t*-Butoxide in *t*-Butyl

Alcohol: Formation of **24**

5-Benzoyl-1-phenacyltetrazole (**3**) (0.69 g) was treated with potassium *t*-butoxide as in the case of **4** above, except that the reaction period was reduced to 66 h. Chromatography gave 1-phenacyltetrazole (**24**) (120 mg, 28%), which, after recrystallization from benzene with treatment with Norit, had m.p. 111-111.5°, undepressed on admixture with an authentic sample; its infrared spectrum was identical with that of the authentic sample.

Reaction of 5-Benzoyl-2-Phenacyltetrazole (**4**) with

Potassium *t*-Butoxide in Ether

(a) In Commercial "Anhydrous" Ether

The tetrazole **4** (0.73 g) was dissolved in commercial "anhydrous" ether (350 ml) by heating. The solution was cooled to room temperature and poured into a stirred slurry of potassium *t*-butoxide (1.25 g) in ether (25 ml). The solution became red momentarily and then turned pale orange-yellow. It was stirred at room temperature for 10 min and then filtered, giving a whitish-yellow solid whose color deepened on exposure to air. Aqueous ammonium chloride was added to the filtrate, and the organic layer was separated, dried, and evaporated to give 2-phenacyltetrazole (**22**) (0.030 g), m.p. and mixed m.p. 103-104°. Its infrared spectrum was identical with that of authentic material. The whitish-yellow solid from above was added to the aqueous ammonium chloride solution and the mixture was extracted with ether. The extract was dried and stripped of solvent to give additional 2-phenacyltetrazole (0.40 g), identified as before. The total yield of **22** was 0.43 g (91%). Benzoic acid (0.30 g, 99%) was isolated from the aqueous layer after acidification.

(b) In Anhydrous Ether

Commercial "anhydrous" ether was boiled under reflux over lithium aluminium hydride and distilled therefrom immediately prior to use. A solution of **4** (1.00 g) in anhydrous ether (400 ml) was rapidly added to a suspension of potassium *t*-butoxide (1.54 g) in anhydrous ether (30 ml) whereupon the mixture turned red. This color persisted while the reaction mixture was stirred at room temperature for 10 min. The mixture was then added to a solution of deuterium chloride in acetic acid-*d*, prepared by mixture of acetyl chloride (12 ml) and deuterium oxide (4 ml). The ethereal solution became colorless (with concomitant salt precipitation) and was extracted with aqueous sodium bicarbonate. The organic phase was dried and stripped of solvent to give a residue which was recrystallized from ethanol. The infrared, n.m.r., and mass spectra of this product (0.59 g) indicated

it to be 5-benzoyl-2-phenacyltetrazole partially deuterated at the methylene group. Its n.m.r. spectrum showed a relative intensity of the methylene to phenyl proton signals of ca. 1.5:10. Its mass spectrum showed a ratio of 1:1 in the abundances of the *m/e* 293 and 292 ions, as compared with a ratio of 1:5 in the spectrum of non-deuterated **4**.

A control experiment showed that in the absence of base no deuterium was incorporated into **4**.

(c) In Anhydrous Ether and Deuterium Oxide

The tetrazole **4** (0.61 g) was dissolved in anhydrous ether (rigorously dried as in (b), 300 ml) and deuterium oxide (0.7 ml) was well stirred into the solution. This mixture was then added to potassium *t*-butoxide (0.90 g) in ether (25 ml). A red color developed momentarily, rapidly turning to a pale yellow. The solution was stirred for 10 min and then added to aqueous ammonium chloride, whereupon the color was discharged. The ethereal layer was separated, and the aqueous layer was extracted with dichloromethane. The combined organic layers were dried and stripped of the solvent; the residue was crystallized from benzene - hexane affording 2-phenacyltetrazole-5-*d* (**27**) (0.25 g, 64%), m.p. 101.5-103°; δ 6.18 (2H, s), 7.5-8.2 (5H, m), 8.69 (0.3H, s). Its infrared spectrum differed in minor respects from that of 2-phenacyltetrazole (**22**). Its mass spectrum showed a ratio of 2:1 in the abundances of the *m/e* 189 and 188 ions, as compared with a ratio of 1:7 in the spectrum of **22**.

2-(1,1-Dimethylphenacyl)tetrazole (**28**)

A solution of **4** (0.73 g) in commercial "anhydrous" ether (not further dried, 350 ml), was added to a suspension of potassium *t*-butoxide (1.22 g) in ether (25 ml), and the mixture was stirred for 10 min. The precipitate was collected by filtration and rapidly transferred to a flask containing a solution of methyl iodide (10 ml) in dimethylformamide (50 ml) under nitrogen. The contents of the flask were stirred for 54 h under nitrogen at room temperature. The solution was added to aqueous ammonium chloride, and the mixture was extracted with dichloromethane. The extract was dried, and stripped of solvent to give an oily crystalline product which possessed the characteristic odor of methyl benzoate. Recrystallization from cyclohexane and sublimation gave **28** (0.23 g, 53%), m.p. 81.5-82°; λ_{\max} 5.96, 6.28, 7.23, 7.33 μ ; δ 2.11 (6H, s), 7.2-7.6 (5H, m), 8.56 (1H, s).

Anal. Calcd. for $C_{11}H_{12}N_4O$: C, 61.09; H, 5.59; N, 25.91. Found: C, 60.92; H, 5.68; N, 25.73.

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