Interaction of a Phenylpyrazolidine Urethane with Meerwein's Salt

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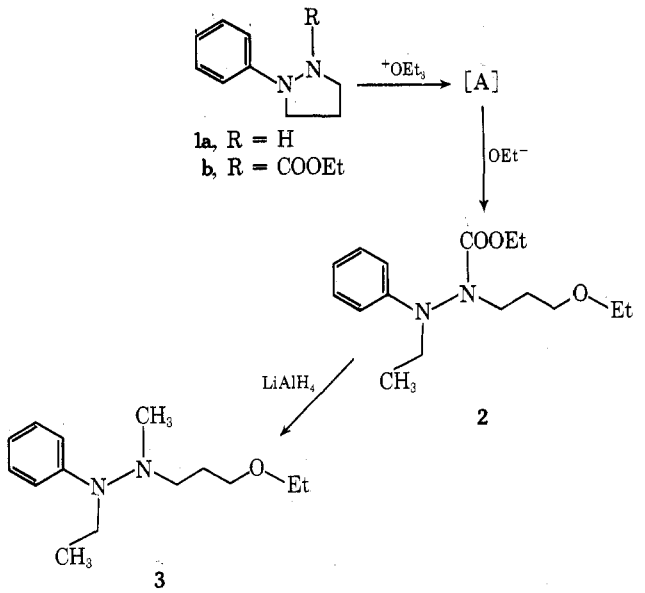
Reaction of 1-carbethoxy-2-phenylpyrazolidine with Meerwein's salt followed by neutralization with ethoxide gave 1-carbethoxy-1-(3-ethoxypropyl)-2-ethyl-2-phenylhydrazine. This product was independently synthesized from 1-ethylphenylhydrazine.

In our studies of 1-phenylpyrazolidine[1] we were interested in the course of ethylation of the carbethoxy derivative of **1a.** Treatment of **1b** with Meerwein salt[2] followed by sodium ethoxide gave a compound containing NEt, OEt, and COOEt groups (from ^{1}H NMR data) and was assigned ring-opened structure **2.** Reduction with $LiAlH_4$ gave the *N*-methyl compound **3.** Structures **2** and **3** were consistent

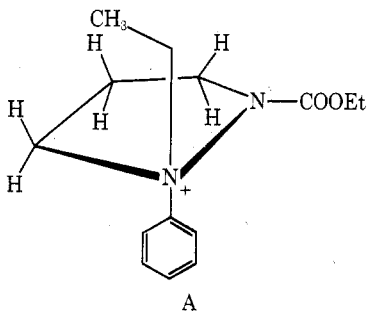


2 3

with ^{1}H NMR and ^{13}C NMR data (see paragraph at end of paper regarding supplementary material). The latter allowed positive identification of the site of ethylation and also revealed the course of the ring opening upon treatment with ethoxide (see Table I).

For confirmation, the urethane **2** was synthesized independently by reaction of the known 1-ethylphenylhydrazine[3] with 3-ethoxypropionyl chloride to give the corresponding hydrazide which was reduced with $LiAlH_4$ to the 1-ethyl-2-(3-ethoxypropyl)-1-phenylhydrazine. This was converted to **2** upon reaction with ethyl chloroformate and found to be identical with an authentic sample by comparison of GLC and thin film spectra.

From these results it may be concluded that the attack of the triethyloxonium fluoroborate on **1b** occurred on the nitrogen attached to the phenyl ring to yield the quaternary ammonium salt A. The addition of base resulted in an SN2



A

Table I. ^{13}C NMR Shifts and Multiplicities Observed for Compounds (ppm[a])

Assignment	1b	2	3	3 (sford)[b]	
NCOO[c]	156.7[c]	Not observed[c]			
N-C_{arom}	150.4	148.9	149.7	s	free rotation
m-C_{arom}	128.9	129.5	129.0	d	
p-C_{arom}	121.6	119.2	117.0	d	
o-C_{arom}	115.6	112.9	112.5	d	
C–CH_2OEt		68.9	69.2	t	
$COCH_2CH_3$		66.6	66.4	t	
$NCOOCH_2CH_3$	62.3	62.1			
CH_3NCH_2			53.0	t	
$CH_2NCOOEt$	54.6	48.6[d]			
CH_3NCH_2			40.2	q	
$PhNCH_2CH_2$	45.4				
$PhNCH_2CH_3$		48.0[d]	36.4	t	
C–CH_2C	25.5	29.5	28.2	t	
$CH_3CH_2OCH_2$		15.4	15.3	q	
NCH_2CH_3		14.8	14.7	q	
$COOCH_2CH_3$	14.8	13.5			

[a] Data converted using $\delta_C^{CS_2}$ 193.0 ppm from Me_2Si. [b] Single frequency off-resonance decoupling. [c] The ^{13}C NMR spectrum of **2** was recorded without the presence of paramagnetic additive[4] [iron tris(pentane-2,4-dionate)]. The ^{13}C NMR spectrum of **1b** however, was recorded in the presence of the decontrasting agent and the carbonyl carbon gave rise to a distinguished peak. [d] Interchangeable.

type ring opening rather than in an E2 elimination reaction since no protons in periplanar position are readily available for ring opening with formation of a double bond.

Experimental Section

Proton NMR (^{1}H NMR) spectra were recorded on either a Varian A-60 or T-60 spectrometer and are recorded in δ values (parts per million) from Me_4Si as internal standard. The ^{13}C NMR spectra were measured on a Bruker HX-90 spectrometer and are recorded in parts per million values from Me_4Si (data converted using $\delta_C^{CS_2}$ 193.0 ppm from Me_4Si). Ir spectra were taken on a Perkin-Elmer Model 257 or 457. Gas–liquid chromatography was carried out on a Hewlett-Packard 5750 chromatograph. Mass spectra were taken on a LKB 9000 mass spectrometer. Ultraviolet spectra were determined in 95% ethanol with a Cary recording spectrophotometer, Model 14.

1-Carbethoxy-2-phenylpyrazolidine (1b). To the ice-cold mixture of 36.8 g (0.20 mol) of phenylpyrazolidine[1a] hydrochloride (**1a**), 500 ml of ether, and 250 ml of 2 N NaOH solution there was slowly added 21.6 g (0.20 mol) of ethyl chloroformate. After 20 min the organic phase was separated and the aqueous phase was extracted with ether. The combined organic phases were washed with water and dried over K_2CO_3. The solvent was evaporated to yield 41.4 g (94%) of crude **1b** which was distilled (bp 120–140 °C, 0.6 mm) to give 38.6 g (88%) of pure **1b:** ^{1}H NMR ($CDCl_3$) δ 1.23 (t, 3, J = 7 Hz, CH_3), 1.97 (quintet, 2, J = 7 Hz, $CH_2CH_2CH_2$), 3.53 (t, 2, J = 7 Hz, NCH_2CH_2), 3.65 (t, 2, J = 7 Hz, NCH_2CH_2), 4.21 (q, 2, J = 7 Hz, OCH_2CH_3), 6.7–7.5 (m, 5, C_6H_5); ^{13}C NMR (see Table I); ir (film) 1700 (C=O) 1600 cm^{-1} (aromatic); uv 237 nm (ϵ 10 600) 278 (1060). Anal. Calcd for $C_{12}H_{16}N_2O_2$ (220.26): C, 65.4; H, 7.3; N, 12.7. Found: C, 65.1; H, 7.4; N, 12.8.

1-Carbethoxy-1-(3-ethoxypropyl)-2-ethyl-2-phenylhydrazine (2). From 34.5 g of boron trifluoride etherate and 16.5 g of epi-

chlorohydrin there was prepared 31.5 g (0.17 mol) of Meerwein salt[2] following the published procedure. The salt was dissolved in 100 ml of dry methylene chloride. A solution of 33.9 g (0.15 mol) of **1b** in 50 ml of methylene chloride was added and the mixture was kept at room temperature overnight. This was poured on a solution prepared from 3.8 g (0.17 mol) of sodium in 200 ml of absolute ethanol. The mixture was stirred at room temperature for 4 h. The solvent was evaporated and the residue was extracted with ether, washed with water, and dried over K_2CO_3. After evaporation of the solvent 28.2 g (62%) of a liquid was obtained which was distilled (bp 110–130 °C, 0.13 mm) to yield 27.8 g (61%) of **2**: *m/e* 294 (M^+); ^1H NMR ($CDCl_3$) δ 0.9–1.5 (m, 9, 3 CH_3), 1.6–2.2 (m, 2, CH_2), 3.1–3.8 (m, 8, 4 CH_2), 4.10 (q, 2, J = 7 Hz, OCH_2CH_3), 6.5–7.4 (m, 5, C_6H_5); ^1H NMR ($CDCl_3$ + CCl_4 + shift reagent at 60 °C) δ 0.90 (t, 3, J = 7 Hz, NCH_2CH_3), 1.45 and 1.57 (t, 3, J = 7 Hz, 2 OCH_2CH_3), 2.0–3.0 (broad, 2, $NCH_2CH_2CH_2$), 3.20 (q, 2, J = 7 Hz, NCH_2CH_3), 3.40 (t, 2, J = 6 Hz, CH_2CH_2OEt), 4.07 (q, 2, J = 7 Hz, $CH_2OCH_2CH_3$), 5.3–6.0 (broad, 2, $COOCH_2CH_3$), 6.4–6.9 (m, 2, NCH_2CH_2); ^{13}C NMR (see Table I); ir (film) 1710 (COOEt), 1608 cm^{-1} (aromatic). Anal. Calcd for $C_{16}H_{26}N_2O_3$ (294.38): C, 65.3; H, 8.9; N, 9.5. Found: C, 65.3; H, 9.2; N, 9.7.

1-(3-Ethoxypropyl)-2-ethyl-1-methyl-2-phenylhydrazine (3). To the suspension of 1.5 g (0.04 mol) of lithium aluminum hydride in 100 ml of dry ether, a solution of 7.0 g (0.024 mol) of **2** was added dropwise. The mixture was heated to reflux for 3 h and then worked up following the usual procedures to give 4.6 g (82%) of **3**: GLC one component, a sample was distilled in a Kugelrohr; *m/e* 236 (M^+); ^1H NMR ($CDCl_3$) δ 1.17 (t, 3, J = 7 Hz, CH_2CH_3), 1.22 (t, 3, J = 7 Hz, CH_2CH_3), 1.72 (quintet, 2, J = 6.5 Hz, $CH_2CH_2CH_2$), 2.45 (s, 3, NCH_3), 2.77 (t, 2, J = 6.5 Hz, NCH_2CH_2), 3.30 (q, 2, J = 7 Hz, NCH_2CH_3), 3.46 (q, 2, J = 7 Hz, OCH_2CH_3), 3.48 (t, 2, J = 6.5 Hz, OCH_2CH_2), 6.5–7.4 (m, 5, C_6H_5); ^{13}C NMR (see Table I); ir (film) 1598 cm^{-1} (aromatic). Anal. Calcd for $C_{14}H_{24}N_2O$ (236.35): C, 71.1; H, 10.2; N, 11.9. Found: C, 71.4; H, 10.5; N, 11.8.

1-Ethyl-2-(3-ethoxypropionyl)-1-phenylhydrazide. This compound was prepared from 7.2 g (0.042 mol) of 1-ethylphenylhydrazine[3] hydrochloride and 6.8 g (0.05 mol) of 3-ethoxypropionyl chloride in the presence of 150 ml of 2 N NaOH solution following the usual procedures to give 7.1 g (72%) of product: ^1H NMR ($CDCl_3$) δ 1.0–1.4 (m, 6, 2 CH_3), 2.4–2.8 (m, 2, $OCH_2CH_2C{=}O$), 3.3–3.9 (m, 6, 3 CH_2), 6.7–7.5 (m, 5, C_6H_5), 7.9 (broad, 1, NH); ir (film) 3250 (NH), 1675 cm^{-1} (NC=O).

1-Ethyl-2-(3-ethoxypropyl)-1-phenylhydrazine. To the suspension of 1.5 g (0.04 mol) of $LiAlH_4$ in 100 ml of dry THF the solution of 5.0 g (0.02 mol) of the above hydrazide was added slowly. The mixture was heated to reflux overnight. The mixture was worked up the usual way to give 3.8 g (85%) of the product as a liquid: *m/e* 222 (M^+); ir (film) 3250 cm^{-1} (NH). This sample was contaminated with approximately 10% starting material (GLC).

1-Carbethoxy-1-(3-ethoxypropyl)-2-ethyl-2-phenylhydrazine (2). A sample (1.0 g, 0.004 mol) of the above product in 30 ml of ether was treated with 0.7 g (0.006 mol) of ethyl chloroformate in the presence of 4 ml of 2 N NaOH solution. The mixture was stirred at room temperature overnight and then worked up the usual way. The liquid was distilled two times to give 0.8 g (60%) of **2**: bp 80–90 °C (0.07 mm); GLC one component, identical with a sample of **2** prepared via **1b** (coinjection); ir (film) identical in every respect with that of **2**.

Registry No.—**1a**, 35267-14-2; **1b**, 58074-51-4; **2**, 58074-52-5; **3**, 58074-53-6; ethyl chloroformate, 54-41-3; Meerwein salt, 368-39-8; 1-ethyl-2-(3-ethoxypropionyl)-1-phenylhydrazide, 58074-54-7; 1-ethyl-1-phenylhydrazine hydrochloride, 58074-55-8; 3-ethoxypropionyl chloride, 49775-37-3; 1-ethyl-2-(3-ethoxypropyl)-1-phenylhydrazine, 58074-56-9.

Supplementary Material Available. A discussion of the NMR spectral data (2 pages). Ordering information is given on any current masthead page.

References and Notes

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Novel Pyridazine Formation in the Base-Catalyzed Reaction of *trans*-1,2-Dibenzoyl-3,3-diphenylcyclopropane with Hydrazine[1a,b]

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The synthesis of *exo*-2,5,7-triphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (**1**) from *trans*-1,2-dibenzoyl-3-phenylcyclopropane (**2a**) has been accomplished in good yield by adding sodium hydroxide to a mixture of **2a** and hydrazine in ethanol. An attempt at producing 2,5,7,7-tetraphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (**4**) from *trans*-1,2-dibenzoyl-3,3-diphenylcyclopropane (**3a**) by an analogous reaction produced only 3,6-diphenyl-4-benzhydrylpyridazine (**5**). It was the purpose of this study to investigate the mechanistic pathway followed in the formation of **5** and to elucidate the reasons for preferred production of **5** from **3a**. The desired heterocyclic **4** was synthesized by addition of either phenylmagnesium bromide or diphenylcadmium to 6,6-diphenyl-3-oxabicyclo-[3.1.0]hexane-2,4-dione (**6**) to form 4,6,6-triphenyl-3-oxabicyclo[3.1.0]hexan-2-on-4-ol (**7**), which, on treatment with hydrazine, gave 5,7,7-triphenyl-3,4-diazabicyclo[4.1.0]hept-4-en-2-one (**8**), which, on treatment with phenyllithium, gave **4**. The heterocyclic **4** gave **5** on heating under acidic, but not basic, conditions, thus ruling out the presence of **4** during the production of **5** from **3a**. A mechanistic scheme involving 1,4,4-triphenyl-3-benzoylbut-2-en-1-one (**12**) and/or 1,4,4-triphenyl-3-benzoylbut-3-en-1-one (**13**) is presented. It is concluded that diazanorcaradiene formation from *trans*-1,2-diacylcyclopropanes under base catalysis is synthetically feasible only in cases where the *cis*-diacylcyclopropanes are sterically accessible and/or the anionic ring opening process is energetically unfavorable.

In their investigation of *exo*-2,5,7-triphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene (diazanorcaradiene, **1**), Amiet and Johns[2] reported that **1** could be synthesized in only low yields (7%) from *trans*-1,2-dibenzoyl-3-phenylcyclopropane (**2a**) by heating **2a** with hydrazine in ethanol for extended periods of time, whereas the cis isomer **2b** reacted rapidly and quantitatively at room temperature. In our laboratory, **1** was produced in satisfactory yield (55%) from **2a** and hydrazine in ethanol at room temperature, if sodium hydroxide was added to the mixture.[3] In view of the ready availability of *trans*-1,2-dibenzoylcyclopropane derivatives, the alkaline base–hydrazine treatment appeared to offer a