[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Relative Extents of Rearrangement of Some Primary Amines of the Neopentyl Type with Nitrous Acid. Electronic *vs.* Steric Factors[1]

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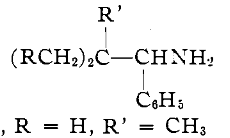
Four primary amines of the α-phenylneopentyl type (Ia-d) have been prepared and their products of reaction with nitrous acid determined. α-Phenylneopentylamine (Ia) gave exclusively the corresponding unrearranged alcohol or its nitrite ester, whereas amine Ib, having three ethyl groups on the β-carbon atom, and amines Ic and Id, having a phenyl group and two methyl or ethyl groups on the β-carbon atoms, formed rearranged products as well as the unrearranged alcohols. The rearranged products consisted of two isomeric olefins and the rearranged alcohol. All of the rearranged and unrearranged alcohols, some of the olefins, and certain of the ketones produced on ozonization of the olefins were independently synthesized for comparisons. In connection with the synthesis of amines Ic and Id, the intermediate oximes were obtained more readily from the corresponding imines and hydroxylamine than from the corresponding ketones. The relative importance of electronic and steric factors in determining the extents of rearrangement have been considered.

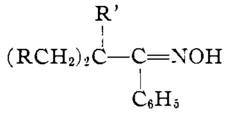
It is well known that neopentyl compounds undergo essentially complete rearrangement with appropriate acidic reagents to form *t*-amyl derivatives. Thus, neopentyl iodide and neopentylamine yield *t*-amyl alcohol with silver nitrate[3] and nitrous acid,[4] respectively. However, α-phenylneopentyl bromide is converted to the corresponding alcohol by silver nitrate,[5-7] and this alcohol is reconverted to the original bromide by hydrogen bromide.[5]

We have found that the corresponding α-phenylneopentylamine (Ia) similarly forms only unrearranged products with nitrous acid but that the three related amines, Ib, Ic and Id, give rearranged as well as unrearranged products under the same conditions (at 25–50°).



$(RCH_2)_2\overset{R'}{C}{-}\underset{C_6H_5}{C}HNH_2$

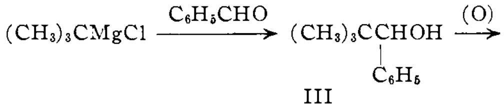
Ia, R = H, R' = CH_3
Ib, R = CH_3, R' = C_2H_5
Ic, R = H, R' = C_6H_5
Id, R = CH_3, R' = C_6H_5



$(RCH_2)_2\overset{R'}{C}{-}\underset{C_6H_5}{C}{=}NOH$

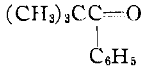
IIa, R = H, R' = CH_3
IIb, R = CH_3, R' = C_2H_5
IIc, R = H, R' = C_6H_5
IId, R = CH_3, R' = C_6H_5

The amines (Ia–d) were obtained from the corresponding oximes (IIa–d) which were prepared from the ketones or imine hydrochlorides[8] synthesized as represented in equations 1–3. Ketone VII (R = CH_3) also was synthesized starting with benzene and α-bromoisobutyric acid, but the oxime subsequently obtained was difficult to purify.[9]



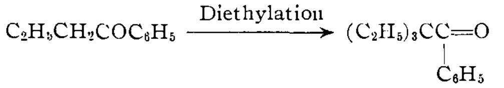
$(CH_3)_3CMgCl \xrightarrow{C_6H_5CHO} (CH_3)_3C\underset{C_6H_5}{CH}OH \xrightarrow{(O)}$

III



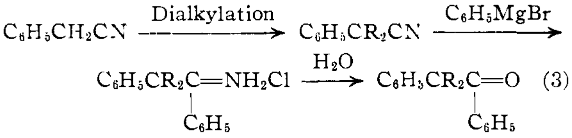
$(CH_3)_3C\underset{C_6H_5}{C}{=}O$ (1)

IV



$C_2H_5CH_2COC_6H_5 \xrightarrow{\text{Diethylation}} (C_2H_5)_3C\underset{C_6H_5}{C}{=}O$ (2)

V

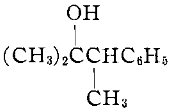


$C_6H_5CH_2CN \xrightarrow{\text{Dialkylation}} C_6H_5CR_2CN \xrightarrow{C_6H_5MgBr}$

$C_6H_5CR_2\underset{C_6H_5}{C}{=}NH_2Cl \xrightarrow{H_2O} C_6H_5CR_2\underset{C_6H_5}{C}{=}O$ (3)

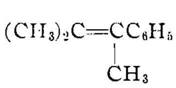
VI VII

On reaction with nitrous acid, amine Ia gave the unrearranged alcohol III and a small amount of its nitrite ester. Alcohol III was obtained contaminated with a slight impurity which appeared to be the corresponding ketone IV. The impurity was evidently not the isomeric rearranged alcohol VIII since the residual oil left after isolating a high yield of pure III produced no olefin with refluxing 20% sulfuric acid, and was converted by hot permanganate to pivalophenone (IV) which is the oxidation product of III. Alcohol VIII (prepared by an unequivocal method) was dehydrated readily by acid to form olefin IX from which acetophenone was obtained on oxidation.



$(CH_3)_2\overset{OH}{C}\underset{CH_3}{C}HC_6H_5$

VIII



$(CH_3)_2C{=}\underset{CH_3}{C}C_6H_5$

IX

However, amines Ib, Ic and Id gave not only the unrearranged alcohol (Xb–d), but also the rearranged alcohol (XIb–d), and two rearranged olefins (XIIb–d and XIIIb–d). These four types of products may be accounted for in the classical manner (Scheme A).[10] The yields and analyses for the olefin and alcohol fractions are given in Table I,

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[1] Supported in part by the Office of Naval Research.

[2] American Cyanamid Company Fellow, 1951–1952.

[3] F. C. Whitmore, E. L. Wittle and A. H. Popkin, THIS JOURNAL, **61**, 1586 (1939).

[4] M. Freund and F. Lenze, *Ber.*, **24**, 2150 (1891).

[5] P. S. Skell and C. R. Hauser, THIS JOURNAL, **64**, 2633 (1942).

[6] S. Winstein and B. K. Morse, *ibid.*, **74**, 1133 (1952).

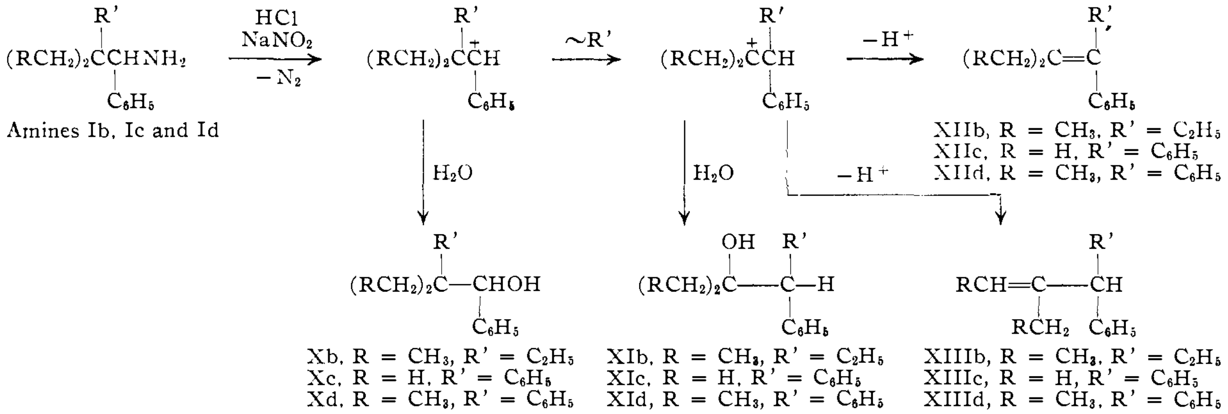
[7] I. Dostrovsky and D. Samuel, *J. Chem. Soc.*, 658 (1954).

[8] Oximes IIc and IId were obtained more conveniently from the imine hydrochlorides VI than from the corresponding ketones VII. Earlier workers (refs. 36 and 41) have similarly observed that certain ketimines form oximes more readily than the corresponding ketones.

[9] Apparently the dimethylphenylacetic acid resulting from the Friedel–Crafts type of alkylation of benzene with α-bromoisobutyric acid was contaminated with the isomeric acid, α-methyl-β-phenylpropionic acid, since an acid corresponding to the latter was shown to be formed in the analogous reaction of toluene with ethyl α-bromoisobutyrate; A. Lambert, J. D. Rose and B. C. L. Weedon, *J. Chem. Soc.*, 42 (1949).

[10] The type XII olefin arises by the loss of an original α-hydrogen from the rearranged carbonium ion, and type XIII olefin, by the loss of an original γ-hydrogen from this carbonium ion. Since the unrearranged carbonium ion has no β-hydrogen, unrearranged olefins are not possible. Although only olefins XIIb and XIIIb are possible from amine Ib, in which R and RCH_2 are both ethyl, two other olefins (and one other rearranged alcohol) would have been produced from amine Ic or amine Id had the β-alkyl group (RCH_2) migrated instead of the β-phenyl group (R'). However, only those olefins resulting from migration of the phenyl group were found.

SCHEME A



the results of ozonization of the olefin fractions, in Table II (first three entries), and the physical constants for further cuts of the alcohol fractions, in Table III. The unrearranged and rearranged alcohols were synthesized independently by unequivocal methods, their physical constants being given in Table III. Also, certain of the olefins and some of the ketones produced on ozonization of olefins were synthesized independently by unequivocal methods.

TABLE I

OLEFIN AND ALCOHOL FRACTIONS FROM AMINES Ib, Ic AND Id WITH NITROUS ACID

Amines		Olefin fraction[a]								Alcohol fraction[a]						
		Yield,[b]	B.p.,			Carbon, %		Hydrogen, %		Yield,[b]	B.p.,		Carbon, %		Hydrogen, %	
No.	Mole	%	°C.	Mm.	$n^{25}D$	Calcd.	Found	Calcd.	Found	%	°C.	Mm.	Calcd.	Found	Calcd.	Found
Ib	0.336	18	112–115	15	1.4962	89.29	88.84	10.71	11.43	60	150–157	16	81.50 81.50	81.44[c] 81.25[d]	10.75 10.75	10.90[c] 10.77[d]
Ic	.247	18	144–147	12	1.5731	92.25	91.98	7.75	7.73	56	172–178	11.5	84.91	85.04	8.02	8.07
Id	.224	34	162–166	12	1.5602	91.47	91.35	8.53	8.78	44[e]	194–198	12	84.99	84.87	8.72	8.79

[a] Analyses were determined on mid-cuts of fractions except as noted. [b] Based on product obtained after refluxing with 10–20% NaOH and redistilling, except as noted. [c] Analysis of cut boiling at 156–157° at 16 mm. [d] Analysis of cut boiling at 150–152° at 16 mm. [e] The treatment with alkali was not employed in this case.

TABLE II

KETONES AND ALDEHYDES FROM OZONOLYSIS OF MIXTURES OF OLEFINS OF TYPES XII AND XIII

		Products from type XII olefin				Products from type XIII olefin					Approx. ratio of type XII to XIII olefin[b]
		$(RCH_2)_2C{=}O$		$R'COC_6H_5$		R—CHO		$RCH_2COCH(C_6H_5)R'$			
Expt.	Source of olefin mixture	R	Yield, %[a]	R'	Yield, %[a]	R	Yield, %[a]	R	R'	Yield, %[a]	
1	Amine Ib[c]	CH_3	..	C_2H_5	1–2[d]	CH_3	45[e,f]	CH_3	C_2H_5	59	1:30
2	Amine Ic[g]	H	20[d,f]	C_6H_5	34[d]	H	10[e]	H	C_6H_5	13[d]	2–3:1
3	Amine Id[c]	CH_3	..	C_6H_5	12–13[d]	CH_3	38[e]	CH_3	C_6H_5	48[h]	1:4
4	Alc. fraction from amine Ic[c,i]	H	11[d]	C_6H_5	23[d]	H	Trace	H	C_6H_5	7[d]	3–4:1
5	Alcohol XIc[c,i] (independently synthesized)	H	20[d,f]	C_6H_5	29[d]	H	...	H	C_6H_5	6[d]	4–5:1

[a] Based on olefin mixture. [b] Based on highest yield of carbonyl compound from each olefin. [c] Ethanol used in cleavage of ozonide. [d] Isolated as the 2,4-dinitrophenylhydrazone. [e] Isolated as the dimethone. [f] This is an estimated yield, some of the carbonyl compound being lost. [g] Ethyl acetate used in the ozonization, the cleavage being effected directly in this solvent. [h] Isolated as the semicarbazone. [i] After dehydration with phenyl isocyanate.

TABLE III

DATA ON ALCOHOL CUTS FROM AMINES AND ON INDEPENDENTLY SYNTHESIZED ALCOHOLS

	Alcohol cuts from amines				Independently synthesized alcohols				Yields of isomeric alcohols from amines	
Amines	Yield, %	B.p. °C.	Mm.	$n^{25}D$	Alcohol	B.p. °C.	Mm.	$n^{25}D$	Rearr., %	Unrearr., %
Ib	3.4	150–152	16	1.5138	XIb	137–138	16	1.5096	XIb 7–8	Xb 52
	6.7	152–154	16	1.5163	Mixture, XIb (50.3%) Xb (49.7%)			1.5146		
	20	154–156	16	1.5185						
	29	156–157	16	1.5194	Xb	156	15	1.5198		
Ic	15	172–174	11.5	1.5724	XIc	168–169	11.5	1.5722	XIc 20	Xc 36
	41	174–178	11.5	1.5730	Xc	178–179	11.5	1.5735		
Id	18	194–196	12	1.5668	XId	181–182 M.p. 62.5–63.5	12	....	XId 8–9	Xd 35
	26	196–198	12	1.5680	Xd	197	12	1.5686		

It can be seen from Table I that the analyses for the olefin and alcohol fractions, each of which consists of isomers, agree satisfactorily with the calculated values except for the olefin fraction from amine Ib. Since these fractions generally were treated with alkali to remove traces of nitrite ester or nitric oxide and redistilled, the total yields (74–78%) are considered reasonably good.

It can be seen from Table II that three or four carbonyl products were obtained from each of the olefin fractions, and that they correspond to the isomeric olefins of types XII and XIII (Scheme A). The yields are based on essentially pure carbonyl compounds or appropriate derivatives, certain of which were difficult to isolate. Attempts to isolate ketones corresponding to olefins that would have resulted if a β-alkyl group (RCH_2) of amines Ic and Id had migrated were unsuccessful. For example, no acetophenone was found among the ozonization products of the olefin fraction from amine Ic. This ketone, which is detected readily, should have been present had a β-methyl group migrated, since then *cis-* or *trans*-dimethylstilbene undoubtedly would have been formed. It can be further seen from Table II (column of ratios) that, although the olefin fraction from amine Ic consisted mainly of the type XII isomer, the olefin fractions from amines Ib and Id consisted largely of the type XIII isomer in which the olefinic double bond is not conjugated with the benzene ring.[11]

Consideration of the boiling points and refractive indices given in Table III indicated that the alcohol fractions from the amines consisted mainly of the unrearranged alcohols with smaller amounts of the rearranged alcohols. This was confirmed by chemical means. Thus, the alcohol fraction from amine Ib gave a high yield of the acid phthalate of the unrearranged alcohol with phthalic anhydride, and the alcohol fractions from amines Ic and Id produced good yields of the phenylurethans of the unrearranged alcohols with phenyl isocyanate. These reactions yielded smaller amounts of olefin which resulted from dehydrations of the rearranged alcohols. Also, one of the unrearranged alcohols (XId) was isolated. The olefinic product from the dehydration of the alcohol fraction of amine Ic was shown by ozonization to consist of isomers XIIc and XIIIc (expt. 4, Table II). Similar results were obtained on ozonizing the olefinic product produced by dehydrating independently synthesized alcohol XIc with phenyl isocyanate (expt. 5, Table II). The yields of the isomeric alcohols given in Table III were estimated in the first case from a composition-refractive index graph, and in the second and third cases, from the yields of materials produced with phenyl isocyanate taking into account the yields obtained on separately treating samples of independently synthesized unrearranged and rearranged alcohols with this reagent.

In Table IV are summarized the yields of the rearranged and unrearranged products from the reactions of amines Ia-d with nitrous acid, together with the ratios of these products. The yields of products from amine Ic were reproduced within 5%; in general the yields and ratios are considered reproducible within ±5%. It should be pointed out that much of the olefin, which was considered above to be formed directly from the amine (Table I), apparently arose through the intermediate formation of the rearranged alcohol since a sample of independently synthesized alcohol XIc was dehydrated approximately 50% under conditions similar to those employed with the amines.[12]

TABLE IV

YIELDS AND RATIOS OF REARRANGED AND UNREARRANGED PRODUCTS

No.	Amine R	R′	Re-arranged olefin + alcohol yield, %	Unre-arranged alcohol yield, %	Ratio rearranged to unrearranged
Ia	H	CH_3	0	80(92)[a]	0:100
Ib	CH_3	C_2H_5	25–26	52	1:2
Ic	H	C_6H_5	38	36	1:1
Id	CH_3	C_6H_5	42–43	35	1.2:1

[a] Yield of crude alcohol plus its nitrite ester.

Electronic *vs.* Steric Factors.—The relative extents of rearrangement of amines Ia-d (Table IV), as well as certain related results likewise obtained under relatively mild conditions,[13] may be accounted for qualitatively on the basis of electronic and steric factors as summarized in Scheme B.[14] Thus, a consistent pattern is derived starting with the common assumption that the complete rearrangement of the neopentyl ion, which is the first member of the series of initial carbonium ions listed in Scheme B, is due mainly to an electronic factor. This may be expressed as stabilization through hyperconjugation in the resulting tertiary amylcarbonium ion.[15] The lack of rearrangement of the α-phenylneopentylcarbonium ion, which is the second member of the series, would then also be ascribed to an electronic factor. This is the result of stabilization of the initial carbonium ion through resonance with the α-phenyl group as has been pointed out previously.[5] However, the partial rearrangement of the initial carbonium ion from amine Ib must not be due to hyperconjugative

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(11) Although the olefin fractions were treated with alkali, it cannot be considered as established that the more thermodynamically stable isomer predominated. A more thorough study of this problem is in progress in this Laboratory.

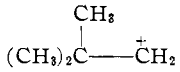
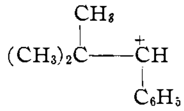
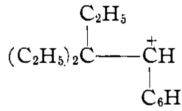
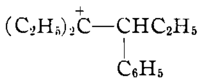
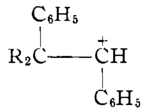
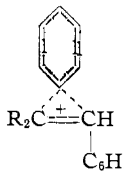
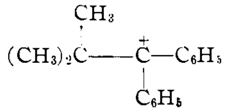
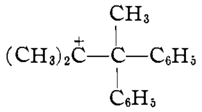
(12) In this experiment, 0.0742 mole of the alcohol was stirred with a solution of 0.75 mole of sodium nitrite and 0.25 mole of 12 *M* hydrochloric acid in one liter of water at 30–35° for three hours. The yield of olefin was 41%, and 38% of the alcohol was recovered.

(13) Only those cases effected at 50° or less will be considered since even α-phenylneopentyl bromide, which is converted to the corresponding alcohol by silver nitrate at room temperature (ref. 5, 6, 7), undergoes rearrangement to form olefin on heating at 180–220°; A. Lepin, *J. Russ. Phys. Chem. Soc.*, **44**, 1178 (1912); *Chem. Zentr.*, **83**, II, 2081 (1912).

(14) In this scheme only the driving force resulting from the rearrangement of the initial carbonium ion to the rearranged carbonium ion or bridge structure is considered. This would appear to be adequate generally when substitution products are formed. However, when elimination products result, the loss of the proton may occur simultaneously with the rearrangement and thereby furnish an additional driving force.

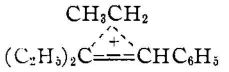
(15) See E. R. Alexander, "Principles of Ionic Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 41. In certain cases tertiary carbonium ions appear to rearrange to the less stable secondary or even primary carbonium ions. One of these, the conversion of camphene hydrochloride to isobornyl chloride, seems to be controlled by the relative ease of ionization of the two halides. See J. D. Roberts, R. E. McMahon and J. S. Hine, THIS JOURNAL, **72**, 4240 (1950).

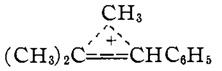
SCHEME B

Source	Initial carbonium ion	Extent of rearrangement	Rearranged carbonium ion or bridge	Main factor
Halide or amine[a]	 $(CH_3)_2\overset{CH_3}{C}-\overset{+}{C}H_2$	Complete	$(CH_3)_2\overset{+}{C}-CH_2CH_3$	Stabilization through hyperconjugation
Amine Ia, halide or alcohol	 $(CH_3)_2\overset{CH_3}{C}-\underset{C_6H_5}{\overset{+}{C}}H$	None	—	Initial carbonium ion stabilized by resonance
Amine Ib	 $(C_2H_5)_2\overset{C_2H_5}{C}-\underset{C_6H_5}{\overset{+}{C}}H$	One-third	 $(C_2H_5)_2\overset{+}{C}-\underset{C_6H_5}{C}HC_2H_5$	Partial relief of steric strain at β-carbon
Amines Ic and Id	 $R_2\overset{C_6H_5}{C}-\underset{C_6H_5}{\overset{+}{C}}H$	One-half or more		Stabilization through resonance
Alcohol XVI	 $(CH_3)_2\overset{CH_3}{C}-\underset{C_6H_5}{\overset{+}{C}}-C_6H_5$	—	 $(CH_3)_2\overset{+}{C}-\underset{C_6H_5}{\overset{CH_3}{C}}-C_6H_5$	Forms less strained carbonium ion (more planar)

[a] Although the reaction of neopentylamine with nitrous acid has been effected apparently only at 100° (ref. 4), essentially complete rearrangement probably would occur also at lower temperatures, since the reaction of neopentyl iodide with silver nitrate produced complete rearrangement at room temperatures (ref. 3).

stabilization in the rearranged carbonium ion, since such an electronic effect should be less in this case than in that possible with the α-phenylneopentylcarbonium ion which failed to rearrange. Neither is this rearrangement due to the formation of a resonance stabilized bridge structure XIV, since not only is such an intermediate quite unlikely,[16] but even if it were formed it should be less stabilized by hyperconjugation than XV (corresponding to the α-phenylneopentylcarbonium ion) which fails to form.[17] Evidently the initial carbonium ion from amine Ib undergoes partial rearrangement in order to relieve steric strain of the type proposed by Brown[18] for certain reactions. The simulation of the rearrangement employing Fisher–Hirschfelder–Taylor molecular models indicates that some strain at the β-carbon atom thereby is relieved.[19]


XIV


XV

The considerable rearrangements of the initial carbonium ions from amines Ic and Id may be ascribed to resonance stabilization in forming the bridge intermediates represented by the general formula[20] in Scheme B or similar complexes,[21,22] which, in contrast to XIV and XV, seem quite likely to be formed. Such intermediates may react with the solvent to form either the rearranged or unrearranged alcohol or lose a proton to give the rearranged olefins. However, the 50% rearrangement observed with amine Ic is coincidental since the bridge intermediate is unsymmetrical. The slightly greater rearrangement with amine Id than with amine Ic (Table IV) may indicate the slight operation of the type of steric factor considered with amine Ib; but this is evidently not the main factor since such strain is probably greater in amine Ib than in amine Ic yet the latter amine rearranged to the larger extent. Actually the loss of nitrogen from amines Ic and Id through their diazonium ions may be accompanied by the simultaneous formation of the bridge intermediates; that is, the phenyl group may participate. Such participation has been demonstrated in solvolytic types of reaction.[20] However, there does not appear to be complete participation of the phenyl group in the decomposition of certain diazonium ions.[23] The great tendency for rearrangement of β-phenyl compounds, even when an α-phenyl is present, is illustrated still further by an earlier observation[5] that 1,2,2,2-tetraphenylethanol produces largely tetraphenylethylene with hydrogen bromide at 40° or less, whereas α-phenylneopentyl alcohol

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[16] S. Winstein and B. K. Morse (ref. 6) have shown that even XV is probably not an intermediate in the solvolysis of an α-phenylneopentyl system since, when the α-carbon is optically active, the reaction is accompanied by much racemization.

[17] In this connection it should be mentioned that, although the ethyl group generally has a greater migration aptitude than the methyl group (as in the pinacol rearrangement), the latter group evidently has the greater migration aptitude in the type of rearrangement under consideration. Thus D. J. Cram and J. D. Knight, THIS JOURNAL, **74**, 5839 (1952), observed that the solvolysis of the *p*-bromobenzoate of 3,4-dimethyl-4-phenyl-3-hexanol was accompanied by the migration of the methyl and phenyl groups, but not the ethyl group.

[18] H. C. Brown and R. S. Fletcher, *ibid.*, **71**, 1845 (1949).

[19] These models also indicate that the triethylcarbinyl group in the initial carbonium ion from amine Ib pushes the phenyl group slightly out of the planar configuration thereby decreasing the stabilizing effect of its resonance with the cationic center, although such distortion appears to operate to only a slightly greater degree than that in the relatively stable unrearranged carbonium ion from amine Ia.

[20] S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, THIS JOURNAL, **74**, 1113 (1952).

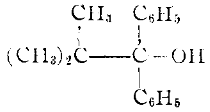
[21] D. J. Cram, *ibid.*, **71**, 3863 (1949).

[22] M. J. S. Dewar, "Electronic Theory of Organic Chemistry," Oxford Univ. Press, Oxford, 1949, p. 215.

[23] See J. D. Roberts and C. M. Regan, THIS JOURNAL, **75**, 2069 (1953).

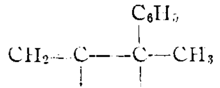
(III) is converted to the corresponding bromide under similar conditions.

Finally α,α-diphenylneopentyl alcohol (XVI) has been observed to undergo rearrangement of a methyl group to form olefin XVII on treatment with acetyl chloride[24] or acetyl bromide,[25] apparently even under mild conditions. This rearrangement of the α,α-diphenylneopentylcarbonium ion appears to be ascribable to the formation of a less strained carbonium ion (last case in Scheme B). Molecular models indicate that the two α-phenyl groups of the unrearranged carbonium ion cannot lie in a plane; consequently they cannot resonate as effectively. Thus, although the substitution of one phenyl group on the α-carbon of the neopentylcarbonium ion greatly decreases the tendency to rearrange, the substitution of a second phenyl group on the α-carbon again increases the tendency to rearrange.



$(CH_3)_2C(CH_3)-C(C_6H_5)_2-OH$

XVI



$CH_2=C(CH_3)-C(C_6H_5)-CH_3$

XVII

Experimental[26]

Oxime IIa.—*t*-Butylmagnesium chloride[27] was treated with benzaldehyde[28] to give a 60% yield of α-phenylneopentyl alcohol (III), b.p. 97–100° at 7 mm., m.p. 43–44° (recrystallized from petroleum ether); reported b.p. 98–105° at 7 mm., m.p. 45°.[28] This alcohol was oxidized with potassium dichromate and sulfuric acid[29] to give a 50% yield of pivalophenone (IV), b.p. 104–106° at 13 mm. (reported 103–104° at 13 mm.[30]). This ketone was converted in 90% yield to oxime IIa, m.p. 165–166° (recrystallized from ethanol–water); reported m.p. 165°,[31] 166–167°.[30]

Oxime IIb.—*n*-Butyrophenone (62 g., 0.42 mole) was metalated with a benzene suspension of 0.439 mole of sodium amide[32] (1.5 hr. refluxing), and the sodio ketone ethylated with 72 g. (0.46 mole) of ethyl iodide[33] (1 hr. refluxing) to give 64 g. (86%) of α,α-diethylacetophenone, b.p. 124–128° at 18 mm. This ketone was metalated with a benzene suspension of 0.38 mole of sodium amide (3 hr. refluxing) and the sodio ketone ethylated with 62.4 g. (0.4 mole) of ethyl iodide (3 hr. refluxing) to give, after fractionating through a 38-cm. glass-helices packed column, 52 g. (61%) of triethylacetophenone (V), b.p. 147–148° at 16 mm., reported b.p. 145–146° at 16 mm.[33] This ketone was converted to oxime IIb in 84% yield by refluxing 3 days with hydroxylamine hydrochloride, anhydrous pyridine and absolute ethanol and recrystallizing the product from 95% ethanol. The oxime melted at 162–163°, reported 160–161°.[33]

Anal. Calcd. for $C_{14}H_{21}NO$: N, 6.39. Found: N, 6.57.

Oxime IIc. (A) Through Imine.—Phenylacetonitrile (50.0 g., 0.428 mole) in 50 ml. of ethyl ether was metalated with a suspension of 0.449 mole of sodium amide[32] in 500 ml. of liquid ammonia (10 minutes stirring), and the sodio nitrile methylated with 67.1 g. (0.437 mole) of methyl iodide (1.5 hr. stirring) to give 50 g. (89%) of α-methylphenylacetonitrile, b.p. 116–117° at 20 mm. This nitrile was metalated with 0.42 mole of sodium amide in ether (10 minutes stirring), and the sodio nitrile methylated with 59.5 g. (0.419 mole) of methyl iodide (1 hr. stirring) to give after fractionating through the 38-cm. column, 40 g. (65% over-all yield) of α,α-dimethylphenylacetonitrile,[34] b.p. 113.5–114° at 20 mm., n^{25}D 1.5032 (reported b.p. 114–116° at 20 mm.)[35]. These constants were the same after retreatment with sodium amide and methyl iodide.

Anal. Calcd. for $C_{10}H_{11}N$: C, 82.71; H, 7.64; N, 9.65. Found: C, 82.88; H, 7.67; N, 9.64.

This nitrile (83.5 g., 0.575 mole) was refluxed 12 hours with a xylene suspension of phenylmagnesium bromide (prepared from 0.822 mole of bromobenzene and magnesium in ether). The cooled mixture was filtered rapidly, and, after washing with dry xylene, the solid addition complex was decomposed with cold ammonium chloride solution. The liberated dimethyldesoxybenzoin imine was taken up in ether[36] from which it was precipitated as its hydrochloride (VI, R = CH_3), yield 91 g. (60%).

The imine hydrochloride (25 g., 0.0963 mole) was treated with hydroxylamine hydrochloride (10.1 g., 0.145 mole) and sodium acetate (20.5 g., 0.25 mole) in aqueous ethanolic solution to precipitate immediately oxime IIc, m.p. 189.5–190.5° (recrystallized from ethanol–water), reported m.p. 192–193°,[36] yield 20.8 g. (90%).

(B) Through Ketone.—Dimethyldesoxybenzoin imine hydrochloride (VI, R = CH_3) (47 g., 0.181 mole), prepared as described in (A), was hydrolyzed with a mixture of hot concentrated hydrochloric acid and 95% ethanol to give 35 g. (86%) of dimethyldesoxybenzoin (VII, R = CH_3), m.p. 46–47° (recrystallized from petroleum ether), reported m.p. 46–47°.[36] This ketone was converted in 91% yield to oxime IIc, m.p. 189–190°, by refluxing 20 hr. with hydroxylamine hydrochloride in pyridine and ethanol.

Oxime IIc (m.p. 187°) was also obtained through the ketone prepared from thiophene-free benzene (600 ml.), α-bromoisobutyric acid (110 g., 0.65 mole), and anhydrous aluminum chloride (175 g., 1.31 moles) (refluxed 15 hours). The resulting dimethylphenylacetic acid (VIII, 71% yield), b.p. 167–168° at 15 mm., m.p. 75.5–77° (reported b.p. 150–155° at 10 mm., m.p. 77–78°),[37] was converted by means of thionyl chloride to the acid chloride (98% yield), b.p. 105–106° at 13 mm. (reported 109° at 13 mm.[38]), which was treated with cadmium phenyl[39] to give dimethyldesoxybenzoin (VII, R = CH_3, 82% yield), m.p. 44.5–46°, after two recrystallizations from petroleum ether.

Oxime IId. (A). Through Imine.—Phenylacetonitrile was diethylated as described above for the dimethylation, employing first 40 g. (0.342 mole) of the nitrile, 0.359 mole of sodium amide[32] and 41 g. (0.376 mole) of ethyl bromide, and secondly, all (33.4 g.) of the monoethylated product (b.p. 112–117° at 13 mm.), 0.241 mole of sodium amide and 27.6 g. (0.253 mole) of ethyl bromide. There was obtained 34 g. (57%, over-all yield) of α,α-diethylphenylacetonitrile, b.p. 119–120° at 13 mm., n^{28}D 1.5003 (reported b.p. 115–118° at 13 mm.[40]). These constants were the same after retreatment with sodium amide and ethyl bromide.

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.19; H, 8.73; N, 8.08. Found: C, 83.38; H, 8.78; N, 8.26.

This nitrile (34 g., 0.196 mole) was refluxed 24 hours with a toluene suspension of phenylmagnesium bromide[41] (prepared from 0.34 mole of bromobenzene and magnesium in ether) to give, after treatment of the reaction mixture with the calculated amount of 6 *N* hydrochloric acid, the hydro-

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[24] Mme. Ramart-Lucas, *Ann. chim.*, [8] **30**, 390 (1913).

[25] D. E. Bateman and C. S. Marvel, THIS JOURNAL, **49**, 2914 (1927).

[26] Boiling points and melting points are uncorrected. Analyses are by Clark Microanalytical Laboratory, Urbana, Ill.

[27] S. V. Puntambeker and E. A. Zoellner, "Organic Syntheses," Coll. Vol. I, 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 524.

[28] J. B. Conant and A. H. Blatt, THIS JOURNAL, **50**, 551 (1928); A. Lepin, *Chem. Zentr.*, **83**, II, 2080 (1912).

[29] See L. T. Sandborn, ref. 27, p. 34.

[30] A. Haller and Ed. Bauer, *Compt. rend.*, **148**, 72 (1909).

[31] J. U. Nef, *Ann.*, **310**, 320 (1899).

[32] This reagent was prepared from the calculated amount of sodium in liquid ammonia assuming quantitative conversion to the sodium amide. The liquid ammonia was replaced by ether or benzene, most of the ammonia being allowed to evaporate before adding the latter solvent. See J. T. Adams and C. R. Hauser, THIS JOURNAL, **66**, 1220 (1944).

[33] See A. Haller and Ed. Bauer, *Compt. rend.*, **148**, 73 (1909).

[34] Acid hydrolysis of a sample of this nitrile gave α,α-dimethylphenylacetic acid, m.p. 79–80°, reported 80–81° (ref. 35).

[35] A. Haller and Ed. Bauer, *Compt. rend.*, **155**, 1582 (1912).

[36] See Mme. Bruzau, *Ann. chim.*, [11] **1**, 332 (1934).

[37] O. Wallach, *Chem. Zentr.*, **70**, II, 1047 (1899).

[38] I. Heilbron, "Dictionary of Organic Compounds," Vol. III, Oxford University Press, New York, N. Y., 1938, p. 425.

[39] See J. Cason, *Chem. Revs.*, **40**, 15 (1947).

[40] M. M. Rising and E. W. Lowe, THIS JOURNAL, **52**, 2524 (1930).

[41] (a) Mme. Ramart-Lucas and M. F. Salmon-Legagneur, *Bull. soc. chim.*, [4] **43**, 321 (1928); (b) Mme. Ramart-Lucas and M. Anagnostopoulos, *ibid.*, [4] **43**, 1315 (1928).

TABLE V

AMINES Ia-d FROM THE REDUCTION OF OXIMES

Oxime	Amine	B.p. °C.	Mm.	$n^{25}D$	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
IIa	1-Phenylneopentyl (Ia)[a]	115–115.5	22	....	95	80.92	80.80	10.50	10.49		
IIb	1-Phenyl-2,2-diethylbutyl (Ib)[b]	144–145	12	1.5170	80	81.88	81.80	11.29	11.44	6.82	6.79
IIc	1-Phenylneophyl (Ic)[c]	155 m.p. 35–37.5	5	....	88	85.27	85.39	8.51	8.77	6.22	6.26
IId	1,2-Diphenyl-2-ethylbutyl (Id)	172–173	5	1.5685	87	85.32	85.13	9.15	9.10	5.53	5.56

[a] Billon (ref. 42, p. 348) reported this amine, b.p. 115° at 22 mm. [b] The substituted phenylthiourea prepared from amine Ib and phenyl isothiocyanate melted at 161–162°. *Anal.* Calcd. for $C_{21}H_{28}N_2S$: S, 9.42. Found: S, 9.67. [c] The substituted benzamide, prepared from amine Ic and benzoyl chloride, melted at 134.5–135.5°. *Anal.* Calcd. for $C_{23}H_{23}NO$: N, 4.25. Found: N, 4.28.

chloride of diethyldesoxybenzoin imine (VI, R = C_2H_5) (39.5 g.) (70%).

The imine hydrochloride (39.5 g., 0.137 mole) was treated with hydroxylamine hydrochloride (19.0 g., 0.274 mole) and potassium acetate (40.3 g., 0.411 mole) in aqueous ethanolic solution to precipitate almost immediately oxime IId, m.p. 188–189° (recrystallized from 95% ethanol), reported m.p. 187–188°,[41a] yield 30 g. (82%).

(B) **Through Ketone.**—Diethyldesoxybenzoin imine hydrochloride, prepared as described in (A), was hydrolyzed to diethyldesoxybenzoin (VII, R = C_2H_5), m.p. 48.5–49.5° (reported 48–49°[41a]) which on refluxing 24 hr. with hydroxylamine hydrochloride in pyridine and ethanol, gave only a 41% yield of pure oxime IId, m.p. 188–189°.

Amines Ia–d from Reduction of Oximes IIa–d.—To a stirred solution of 0.3–0.5 mole of the oxime in 0.6–1 liter of absolute ethanol was added in small portions 3.6–6.0 g. atoms of sodium,[42] the mixture being warmed and more ethanol added during the later stages of the reaction. After adding water and distilling most of the ethanol, the amine was taken up in ether from which it was extracted with dilute hydrochloric acid and recovered. The hydrochloride of amine Ic partially precipitated during the extraction. The yields of amine and other data are summarized in Table V.

Reactions of Amines Ia–d with Nitrous Acid. General Procedure.—In a three-necked, round-bottomed flask fitted with mechanical stirrer, thermometer and a short condenser (to the end of which was attached a bent piece of glass tubing dipping below the surface of water in a beaker) were placed 0.2–0.5 mole of the amine and 800–900 ml. of water. To the vigorously stirred mixture was added an amount of concentrated hydrochloric acid equivalent to the amine. After the amine had dissolved, two to three equivalents of solid sodium nitrite were added (in small portions to amine Ia), the temperature of the reaction mixture being kept at 25–50°. Some nitrogen was evolved immediately and an oil separated. The mixture was warmed at 40–50° until nitrogen ceased to be evolved (3–6 hr.), then was extracted several times with ether. The ether solution was washed successively with cold 2 *N* hydrochloric acid, 10% sodium hydroxide (until the washings were no longer colored), and water, and dried. The solvent was removed, and the residue fractionated *in vacuo* through a glass-helices packed column or a 60-cm. tantalum spiral Podbielniak column.[43] Small amounts of the amine usually were recovered from the hydrochloric acid extracts of the reaction mixtures, and these were either retreated with nitrous acid or taken into account in calculating the yields of products.

Results with Amine Ia.—This amine (0.451 mole) gave 4 g. of nitrite ester, b.p. 80–85° at 8 mm., and 65 g. of an alcohol fraction, b.p. 98–102° at 8 mm., which became semi-solid at room temperature. No olefin was found. The nitrite ester gave a positive sodium fusion test for nitrogen, evolved nitric oxide with cold sulfuric acid, and underwent alkaline hydrolysis to form the unrearranged alcohol III (3 g.), m.p. and mixed m.p. 43–44°. The semi-solid alcohol fraction (65 g.) was filtered with suction to give 49.5 g. of solid, m.p. 39–42°, and 15 g. of oil. Two recrystallizations of the solid from petroleum ether yielded 46 g. of the pure unrearranged alcohol III, m.p. and mixed m.p. 43–44°. More (9.6 g.) of this pure alcohol was obtained on treating the 15 g. of oil with 14.2 g. of phthalic anhydride and 14.5 g. of dry pyridine,[6] followed by saponification of the resulting phthalate acid ester with 25% sodium hydroxide. The total yield of the pure unrearranged alcohol III including that from the hydrolysis of the nitrite ester was 80%.

The phthalic anhydride treatment left 5 g. of oil, 3.5 g. boiling at 95–97° at 11 mm., which was apparently unaffected on refluxing 2 hours with 20% sulfuric acid. The oil recovered from this treatment, on oxidation with alkaline permanganate, gave pivalophenone which was identified as its oxime (1.6 g.). Under similar conditions, an authentic sample of α-phenylneopentyl alcohol (III, see oxime IIa) gave an analogous result, whereas a sample of the isomeric alcohol, 2-methyl-3-phenyl-2-butanol (VIII) was dehydrated by the sulfuric acid to form mainly α,β,β-trimethylstyrene (IX) which was oxidized by the permanganate to give acetophenone (identified as the 2,4-dinitrophenylhydrazone and semicarbazone). Alcohol VIII was synthesized in 41% yield by methylating phenylacetone[44] and condensing the resulting ketone with methylmagnesium iodide.[6] The product boiled at 104–105° at 12 mm., $n^{25}D$ 1.5154; reported b.p. 105–107° at 12 mm.,[13] $n^{25}D$ 1.5158.[6]

Results with Amines Ib, Ic and Id.—These amines gave olefin and alcohol fractions which generally were refluxed with 10–20% sodium hydroxide to remove the yellow color and refractionated through the column. The results are summarized in Table I. The constituents of the olefin and alcohol fractions were determined and the independent syntheses of authentic samples of compounds employed in these determinations were effected as described below.

Constituents of the Olefin Fractions. Ozonolysis.—The olefin mixture (4–6 g.) in 100 ml. of chloroform, cooled to 0°, was treated with oxygen containing 4% of ozone[45] until the calculated amount of ozone had been absorbed. The solvent was removed at room temperature under reduced pressure (water aspirator) and a solution of the oily residue of ozonides in 50–60 ml. of absolute ethanol or ethyl acetate hydrogenated at atmospheric pressure using palladium-on-calcium carbonate as a catalyst.[46] The amount of hydrogen absorbed varied from 50–100% of the calculated quantity. The solvent was distilled[47] and aliquots of the distillate, collected in a Dry Ice-cooled trap, treated with methone[48] or 2,4-dinitrophenylhydrazine to produce appropriate derivatives of the low-boiling carbonyl compounds. The residue, after treatment with a little dilute acid to destroy the calcium carbonate of the catalyst, was extracted with ether and the ether solution fractionated to yield the higher boiling ketones. The catalyst was sometimes removed from the reaction mixture by centrifuging prior to the removal of the solvent. The fractional distillation afforded a satisfactory separation of propiophenone and 4-phenyl-3-hexanone but not of benzophenone and α,α-diphenylacetone or ethyl benzhydryl ketone. The mixture of benzophenone and α,α-diphenylacetone was treated with excess 2,4-dinitrophenylhydrazine reagent and the derivatives of the two ketones separated by fractional crystallization from ethanol. The mixture of benzophenone and ethyl benzhydryl ketone was treated with semicarbazide under conditions that produced the semicarbazone of only the latter ketone. The benzophenone was then separated from this derivative and identified as its 2,4-dinitrophenylhydrazone.

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(42) See P. Billon, *Ann. chim.*, **7**, 333 (1927).

(43) J. Cason and H. Rapoport, "Laboratory Text in Organic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1950, p. 237.

(44) C. M. Suter and A. W. Weston, THIS JOURNAL, **64**, 533 (1942).

(45) See L. I. Smith, F. L. Greenwood and O. Hudrlik, *Org. Syntheses*, **26**, 63 (1946).

(46) See F. G. Fischer, H. Düll and L. Ertel, *Ber.*, **65**, 1467 (1932).

(47) When less than the calculated amount of hydrogen was absorbed, 1–2 ml. of water was added to the reaction mixture before distilling the solvent.

(48) D. Vorländer, *Z. anal. Chem.*, **77**, 241 (1929).

The results are summarized in Table II (expts. 1, 2 and 3), the yields being based on essentially pure compounds. The derivatives of the aldehydes and ketones were identified by the mixed melting point method. Three ketones and two olefins were independently synthesized for comparative purposes.

Independent Synthesis of Ketones of Type $RCH_2COCH(C_6H_5)R'$.—α,α-Diphenylacetone was prepared as described previously.[49] The 2,4-dinitrophenylhydrazone melted at 142–143°.

4-Phenyl-3-hexanone was prepared from cadmium ethyl and α-phenylbutyryl chloride according to the general method described by Cason.[39] The product boiled at 121–122° at 20 mm., $n^{25}D$ 1.4977 and d^{20}_4 0.931; reported b.p. 114–116° at 13 mm.[50]

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.68; H, 9.32.

The semicarbazone melted at 141–141.5° after recrystallization from ethanol–water; reported 139–140°.[50]

Anal. Calcd. for $C_{13}H_{19}N_3O$: C, 66.92; H, 8.21; N, 18.01. Found: C, 67.10; H, 7.99; N, 18.05.

Ethyl benzhydryl ketone was prepared by adding 0.24 mole of propionyl chloride in 30 ml. of ether to a stirred suspension of potassium diphenylmethide (from 0.475 mole of potassium amide and 0.475 mole of diphenylmethane)[51] in 400 ml. of ether. After refluxing 10 hours and adding water, the ether layer was washed with sodium bicarbonate solution, dried and distilled to give a 39% yield of the ketone boiling at 169–170° at 8 mm., m.p. 36–37° after recrystallization from petroleum ether; reported b.p. 184–188° at 17 mm.,[52] m.p. 35–36°.[53] The semicarbazone, obtained in 80% yield from 1 g. of the ketone, melted at 190–191°; reported m.p. 190–191°.[53]

Independent Synthesis of Type XII Olefin (Scheme A).—Diphenylisopropylcarbinol (11.4 g.), prepared from ethyl isobutyrate and phenylmagnesium bromide, was dehydrated with acetic anhydride (30 ml.) and sulfuric acid (5 drops) at 100° for 12 hours to give 8.4 g. (80%) of **1,1-diphenyl-2,2-dimethyl ethylene (XIIc)**, b.p. 153–154° at 16 mm., $n^{25}D$ 1.5871, d^{20}_4 0.975; reported b.p. 150–152° at 15 mm.[54] Samples of the olefin were converted by monoperphthalic acid[55] in ether at room temperature to the corresponding oxide, m.p. 61–62° after recrystallization from ligroin, and by chromic anhydride in acetic acid to only acetone and benzophenone which were identified by suitable derivatives.

1,1-Diphenyl-2-ethyl-1-butanol was obtained in 65% yield from methyl 2-ethylbutyrate and excess phenylmagnesium bromide (15 hr. refluxing). The product boiled at 192–193° at 14 mm., $n^{25}D$ 1.5611; reported b.p. 186° at 15 mm.[41b] The carbinol (35 g.) was dehydrated with acetic anhydride (32 ml.) and sulfuric acid (3 drops) at 100° for 3 hours to give 27.5 g. (85%) of **1,1-diphenyl-2,2-diethylethylene (XIId)**, b.p. 162–163° at 12 mm., $n^{25}D$ 1.5698, d^{20}_4 0.955, reported 160° at 11 mm.[41b]

Anal. Calcd. for $C_{18}H_{20}$: C, 91.47; H, 8.53. Found: C, 91.60; H, 8.62.

Oxidation of the olefin with chromic anhydride in acetic acid at 70–80° gave only diethyl ketone and benzophenone (identified as their 2,4-dinitrophenylhydrazones).

Constituents of the Alcohol Fractions.—The alcohol fractions from amines Ib–d (Table I) were further fractionated, and the physical constants of the resulting cuts compared with those of authentic samples of the unrearranged and rearranged alcohols (Table III). The constituents of the alcohol fractions were determined (usually after combining the cuts), as described below.

A 3-g. sample of the highest boiling cut of **the alcohol fraction from amine Ib** was heated at 80–90° for 24 hours with 2.26 g. of phthalic anhydride and 2.31 g. of pyridine. After adding 35 ml. of chloroform, the mixture was stirred with ice containing 2.5 ml. of 12 *N* hydrochloric acid. The organic layer was washed with water, dried and the solvent removed. After stirring with a little hexane, the residue was recrystallized from ethanol–water to give 4.1 g. (80%) of the phthalate ester of the unrearranged alcohol (Xb), m.p. 182–183°.

Anal. Calcd. for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.30; H, 7.38.

A mixed melting point with an authentic sample of this phthalate was the same. The authentic sample was obtained (also in 80% yield) from independently synthesized alcohol Xb. Independently synthesized alcohol XIb failed to give a phthalate under similar conditions.

The remainder of the highest boiling cut and the three other cuts of **the alcohol fraction from amine Ib** (see Table III) were combined (38 g.) and similarly treated with 27.3 g. of phthalic anhydride and 29.1 g. of pyridine to give 46 g. (70%) of the phthalate of the unrearranged alcohol, m.p. 180–182°, and 7 g. of oil. After washing with 5% sodium carbonate, this oil was fractionated to give 2.6 g. of olefin (b.p. 116–118° at 16 mm., $n^{25}D$ 1.5065), 2.4 g. of the unrearranged alcohol, and small amounts of mid-fractions. The olefin gave qualitative tests for unsaturation.

The combined cuts of **the alcohol fraction from amine Ic** (31.7 g., 0.14 mole) was heated with 25.0 g. (0.21 mole) of phenyl isocyanate at 80–90° for 10 hours and allowed to stand at room temperature 24 hours, care being taken to exclude atmospheric moisture. The viscous mixture was heated with 250 ml. of dry carbon tetrachloride, and the insoluble diphenyl urea (a by-product of the reaction) removed by filtration. The filtrate was concentrated to 100 ml., and 25 ml. of hexane added to give, after recrystallization from carbon tetrachloride, 24.5 g. (51%) of the urethan of the unrearranged alcohol (Xc), m.p. 143–145°. A mixed melting point with an authentic sample of the urethan of alcohol Xc was the same.

The filtrates from these operations were combined, concentrated, and chromatographed through an alumina column which had been previously wetted with hexane. Elution with hexane produced an oil which, on distillation, gave 6.7 g. (23%) of a mixture of the isomeric olefins, XIIc and XIIIc, b.p. 151–152° at 15 mm., $n^{25}D$ 1.5774 (see Table II, expt. 4).

Anal. Calcd. for $C_{16}H_{16}$: C, 92.25; H, 7.75. Found: C, 91.85; H, 8.11.

No attempt was made to characterize non-olefinic material remaining in the alumina column.

When 10.4 g. (0.0459 mole) of independently synthesized alcohol Xc was treated with 8.2 g. (0.069 mole) of phenyl isocyanate under similar conditions, there was obtained 14 g. (88%) of the urethan, m.p. 144–145° after recrystallization from carbon tetrachloride; reported 137°.[56]

Anal. Calcd. for $C_{23}H_{23}NO_2$: C, 79.97; H, 6.71. Found: C, 80.22; H, 6.86.

No olefinic material was recovered on chromatographing the residual oil (1–2 g.), obtained as a by-product in the preparation of the urethan, using hexane as an eluting agent.

When 10.0 g. (0.0442 mole) of independently synthesized alcohol XIc was treated similarly with 7.9 g. (0.0663 mole) of phenyl isocyanate there was obtained 6.0 g. (65%) of isomeric olefins, XIIc and XIIIc (see Table II, expt. 5), b.p. 148–150° at 14 mm., $n^{25}D$ 1.5786.

Anal. Calcd. for $C_{16}H_{16}$: C, 92.25; H, 7.75. Found: C, 91.86; H, 7.97.

The combined cuts of **the alcohol fraction from amine Id** (25.0 g., 0.098 mole) was heated at 100° for 5 hours with 11.7 g. (0.0985 mole) of phenyl isocyanate and allowed to stand at room temperature for 15 hours. After cooling, the mixture was heated with 150 ml. of carbon tetrachloride and filtered to remove a small amount of diphenylurea. The filtrate was concentrated to give, after recrystallization from carbon tetrachloride, 26.7 g. (73%) of the urethan of the unrearranged alcohol, m.p. 160–161°. A mixed melting point with an authentic sample of the urethan of the unrearranged alcohol was the same.

The combined carbon tetrachloride filtrates were concentrated, and stirred for several hours with cold water. After adding some carbon tetrachloride and filtering, the organic layer of the filtrate was dried and chromatographed through an alumina column wetted with hexane. Elution with this solvent gave 1.69 g. (0.0715 mole, 7.3%) of an olefin boiling at 160–164° at 11 mm., $n^{25}D$ 1.5650. The column was then

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"stripped" with a mixture of hexane and acetone, followed by evaporation of the solvent to give a brown oil from which was isolated 1.7 g. (7%) of the rearranged alcohol, m.p. 62–63°, after two recrystallizations from petroleum ether. A mixed melting point with an authentic sample of the rearranged alcohol was the same.

When 10.0 g. (0.0393 mole) of independently synthesized alcohol Xd was treated with 4.68 g. (0.0393 mole) of phenyl isocyanate under similar conditions, there was obtained 13.4 g. (91%) of the urethan, m.p. 161–161.5° after recrystallization from carbon tetrachloride, reported m.p. 157°.[41b]

Anal. Calcd. for $C_{25}H_{27}NO_2$: C, 80.39; H, 7.29; N, 3.75. Found: C, 80.52; H, 7.41; N, 3.82.

When 5.95 g. (0.0234 mole) of independently synthesized alcohol XId was treated similarly with phenyl isocyanate (2.79 g., 0.0234 mole) and chromatographed there was obtained 2.4 g. (43%) of an olefin, b.p. 161–162° at 11 mm., $n^{25}\text{D}$ 1.5659, and 2.5 g. (42%) of recovered alcohol, m.p. 62–63°.

Independent Syntheses of Alcohols of Types X and XI (Scheme A).—**1-Phenyl-2,2-diethyl-1-butanol** (Xb) was prepared by adding 12 g. (0.059 mole) of triethylacetophenone (V) in 30 ml. of ether to a stirred suspension of 2.23 g. (0.06 mole) of lithium aluminum hydride in 30 ml. of ether. After 2 hours at room temperature, the reaction mixture was hydrolyzed with 10% sodium hydroxide to give 10.5 g. (87%) of the alcohol, b.p. 156° at 15 mm., $n^{25}\text{D}$ 1.5198.

Anal. Calcd. for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.68; H, 10.90.

3-Ethyl-4-phenyl-3-hexanol (XIb) was synthesized from 20.0 g. (0.112 mole) of methyl α-phenylbutyrate (b.p. 113–114° at 17 mm., $n^{25}\text{D}$ 1.4951) and a benzene suspension (100 ml.) of ethylmagnesium bromide (prepared from 0.25 mole of ethyl bromide and magnesium in ether). After refluxing 24 hours, the reaction mixture was decomposed with ammonium chloride to give 16 g. (69%) of the alcohol, b.p. 137–138° at 16 mm., $n^{25}\text{D}$ 1.5096, d^{20}_4 0.937.

Anal. Calcd. for $C_{14}H_{22}O$: C, 81.49; H, 10.75. Found: C, 81.69; H, 10.69.

1-Phenylneophyl alcohol (Xc) was prepared from 8.70 g. (0.0388 mole) of dimethyldesoxybenzoin (VII, R = CH_3) and 1.47 g. (0.0388 mole) of lithium aluminum hydride in ether by the method described above; yield 6.8 g. (78%), b.p. 184° at 14 mm. (179° at 11.5 mm.), $n^{25}\text{D}$ 1.5735, reported b.p. 185–190° at 18 mm.[56]

Anal. Calcd. for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 85.17; H, 7.99.

2-Diphenylmethyl-2-propanol (XIc) was obtained by adding during 12 hours benzhydryl chloride (60.0 g., 0.296 mole) in 300 ml. of anhydrous ether to a stirred, refluxing suspension of 216 g. (8.9 g. atoms) of powdered magnesium in 400 ml. of ether,[57] followed (after cooling), by 17.2 g. (0.296 mole) of purified acetone. After 4 hours at room temperature, the mixture was poured onto ice and ammonium chloride to give (after dissolving the precipitated magnesium salts with cold 5% sulfuric acid) 30.6 g. (46%) of the alcohol, b.p. 151–152° at 5.5 mm. (168–169° at 11.5 mm.), $n^{25}\text{D}$ 1.5722.

Anal. Calcd. for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 85.19; H, 8.14.

1,2-Diphenyl-2-ethyl-1-butanol (Xd) was synthesized from 15.0 g. (0.0595 mole) of diethyldesoxybenzoin (VII, R = C_2H_5) and 2.25 g. (0.0595 mole) of lithium aluminum hydride in ether by the method described above; yield 12.8 g. (85%), b.p. 197–197.5° at 12 mm., $n^{25}\text{D}$ 1.5686, reported b.p. 209° at 20 mm.[41b]

Anal. Calcd. for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 85.21; H, 8.69.

3-Diphenylmethyl-3-pentanol (XId) was prepared from 21.0 g. (0.0936 mole) of ethyl benzhydryl ketone (see above) and ethylmagnesium bromide (from 0.109 mole of ethyl bromide and magnesium) in 150 ml. of ether. After refluxing 24 hours, the mixture was hydrolyzed with saturated ammonium chloride solution to give 5.0 g. (21%) of the alcohol boiling at 161–162° at 5 mm. (181–182° at 12 mm.), m.p. 62.5–63.5° after recrystallization from petroleum ether.

Anal. Calcd. for $C_{18}H_{22}O$: C, 84.99; H, 8.72. Found: C, 84.95; H, 8.52.

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DURHAM, N. C.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF REED COLLEGE, UNIVERSITY OF WASHINGTON AND UNIVERSITY OF CALIFORNIA]

The α-Hydrogen Reactivity of Thiolesters[1,2]

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Ethyl thiolacetate has been found to undergo Claisen condensation with isopropylmagnesium bromide to give 60–70% yields of ethyl acetothiolacetate and the relative rate of reaction of benzaldehyde with ethyl dithiolmalonate in the Knoevenagel condensation has been found to be about four times the rate for the corresponding reaction with ethyl malonate. These observations are indicative of an increase in the acidity of the hydrogen alpha to a carbethoxy group upon replacement of oxygen by sulfur to give a thiolester. Isopropylmagnesium bromide reacts with *t*-butyl thiolacetate to give a relatively stable Grignard of the thiolester, $BrMgCH_2COSC(CH_3)_3$. This reagent reacted with cyclohexanone in a Reformatsky-type reaction to give 65% of *t*-butyl 1-hydroxycyclohexylthiolacetate which was desulfurated with Raney nickel to give 80% of 2-(1-hydroxycyclohexyl)-ethanol.

Although there have been some indications of differences in the behavior of esters and thiolesters[4–8] the chemical and physical properties of thiolesters have not been investigated extensively. The discovery of coenzyme A and its importance in acylation and other metabolic processes[9,10] and the finding that acyl derivations of coenzyme A are thiolesters[11] has created additional interest in the chemistry of these esters.[12–14]

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