Table I. Pyrolysis of Acetophenone over UOP No. 1

reactant[a]	temp, °C	pressure,[b] mmHg	% 2a[f]
1a	400	0.4	2
1a	500	0.6	11
1a	630	0.7	28
1a	500	33	4
1a	582	760[e]	2
1a[c]	614	760[e]	3
1a[c]	600	0.5	21
1a[d]	600	0.5	0

[a] 5 g of acetophenone and 5 g of UOP No. 1 were used. [b] All of the acetophenone had passed through the tube in 30–60 min. This corresponds at 600 °C (1 mmHg) to a residence time of 0.3–0.6 s. [c] 20 g of UOP No. 1 was used. [d] Run without UOP No. 1 present. [e] 0.5 SCFM flow of N_2 was used. [f] Acetophenone (1a) and small amounts of water were also recovered. A mass greater than 90% was typically observed.

Table II. Pyrolysis of 7 at Various Temperatures[a]

reagent	temp, °C	pressure, mmHg	% 2a	% 1a	% 7	% 8
7	420	0.03			95	
7	534	0.03			92	tr
7[b]	529	0.05			95	tr
7	650	0.05	5	6	9	72
7	700	0.05	6	12	36	36
7	760	0.7	30	30		
8	760	0.4	37	60		
2a	700	0.2	95			

[a] Without catalyst, product collected in dry ice bath. [b] Contained large acidic glass surface area.

was placed in the reactor and allowed to flash distill through the tube. Reactions at atmospheric pressure were carried out under a nitrogen flow of 0.5 SCFM. Volatile products were collected in dry ice/acetone. Then the products were dissolved in ether and dried over anhydrous magnesium sulfate and the ether was removed in vacuo under conditions where losses of phenylacetylene or acetophenone were minimized. The products were analyzed by NMR and GC on a 2-ft UCW 982 column and by comparison with authentic samples. Results are shown in Table I.

Synthesis of Diethyl 1-Phenylvinyl Phosphate (5). To 15.5 g (0.1 mol) of phenacyl chloride in a 200-mL one-neck flask was added 16.6 g (0.1 mol) of triethyl phosphite. This was heated at 86 °C for 4 h with stirring. The product was then distilled at 121 °C (0.03 mm) [lit.[10] bp 101–105 °C (0.005 mm)], and 21.9 g was recovered: 86% yield; NMR ($CDCl_3$) δ 7.2–7.8 (m, 5 H, aromatic H), 5.25 (d, 2 H, C=CH_2, J = 3 Hz), 4.20 (q, 2 H, OCH_2, J = 8 Hz), 4.33 (q, 2 H, OCH_2, J = 8 Hz), 1.38 (t, 6 H, CH_3, J = 8 Hz).

Preparation of 1-Phenylvinyl Acetate (7). To 40 mL of isopropenyl acetate in a flask equipped with a magnetic stirrer and distillation head was added 24 g (0.2 mol) of acetophenone and 0.2 g of *p*-toluenesulfonic acid. After heating for 7 h at 98–118 °C, 15 mL of acetone had distilled and approximately 75% conversion to 7 was observed by NMR sampling of the product mixture. The reaction was then cooled, extracted with ether, and washed once with 10 g of sodium bicarbonate in 100 mL of ice water. The ether was then dried over anhydrous magnesium sulfate and removed in vacuo. The product distilled at 90 °C (4 mm)[lit. 92–95 °C (4.5 mm)][14] and 18 g was recovered: 56% yield; NMR ($CDCl_3$) δ 7.4 (m, 5 H, ring H's), 5.60 (d, 1 H, C=CH, J = 2 Hz), 5.10 (d, 1 H, C=CH, J_1 = 2 Hz), 2.30 (s, 3 H, CH_3).

Pyrolysis on 7 to Form 1-Phenyl-1,3-butanedione. Enol acetate (7; 2.0 g) was flash distilled through a quartz pyrolysis tube at 650 °C at 0.5 mm of vacuum. The product 8 (1.81 g, 90% yield) was collected in an ice bath and recrystallized from ethanol–water: mp 56–57 °C (lit.[11] mp 60 °C); NMR ($CDCl_3$) δ 7.2–8.0 (m, 5 H, ring H), 6.20 (s, 1 H, vinyl H), 2.60 (s, 2 H, CH_2 keto form), 2.20 (s, 3 H, CH_3). The product 8 was present in keto and enol forms and gave a positive ferric chloride test. Results for pyrolysis of 7 at other temperatures are reported in Table II. All products were identified by comparison with authentic samples (NMR, GC).

(14) D. S. Noyce and R. M. Pollack, *J. Am. Chem. Soc.*, **91**, 119 (1969).

Registry No. 1a, 98-86-2; **2a**, 536-74-3; **5**, 1021-45-0; **6a**, 93-55-0; **6b**, 673-32-5; **7**, 2206-94-2; **8**, 93-91-4; phenacyl chloride, 532-27-4; triethyl phosphite, 122-52-1; isopropenyl acetate, 591-87-7.

Convenient One-Step Synthesis of N-Substituted α-Methylphenethylamines via Aminomercuration–Demercuration

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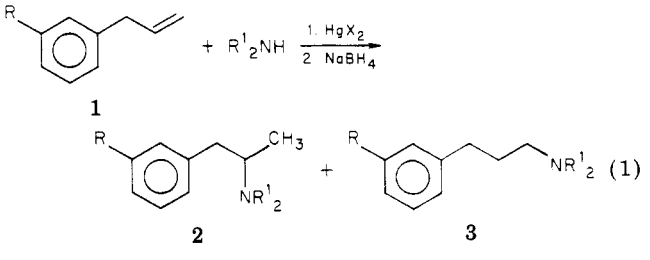
Phenethylamines are important natural precursors to a variety of alkaloid systems[1] as well as large ring benzoheterocycles[2] and are themselves also widely used as drugs.[3]

In our present work, we considered the recently developed[4] aminomercuration–demercuration reaction as a possible general route to N-substituted α-methylphenethylamines via a reaction of type 1, the Markownikoff product 2 being the desirable addend for our purposes. No such route to N-substituted amphetamines has been previously described. Of particular interest to us was the synthesis of the aminoacetaldehyde diethyl acetal derivative **2a** (R = OCH_3; R^1 = H, $CH_2CH(OEt)_2$), which is a useful synthon for the preparation of 3*H*-3-benzazepines.[5]



Our initial studies involved, as a prototype reaction, the addition of *m*-methoxyallylbenzene (1.2 equiv) to a mixture of the appropriate mercuric salt (1.5 equiv) and aminoacetaldehyde diethyl acetal (4 equiv) in THF with subsequent heating to 60 °C to expedite formation of the intermediate organomercurials. In all cases, rapid formation of amine–mercury complexes was observed prior to the addition of the olefin substrate. The rate of aminomercuration proved to be a sensitive function of the mercuric salt employed. The order of reactivity of the various mercury salts increased in the order $HgCl_2$ <

(1) S. W. Pelletier, "Chemistry of the Alkaloids", Van Nostrand-Reinhold, New York, 1970.
(2) Georges Hazebroucq, "Access to 1*H*-Tetrahydro-2,3,4,5-benzazepine-3-ones", Ph.D. Thesis, University of Paris, in Annales De Chimie, Series 14, Vol. 1, 1966.
(3) C. D. Leake, "The Amphetamines: Their Actions and Uses", Charles C. Thomas Co., Springfield, Ill., 1958.
(4) (a) A. Lattes and J. J. Perie, *C. R. Hebd. Seances Acad. Sci.*, **262**, 1591 (1966); (b) A. Lattes and J. J. Perie, *Tetrahedron Lett.*, 5165 (1967); (c) A. Lattes and J. J. Perie, *ibid.*, 2289 (1969).
(5) J. Likforman and J. Gardent, *C. R. Hebd. Seances Acad. Sci.*, **268**, 2340 (1969).

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$Hg(OAc)_2 \ll Hg(NO_3)_2 \sim Hg(ClO_4)_2$, which parallels the degree of ionization of these salts. The use of $Hg(NO_3)_2$ resulted in nearly complete conversion to the organomercurial (based on loss of the olefin) after 10 h.

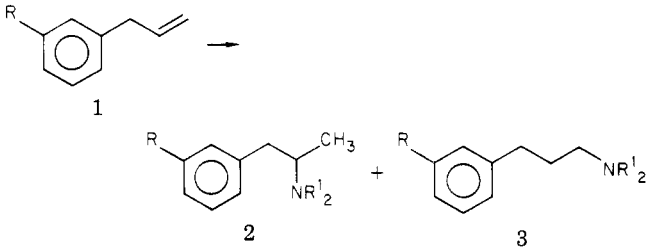
For our purposes, this organomercurial intermediate had to be cleaved (preferably in situ) to yield the desired amine product(s) (**2**, **3**). Reduction of such species has been readily achieved previously, and as reported,[6] we have found sodium borohydride to be effective and convenient. A serious drawback to this procedure in the past has been the large percentage of elimination (to 1) encountered during the reductive process. This pathway can exercise a leveling effect in the overall aminomercuration–demercuration process, as we have observed that the amine–mercury salt combination which results in the most rapid and complete mercuration often yields a high proportion of elimination product (olefin) during reduction. For example, the combination of $Hg(NO_3)_2$, aminoacetaldehyde diethyl acetal, and *m*-methoxyallylbenzene (60 °C, 18 h, THF) results in >95% conversion (based on loss of olefin) to the organomercurial intermediate; however, subsequent borohydride reduction (20 °C, THF) gave 45% of **2a** and 55% of **1a**. We have found that the proportion of elimination which occurs during this reduction can be diminished nearly totally by treatment of the organomercurial with 10% NaOH prior to the reduction.[7] Pretreatment with base and subsequent acid workup resulted in an 87% (isolated) yield of the desired amine **2**. This increase in the amine/olefin ratio is presumably due to ligand exchange (OH for NO_3) at the mercury moiety with consequent diminution in the reductive elimination pathway.

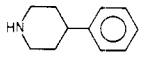
The aminomercuration, ligand exchange and reduction steps are all mutually compatible and can be easily performed successively in a single reaction vessel, using THF as solvent. Using our optimal conditions for the synthesis of the acetal **2a**, we explored the generality of this reaction sequence with a variety of amines, including primary and secondary alkyl, aryl, benzyl, cycloalkyl, and heterocyclic amines, and with three variations in allylbenzene substrates (Table I). With the exception of **2a**, the data presented represent the results of a single trial with no efforts made to optimize yield or product distribution.

It is obvious from the table that the reaction may be performed successfully in good to excellent yields, irrespective of major variations in amine substrates. No clear-cut relationship has emerged through variation of the amine addends, as both steric and basicity effects may play a role in determining the overall reaction rate and the degree of Markownikoff vs. anti-Markownikoff (**2**/**3**) addition. The formation, in some cases, of minor amounts of the isomeric amine (anti-Markownikoff) product may detract somewhat from the overall synthetic utility in certain instances; however, we have found these isomeric products to be readily separated by simple chromatography, and it is highly likely that changes in the reaction conditions may result in alterations of the product ratios. This awaits further investigation.

In contrast to the related oxomercurations, the direct formation of mercurinium ions does not appear to be rate determining for intermolecular aminomercurations.[8]

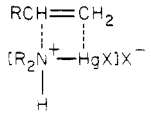
Table I. Aminomercuration of Allylbenzenes with Various Amines



R	amine (NR'_2)	2/3	isolated yield, %
a, OCH_3	$NH_2CH_2CH(OEt)_2$	100/0	87
b, OCH_3	$NH_2CH_2CH_2CH_2CH_3$	100/0	48
c, OCH_3	NH_2CH_2Ph	90/10	78
d, OCH_3	$NH(CH_2CH_3)_2$	60/40	39
e, OCH_3	NH_2Ph	100/0	41
f, OCH_3		100/0	68
g, OCH_3		80/20	86
h, H	NH_2CH_2Ph	90/10	71
i, CF_3	NH_2CH_2Ph	100/0	57
j,[a] OCH_3	$NH_2CH_2CH_3$[b]	80/20	87
k,[a] CF_3	$NH_2CH_2CH_3$[b]	82/18	93
l, CF_3	$NH_2CH_2CH(OEt)_2$	90/10	62

[a] $Hg(ClO_4)_2$ substituted for $Hg(NO_3)_2$. [b] 30% aqueous ethylamine.

Currently, the rate-determining step is thought to be either slow dissociation of HgX^+ from the strong amine–mercury complexes (i.e., $[R_2NHHgX]^+X^-$) or direct addition of these complexes to the olefin substrate via a four-centered transition state (**4**).[9]



4

We have observed that the aminomercuration reactions can be performed in aqueous THF (examples **2j,k**) as well as under anhydrous conditions with no detectable formation of the analogous oxomercurated alcohol products. This result suggests either that hydroxide does not compete successfully with ethylamine as a nucleophile for intermediate mercurinium ions or that direct addition of the amine–mercury complexes may be involved.

Experimental Section

General. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 225 grating spectrometer. NMR spectra were recorded on a Varian A60 spectrometer, using Me_4Si or DDS as an internal standard. Ultraviolet spectra were obtained on a Cary 14 spectrometer. Elemental analyses were performed by Galbraith Laboratories. All solvents were ACS Reagent grade and were used without additional purification. Allylbenzene was purchased from Aldrich Chemical Corp., 3-methoxyallylbenzene was prepared by the procedure of Horeau,[10] and 3-(trifluoromethyl)allylbenzene was prepared as described by Rocca.[11]

(6) J. J. Perie and A. Lattes, *Bull. Soc. Chim. Fr.*, 1378 (1971).

(7) See: (a) H. C. Brown and J. T. Kurek, *J. Am. Chem. Soc.*, **91**, 5647 (1969); (b) V. Gomez Aranda et al., *Tetrahedron Lett.*, 3621 (1972); (c) H. Hodjat-Kachani et al., *Chem. Lett.*, 409 (1976).

(8) This is based primarily on the fact that with like substrates oxomercuration proceeds at a much greater rate than aminomercuration. See: J. J. Perie and A. Lattes, *Bull. Soc. Chim. Fr.*, 583 (1970), and references therein.

(9) For an excellent review of intramolecular aminomercuration, see: A. Lattes, *Chem. Heterocycl. Compd.*, 11 (1), 4 (1975).

(10) A. Horeau, L. Menager, and H. Kagan, *Bull. Soc. Chim. Fr.*, 3571 (1971).

General Procedure for the Preparation of α-Methylphenethylamines (Table I). The following are typical examples of the aminomercuration–demercuration procedures used for the preparation of **2a–l**.

***N*-(2,2-Diethoxyethyl)-1-(3-methoxyphenyl)-2-propylamine (2a).** To a stirred solution of $Hg(NO_3)_2 \cdot H_2O$ (51.4 g, 0.15 mol) in tetrahydrofuran (100 mL) under nitrogen was added aminoacetaldehyde diethyl acetal (64.0 g, 0.48 mol) and then 3-methoxyallylbenzene (17.8 g, 0.12 mol), and the mixture was heated to 60–65 °C for 24 h. After the solution was cooled to ambient temperature, 10% NaOH (100 mL) and $NaBH_4$ (12.0 g, 0.32 mol) were added, and the mixture was stirred for 18 h, acidified to pH 1 with 10% HCl, stirred until no more gas evolution was observed upon the addition of small amounts of 10% HCl (ca. 1–2 h), then basified to pH 11 with 20% NaOH, and extracted with chloroform. The extracts were dried over $MgSO_4$ and evaporated to an oil, which was distilled under vacuum to remove the excess aminoacetaldehyde diethyl acetal and traces of 3-methoxyallylbenzene (bp 45–68 °C (0.05 mm)). Distillative or chromatographic (silica gel) purification of the residue affords **2a** as a pale yellow oil (29.4 g, 87% yield): bp 135–142 °C (0.05 mm); IR (neat) 3330, 1600, 1582, 1258, 1150, 1055 cm^{-1}; NMR ($CDCl_3$) δ 1.0–1.4 (m, 9 H), 1.7 (s, 1 H), 2.5–3.2 (m, 5 H), 3.2–3.75 (m, 4 H), 3.8 (s, 3 H), 4.6 (t, 1 H), 6.5–7.0 (m, 3 H), 7.0–7.3 (m, 1 H).

Anal. Calcd for $C_{16}H_{27}NO_3$: C, 68.29; H, 9.67; N, 4.98. Found: C, 68.06; H, 9.66; N, 4.92.

***N*-Ethyl-1-(3-(trifluoromethyl)phenyl)-2-propylamine (2k) and *N*-Ethyl-3-(3-(trifluoromethyl)phenyl)-1-propylamine (3k).** To a stirred solution of $Hg(ClO_4)_2 \cdot 3H_2O$ (68.0 g, 0.15 mol) in tetrahydrofuran (200 mL) under nitrogen at 0 °C was added 70% aqueous ethylamine (46.3 g, 0.72 mol) and then 3-(trifluoromethyl)allylbenzene (22.4 g, 0.12 mol), and the mixture was heated to 65 °C for 72 h. After the solution was cooled to ambient temperature, 10% NaOH (100 mL) and $NaBH_4$ (12.0 g, 0.32 mol) were added, and the mixture was stirred for 18 h and acidified with 10% HCl to pH 1. An additional portion of concentrated HCl (50 mL) was added, the mixture was stirred for 5 h and extracted with petroleum ether, and the aqueous phase was basified to pH 11 with 20% NaOH and extracted with chloroform. The chloroform extracts were dried over $MgSO_4$ and evaporated in vacuo to a yellow oil (26.0 g, 93% yield) consisting (GLC) of 82% **2k** and 18% *N*-ethyl-3-(3-(trifluoromethyl)phenyl)-1-propylamine (**3k**), which were separated by preparative column chromatography on silica gel and isolated as the hydrochloride salts from ethanol/ether.

2k: mp 166–167 °C (lit.[12] mp 166 °C); IR (KBr) 2900–2300, 1585, 1455, 1330, 1160, 1065 cm^{-1}; NMR ($CDCl_3$) δ 1.19 (d, 3 H, J = 7 Hz), 1.35 (t, 3 H, J = 7 Hz), 2.5–4.7 (m, 5 H), 7.65 (s, 4 H), 9.5 (br s, 2 H).

Anal. Calcd for $C_{12}H_{17}F_3NCl$: C, 53.83; H, 6.40; F, 21.28; N, 5.23; Cl, 13.24. Found: C, 53.90; H, 6.30; F, 21.10; N, 5.22; Cl, 13.42.

3k: mp 144–145 °C; IR (KBr) 2900–2300, 1590, 1450, 1332, 1065 cm^{-1}; NMR ($CDCl_3$) δ 1.4 (t, 3 H), 2.3 (m, 2 H), 2.9 (m, 6 H), 7.4 (s, 4 H), 9.2 (br s, 2 H).

Anal. Calcd for $C_{12}H_{17}F_3NCl$: C, 53.83; H, 6.40; F, 21.28; N, 5.23; Cl, 13.24. Found: C, 53.74; H, 6.40; F, 21.42; N, 5.23; Cl, 13.22.

Physical Properties of the New Propylamines (Table I). The propylamines (Table I) which were isolated were obtained as the hydrochloride salts recrystallized from alcohol/ether mixtures, with the exception of the acetals **2a** and **2l** which were analyzed as the bases. The physical data for **2a**, **2k**, and **3k** are presented above in the experimental descriptions.

***N*-Butyl-1-(3-methoxyphenyl)-2-propylamine (2b)**: mp 155–156 °C; IR (KBr) 2960, 2800, 1605, 1590, 1465, 1255, 1170, 1035, 785, 740 cm^{-1}; NMR ($CDCl_3$) δ 0.9 (t, 3 H, J = 6 Hz), 1.4 (d, 3 H, J = 6 Hz), 1.6–2.5 (m, 4 H), 2.8–3.75 (m, 5 H), 3.8 (s, 3 H), 6.6–7.4 (m, 4 H), 9.7 (br s, 2 H).

Anal. Calcd for $C_{14}H_{24}ClNO$: C, 65.23; H, 9.38; Cl, 13.75; N, 5.43; O, 6.21. Found: C, 65.44; H, 9.15; Cl, 13.72; N, 5.41; O, 6.26.

***N*-Benzyl-1-(3-methoxyphenyl)-2-propylamine (2c)**: mp 143–143.5 °C; IR (KBr) 2930, 2760, 1600, 1490, 1445, 1265, 1165, 1040, 990, 835, 785 cm^{-1}; NMR ($CDCl_3$) δ 1.33 (d, 3 H, J = 7 Hz), 2.8–3.6 (m, 3 H), 3.73 (s, 3 H), 4.10 (br t, 2 H), 6.5–7.8 (m, 9 H), 10.4 (br s, 2 H).

Anal. Calcd for $C_{17}H_{22}ClNO$: C, 69.97; H, 7.60; Cl, 12.15; N, 4.80; O, 5.48. Found: C, 69.91; H, 7.62; Cl, 12.16; N, 4.85; O, 5.40.

***N,N*-Diethyl-1-(3-methoxyphenyl)-2-propylamine (2d)**: mp 123–124 °C; NMR ($CDCl_3$) δ 1.31 (d, 3 H, J = 6.7 Hz), 1.56 (t, 6 H, J = 7 Hz), 2.2–3.7 (m, 7 H), 3.80 (s, 3 H), 6.8–7.5 (m, 4 H), 12.4 (s, 1 H).

Anal. Calcd for $C_{14}H_{24}ClNO$: C, 65.23; H, 9.38; Cl, 13.75; N, 5.43; O, 6.21. Found: C, 65.36; H, 9.46; N, 5.32; O, 6.18.

***N*-Phenyl-1-(3-methoxyphenyl)-2-propylamine (2e)**: mp 176–177 °C; IR (KBr) 2940, 2830, 1600, 1490, 1450, 1260, 1165, 1035, 857, 780, 750 cm^{-1}; NMR (Me_2SO-d_6) δ 1.17 (d, 3 H, J = 6.5 Hz), 2.7–3.6 (m, 2 H), 3.78 (s, 3 H), 3.8–4.2 (m, 1 H), 6.7–7.0 (m, 4 H), 7.0–7.8 (m, 6 H).

Anal. Calcd for $C_{16}H_{20}ClNO$: C, 69.17; H, 7.25; Cl, 12.76; N, 5.04; O, 5.75. Found: C, 68.96; H, 6.93; Cl, 12.62; N, 5.16; O, 6.24.

***N*-[2-(3-Methoxyphenyl)-1-methylethyl]morpholine (2f)**: mp 145–146 °C; IR (KBr) 2950, 2590, 1600, 1595, 1490, 1460, 1260, 1175, 1040, 785, 745 cm^{-1}; NMR ($CDCl_3$) δ 1.31 (d, 3 H, J = 6 Hz), 2.4–3.0 (m, 1 H), 3.0–3.7 (m, 6 H), 3.77 (s, 3 H), 4.0–4.7 (m, 4 H), 6.6–7.5 (m, 4 H), 12.7 (s, 1 H).

Anal. Calcd for $C_{14}H_{22}ClNO_2$: C, 61.86; H, 8.15; Cl, 13.04; N, 5.15; O, 11.77. Found: C, 61.85; H, 8.14; Cl, 13.07; N, 5.20; O, 11.69.

***N*-[2-(3-Methoxyphenyl)-1-methylethyl]-4-phenylpiperidine (2g)**: mp 240–242 °C; IR (KBr) 2930, 2630, 1600, 1490, 1460, 1260, 1160, 1030, 790, 760 cm^{-1}; NMR ($CDCl_3$) δ 1.31 (d, 3 H, J = 6 Hz), 1.9–3.7 (m, 12 H), 3.77 (s, 3 H), 4.0–4.7 (m, 4 H), 6.6–7.5 (m, 4 H), 12.7 (s, 1 H).

Anal. Calcd for $C_{21}H_{28}ClNO$: C, 72.91; H, 8.15; Cl, 10.24; N, 4.04; O, 4.62. Found: C, 73.02; H, 8.02; Cl, 10.32; N, 4.10; O, 4.54.

***N*-[3-(3-Methoxyphenyl)propyl]-4-phenylpiperidine (3g)**: mp 181–183 °C; IR (KBr) 2940, 2650, 1605, 1580, 1455, 1265, 1155, 1050, 775, 760, 700 cm^{-1}; NMR (Me_2SO-d_6) δ 1.3–3.6 (m, 15 H), 3.70 (s, 3 H), 6.5–6.9 (m, 3 H), 6.9–7.4 (m, 6 H).

Anal. Calcd for $C_{21}H_{28}ClNO$: C, 72.91; H, 8.15; Cl, 10.24; N, 4.04; O, 4.62. Found: C, 72.74; H, 8.17; Cl, 10.08; N, 4.04; O, 4.65.

***N*-Benzyl-1-phenyl-2-propylamine (2h)**: mp 197.5–198.5 °C (lit.[13] mp 199 °C); IR (KBr) 2940, 2770, 1602, 1500, 1458, 1145, 1000, 742, 702 cm^{-1}; NMR (Me_2SO-d_6) δ 1.20 (d, 3 H, J = 6 Hz), 2.5–3.0 (m, 1 H), 3.1–3.6 (m, 2 H), 4.20 (m, 2 H), 7.1–7.9 (m, 10 H), 9.75 (s, 2 H).

Anal. Calcd for $C_{16}H_{20}ClN$: C, 73.40; H, 7.70; Cl, 13.54; N, 5.35. Found: C, 73.44; H, 8.00; Cl, 13.84; N, 5.13.

***N*-Benzyl-1-(3-(trifluoromethyl)phenyl)-2-propylamine (2i)**: mp 165–166 °C (lit.[14] mp 170–172 °C); IR (KBr) 2940, 2780, 1580, 1460, 1330, 1170, 1120, 795, 750 cm^{-1}; NMR ($CDCl_3$/Me_2SO-d_6) δ 1.38 (d, 3 H, J = 6.5 Hz), 3.0–3.9 (m, 3 H), 4.20 (br d, 2 H), 7.4–7.9 (m, 9 H), 11.5 (s, 2 H); mass spectra m/e (intensity) 292 (1), 278 (2), 196 (3), 134 (53), 106 (12), 91 (100), 89 (2), 77 (2).

***N*-Ethyl-1-(3-methoxyphenyl)-2-propylamine (2j)**: mp 142–143 °C (lit.[15] mp 137–139 °C); IR (KBr) 2960, 2800, 1600, 1490, 1450, 1265, 1025, 870, 790, 700 cm^{-1}; NMR ($CDCl_3$) δ 1.38 (d, 3 H, J = 6 Hz), 1.55 (t, 3 H, J = 6.5 Hz), 2.5–3.7 (m, 5 H), 3.78 (s, 3 H), 6.6–7.4 (m, 4 H), 9.56 (br s, 2 H).

Anal. Calcd for $C_{12}H_{20}ClNO$: C, 62.73; H, 8.77; Cl, 15.43; N, 6.09; O, 6.96. Found: C, 62.66; H, 8.80; Cl, 15.26; N, 6.12; O, 7.02.

***N*-Ethyl-3-(3-methoxyphenyl)-1-propylamine (3j)**: mp 103–104 °C; IR (KBr) 2950, 2820, 1600, 1445, 1260, 1175, 1035, 790, 700 cm^{-1}; NMR (D_2O) δ 1.40 (t, 3 H, J = 6.5 Hz), 1.7–2.5 (m, 2 H), 2.70 (br d, 2 H, J = 7 Hz), 3.09 (q, 4 H, J = 7 Hz), 3.87 (s, 3 H), 6.7–7.1 (m, 3 H), 7.1–7.5 (m, 1 H).

Anal. Calcd for $C_{12}H_{20}ClNO$: C, 62.73; H, 8.77; Cl, 15.43; N, 6.09; O, 6.96. Found: C, 62.90; H, 8.84; Cl, 15.54; N, 6.29; O, 6.73.

(11) A. Rocca, French Patent 1 457 540 (1964).
(12) L. Beregi, P. Hugon, J. LeDouarec, and H. Schmitt, French Patent M1658 (1963).
(13) A. Lespagnol, M. Debaert, and M. Devergnies, *Bull. Soc. Chim. Fr.*, **12**, 2744 (1963).
(14) J. Boissier, R. Batonis, and C. Dumont, *Ann. Pharm. Fr.*, **24** (1), 57 (1966).
(15) R. Tessel, J. Woods, R. Counsell, and M. Lu, *J. Pharmacol. Exp. Ther.*, **192** (2), 310 (1975).

***N*-(2,2-Diethoxyethyl)-1-(3-(trifluoromethyl)phenyl)-2-propylamine (21)**: bp 109–111 °C (0.05 mm); IR (neat) 2980, 2900, 1600, 1450, 1320, 1200, 1150, 1060, 800, 705 cm^{-1}; NMR ($CDCl_3$) δ 1.15 (m, 9 H), 2.4–3.4 (m, 6 H), 3.4–4.2 (m, 4 H), 4.85 (t, 1 H, J = 6 Hz), 7.9 (s, 4 H).

Anal. Calcd for $C_{16}H_{24}F_3NO_2$: C, 60.17; H, 7.57; F, 17.84; N, 4.38; O, 10.01. Found: C, 60.08; H, 7.55; F, 18.01; N, 4.47; O, 9.89.

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Registry No. 1a, 24743-14-4; **1h**, 300-57-2; **1i**, 1813-96-3; **2a**, 71250-18-5; **2b**, 71250-19-6; **2c**, 71250-20-9; **2d**, 71250-21-0; **2e**, 71250-22-1; **2f**, 71250-23-2; **2g**, 71250-24-3; **2h**, 1085-43-4; **2i**, 14818-01-0; **2j**, 71250-25-4; **2k**, 404-82-0; **2l**, 71250-26-5; **3c**, 71250-27-6; **3d**, 71250-28-7; **3g**, 71250-29-8; **3h**, 53578-37-3; **3j**, 71250-30-1; **3k**, 71250-31-2; **3l**, 71250-32-3; aminoacetaldehyde diethyl acetal, 645-36-3; 1-butanamine, 109-73-9; benzenemethanamine, 100-46-9; diethylamine, 109-89-7; benzenamine, 62-53-3; morpholine, 110-91-8; 4-phenylpiperidine, 771-99-3; ethanamine, 75-04-7; mercury perchlorate, 7616-83-3; mercury nitrate, 10045-94-0.

Stereochemistry of the Diels–Alder Reaction of Vinylcyclohexene or 1-[α-(*tert*-Butyldimethylsilyloxy)vinyl]-Δ^1-cyclohexene and 2-Methylcyclopentenone

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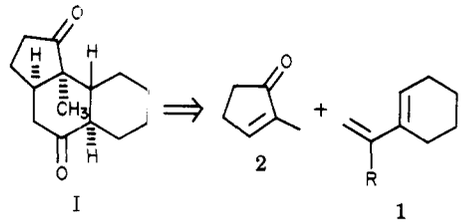
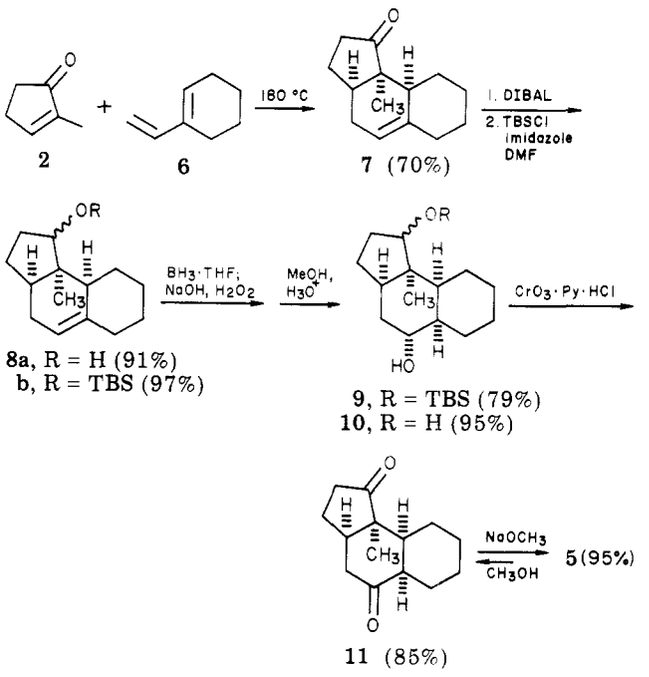
As part of an investigation on the total synthesis of the macrolide antibiotic chlorothricolide,[1] an efficient synthesis of a cis-anti-trans fused tricyclic ring system such as I was required. A simple, convergent approach to the construction of such a tricyclic I might be the Diels–Alder reaction of a vinylcyclohexene (1) with 2-methylcyclopentenone (2).



I 2 1

Indeed, the reaction between vinylcyclohexene (1, R = H) and 2-methylcyclopentenone (2) was reported in 1939 by Bockemuller to give an adduct of unknown structure.[2] While many examples of this type of Diels–Alder reaction have been reported, evidence for the stereochemical outcome of the reaction resulting from the two possible modes of cycloaddition is usually only speculative.[3] Of those rare cases where a rigorous structure proof is given, anti or syn products resulting from either predominant exo or endo cycloaddition can be found.[4] We report here the results of a single-crystal X-ray diffraction analysis of the tricyclic dione **5** from the Diels–Alder reaction of 1-[α-(*tert*-butyldimethylsilyloxy)vinyl]-Δ^1-cyclohexene (**3**) and 2-methylcyclopentenone (**2**). The diene **3** was prepared in 79% distilled yield by enolization of acetylcyclohexene with lithium diisopropylamide (LDA) at −78 °C, and then trapping the resulting dienolate anion with *tert*-butyldimethylsilyl chloride (TBSCl) in hexamethylphosphoramide (HMPA). The Diels–Alder adduct **4**, which consisted of a mixture of silyl enol ether double bond isomers, was converted quantitatively to the dione **5** by treatment with tetra-*n*-butylammonium fluoride in tetrahydrofuran (THF).[5]

Scheme I

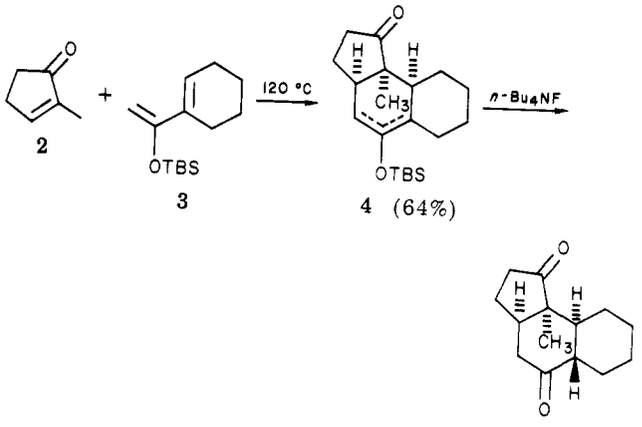


2 6 7 (70%)

8a, R = H (91%)
b, R = TBS (97%)

9, R = TBS (79%)
10, R = H (95%)

11 (85%)



2 3 4 (64%)

5 (100%)

(1) W. Keller-Schierlein, R. Muntwyler, W. Pache, and H. Zähner, *Helv. Chim. Acta*, **52**, 127 (1969); R. Muntwyler, J. Widmer, and W. Keller-Schierlein, *ibid.*, **53**, 1544 (1970); R. Muntwyler and W. Keller-Schierlein, *ibid.*, **55**, 2071 (1972); M. Brufani, S. Cerrini, W. Fedeli, F. Mazza, and R. Muntwyler, *ibid.*, **55**, 2094 (1972).

(2) W. Bockemuller, U.S. Patent 2 179 809 (1939); *Chem. Abstr.*, **34**, 1823 (1940).

(3) A. S. Onischenko, "Diene Synthesis", Israel Program for Scientific Translations, Jerusalem, 1964, pp 416–425, and references cited therein.

(4) M. F. Ansell and G. T. Brooks, *J. Chem. Soc.*, 4518 (1956); I. N. Nazarov, V. F. Kucherov, and G. M. Segal, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1215 (1956); I. N. Nazarov, V. F. Kucherov, and V. M. Andreev, *ibid.*, 331 (1957); I. N. Nazarov, V. F. Kucherov, V. M. Andreev, and G. M. Segal, *Croat. Chim. Acta*, **29**, 369 (1957); F. Winternitz and C. Balmossiere, *Tetrahedron*, **2**, 100 (1958).

(5) E. J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, **94**, 6190 (1972).

0022-3263/79/1944-3583$01.00/0