showed weak absorption at 2210 cm^{-1}, attributable to a nitrile group, and no NH or OH absorption. The nmr spectrum showed only aromatic protons and *no* CH_3 protons. These data were consistent with phenyl(phenylimino)acetonitrile (**3**), and this structure was confirmed by comparison (infrared, melting point, and nuclear magnetic resonance) with an authentic sample.[5]

Subsequently, it was found that the reaction could be carried out somewhat more conveniently by simply heating equimolar amounts of 1,5-diphenyl-3-methyl-4-nitrosopyrazole (**1**) and triethyl phosphite on the steam bath. An exothermic reaction took place and a small amount of liquid distilled from the reaction mixture. Redistillation of the distillate gave a colorless liquid boiling at 80° which was identified as acetonitrile. Phenyl(phenylimino)acetonitrile (**3**) was obtained from the reaction mixture in 70% yield.

The products obtained may be explained by the mechanism outlined in Scheme I. The reaction is thus a type of heterolytic fragmentation[6] which differs from those investigated previously in that a nitrene **2** may be involved as an intermediate. However, it is possible that a concerted reaction (*e.g.*, **4**) takes place without the formation of an intermediate nitrene.[7]

Experimental Section[8]

Phenyl(phenylimino)acetonitrile (**5**).—A mixture of 7.89 g (0.03 mol) of 1,5-diphenyl-3-methyl-4-nitrosopyrazole,[4] 4.98 g (0.03 mol) of triethyl phosphite, and 120 ml of dry benzene was heated under reflux for 13 hr using a condenser closed off with a calcium chloride tube. The benzene was removed by distillation and the residue was heated on the steam bath under vacuum (<1 mm). The oil was allowed to cool and was poured into water. The solid was removed by filtration and was recrystallized from ethanol. There was obtained 3.05 g of yellow prisms melting at 73–74°.

Anal. Calcd for $C_{14}H_{10}N_2$: C, 81.53; H, 4.89; N, 13.58. Found: C, 81.40; H, 4.82; N, 13.70; *m/e*, 206.

When equimolar amounts [7.89 g (0.03 mol) of 1,5-diphenyl-3-methyl-4-nitrosopyrazole and 4.98 g (0.03 mol) of triethyl phosphite] of reactants were heated on the steam bath without any solvent in a flask containing a side arm for distillation, an exothermic reaction took place and several milliliters of distillate was obtained. The residue was poured into water and the solid was removed by filtration and recrystallized from ethanol. There was obtained 4.34 g (70%) of yellow-green platelets melting at 67–71°. Further recrystallization from ethanol raised the melting point to 73–74°. The product was identical (mixture melting point and comparison infrared spectra) with that obtained above.

Registry No.—**1**, 7171-64-4; **3**, 4686-14-0; triethyl phosphite, 122-52-1.

Acknowledgment.—The author is indebted to Professors Donald J. Cram, Kenneth Rinehart, and William Doering for stimulating discussions and to Mr. Albert Lallinger for technical assistance.

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(5) F. Kröhnke, *Ber.*, **71B**, 2583 (1938). The reported melting point is 72°.

(6) *Cf.* C. A. Grob and P. W. Schiess, *Angew. Chem. Intern. Ed. Engl.*, **6**, 1 (1967).

(7) W. D. Crow and C. Wentrup [*Chem. Commun.*, 1082 (1968)] have recently investigated heterocyclic nitrenes in the pyridine and pyrimidine series and found that in these cases ring contraction takes place. The nitrenes were prepared by pyrolysis of triazolo[4,5-*b*]pyridine, tetraazolo-[1,5-*a*]pyrimidines, and related substances.

(8) All melting points and boiling points are corrected.

Formation of Thiols from Thiophene and Benzyne at 690°

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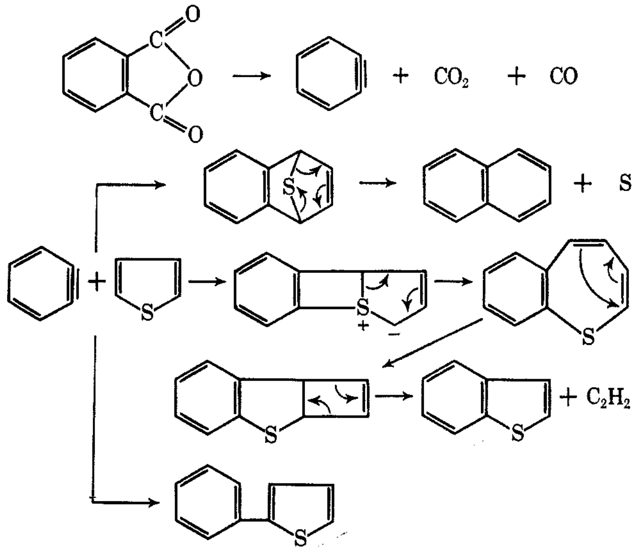
Benzyne from phthalic anhydride reacts with thiophene at 690° to give naphthalene and benzothiophene by 1,4 and 1,2 addition, respectively, as well as phenylthiophene by insertion (Scheme I).[1] The ratio of naphthalene to benzothiophene is about 9:1, implying nearly the same preference for 1,4 over 1,2 addition as was inferred from the reaction of benzyne with dichlorobenzenes and pyridine at the same temperature,[2,3] and reflecting the strong tendency of benzyne to act as a dienophile at high temperatures as well as in solution.[4]

SCHEME I



As the formation of naphthalene from phthalic anhydride and thiophene requires the extrusion of a sulfur atom, products arising from the reaction of such sulfur, possibly monatomic and hence highly reactive,[5] with thiophene might be expected. Sulfur atoms have been formed by photolysis of COS rather than by heating sulfur; the high S–S bond energy of about 101 kcal/mol[6] would ordinarily require temperatures at which

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(1) (a) E. K. Fields and S. Meyerson, *Chem. Commun.*, 708 (1966); (b) E. K. Fields and S. Meyerson in "Organosulfur Chemistry," M. J. Janssen, Ed., John Wiley & Sons, Inc., New York, N. Y., 1967, p 143.

(2) S. Meyerson and E. K. Fields, *Chem. Ind.* (London), 1230 (1966).

(3) E. K. Fields and S. Meyerson, *J. Org. Chem.*, **31**, 3307 (1966).

(4) G. Wittig, *Angew. Chem.*, **69**, 245 (1957); T. G. Corbett and O. N. Porter, *Aust. J. Chem.*, **18**, 781 (1965); W. L. Dilling, *Tetrahedron Lett.*, 939 (1966).

(5) K. S. Sidhu, E. M. Lown, O. P. Strausz, and H. E. Gunning, *J. Amer. Chem. Soc.*, **88**, 254 (1966).

(6) R. F. Palmer and F. P. Lossing, *ibid.*, **84**, 4661 (1962); J. Berkowitz and J. R. Marquart, *J. Chem. Phys.*, **39**, 275 (1963); H. Mackle, Abstracts of the Sulfur Symposium, Calgary, March 1964.

most reaction products decompose.[7] Indeed, the mass spectrum of the products revealed a substance of molecular weight 116 and an isotopic distribution establishing the elemental composition as $C_4H_4S_2$, apparently thiophenethiol. The relative amounts of the major products are shown in Table I. The product mixture was extracted with potassium hydroxide and the recovered alkali-soluble products were analyzed by directly coupled gas chromatography–mass spectrometry[8] and compared with an authentic sample of thiophene-2-thiol. The latter was synthesized from 2-thienylmagnesium bromide and sulfur;[9] its mass spectrum showed it to consist essentially of two components, thiophenethiol, presumably the 2 isomer, and dithienyl sulfide, presumably the 2,2′ isomer. An attempt was made to purify the material by gas chromatography. The mass spectrum of the supposedly purified thiol showed again the same two components, but, unexpectedly, enriched in the sulfide. The relative concentrations in the two samples differed sufficiently to permit use of the procedure described by Meyerson[10] to derive reference spectra for the components and to analyze the two mixtures quantitatively. The concentrations (volume per cent) of thiophenethiol and dithienyl sulfide, respectively, were, in the original sample, 92.4 and 7.6 and, in the chromatographed sample, 63.0 and 37.0.

Table I

Product	Rel concn[a]
Thiophenethiol	9.2
Naphthalene	100.0
Benzothiophene	11.3
Phenylthiophene	83.4
Bithiophene	62.6

[a] Relative intensity in the low-voltage (7.5 V, uncorrected) mass spectrum, normalized to naphthalene = 100.

In deriving the spectra of these two compounds we ignored the possible presence of any other components; we assumed that the peak at 198 was due solely to the dithienyl sulfide, and that the peak at 116, after removal of heavy-isotopic contributions, was due solely to the thiophenethiol. The fact that the derived spectra contain very few and very small negative values supports the validity of these assumptions.

The unexpected enrichment of the gas-chromatographic trapout in the sulfide suggests that it was formed by a reaction on the column and, further, that it had a retention time identical with that of the thiophenethiol. Gas chromatography was run on a 6 ft × 0.25 in. diameter column containing diethylene glycol sebacate on 30–60 mesh Chromosorb W. Other thiols, *n*-octyl- and *n*-decylthiol, thiophenol, and thio-*o*-cresol, did not show the same behavior; they were unchanged after several passages through the column.

The separated product from the reaction of phthalic anhydride with thiophene, with the parent peak at mass 116, again accompanied by heavy-isotopic satellites with an intensity distribution indicating the formula $C_4H_4S_2$, gave a spectrum qualitatively similar to that of thiophene-2-thiol in the API Catalog[11] and to that of our synthesized sample. Partial spectra, consisting of most prominent peaks, are shown in Table II. The derived spectrum of the synthesized thiophenethiol is in good agreement with the published spectrum, but differs appreciably from that of the benzyne reaction product. The differences, in the light of correlations described by Foster, *et al.*,[12] suggest that the material from the benzyne reaction consists largely of the 3 isomer. The substantially lower relative intensity at the parent mass parallels the known lower stability of this isomer to light, heat, and air.[9]

Table II

Mass	Product of mol wt 116	API Spectrum No. 162[11]	Synthesized thiophene-2-thiol[a]
45	69.6	45.5	33.0
71	100.0	93.4	89.6
115	7.22	9.25	8.66
116	45.4	100.0	100.0

[a] Spectrum derived from those of thiol–sulfide mixtures.[10]

Thiophenethiol, about 10% as much as bithiophene, was also found in the product when a solution of sulfur in thiophene was pyrolyzed under the identical conditions as for phthalic anhydride and thiophene.

Major alkali-soluble products from the reaction of phthalic anhydride with thiophene and of thiophene with sulfur, both at 690°, are shown in Table III. Relative concentrations are approximated by relative intensities in the low-voltage mass spectra. Sensitivity, *i.e.*, the proportionality factor between parent peak intensity and concentration, differs from one compound to another; however, closely related compounds have roughly equal sensitivities at the ionizing voltage employed in our work.[13] For example, from the reaction of phthalic anhydride with thiophene, relative intensities of the four products listed in Table IV, normalized to a total of 100.0, agree quite well with relative areas in the gas chromatogram.

Table III

Alkali-Soluble Products from Phthalic Anhydride with Thiophene and Thiophene with Sulfur[a]

Mass	Probable structure	Rel concn[b] of product Expt A[c]	Expt B[d]
116	Thiophenethiol	100	100
160	Naphthalenethiol	78	
198	Bithiophenethiol	4	3
230	Bithiophenedithiol	1	147

[a] Conditions: 690°, 12-sec contact time. [b] Relative intensities in the low-voltage (7.5 V, uncorrected) mass spectrum. [c] Phthalic anhydride (0.2 mol) and thiophene (2.0 mol). The products weighed 3.2 g. [d] Sulfur (0.2 g-atom) and thiophene (0.4 mol). The products weighed 1.35 g.

The thiol of mol wt 230 listed as bithiophenedithiol in Table III, but which may also contain isomeric dithienyl sulfide thiols, was present in larger concentration than any other component. However, there seems no obvious reason why such large amounts of these com-

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[7] H. E. Gunning and O. P. Strausz, *Advan. Photochem.*, **4**, 141 (1966).

[8] R. S. Gohlke, *Anal. Chem.*, **31**, 535 (1959); L. P. Lindeman and J. L. Annis, *ibid.*, **32**, 1742 (1960); J. T. Watson and K. Biemann, *ibid.*, **36**, 1135 (1964).

[9] N. H. Houff and R. D. Schultz, *J. Amer. Chem. Soc.*, **75**, 6316 (1953).

[10] S. Meyerson, *Anal. Chem.*, **31**, 174 (1959).

[11] American Petroleum Institute, Research Project 44, "Catalog of Mass Spectral Data," Chemical Thermodynamics Properties Center, Agricultural and Mechanical College of Texas, College Station, Texas, 1947–1967.

[12] N. G. Foster, D. E. Hirsch, R. F. Kendall, and B. H. Eccleston, U. S. Department of the Interior, Bureau of Mines, Report of Investigations, No. 6433, 1963.

[13] G. F. Crable, G. L. Kearns, and M. S. Norris, *Anal. Chem.*, **32**, 13 (1960).

TABLE IV

Component	Rel intensity in mass spectrum	Rel area in gas chromatogram
Naphthalene	38.9	47.8
Benzothiophene	4.4	5.1
Phenylthiophenes	32.4	27.7[a]
Bithienyls	24.3	19.4

[a] 2-Phenyl, 20.9; 3-phenyl, 6.8.

TABLE V

ISOTOPIC PROFILES OF THIOLS

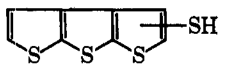
Thiol	Formula	Mass	Rel intensity[a]: Measd: Phthalic anhydride with thiophene	Rel intensity[a]: Measd: Sulfur with thiophene	Rel intensity[a]: Calcd
Thiophenethiol	$C_4H_4S_2$	116	100	100	100
		117	6.97	6.81	5.99
		118	9.03	9.14	8.99
		119	0.47	0.49	0.45
		120			0.23
Naphthalenethiol	$C_{10}H_8S$	160	100	0	100
		161	12.5		11.7
		162	5.6		5.06
		163	0.9		0.49
		164			0.04
Bithiophenethiol	$C_8H_6S_3$	198	100	100	100
		199	13	14.7	11.1
		200	13	13.3	13.8
		201			1.37
		202			0.69
Bithiophenedithiol	$C_8H_6S_4$	230	100	100	100
		231	33[b]	12.4	11.9
		232	33[b]	18.1	18.3
		233		2.1	2.0
		234		1.4	1.3

[a] 7.5-V spectrum. [b] Quite different from the calculated values, most likely due to the very low signal-to-noise ratio.

pounds should be formed, whatever their structure. Further work to answer this question is in progress.

At the mole ratio of phthalic anhydride/thiophene of 1:5, the relative amount of thiols changed appreciably. Determined by gas chromatography, these follow, volume per cent: thiophene-3-thiol, 2.3; thiophene-2-thiol, 12.0; naphthalenethiol, 84.5; unknown thiols, 1.2. The naphthalenethiol may be a mixture of the 1 and 2 isomers; we were unable to separate authentic samples of the two.

Table V compares the measured isotopic profiles of the thiols listed in Table III with calculated profiles. There was additionally some product of mol wt 228 in the alkali-soluble material (7 on the scale of Table III) from thiophene and sulfur, possibly thienothiophthenethiol. However, its isotopic profile overlapped that of the thiol of mol wt 230 and could not be determined. The agreement between measured and calculated isotopic profiles is generally good, and together with the solubility in alkali indicates the nature of the thiols formed in the two reactions. This method of analysis does not, of course, differentiate among possible structural isomers. Such an analysis would be extremely difficult, even assuming no fortuitous coincidences of retention times among isomers of their impurities, as we have described for 2-thiophenethiol and the corresponding sulfide.



To confirm the origin of the product from phthalic anhydride with thiophene, we ran the same reaction using phthalic anhydride-d_4. The major products are shown in Table VI, together with those from the unlabeled anhydride for comparison.

We had hoped to find naphthalenethiol-d_4 from the labeled phthalic anhydride reaction; if present, however, it was obscured by phenylthiophene-d_4 of the same molecular weight (164) and formed in much greater amount. Both reactions showed the same preference, 9:1, for benzyne to act as a dienophile and add 1,4 rather than 1,2 to thiophene.

TABLE VI

PRODUCTS FROM THIOPHENE WITH PHTHALIC ANHYDRIDE-d_0 AND -d_4[a]

Product	Rel concn[b]: Phthalic-d_0	Rel concn[b]: Anhydride-d_4[c]
Thiophenethiol	2	2
Naphthalene	26	
Naphthalene-d_4		27
Benzothiophene	3	
Benzothiophene-d_4		3
Thiophthene	0.5	0.9
Phenylthiophene	10	
Phenyl-d_4-thiophene		9
Bithiophene	12	17
Benzothiophthene	12	
Benzothiophthene-d_4		9

[a] Conditions: 690°, 7-sec contact time, mole ratio of phthalic anhydride/thiophene, 10:1. [b] Relative intensities in the low-voltage mass spectrum, normalized to mass 116, thiophenethiol = 2. [c] 94.3% d_4, 5.7% d_3.

Although the amount of sulfur from the reaction of phthalic anhydride with thiophene could theoretically be no greater than that in the sulfur–thiophene reaction and from the total product analysis[1] was appreciably less, the yield of thiols in the first reaction was far greater than that in the second. This result, coupled with Hartough's findings that sulfur and thiophene failed to react at 600°,[14] is good evidence for the high reactivity of sulfur lost from the benzyne–thiophene 1,4 adduct I. The formation of thiols in the reactions of other arynes with thiophene and benzothiophene is being investigated; in addition, we are looking at the reactions of other arynes generated by pyrolysis of aromatic anhydrides with sulfur, carbon disulfide, and S-containing heterocyclic compounds other than thiophene.

Experimental Section

Reaction of Phthalic Anhydride with Thiophene.—A filtered solution of 14.8 g (0.1 mol) of phthalic anhydride in 78.65 ml (1 mole) of thiophene was pyrolyzed at 690° in a Vycor tube filled with Vycor chips in a stream of dry nitrogen flowing at 20 cc/min. The pyrolysate was distilled to recover 67.5 ml of thiophene and obtain 12.15 g of residue.

A solution of the residue in 200 ml of ether was extracted with two 50-ml portions of 10% aqueous potassium hydroxide; the acidified aqueous extract was extracted with three 50-ml portions of ether. The dried ether solution, evaporated on the steam bath, gave 1.6 g of a light yellow semisolid mixture of thiols.

Reaction of Sulfur with Thiophene.—A mixture of 3.2 g (0.1 g-atom) of sulfur and 31.46 ml (0.4 mol) of thiophene was refluxed for 18 hr, by which time all of the sulfur was in solution. Although a small amount of hydrogen sulfide evolved during the refluxing, there had been no appreciable reaction; both sulfur and thiophene were recovered unchanged in a separate experiment. The thiophene solution was pyrolyzed and the thiols were worked up as described in the phthalic anhydride reaction. Yield of mixed thiols was 0.25 g.

Phthalic anhydride-d_4 was made by oxidation of naphthalene-d_8 with potassium permanganate.

Analysis.—Mass spectral analyses were performed on a Consolidated Model 21-103c instrument with the inlet system at 250°. The usual 70-V spectrum was supplemented by a low-voltage (7.5 ionizing V, uncorrected) spectrum to help identify parent peaks.

Gas chromatographic analyses were performed on a stainless steel column 6 ft long and 0.25-in. o.d., packed with 10% diethylene glycol sebacate on 30–60 mesh acid-washed Chromosorb W. The column temperature was programmed from 70 to 200° at 2°/min; helium flow was 50 cc/min. Temperature of the injector was 240°; that of the thermal conductivity cell was 300°.

Directly coupled gas chromatography–mass spectrometry is described in ref 8.

Registry No.—Thiophene, 110-02-1; benzyne, 462-80-6.

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[14] H. D. Hartough, "Thiophene and Its Derivatives," Interscience Publishers, Inc., New York, N. Y., 1952, p 61.

Synthesis of Isoquinolines. X.
1-Alkyl-1,2,3,4-tetrahydroisoquinolines[1]

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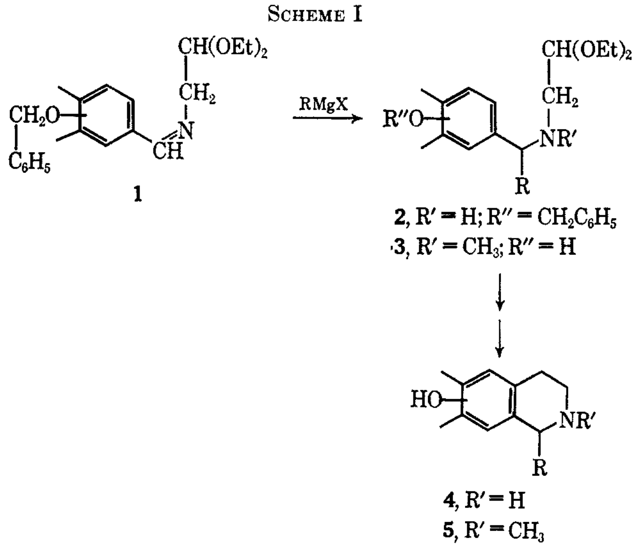
Received December 30, 1968

In recent years, we have developed some facile syntheses of various oxygenated isoquinolines.[3] In connection with our work on the oxidative coupling of phenolic isoquinolines,[4,5] we required a series of 1-alkyl-N-methyl-1,2,3,4-tetrahydroisoquinolines. In this paper, we would like to describe a general synthesis of these compounds.[6] The reactions are shown in Scheme I.

SCHEME I



This route for the preparation of 1-alkylisoquinolines was originally developed by Quelet and Vinot.[7] However, their method involved the use of boron trifluoride as a cyclizing agent. This was found to be generally unsuitable for the preparation of oxygenated isoquinolines, and thus, for the various cactus alkaloids.[8] Vanillin and isovanillin were benzylated[9] (75–85% yield) and allowed to react with aminoacetaldehyde diethyl acetal to yield the Schiff bases **1** (95% yield). Veratraldehyde was converted directly to the Schiff base. The Schiff bases were allowed to react with various aliphatic Grignard reagents to yield the amines (**2**, R = CH_3, CH_3CH_2, and $CH_3CHCH_3CH_2$). At this point, there were two alternatives. Compounds **2** could be debenzylated (H_2-Pd/C), hydrolyzed, and cyclized (HCl), and reduced to give 1-alkyl-1,2,3,4-tetrahydroisoquinolines (**4**, Table I).[10] Second, compounds **2** could be debenzylated, N-methylated (HCHO, H_2, Pt) to **3**, hydrolyzed, cyclized, and reduced to yield 1-alkyl-N-methyl-1,2,3,4-tetrahydroisoquinolines (**5**, Table II).[11]

Several alkaloids were prepared in this work. These are salsoline (**6**),[8] salsolidine (**8**),[8] carnegine (**13**),[8] and lophocerine (**16**).[12]

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[1] (a) Paper IX. M. Bobbitt and C. P. Dutta, *J. Org. Chem.*, **34**, 2001 (1969). (b) This work was sponsored, in part, by Training Grant GM-1139 from the National Institutes of Health.

[2] Abstracted in part from the Ph.D. Dissertations of A. S. S. (University of Connecticut, 1968) and K. H. W. (University of Connecticut, 1969).

[3] See ref 1 and the preceding papers of this series.

[4] J. M. Bobbitt, R. Ebermann, and M. Schubert, *Tetrahedron Lett.*, 575 (1963).

[5] J. M. Bobbitt, J. T. Stock, A. Marchand, and K. H. Weisgraber, *Chem. Ind.* (London), 2127 (1966).

[6] This work was partially reported at the 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1967.

[7] N. Vinot, *Ann. Chim.* (Paris), [13] **3**, 461 (1958); N. Vinot and R. Quelet, *Bull. Soc. Chim. Fr.*, 1164 (1959).

[8] These compounds have been previously synthesized, generally by more laborious routes. The work is summarized by L. Reti in "The Alkaloids," Vol. IV, R. H. F. Manske and H. L. Holmes, Ed., Academic Press Inc., New York, N. Y., 1954, p 7.

[9] R. Dickinson, I. M. Heilbron, and F. Irving, *J. Chem. Soc.*, 1888 (1927).

[10] J. M. Bobbitt, J. M. Kiely, K. W. Khanna, and R. Ebermann, *J. Org. Chem.*, **30**, 2247 (1963).

[11] J. M. Bobbitt, D. N. Roy, A. Marchand, and C. W. Allen, *ibid.*, **32**, 2225 (1967).

[12] J. M. Bobbitt and T.-t. Chou, *ibid.*, **24**, 1106 (1959).