DISCUSSION OF SOME PROBLEMS INVOLVED IN USING THE CHEMICAL LITERATURE*

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These comments should perhaps more appropriately have been titled "A Synthetic Organic Chemist....." for it is from this point of view that the literature will be discussed.

The first half of the discussion will outline briefly some sources of information which the chemist has available to help him in the use of the literature. The second part will deal with Chemical Abstracts, some problems involved in its use, and ways in which it might be improved.

The organic chemist has four major interests in the use of the chemical literature:

I. Searching for specific compounds.
II. Searching for related compounds and classes of compounds.
III. Searching for methods of synthesis or experimental techniques.
IV. Keeping abreast of current literature.

There are, of course, other uses of the literature, but these are specific uses and do not fit into the general category to be discussed here.

I. Let us consider first the simplest task, the search for a specific compound. Some of the sources available to help us are: Beilstein and Elsevier, Chemical Abstracts, United States Patent Office Steroid Punch Cards, and Index Chemicus.

Certainly the first source to be consulted is the chemist's monumental reference book, Beilstein.[1] For the period covered, up to 1939, a search of Beilstein probably will pick up 99% of all organic compounds that appeared.

Elsevier,[2] for some reason, does not seem to be as well known among organic chemists. It is essentially a Beilstein published in English. In addition to being in English, it has certain other advantages over Beilstein. It is more current (covering some areas up to 1958), it makes greater use of structural formulas, so that it is easier to recognize specific compounds; and it often makes use of summary flow diagrams to show the relationship or interconversion of various compounds, particularly when these are complex (see Fig. 1).

Scheme I*

Some Oxidation Reactions of Santonin

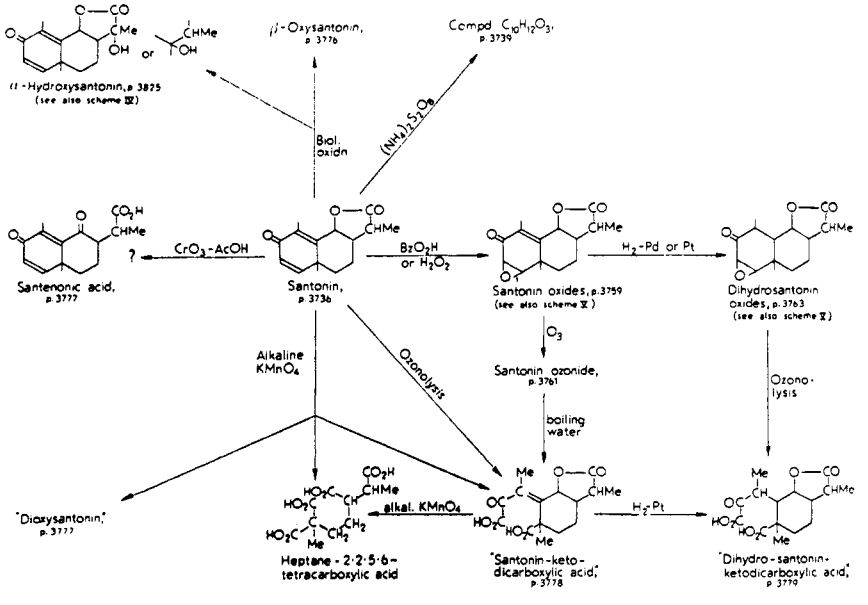


Fig. 1.—Typical summary flow diagram from Elsevier's "Encyclopedia of Organic Chemistry."

*Presented at the Symposium on Information Retrieval and Analysis, sponsored jointly by the Division of Medicinal Chemistry and the Division of Chemical Literature, New York City, September, 1960.

The big disadvantage is, of course, that it terminated before covering all areas of organic chemistry. Fortunately, it covers the polycyclic carbocyclic compounds, an area where Beilstein is weak.

The next source that would be consulted is Chemical Abstracts[3] with its three decennial indices and four annual indices. The problems involved in its use will be discussed further on in the paper.

In the steroid area, one has available the United States Patent Office Steroid Punch Cards.[4] These cover all United States and foreign references from 1957 on, and all United States patents prior to 1957. Use of these cards permits rapid retrieval of specific compounds for this period.

A wonderful new tool for the organic chemist is the "Index Chemicus."[5] "Index Chemicus" is a monthly magazine which claims that it will index all new compounds within 30 days of appearance in a journal. Cumulative molecular formula indices are to appear quarterly and then annually. Thus, one may anticipate that a search for a compound will be no more than 30 days behind the current literature, rather than the period of up to three years that one now has if he depends on Chemical Abstracts indices.

This publication has other outstanding features. All compounds are listed by the unambiguous molecular formula and also frequently the structural formula. This greatly expedites searching, and eliminates the problems arising due to arbitrary nomenclature systems. It has one drawback in that the present molecular formula index to this magazine does not distinguish between different compounds having the same molecular formula.

This remarkable publication will not completely replace the compound indexing by Chemical Abstracts, for "Index Chemicus" will stress the reporting of new compounds, whereas Chemical Abstracts reports and indexes all compounds mentioned in a publication.

II. The search for compounds related to one in hand, or desired, is a more complicated problem. Some of the sources available are Beilstein and Elsevier, Chemical Abstracts, Review Articles, Review Books, and Uniterm Index to Chemical Patents.

Here again, one will very likely start with Beilstein and Elsevier, for closely related compounds--homologs and derivatives--are usually located in the same area. One must exercise caution in their use, however, for closely related compounds are not always in the same vicinity. Thus, phthalic acid, its esters and derivatives, are in Vol. 9, but phthalic anhydride is in Vol. 17.

Once again, one would consult Chemical Abstracts, but the situation with respect to searching for related compounds, or generic searching, is quite unsatisfactory. This will be commented on later.

Very useful sources of information are review articles. These are, in fact, often the most convenient way of locating related classes of compounds. Review articles are found in such journals as Chemical Reviews[3] and Quarterly Reviews.[6] A particularly useful journal carrying review type articles is Angewandte Chemie.[7]

Unfortunately, there is no convenient way of telling whether or not a review article covering the area in which one is interested has ever appeared. As one way to solve this, the Science Information Department at Smith, Kline and French has compiled, for internal use, a list of all review articles that have appeared in some 50 journals in the past 20 years. This list has been of great value to us in our literature searches.[8]

Review books such as ACS monographs, and specialty books such as those on phosphorus, sulfur, or heterocyclic compounds, are in the same category as review articles. They are the ideal source for information, provided they can be located.

Another source for carrying out generic searches in a restricted area is the United States Patent Uniterm Index.[9]

In this index, which has been in existence for only about seven to eight years, each patent is assigned a number. Under each generic heading all patents having pertinent information are listed. Thus, if one wishes to locate all United States patents dealing with phenothiazines appearing in 1960, this is done easily. In order to facilitate more specific searching, the index is issued in duplicate. If one wishes to locate all phenothiazines having trifluoromethyl groups, one places the pages with the items phenothiazine and trifluoromethyl side by side and locates those numbers common to both headings.

The Uniterm Index is really a manual form of punch card system. It is often a useful way of rapidly scanning the U.S. patent literature, but the coverage is far from complete.

None of these sources is entirely satisfactory. Such a search is very laborious and often incomplete.

III. Now let us turn to the third area in which we deal with the literature, i.e., the search for a synthetic method.

Despite the large number of books on synthetic methods, a great need still exists for a ready means of scanning the literature for general or specific synthetic procedures. Some of the sources that may be consulted are: Review Articles, Review Books, Books on Synthetic Techniques, Chemical Abstracts, Company Key-Word Index, and Advertising Brochures.

One first usually consults review articles such as those in "Organic Reactions,"[25] Chemical Reviews,[3] and Quarterly Reviews.[6] Review books, such as the heterocyclic series,[7,10] usually have

thorough reviews of synthetic methods. One would naturally consult the books on synthetic techniques such as "Organic Syntheses" and "Organic Reactions," Weygand, 1938,[11] Hickinbottom, 1948,[12] Shirley, 1951,[13] Wagner and Zook, 1953,[14] Migrdichian, 1957,[15] Theilheimer, 1946+,[16] Houben-Weyl, 4th Edition, 1958,[17] and Rodd, 1951+.[18]

None of these books really provides satisfactory critical comparisons of the various possible techniques for carrying out a given reaction, although Houben-Weyl comes closest to doing this.

One very useful source of information, usually overlooked, is advertising brochures and booklets. Recently, for example, the du Pont Co. distributed a very comprehensive review of oxidations using hydrogen peroxide [19]; Allied Chemical distributed an excellent review booklet on reactions of sulfur trioxide[20]; Metal Hydrides had distributed a number of excellent brochures summarizing the reactions of various metal hydrides.[21]

Unfortunately, unless one sets up his personal file, it is virtually impossible to locate any lists of such brochures. Someone could perform a very valuable service by publishing a list of the technical brochures issued by chemical concerns, covering compounds, reagents, and reactions.

Many chemists find it helpful to set up their own filing system of reactions and reagents as the quickest way of locating reactions and techniques. We have found such a file invaluable.

Companies often find it valuable to set up such key-word type files, particularly to cover the span of several years between the appearance of an article and its indexing by Chemical Abstracts.

The wonderful work of Theilheimer may make such individual files unnecessary, but only if the rather poor indexes are improved.

As far as the use of Chemical Abstracts for such searches is concerned, in general, it is a poor place to search for synthetic techniques as now indexed. A reaction technique is usually not indexed, unless an entire article is devoted to it.

IV. One of the major and most difficult tasks of the chemist is keeping abreast of the latest developments in chemistry.

Some of the ways of doing this are to consult individual journals, Chemical Abstracts, Theilheimer Monthly Service, review journals, Seminar Reports, Dissertation Abstracts, Company Patent Abstracts, Current Chemical Papers, Current Contents, I and EC Tables of Contents, Chemical Titles, and Index Chemicus.

To attempt to keep up with all new developments by reading the hundreds of journals in which chemical articles appear is too ridiculous to consider. Even reducing this to the 15-20 basic journals is a formidable task. Although Chemical Abstracts should serve to help us out of this dilemma, as it now is issued, there is often little advantage to going to Chemical Abstracts as compared to scanning the original articles. It is convenient therefore to have resource to one of the newer publications, whose aim is to rapidly summarize or itemize new work more quickly than even an abstract journal can. By consulting these lists, one can rapidly scan the contents of current chemical journals, and select only those articles for perusal which are really of interest. One such list is the monthly "Current Chemical Papers."[6] In this is printed the title, or 5-10 word summary in instances in which the title is not informative, of articles appearing in 200-300 periodicals each month. These items are roughly classified within sections. Entries usually appear in Current Chemical Papers within one to two months of appearance in a journal.

Current Contents is a similar type of publication.[5] The purpose is the same, i.e., to bring the latest publications rapidly to the attention of the chemist. This is done by reproducing the entire Table of Contents of some 600 chemical and biological journals. This compact magazine usually gives the index pages even before the journals themselves arrive in the libraries, and permits rapid scanning of the latest journals without the necessity of circulating hundreds of journals and hundreds of pounds of journals each month.

I. and E.C. Title Pages[3] is exactly the same, except that it covers only the ACS journals.

Chemical Titles[3] is a recent attempt by the ACS to improve on Current Contents by having each word of each title serve as a separate index heading.

Theilheimer issues a very fine monthly reaction abstract service.[22] It is easy to scan and very current. It consists of a one or two sentence summary with equations of all interesting reactions in an article.

While review journals are useful, they usually are not very up-to-date.

A convenient way of keeping up-to-date on mechanisms is to scan the seminar reports that schools such as MIT, University of Illinois, and Pennsylvania State University make available.

Dissertation Abstracts[23] could be a useful way of keeping up with the latest work in the universities, if the abstracts themselves were not so uninformative.

Most companies handle the patent literature either by circulating the latest chemical patents to the proper persons in the organization, or by issuing a bulletin that gives a one sentence summary of the pertinent patent.

"Index Chemicus," the new index of chemical compounds that was described earlier, may also serve as an alerting service, since not only

can one see what new compounds have appeared, but often the chemical transformations that they undergo.

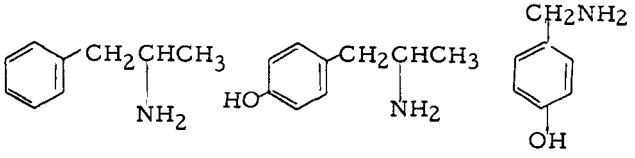
Having discussed some of the sources which the chemist has to assist him in the use of the literature, we shall now turn to the chemist's most important key to the literature, Chemical Abstracts; we shall discuss some of the problems involved in the use of Chemical Abstracts, and suggest ways in which it might be improved.

Let us consider Chemical Abstracts and its relationship to the first item discussed, i.e., locating a specific compound.

One of the most common problems encountered in the use of Chemical Abstracts is the difficulty with which this is done.

In attempting to locate a compound by name in the subject index, usually one must first spend a great deal of time determining the approved name -- with no guarantee that one is right, or that the same name will have been used in all indices. Most chemists, therefore, find it wisest to go directly to the molecular formula index, since this provides the most fool-proof method of locating the desired compound.

We have, for example, had occasion to look up the compounds shown below:



Phenethylamine, ∝-methyl

Phenol, 4-(2-aminopropyl)

p-Cresol, ∝-amino-

To learn the Chemical Abstracts name for amphetamine, recourse was made to the formula index. Subsequently, when we wished to look up the p-hydroxy derivative, we were unable to locate it by any reasonable modification of the previous name and, once again, we had to go to the formula index.

The third example is a particularly atrocious example of naming, and this compound could only be located by recourse to the formula index. In fact, no one in our laboratories, even those "expert" in the Chemical Abstracts nomenclature rules, was able to predict the name under which it was listed.

The use of the formula index as now constructed is not without its problems also. In Fig. 2 we see a portion of a typical Chemical Abstracts formula index.

If one has a great number of compounds to look up, particularly if they are complex

Fig. 2

$C_{12}H_{10}O_2S$ Benzenesulfonic acid, Ph ester, 219cd.
4-Biphenylsulfonic acid, 15475f.
Phenol, (phenylsulfonyl)-, 219e, 223i, 12187c, 14617e.
Phenyl sulfite, 12816a.
2-Thiopheneglycolic acid, ∝-phenyl-, 2579g.
2-Thiophenemethanol,∝-(3,4-methylenedioxphenyl)-13865d.

$C_{12}H_{10}O_4$ (See also Quinhydrone.)
Acetic acid, (6-hydroxy-2-naphthyloxy)-, 16955h.
Benzopyrancarboxylic acid, dimethyl-4-oxo-, 7755c, 15349d.
-, 2-oxo-, Et ester, 10715ch, 10717a.
Biphenyltetrol, 379a, 6402i, 6403b.
Chromone, 3-acetyl-7-hydroxy-2-methyl-, 1788b.
Coumarin, 6-acetyl-5-hydroxy-4-methyl-, 4928b.
Crotonic acid, 3-hydroxy-2-(o-hydroxyphenyl)-, γ-lactone, acetate 2561i.
3,9-Dodecadiene-5,7-diynedioic acid, 185a.
2-Indancarboxylic acid, 1,3-dioxo-, Et ester, 13851d.
7-Indeneacetic acid, 3-carboxy-, 7831a.
Ketone, 3-hydroxy-2-benzofuranyl methyl, acetate, 2561f.
Naphthazarin, 2,6-dimethyl-, 7757f.
-, 2-ethyl-, 10692i.
2-Naphthoic acid, 1-hydroxy-4-methoxy-, 9397g.
1,4-Naphthoquinone, dimethoxy-, 7758c, 9397f.

$C_{12}H_{10}O_4S$ 1,4-Naphthoquinone, 2-(1,2-dihydroxyethylthio)-, 11526f.
Phenol, sulfonyldi-, 223i, P12110h.
Resorcinol, (phenylsulfonyl)- 12038ef.
-, 4,4'-thiodi-, P 98i.

$C_{12}H_{10}O_4S_2$ Phenyl disulfone, 12873f.

$C_{12}H_{10}O_4S_2$ Benzenesulfonic acid, thiol-, anhydrosulfide, 7049g.

$C_{12}H_{10}O_4S_4Te$ Telluride, bis(phenylsulfonylthio), 9091i, 13552f.

$C_{12}H_{10}O_5$ 3,5-Benzofurandiol, diacetate, 3295a.
2H-1-Benzopyran-8-acetic acid, 7-methoxy-2-oxo-, 15743g.
4H-1-Benzopyran-6-carboxaldehyde, 5,7-dihydroxy-2, 8-dimethyl-4-oxo-, 4928g.
-, 7-hydroxy-5-methoxy-2-methyl-4-oxo-, 1792b.
2H-1-Benzopyrancarboxylic acid, hydroxy-4-methyl-2-oxo-, Me ester, 4928ab.
-, hydroxy-2-oxo-, Et ester, 13895c, 14727g.
2,3',4,5',6-Biphenylpentol, 11991g.
Citropten, 6-formyl-, 8614a.
Dicarboxylic acid, m. 278-80°, 370d.
2-Furaldehyde, 5,5'-(oxydimethylene)di-, 10073g.
2-Indancarboxylic acid, 2-hydroxy-1,3-dioxo-, Et ester, 13851f.
1,4-Naphthoquinone, 2-hydroxydimethoxy-, 7758bf, 7760h, 7762a.
Phloroglucide, 11991g.

$C_{12}H_{10}O_5S$ 1,4-Naphthoquinone, 2-(1,2-dihydroxyethylthio)-3-hydroxy-, 11526f.
Resorcinol, 4,4'-sulfinyldi-, P98i.

$C_{12}H_{10}O_6$ 4H-1-Benzopyran-6-carboxaldehyde, 7-hydroxy-2-(hydroxymethyl)-5-methoxy-4-oxo-, 1792b.
1H-2-Benzopyran-3-carboxylic acid, 7,8-dimethoxy-1-oxo, 2563e.
2,2',4,4',6,6'-Biphenylhexol, 11992f.
Terephthalaldehyde, 2,5-dihydroxy-, diacetate, 7099b.

$C_{12}H_{10}O_6P_2Th$, 2360i.

$C_{12}H_{10}O_6S_2$ 4,4'-Biphenyldisulfonic acid, 9743i, 15475f.

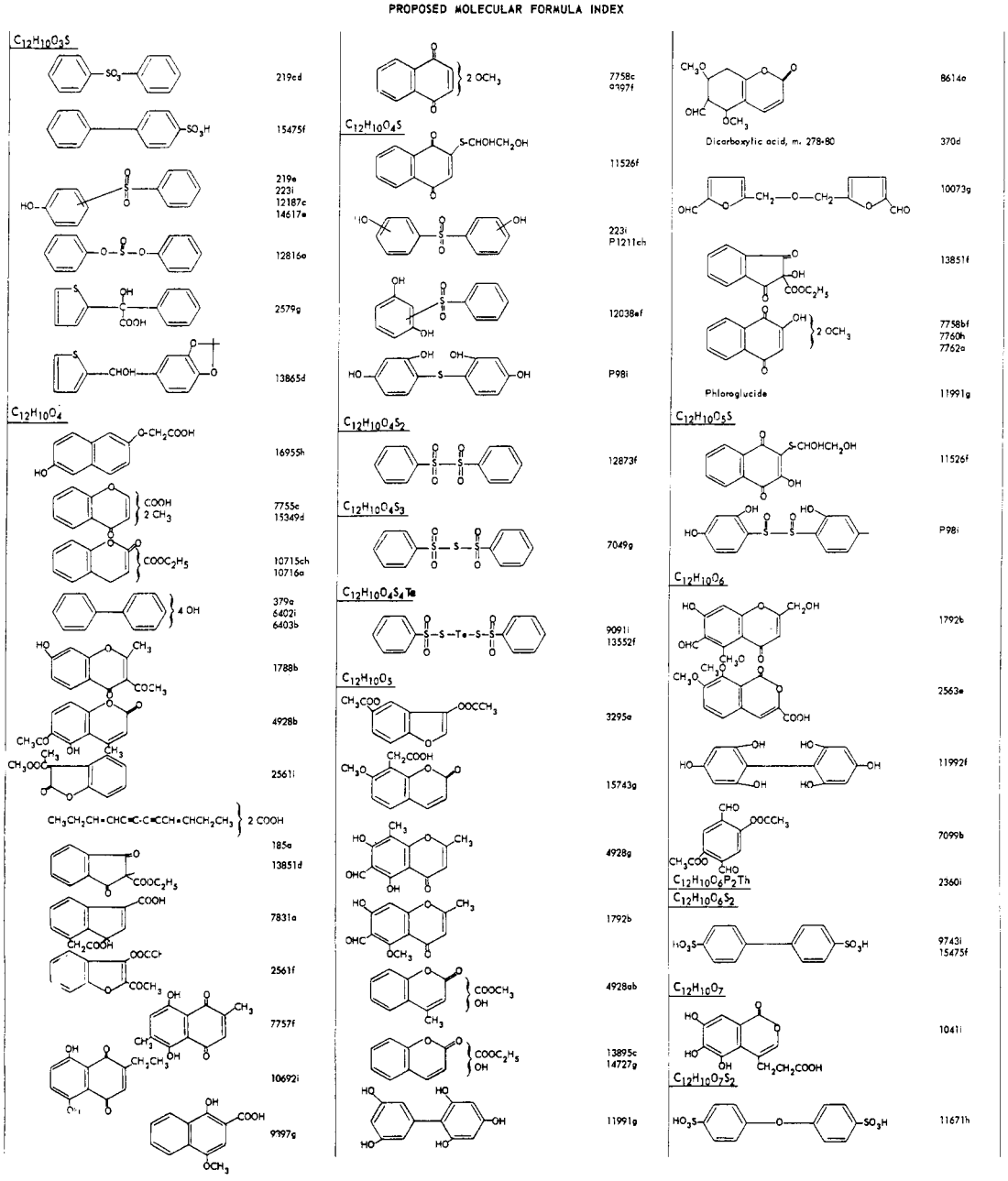
$C_{12}H_{10}O_7$ 1H-2-Benzopyran-4-propionic acid, 5,6,7-trihydroxy-1-oxo-, 1041i.

$C_{12}H_{10}O_7S_2$ Benzenesulfonic acid, 4,4'-oxydi-, 11671h.

substances, a considerable amount of time must be spent just in the deciphering of each systematic name.

We suggest, therefore, that the structural formulas be included under the molecular formulas as shown in Fig. 3. This would certainly provide the most rapid and fool-proof method of searching for a particular compound.

Fig. 3



Whenever this suggestion is made, the usual response is -- fine! But what about the space and cost problems?

There would be little, if any, increase in cost, since one would employ the very inexpensive photographic reproduction technique, rather than the currently employed, very expensive, letterpress technique.

It has been estimated that by the use of microprint formulas, there would be at most only a 10% increase in space. This is a small price to pay for the greater speed, reliability, and convenience that would result.

Furthermore, since this type of structural molecular formula index provides an unequivocal means of locating a compound, the inclusion

of compound names in the subject index becomes expendable, and the vast time, money, and effort going into chemical naming for the subject index could be sharply curtailed. It is not, in fact, inconceivable that single compound names could be dropped from the subject index. Elimination of compound names from the subject index probably would result in a saving of 30% in space; thus, the use of this structural molecular formula index system would result in an overall 20% decrease in volume of the indices.

Elimination of systematic names from the subject index would not only give this great saving in space and expense, but would greatly speed up publication of the indices by eliminating the very time-consuming process of naming of the compounds. Since the compilation of such a structural formula index can be done so readily (probably mechanically), there should be little or no time lag between the appearance of an abstract and the pertinent index reference.

We have just suggested reducing the size of the subject index by elimination of single compound names. Now we would like to suggest expansion of the subject index by having more complete cross-indexing and generic listing. Inasmuch as single compounds would be more readily accessible from the structural formula index, we propose a shift in emphasis to more complete generic listing.

As an illustration of the deficiencies of the present system, let us consider a search for phenothiazines. At present, if one searches under this heading, one might locate alkyl, amino, or halo derivatives, but not carboxy or carboxamide derivatives. In fact, we made a careful study of the subject index one year and found that at least 30% of the phenothiazines in the index were not listed under that generic heading. We make the obvious suggestion that all related compounds be listed under the appropriate generic heading.

By generic listing we refer not only to more complete indexing under compound class (e.g., tetrazines, naphthoquinones, phenothiazines), but under other generic headings, such as use (antihistamines, insecticides, etc.), and particularly types of reactions (oxidations, sulfonation, amination, etc.). Under this latter generic heading we could have indexing such as is used in "Organic Syntheses," and illustrated below. Thus, a search for dehydration techniques would list all techniques described that year.

Dehydration
by Anhydrides, 231f
heat, 1722 g, 9463a
H_2SO_4, 364b, 12364g
$KHSO_4$, 426d
I_2, 1733b
$(H_3PO_4)_n$, 6423a, 1473d, 27c.

This service of the subject index would be invaluable to the practicing organic chemist.

As part of this expansion of generic listing in the subject index, we recommend the incorporation of Patterson's Ring Index System[24] into the subject index. So frequently, when looking up an unfamiliar or complex ring or heterocyclic system, one must first consult this source anyway. By incorporating this into Chemical Abstracts subject index, one could simplify and facilitate searches, particularly for complex heterocycles.

Let us now turn from comments about the abstract indexes to comments regarding the abstracts themselves.

Abstracts should have two functions: (1) they should serve as a means of locating information in the original literature, and (2) they should serve to alert or make the reader aware of the latest developments in a given area.

By definition, an "abstract" should not (except in the case of obscure journals) be itself the repository of this information; and yet, we find more and more that Chemical Abstracts is stressing this latter objective. The abstracts are becoming increasingly more archival in nature. Often, there is little point to going back to the original article, since all of the information in full detail is given in the abstract. Conversely, there is often little advantage to perusing the abstract, for it is no longer a concise summary of the contents of an article, and is frequently more difficult to read.

Long abstracts of papers from obscure journals are certainly worthwhile, but one wonders about the validity of having page after page of the most detailed abstracts of such journals as J. Am. Chem. Soc., J. Org. Chem., and the like.

The present abstracts are certainly inadequate as far as alerting the reader to new developments. A typical abstract is shown in Fig. 4. The difficulty with which this can be scanned is quite obvious.

An informal survey of chemists in the Philadelphia area shows that rarely does one any longer find someone who "reads" or scans Chemical Abstracts, as one should an alerting service. This is because being in such fine print, and essentially devoid of structural formulas, it takes such a great deal of time and effort to decipher the abstracts. Usually one must employ pencil and paper to translate the abstracts into recognizable reactions and equations.

We suggest that the organic abstracts in Chemical Abstracts be modified to contain flow diagrams of all reactions run with virtually no descriptive matter, unless pertinent to the philosophy of the work. The abstract, modified as we suggest, is shown in Fig. 5.

Fig. 4

1959 16134-16135 PRESENT CA ABSTRACT 16135-36 Vol. 53

2,2-Dimethyl-6-quinuclidone, a mesomerism-free acid amide. Horst Pracejus (Univ. Halle, Ger.). Chem. Ber. 92, 988-9(1959). — 2,2-Dimethyl-6-quinuclidone (I) was prepd. in a 12-step synthesis. I is not capable of acid amide mesomerism because of steric reasons. The basicity, reactivity, and spectral behavior of I are investigated and discussed. $Me_2C{:}CHCO_2H$ and concd. NH_4OH heated in an autoclave at 150°, the crude product refluxed with alc. HCl, and the sirupy ester HCl salt treated with KOH and distd. gave about 50% $Me_2C(NH_2)CHCO_2Et$(II), b_{13} 64-8°. II(145.1g.), 119 cc. $CH_2{:}CHCO_2Et$, and 0.6 cc. glacial AcOH heated 24 hrs. at 50°, and 48 hrs. at 60°, dild. with 300 cc. Et_2O, washed with 20% aq. K_2CO_3, dried, and evapd., and the residue fractionated gave 218-25 g. $EtO_2C\text{-}CCH_2CH_2NHCMe_2CO_2Et$ (III), $b_{1.5}$ 111-14°, n_D^{20} 1.4418, d_{20} 0.988. III(122.5 g.) in 600 cc. dry C_6H_6 treated dropwise with stirring successively with 61 cc. BzCl and 74 cc. Et_3N, kept 3 hrs., heated 1 hr. on the steam bath, cooled, and filtered, the residue washed with C_6H_6 and the combined filtrates worked up gave 157-60 g. N-Bz deriv. (IV) of III, b_{2-3} 210-15°, n_D^{20} 1.5043. IV(139.6 g.) added to 9.40 g. Na sand in 400 cc. dry C_6H_6, treated with about 1 cc. abs. EtOH, heated 12-15 hrs. on the steam bath with stirring, and decompd., with stirring with 280 cc. 10% AcOH, the C_6H_6 layer dild. with an equal vol. Et_2O, filtered, cooled to 0°, and extd. with N NaOH, the alk. ext. acidified immediately with dil. H_2SO_4 and extd. with Et_2O, the ext. washed with dil. aq. $NaHCO_3$ and H_2O, dried, concd. to about 200 cc., and cooled to -10° gave 1-benzoyl-2,2-dimethyl-5(?)-carbethoxy-4-piperidone (V); the mother liquor concd. to 60 cc. gave a 2nd crop; the combined product (44-8 g.) recrystd. from Et_2O gave pure V, m. 79.5-81.0°. V (30.3 g.) and 0.103 mole N KOH shaken to soln., heated 18 hrs. on the steam bath, cooled, washed by decantation with H_2O, dried, boiled 15 min. with 200 cc. Et_2O, allowed to stand at least 2 hrs. under Et_2O, and filtered gave 12.8 g. product; the mother liquor washed with 2N NaOH and H_2O dried, and evapd. gave an addnl. 6.4 g. product (total) yield, 19.2 g.; the crude product recrystd. from Et_2O yielded pure 1-benzoyl-2,2-dimethyl-4-piperidone (VI), m. 116-17°(Et_2O). VI (23.1 g.), 11.9g. $NCCH_2CO_2Et$, 2.3 g. NH_4OAc, 5 cc. glacial AcOH, and 25 cc. C_6H_6 refluxed 4 hrs., dild. with 400 cc. C_6H_6, washed, dried, concd. to 300 cc., filtered through 100 g. Al_2O_3, and evapd., the residue boiled with 100 cc. Et_2O and allowed to stand, and the crude product (29.0 g.) recrystd. from iso-PrOH and then MeOH yielded a mixt. of Et cis- and trans-1-benzoyl-2,2-dimethyl-4-piperidylidenecyanoacetate (VII), m. 131-6.5°. VII (32.6 g.) in 300 cc. dry dioxane hydrogenated about 10-15 hrs. over 340 mg. PtO_2 under ambient conditions yielded the 4-piperidyl analog (VIII) of VII, a mixt. of the diastereoisomers, $b_{0.001}$ 143-7°, m. 81-105°. VIII(0.1 mole) treated with 350 cc. H_2O and 84 g. solid KOH, the mixt. distd. to remove during 2 hrs. 100 cc. H_2O (together with NH_4OH and dioxane), the residue heated 24 hrs. in an autoclave at 140-50°, boiled filtered, acidified with 6N HCl, allowed to stand briefly, and filtered gave 10.7 g. BzOH; the filtrate concd. in vacuo dild. with 2 vols. EtOH, cooled to -10°, filtered after several hrs., and evapd. to dryness in vacuo, the residue heated 1 hr. at 200°, refluxed 2 hrs. with 300 cc. abs. alc. HCl, and evapd. in vacuo, the esterification repeated in the same manner, the mixt. evapd., the sirupy residue dissolved in 35 cc. dry Et_2O, neutralized with shaking dropwise with 10N NaOH, treated with 12 cc. 10N NaOH, and extd. with Et_2O, and the ext. worked up gave 12.0 g. Et dl-2,2-dimethyl-4-piperidylacetate (IX), $b_{0.5}$ 82-3° n_D^{20} 1.4588; the forerun and residue combined with the aq.-alk. residue, acidified with HCl, worked up in the usual manner, and the crude product reësterified gave about 2.7 g. IX. IX in Et_2O contg. a small amt. of EtOH treated in the usual manner with dry HCl gave 93% IX.HCl, m. 144-6.5° (abs. EtOH-Et_2O); picrate m. 169.5-71° (Et_2O). IX (5.98 g.) in 5 cc. abs. EtOH treated with 3.67 g. dibenzoyl-d-tartaric acid monohydrate, $[\alpha]_D^{20}$ — 111° (EtOH), in 30 cc. abs. EtOH, the mixt. dild. with 5 cc. abs. EtOH, kept 6 hrs. at room temp., and 18 hrs at 0°, and filtered, and the residue washed with EtOH and Et_2O, dried, and recrystd. yielded 3.57 g. dibenzoyl-d-tartrate (X) of l-IX, m. 190-3° (decompn.), $[\alpha]_D^{20}$ 62.5 ± 0.5° (c 1, abs. EtOH). The X in 1.8 cc. abs. EtOH treated with dry HCl, the soln. dild. with 20 cc. Et_2O, and then with dry Et_2O to about 90°, kept 1 day at 0°, and the solid deposit filtered and recrystd. from EtOH-Et_2O yielded 2.01 g. l-IX.HCl, m. 131.5-3.5°, $[\alpha]_D^{20}$ — 11.3 ± 0.5° (c 1, abs. EtOH). The 1st mother liquor from X treated with a small excess of abs. alc. HCl, the mixt. evapd. in vacuo, the residue treated with 3 cc. HCl-EtOH and 200 cc. Et_2O kept at -10°, and filtered, and the residual 4.37 g. d-IX. HCl, m. 122-8°, $[\alpha]_D^{20}$ about 5.7°, fractionally crystd. from EtOH-Et_2O yielded 1.7 g. dl-IX. HCl, and about 2.6 g. d-IX. HCl, m. 120-6°, $[\alpha]_D^{20}$ 8.0 ± 0.7° (c 1, abs. EtOH). dl-IX (1.99 g.) (or 2.36 g. dl-IX. HCl) refluxed 3 hrs. with 15 cc. 6N HCl and evapd. in vacuo, the soln. evapd. in vacuo, and the residue dried gave 100% dl-isomer of 2,2-dimethyl-4-piperidylacetic acid-HCl (XI. HCl), m. 222-5° (abs. EtOH-Et_2O). In exactly the same manner was prepd. l-XI. HCl, m. 209-13.5°, $[\alpha]_D^{20}$ — 11.2 ± 0.5° (c 1, H_2O). dl-XI. HCl (1.245 g.) and 5 cc. $SOCl_2$ heated 3 hrs. at 60° and evapd. in vacuo below 35°, the residual glassy acid chloride kept several days under dry Et_2O to crystallize, the cryst. solid washed by decantation with Et_2O powdered, dried in vacuo, mixed with 20 cc. dry Et_2O, some quartz sand, and a few glass beads, stirred 9 hrs. at room temp. with 1.70 cc. Et_3N, kept overnight, and filtered, the residue washed with dry Et_2O, the combined filtrates evapd. in vacuo, and the residue sublimed at 40-65°/0.5-2 mm. gave 370-600 mg. dl-isomer of 2,2-dimethyl-6-quinuclidone (XII), m. 48-51°. Similarly was prepd. l (+)-XII, m. 47-50° $[\alpha]_D^{20}$ 2.5° (c 1.5, C_6H_6), in 26-40% yield. l (+)-XII in abs. C_6H_6 treated with a small excess of dry HCl in C_6H_6 and filtered after 10 min. gave nearly 100% l-XII. HCl, m. 133-6° (decompn.), $[\alpha]_D^{20}$ 45° (c 1, abs. EtOH), 39° (C 1, H_2O). The dissocn. const. of dl-XII was measured to be 5.33. The ultraviolet absorption spectrum of XII in cyclohexane is recorded. l-(+)-XII. HCl (0.17-0.34 millimole) dissolved rapidly in H_2O or abs. EtOH at 20°, dild. to 5.00 cc., and the rotation measured gave a half-life of 16 ± 1 min. for the hydrolysis, and of 12 hrs. for the alcoholysis at 20.0 ± 0.1°. While XII is very rapidly hydrolyzed in acidic soln., it is only very slowly attacked by H_2O at 20°. Cryst. XII is fairly stable at room temp. but small amts. of polymer material is formed during 1-2 days.

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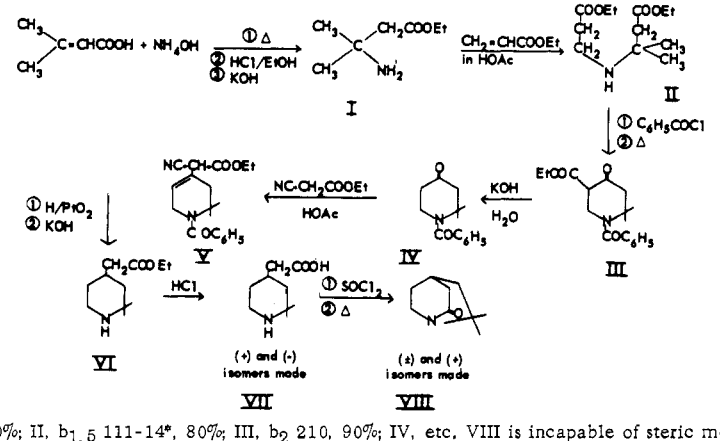
Fig. 5.—PROPOSED ABSTRACT

2,2-Dimethylquinuclidone-6, a mesomerism-free acid amide, H. Pracejus, Chem. Ber. 92, 988-998 (1959).



Cpd., b.p., yield: I, b_3 64-8*, 50%; II, $b_{1.5}$ 111-14*, 80%; III, b_2 210, 90%; IV, etc. VIII is incapable of steric mesomerism. The basicity, reactivity, and spectra of VIII are discussed.

Inclusion of physical constants, reaction conditions, and yields is easily accomplished. A statement of the author's purpose and conclusions might be incorporated, and we believe that this could most reasonably be accomplished by use of the author's own summary -- edited if necessary. This inclusion of the purpose and conclusion of the work is now lacking in present abstracts.

Modification of abstracts as we have recommended would be particularly useful in articles involving organic reaction mechanisms. This is an area essentially ignored by Chemical Abstracts.

In Figure 6 is a Chemical Abstracts abstract of an article in which is described a novel reaction and a proposed mechanism. The Chemical Abstracts abstract makes no mention of the fact that a mechanism is proposed. Our proposed abstract gives the mechanism and reaction and can be scanned at a glance.

Fig. 6

The ortho alkylation of phenols. Alfred J. Kolka, John P. Napolitano, and George G. Ecke (Ethyl Corp., Detroit, Mich.). *J. Org. Chem.* 21, 712–13(1956).—Phenols are alkylated with olefins in the presence of catalytic amts. of $(PhO)_3Al$ (I) to give 2-mono- and 2,6-dialkylated phenols. Heating PhOH with C_2H_4 and 3–4 mole-% I 10 hrs. at 320° and 60–800 lb./sq. in. gives 24% *o*-EtC_6H_4OH, b. 201–2°, $n^{25}D$ 1.5372 (*o*-$EtC_6H_4OCH_2CO_2H$ deriv., m. 138–40°), and 8% 2,6-$Et_2C_6H_3OH$, b. 219°, m. 37–8°. Alkylation of PhOH with $MeCH:CH_2$ 2 hrs. at 230–40° and 200–500 lb./sq. in. gives 61% 2,6-$(Me_2CH)_2C_6H_3OH$, b_{20} 136°, m. 19°, $n^{25}D$ 1.5134. Alkylation of PhOH with $Me_2C:CH_2$ 4 hrs. at 105–15° and 30–100 lb./sq. in. gives 5% recovered PhOH, 46% *o*-Me_3C-C_6H_4OH, b_{20} 120°, $n^{25}D$ 1.5239, 1% *p*-isomer, 36% 2,6-$(Me_3C)_2C_6H_3OH$ (II), b_{20} 147°, m. 36.5°, and some higher-boiling products. By changing the reaction time, pressure, and temp. products contg. from 0 to 80% II may be obtained.

F. E. B.

A statement of the purpose and conclusions (most expertly prepared by the expert -- the author) with perhaps the proposed mechanism illustrated is readily comprehended and most useful.

An abstract journal of the form we have just outlined would be smaller than the present journal, would be issued at less than the present cost, and would be read avidly by the majority of organic chemists.

We suspect that the number of personal subscriptions would show a marked increase, thus further assisting the lowering of price.

It should also be pointed out that abstracts of the type that we have described would be easier to write and proofread, hence should greatly reduce the time lag between appearance of the original article and the appearance of the abstract and indices.

Once again, the objection may be raised as to the cost of printing this type of abstract. Once again, the obvious answer is to change from the present expensive letterpress printing to the much less expensive and more versatile photographic reproduction process.

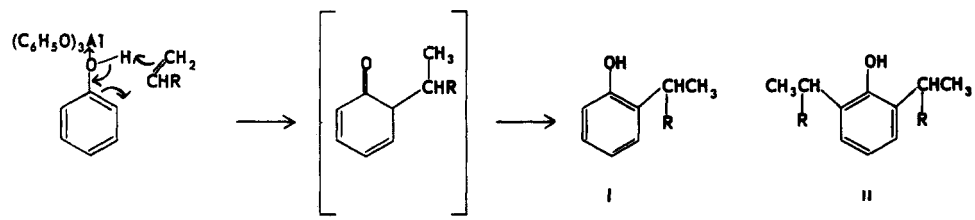
To summarize, we believe that modifying the abstracts to provide flow diagrams would greatly increase the value to the chemist, would markedly reduce abstracting time and space, and facilitate early appearance of the abstract.

We also believe that the use of a structural molecular formula index would greatly facilitate compound searching, and that the ease and rapidity with which such indexes can be prepared would permit issuance of an index with each issue of Chemical Abstracts.

The considerable saving in time, resulting from these modifications, would probably result in issuance of abstract and index within six months of appearance of the original article.

Fig. 7

THE ORTHO ALKYLATION OF PHENOLS. A. J. Kolka, J. P. Napolitano, G. G. Ecke (Ethyl Corp., Detroit, Michigan). J. Org. Chem. 21, 712-13 (1956). - Synthesis of 2-alkyl and 2,6-dialkyl substituted phenols by reaction of an olefin and phenol catalyzed by aluminum phenoxide, at 2-300° and 2-500 psig. Suggested mechanism:



I, R =H, b 201-02°, n_D^{20} 1.5372, 24%; I, 2-t-Bu, b_{30} 120°, 46%; II, R =H, m.p. 37-8°, 8%; II, R =CH_3, m.p. 19°, 61%; II, 2,6-di-t-Bu, m.p. 36.5°, 36%.

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