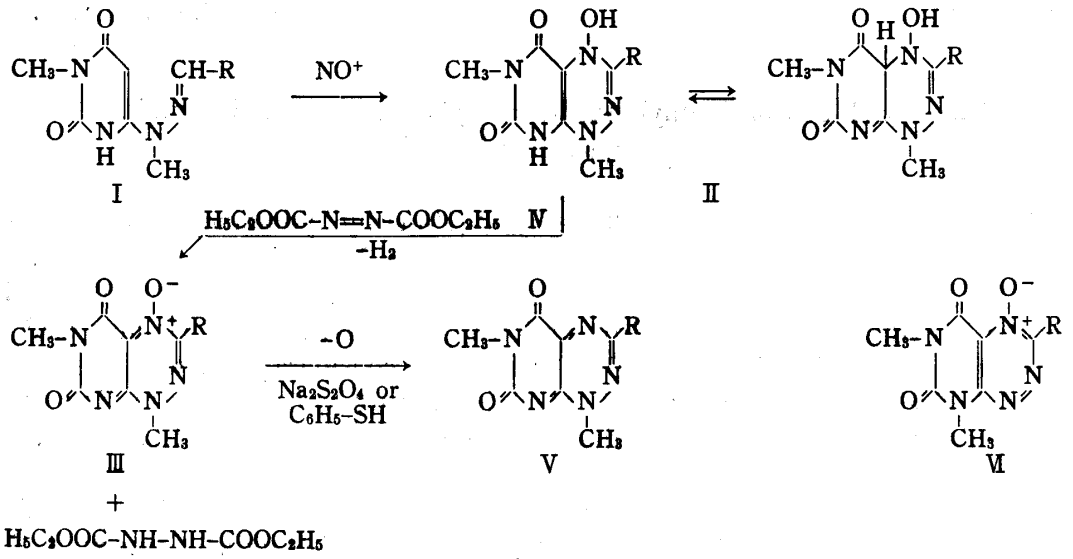


Chart 1

We consider this oxidative cyclization involving hydrogen abstraction as possessing considerable potential utility for the synthesis of other heterocycle-N-oxides. Moreover, it should be noted that the azapteridine-4-oxides mentoned above can not be obtained by the conventional peracid oxidation of the respective azapteridines. This would be connected with the π-electron distributions of the azapteridine system, and in fact the 4-positions are not sufficiently high in the π-electron densities.[7]

Faculty of Pharmaceutical Sciences,
Kumamoto University
Oe-honmachi, Kumamoto

FUMIO YONEDA

Pharmaceutical Institute,
School of Medicine,
Keio University
Shinjuku-ku, Tokyo

SADAO NISHIGAKI
KAZUKO SHINOMURA

Received September 23, 1971

7) Details will be published in the full paper.

[Chem. Pharm. Bull. 19(12)2648—2651(1971)]

UDC 547.745.04

A Wittig Reaction of N-Sulfonyl Lactam

We wish to report here the successful Wittig reaction on substances having an N-sulfonyl lactam grouping,[1] and by utilizing this knowledge, we propose the reaction sequence of Chart 1 with a new synthetic pathway for the purpose of functionalization of the amide-carbonyl group.

1) The Wittig reaction of succinimide and phthalimide has been described. W. Flitsch and H. Peters, *Chem. Ber.*, **103**, 805 (1970).

NII-Electronic Library Service

N-*p*-Toluenesulfonylpyrrolidone[2] (II) was subjected to the Wittig reaction with the resonance-stabilized phosphoranes (Va—d) by heating in refluxing xylene or without a solvent at 165—180° in nitrogen for the period cited in the Table I, and the products (IIIa—d) were easily isolated by column chromatography. Judging from their nuclear magnetic resonance (NMR) spectra, these products are stereochemically pure and the newly-formed double bond is assumed to have a *trans* configuration in view of the stereochemical preference of the *trans* isomer,[3] when the reaction was carried out with stable phosphoranes. The allyl coupling (J=2 Hz) of the olefinic proton with the methylene protons at C-3 position of the pyrrolidine ring is characteristic to all of the Wittig products.

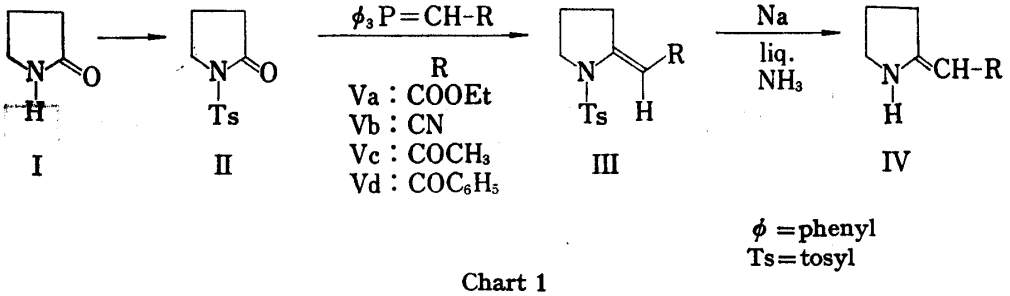


Chart 1

Table I. Synthesis of IIIa—d

	R	Condition	Yield (%)	mp (°C)	IR ν_{max}^{KBr} (cm^{-1})	NMR of >C=CH–R δ (ppm) in CCl_4
IIIa	COOEt	xylene, reflux 26 hr	70	87—88	1706 (C=O) 1631 (C=C)	5.94, t, J=2 Hz
IIIb	CN	170°, 15 hr	84	113—114	2250 (CN) 1625 (C=C)	5.37, t, J=2 Hz
IIIc	$COCH_3$	180°, 22.5 hr	40	106.5—108.5	1668 (C=O) 1590 (C=C)	6.40, t, J=2 Hz
IIId	COC_6H_5	165°, 151 hr	21	118—119	1649 (C=O)	in aromatic protons[a]

a) The methylene protons at C-3 are a double triplet of J=2 and J=7 Hz.

N-Tosyl group of IIIa—d was readily cleaved by means of sodium in liquid ammonia in a usual manner in a moderate yield to produce IVa—d (Table II). IVb[4] with cyano function in the substituent exhibits two different NMR signals assignable to the olefinic proton of *cis* and *trans* forms in a ratio of approximately 1.4:1,[5] reflecting the same observation of Horii, *et al.*[4a] for the compound (IVb), which they synthesized by an alternative route. The NMR spectra of IVa, IVc, and IVd suggest that each of these compounds is a single isomer and the configuration of IVa and IVc is presumed to be *cis*, because of their low-field NH signals at 7.9 δ and 9.3—10.0 δ, due to the hydrogen bonding.[4a] In the case of IVa and IVc, which contain a carbonyl group in the substituent R, such complete conversion of the stereochemistry surrounding the double bond might be explained by assuming the formation of a salt (VI) during the course of the reaction (Chart 2), and its protonation gives rise to the production of only the *cis* isomer.

2) W. Reppe, *et al.*, *Ann.*, **596**, 201 (1955).
3) A. Maercker, *Org. Reactions*, **14**, 313 (1965).
4) *a*) Z. Horii, K. Morikawa, and I. Ninomiya, *Chem. Pharm. Bull.* (Tokyo), **17**, 2230 (1969); Y. Yamada and M. Matsui, *Agr. Biol. Chem.* (Tokyo), **34**, 724 (1970).
5) Assignment of the NMR proton signals of *cis* and *trans* isomers for similar compounds was reported: I. Felner, A. Fischli, A. Wick, M. Pesaro, D. Bormann, E.L. Winnacker, and A. Eschenmoser, *Angew. Chem.*, **79**, 863 (1967); Y. Yamada, K. Hatano, and M. Matsui, *Agr. Biol. Chem.* (Tokyo), **34**, 1536 (1970).

NII-Electronic Library Service

Table II. Synthesis of IVa-d

	R	Yield (%)	mp (°C)	IR ν_{max}^{KBr} (cm^{-1})	NMR of >C=CH–R δ (ppm) in CCl_4
IVa	COOEt	35	59—61	3340 (NH) 1653 (C=O) 1598 (C=C)	4.38, s
IVb	CN	44	61—70	3280 (NH) 2225 (CN) 1618 (C=C)	3.68, s (*cis*) 3.97, s (*trans*)
IVc	$COCH_3$	21	56—57	1618	4.93, s
IVd	COC_6H_5	35	111—112	1620	5.65, s

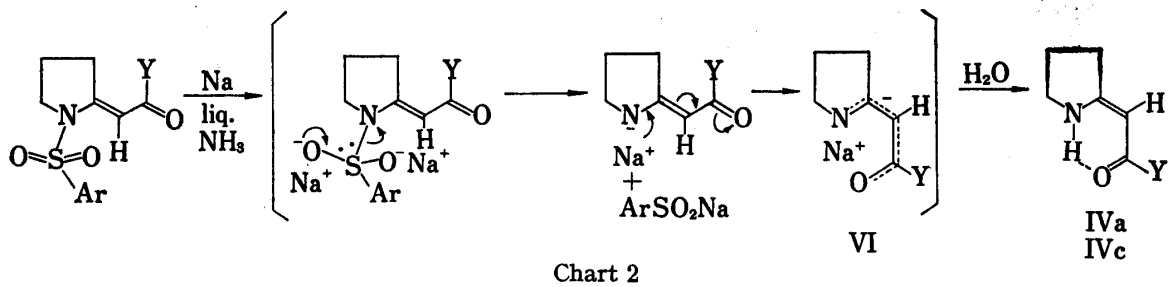
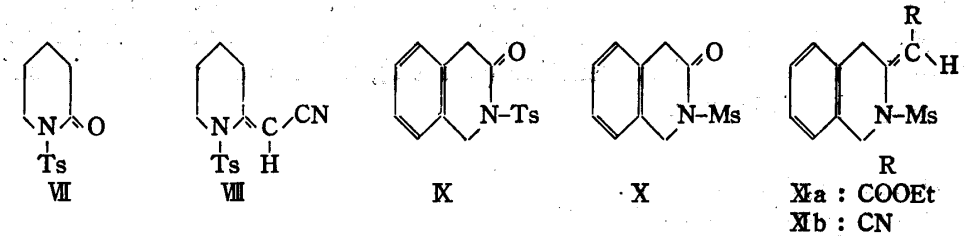


Chart 2

In order to extend the above result to the functionalization of six-membered lactams, N-*p*-toluenesulfonyl-*δ*-valerolactam[6] (VII) was submitted to this reaction with Vb at 180° in nitrogen for 36 hr and it was found that the formation of the expected product (VIII), mp 99—100°, IR ν_{max}^{KBr} cm^{-1}: 2250 (CN), 1596 (>C=C<), NMR ($CDCl_3$) δ: 5.55 (=CH-CN), was observed only in 16% yield, together with 48% recovery of the starting material. This finding coincides with the fact that IX[7] hardly interacted with Vb, which furnished the best result in the case of II. This marked difference might be ascribable to the steric effect of the tosyl group to the carbonyl function of the six-membered lactam, and therefore, X[7] was selected for the model of the N-methanesulfonyl lactam in the six-membered frame-work and it was confirmed that the less-hindered N-mesyl lactam did react with the Wittig reagents, Va and Vb, as shown in Table III. Application of this result to more complex lactams as well as the study on the reaction of the sulfonyl lactams is in progress.

Table III. Synthesis of XIa—b

	R	Condition	Yield (%)	mp (°C)	IR ν_{max}^{KBr} (cm^{-1})	NMR of >C=CH–R δ (ppm) in $CDCl_3$
XIa	COOEt	120—130°, 43 hr	24	77.5—78.5	1732 (C=O) 1642 (C=C)	6.52, s
XIb	CN	140—160°, 20 hr	55	103—104	2253 (CN) 1650 (C=C)	6.85, t, J=1.5 Hz



6) C.A. Grob, H.P. Fischer, W. Raudenbusch, and J. Zergenyi, *Helv. Chim. Acta*, **47**, 1003 (1964); T. Sato and H. Watatsuka, *Bull. Chem. Soc. Japan*, **42**, 1955 (1969).
7) M. Natsume, *et al.*, unpublished data.

NII-Electronic Library Service

Research Foundation, ITSUU Laboratory
Tamagawa 2-28-10, Setagaya-ku, Tokyo

MITSUTAKA NATSUME
MAKOTO TAKAHASHI
KAZUKO KIUCHI
HIDEKI SUGAYA

Received October 2, 1971

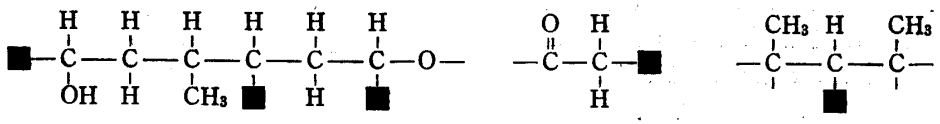
[Chem. Pharm. Bull. 19(12)2651—2652(1971)]

UDC 547.991.02 : 581.192.582.752.1

Stereostructure of Picrasin G, Simaroubolide of *Picrasma quassioides*

Knowledge of the bitter principles of the quassia tree, *Picrasma quassioides* BENNETT (Simaroubaceae) has been fairly accumulated during the past few years.[1-10] We have further isolated another new bitter which is now named picrasin G. In the present communication, we wish to provide evidence that picrasin G is represented by formula I.

Picrasin G has the composition $C_{21}H_{28}O_7$ (M^+ at *m/e* 392 in mass spectrum). Of the seven oxygen atoms, one is involved in a secondary hydroxyl next to a carbonyl (ν_{max} 3440 cm^{-1}, δ 4.84 ppm, formation of a monoacetate (δ 2.12, 5.87 ppm), consumption of periodate), one in an unconjugated ketone in a six- or larger-membered ring (ν_{max} 1710 cm^{-1}), one in an α,β,β-trisubstituted, conjugated ketone in a six- or larger-membered ring (λ_{max} 252 nm, ν_{max} 1685, 1630 cm^{-1}, $[\theta]_{329}$ −5420), two in a δ-lactone (ν_{max} 1722 cm^{-1}, δ 4.62 ppm), one in a methoxyl (δ 3.62 ppm), and the remaining one in a tertiary hydroxyl (ν_{max} 3440 cm^{-1}, no carbinyl hydrogen signal). Picrasin G also contains a secondary methyl (δ 0.92 ppm), two tertiary methyls (δ 1.12, 1.45 ppm), and a vinyl methyl (δ 1.90 ppm) other than the methoxyl. Further analysis of the nuclear magnetic resonance (NMR) spectrum with the aid of double resonance



■ denotes a quaternary carbon

experiments has demonstrated the presence of the following partial structures. The partial structures so arrived at, along with the previously assigned oxygen functions, have many features in common with those of picrasin B (V). Furthermore, the NMR parameters for certain hydrogens of picrasin G are in good agreement with those of picrasin B (V), indicating that picrasin G is similar in structure to picrasin B.

Picrasin G differs from picrasin B in having one extra tertiary hydroxyl. This difference is reflected in the NMR spectra of both the substances, where the C-15 methylene hydrogens

1) T. Murae, T. Tsuyuki, T. Nishihama, S. Masuda, and T. Takahashi, *Tetrahedron Letters*, **1969**, 3013.
2) H. Hikino, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 219 (1970).
3) T. Murae, T. Ikeda, T. Tsuyuki, T. Nishihama, and T. Takahashi, *Bull. Chem. Soc. Japan*, **43**, 969 (1970).
4) H. Hikino, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **18**, 1082 (1970).
5) T. Murae, T. Ikeda, T. Tsuyuki, T. Nishihama, and T. Takahashi, *Bull. Chem. Soc. Japan*, **43**, 3021 (1970).
6) T. Murae, T. Ikeda, T. Tsuyuki, T. Nishihama, and T. Takahashi, *Chem. Pharm. Bull.* (Tokyo), **18**, 2590 (1970).
7) H. Hikino, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **19**, 212 (1971).
8) T. Murae, T. Tsuyuki, and T. Takahashi, *Chem. Pharm. Bull.* (Tokyo), **19**, 1747 (1971).
9) H. Hikino, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **19**, 2203 (1971).
10) H. Hikino, T. Ohta, and T. Takemoto, *Chem. Pharm. Bull.* (Tokyo), **19**, 2211 (1971).

NII-Electronic Library Service