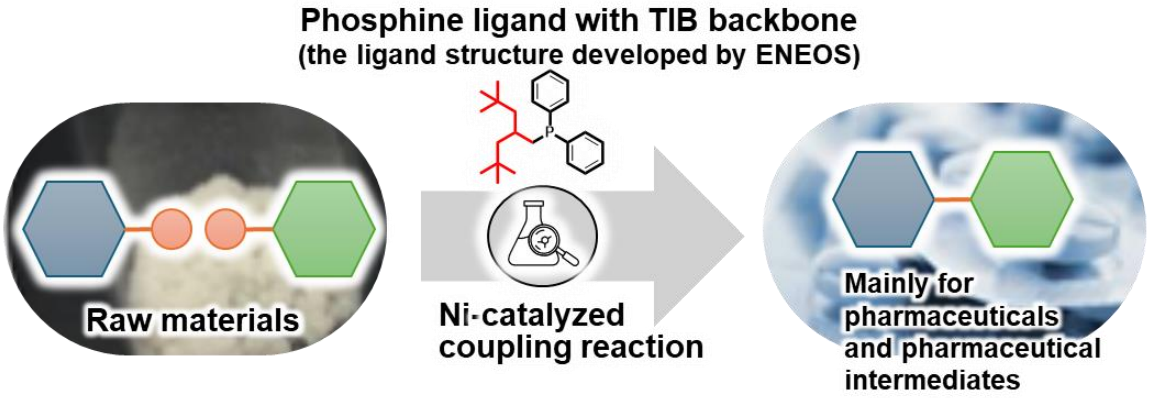
NEWS RELEASE

ENEOS

July 29, 2025

ENEOS Develops High-performance Ligand for Nickel-Catalyzed Coupling Reactions
- Hokko Chemical Industry Co., Ltd. Will Launch Sample Sales in September -

ENEOS Corporation (hereinafter “ENEOS”) has developed “alkylphosphine with a triisobutylene (TIB) backbone (TIB phosphine ligand),” a high-performance ligand for nickel-catalyzed coupling reactions, in collaboration with Prof. Kouki Matsubara, Faculty of Science, Fukuoka University. To apply these results to pharmaceuticals manufacturing and other purposes, ENEOS has signed a licensing agreement with Hokko Chemical Industry Co., Ltd. (hereinafter “Hokko Chemical Industry”), Japan’s largest phosphine compound manufacturer. Hokko Chemical Industry plans to launch sales of small-quantity samples of the TIB phosphine ligand this September.



ENEOS has been utilizing its R&D technologies and knowledge in petrochemistry that it has cultivated over the years, for the licensing business of organic catalysts used in production of pharmaceuticals. *1

Although the Suzuki-Miyaura cross-coupling reaction*2 using palladium catalysts and alkylphosphine ligands is frequently used in production of pharmaceuticals, pharmaceutical intermediates and functional materials, it faces various problems including (1) toxicity and high procurement cost of palladium, (2) high cost of ligand, (3) difficulty in handling alkylphosphine ligands in air, and (4) limited reaction yields. ENEOS developed a solution designed to tackle these problems. Specifically, we developed the world's first catalyst design in which a phosphine ligand consisting of a primary alkyl group*3 with two tert-butyl groups*4 in remote positions attached to a phosphorus atom improves the activity of nickel-catalyzed coupling reactions. This has enabled us to successfully synthesize and isolate phosphine ligands with a TIB backbone that is derived from petrochemicals and can be procured with lower cost. This TIB

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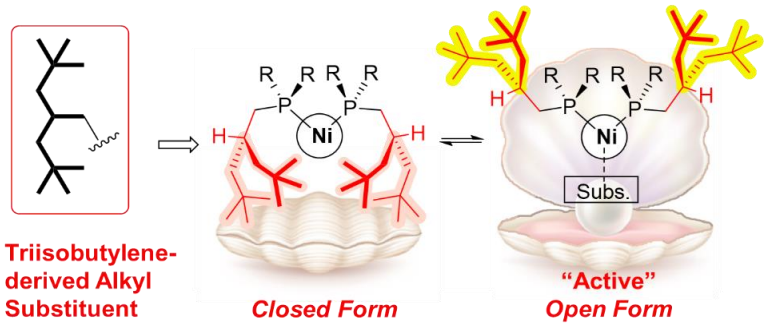
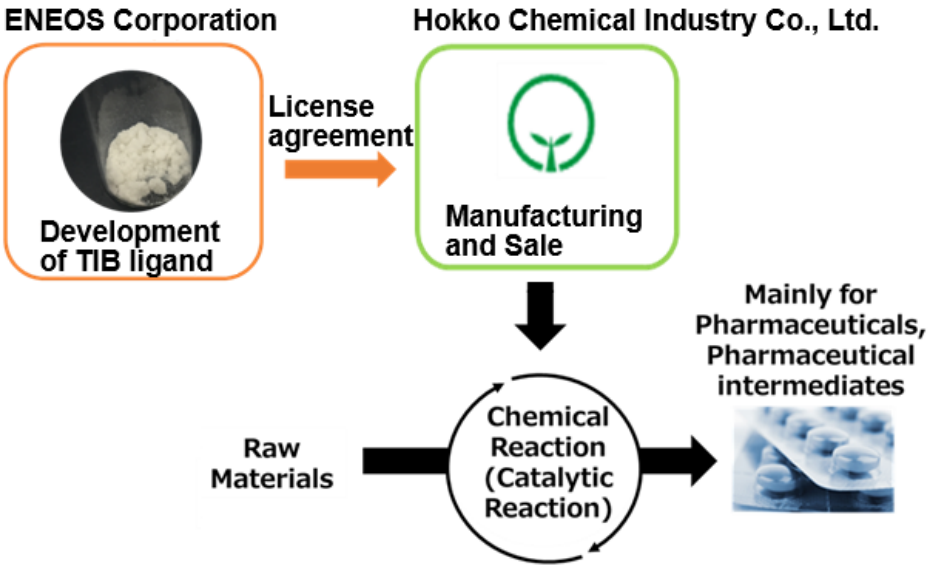
phosphine ligand is stable in air and can achieve a higher yield than before, depending on combinations of reactants, by coupling reactions using nickel catalysts that can be obtained more easily than palladium (patent pending).

The details of these results will be presented at both International Symposium on Organometallic Chemistry Directed Towards Organic Synthesis (OMCOS)[*5] and Symposium on Organometallic Chemistry[*6] scheduled to be held in September this year.



Catalytic design of TIB phosphine ligand



Business Scheme

Through our continuing development of new organic and organometallic catalysts, we are dedicated to achieving both a stable supply of energy and materials and the realization of carbon-neutral society.

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Please refer to the official website of Hokko Chemical Industry for the release regarding this matter.
https://www.hokkochem.co.jp/wp-content/uploads/2025_01_fc_release.pdf

*1 June 26, 2023 News release: ENEOS Signs License Agreement for Organic Catalyst Manufacturing Technology for Pharmaceutical Production

*2 The formation of carbon-carbon bonds, which correspond to the backbone of organic compounds, is one of the fundamental processes in chemical synthesis. Among the various methods that have been developed, the Suzuki-Miyaura cross-coupling reaction, in which an organohalogen compound is caused to react with an organoboron compound by means of a palladium catalyst to link them together via the carbon-carbon bond, is considered one of the excellent methods for its high reliability. The usefulness of this method was highly evaluated, which lead to the awarding of the Nobel Prize in Chemistry in 2010.

*3 An alkyl group is a hydrocarbon group formed by removing one hydrogen atom from an alkane in organic chemistry. An alkyl group is also called a primary, secondary, and tertiary alkyl group depending on how many other carbon atoms are attached to each position of the alkyl chain. A primary alkyl group is a carbon bonded with one other carbon.

*4 The tert-butyl group (also known as tertiary butyl group) is an atomic group in organic chemistry and a type of branched alkyl group. The structural formula is $-C(CH3)_3$, and its IUPAC systematic name is 1,1-dimethylethyl group. Since tert-butyl groups are bulky and electron-donating for their having three methyl groups, compounds with this type of group often show characteristic properties in conformation or reactivity, and their properties are often applied in organic chemistry research.

*5 OMCOS XXII 22nd International Symposium on Organometallic Chemistry Directed Toward Organic Synthesis

*6 71st Symposium on Organometallic Chemistry | Confit (in Japanese)